Alberta Health

Odours and Human Health

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About this document:

This literature review was prepared to inventory and summarize scientific information about the relationship between odour and human health. The intended audience for this report is primarily health professionals or other professionals with related scientific backgrounds, but information is contained in this report that may also be relevant to interested members of the public.

The information in this document is provided on an informative and summative basis only. Recognizing that the topics addressed in this report are areas of current scientific inquiry, users of this report are encouraged to review the latest literature in the field of odour science.

Development of the Clean Air Strategic Alliance's "Good Practices Guide for Odour Management in Alberta" (ISBN 978-1-896250-81-6; available at www.casahome.org) was informed by this document.

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Executive Summary

The effect of odours on health is a recognized environmental issue. Many people, particularly residents living near odour-emitting facilities such as concentrated animal feeding operations, have expressed concerns and questions regarding the physical and psychological health impacts of exposures to environmental odours. An abundance of research has been done in this topic over the last 30 years; however, there remains much debate over the impacts of odours on health, the mechanisms in which odours induce a health response, and the most effective risk-based approaches for regulating health impacts from exposures.

This report explores and summarizes the findings from over 500 peer-reviewed epidemiology and experimental studies assessing odour and health outcomes in humans. The primary objectives are to:

1. present a collection of scientific literature pertaining to odour-induced health responses in humans;
2. provide a summary of the current state-of knowledge regarding odours and health; and
3. evaluate the factors and mechanisms involved in odour-induced responses.

The main outcomes of interest include health symptoms, physiological responses, annoyance, mood and psychological health, quality of life, cognition (task performance), athletic performance, and brain activity.

Epidemiological Studies

Odours from a variety of sources (petrochemical plants, pulp mills, sewage/waste treatment plants, fertilizer plants, pig-rearing facilities) have been found to correlate with frequency and intensity of odour annoyance. Degree of annoyance was generally lowest with pleasant odours and highest with unpleasant odours, indicating a role for odour pleasantness in odour-induced annoyance.

Residents of communities located near odour-emitting facilities generally report a higher number of health symptoms compared to residents of control communities. Reported symptoms included, for example, cough, nausea, congestion, eye irritation, headache, dizziness, sleep problems, diarrhea, chest pain, and respiratory symptoms. Self-reported frequency of odour perception (a subjective measure of exposure) often correlated with symptoms, while residence distance to facility (an objective measure of exposure) typically did not. The use of subjective measures of exposure is a potential source of reporting bias and results should be interpreted with caution.

The relationship between odour exposure and health symptoms also appears to be influenced by odour pleasantness. Exposure to unpleasant odours, such as those from a pig facility, a fat refinery, or a cast-iron factory, results in more symptom reporting than exposure to moderate or pleasant odours.

A consistent finding among the epidemiology studies is that symptom reporting is mediated by odour annoyance. Many studies have found odour annoyance to be a stronger predictor of symptom

reporting than odour perception, odour concentration, and residence distance to facility. The relationship between odour annoyance and symptom reporting may also be influenced by individual or community attitudes towards an odour, method of coping with an odour, environmental worry, and perceiving odour as a threat to health.

Experimental Studies - Physiological Responses, Mood, and Task Performance

Experimental findings demonstrate that odours can significantly impact physiological outcomes, irritant symptoms, mood, and cognition (task performance); however, this is not true for all odours in all situations. Responses appear to be odorant-specific and are also heavily influenced by individual factors and experimental methods.

Odours were found to significantly influence physiological arousal parameters (heart rate, blood pressure, respiratory rate, skin conductance) and reporting of irritant symptoms (headaches, eye irritation, nausea, dry eye) in several studies. However, contradictory or null findings to these results were also found.

For studies of odour and mood, pleasant odours tended to induce more positive moods (mainly increased happiness and improved overall mood) and unpleasant odours tended to induce more negative moods (mainly decreased overall mood or increased anger and disgust). Due to the variation in responses, any further conclusions beyond this basic finding were difficult to identify.

A common finding among the studies evaluating physiological outcomes, symptoms, and mood is that odour-induced responses are impacted by individual cognitive attitudes towards an odour. Subjects given a harmful bias towards an odour were more likely to report irritant symptoms than those given a healthful bias. Similarly, subjects given a healthful bias towards tend to be in a more pleasant mood than those given a harmful bias.

Varied results have been found with studies assessing odours and cognition function (task performance). Both pleasant and unpleasant odours were shown to improve or impair performance on memory and recognition tasks, math tasks, lexical tasks (word recognition, word decoding), and motor reaction tasks. Other studies have demonstrated no effect of odours on task performance. This lack of consistency across studies suggests that the impact of odours on task performance may be odorant-specific, as well as influenced by individual factors.

The relationship between odours and physiological or psychological health is extremely complex and influenced by a wide variety of odour characteristics (e.g., hedonicity, familiarity) and individual factors (e.g., subjective expectations, personal experience with an odour). Different odours induce different responses, and odours appear to have their own cognitive and mood profiles.

Experimental Studies - Brain Responses

In studies localizing odour-induced brain activity, more than 30 different regions have been indicated as being involved in some aspect of olfaction. The pattern of brain activity can be influenced by factors such as odour characteristics (e.g., intensity, pleasantness), the task at-hand (e.g., paying attention to an odour, odour identification), subjective association with an odour (e.g., familiarity, emotional association), and pre-conceived expectations about an odour.

Different studies show varied brain responses following exposure to pleasant and unpleasant odours. The lack of consistency across studies makes it extremely difficult to draw any definitive conclusions regarding how pleasant or unpleasant odours affect the brain. There are a complex array of factors involved in the response to odour pleasantness, such as type of odour (e.g., food vs floral), familiarity, and situational context. The orbitofrontal cortex and the amygdala are two brain regions often found to be activated by both pleasant and unpleasant odours, and are considered to play a strong role in emotional processing. Additionally, the involvement of many of the structures of the limbic system (e.g., amygdala, hippocampus, cingulate gyrus) helps to explain the emotional response to pleasant or unpleasant odour.

At present, the clinical application of odour-induced brain activity studies is rather limited, and the link between changes in activity and health response is poorly understood. Some studies have suggested that odour-induced increases in brain activity can be linked to certain behaviors. For example, changes in odour-induced brain activity have been linked to changes in mood, drowsiness, and alertness. However, studies of this nature are few in number and further research in this area is needed before further conclusions can be drawn.

Conclusions

The association between odours and health has proven to be extremely complex. The evidence demonstrates that all odours are not of equal consequence; a wide range of responses can be induced by different odorants and the health impacts of odours are often odorant-specific. Studies have shown that odour-induced responses are heavily influenced by odour characteristics (e.g., pleasantness, familiarity) as well as individual factors (e.g., past experience, cognitive bias). The variation in odour character and the subjective nature of odour responses make it particularly difficult to examine the health impacts of odours using typical risk assessment approaches.

There are a number of limitations and research needs that were noted throughout the development of this report. The main limitations associated with epidemiological research are the weak exposure assessments and the use of subjective measures for exposures and/or outcomes. The main limitations of human experimental studies are the lack of standardized exposure methods (type of odorant, odorant delivery method), the difficulty in conducting blinded experiments (as subjects are often aware of the presence of odour), and the influence of individual predilections and individual past experience on odour-induced responses.

Odour epidemiological research would benefit from:

- improved exposure assessments; more objective and consistent/standardized assessments of exposure would help to limit bias and improve comparability between studies.
- additional measurements of co-pollutants to allow differentiation of odour-related effects from toxic or irritant effects.
- more prospective studies evaluating community health responses before and after introduction of an odour-emitting facility, or before and after implementation of an odour reduction plan.

For human experimental studies, there is a need for:

- more consistency in terms of odour exposure (concentration, method of odorant delivery, exposure time) to allow for generalizations of the effects of odours.
- evaluations of repeated exposures to odours (i.e., over multiple days).
- more studies assessing physiological and psychological responses simultaneously; correlating objective physiological responses with subjective mood/behavior responses would provide more meaningfulness to the physiological data.
- further research into the clinical application of odour-induced neuronal activity (understanding the link between brain activity changes and behavioral/physiological responses)
- more experimental studies directly evaluating the physiological or psychological effects of complex environmental odours.

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Abbreviations

ASTM: American Society of Testing and Materials
BOLD: Blood oxygen level-dependant
BP: Blood pressure
BTEX: Benzene, toluene, ethylbenzene, *o*-xylene and (*m*+*p*)-xylene
CH_4: Methane
CI: Confidence interval
CNV: Contingent negative variation
CO_2: Carbon dioxide
DBP: Diastolic blood pressure
DDO: Dynamic dilution olfactometry
D/T: Dilution-to-threshold
EEG: Electroencephalography
E-Nose: Electronic nose
H_2S: Hydrogen sulphide
HR: Heart rate
FIDOL: Frequency, Intensity, Duration, Offensiveness, Location
(factors involved in determining impact of odour on a community)
fMRI: Functional magnetic resonance imaging
MEG: Magnetoencephalography
NH_3: Ammonia
NIRS: Near-infrared spectroscopy
NO_2: Nitrogen dioxide
OERF: Olfactory event-related field
OERP: Olfactory event-related potential
OFC: Orbitofrontal cortex
OR: Odds ratio
OU/m^3: Odour units per metre cubed
OU_E: European odour units
PEA: Phenylethyl alcohol
PET: Positron emission tomography
PM_{10}: Particulate matter of diameter $\leq$10 μm
PNS: Parasympathetic nervous system
POC: Primary olfactory cortex
POMS: Profile of Mood States test
ppb: Parts per billion
ppm: Parts per million
ppt: Parts per trillion
rCBF: Regional cerebral blood flow
REM: Rapid eye movement
RR: Respiratory rate
SBP: Systolic blood pressure
SCR: Skin conductance response
SNS: Sympathetic nervous system
SO_2: Sulphur dioxide
SOC: Secondary olfactory cortex
VOC: Volatile organic compound

1. Introduction

The effect of odours on health is a recognized environmental issue. People residing near odour-emitting facilities often have complaints about the impact of odours on their psychological health, physical health, and quality of life. The purpose of this report is to review the scientific literature and provide a summary of the current state of knowledge regarding odours and human health. Both the positive and negative effects of odours are documented.

The health responses evaluated in this report include health symptoms, physiological outcomes, annoyance, mood and psychological health, quality of life, cognition (task performance), athletic performance, and brain activity. Brief discussions of the effects of odour on pain, sleep, and taste/appetite are also included. The following odour-related disciplines were considered beyond the scope of this review and excluded: aromatherapy treatments for medical conditions or procedure-related anxiety, the effect of certain diseases on olfaction, multiple chemical sensitivity/hyper-reactivity, pheromones, massage aromatherapy, lateralization in olfactory processing, occupational exposures, and odour-related marketing. With regards to odour and memory, studies looking at the effect of odours on performance of memory tasks were included; however, studies assessing the involvement of odour in learning mechanisms or odours as triggers of memories were considered out of scope.

Studies evaluating the effects of odour exposure in animals, although applicable to the understanding of olfaction, often have limited relevance to the study of odours and human health. Most animal research focuses on identifying the underlying mechanisms of olfaction, understanding odorant interactions with receptors, and aromatherapy. Additionally, there are significant differences between the olfactory systems of humans and animals, limiting the applicability of animal studies to the assessment of odour-induced effects on human health. For these reasons, an evaluation of animal data was not completed.

The literature search was conducted using the databases *Pubmed*, *Scopus*, and *ISI Web of Science*. Articles considered relevant were epidemiology studies and human experimental studies that specifically evaluated the impact of odours on any of the in-scope outcomes mentioned above. Only original articles published in English were accepted. Supplementary searches included use of the '*Related Citations*' function in *Pubmed* and citation sourcing of relevant original and review articles. The initial literature search was performed in 2011, which included studies published from the 1970's to September 2011. A second literature search was performed in 2013 that included studies published up to July 2013. Although attempts were made to obtain all relevant material, due to the broad and extensive nature of the topic, there is the potential that pertinent studies were not identified by the literature search.

Regarding the technical quality of the studies, a critical evaluation of the studies was considered outside the scope of the review. However, for epidemiology studies, any apparent strengths and weaknesses were noted.

The main objectives for this review are to: (1) Present a collection of scientific literature pertaining to odour-induced health responses in humans; (2) Provide a summary of the current state-of knowledge regarding odours and health; and (3) Evaluate the factors and mechanisms involved in odour-induced responses. The initial list of objectives also included a fourth item: Present a summary of recent literature review documents published by other health organizations. However, this fourth objective was removed due to a lack of information. A search for grey literature was conducted using the websites of several health organizations around the world (e.g., Ontario Ministry of the Environment, Bay Area Air Quality Management District (California), Texas Commission on Environmental Quality, New Zealand Ministry for the Environment, Department of Environment and Conservation New South Wales (Australia), Environment Protection Authority South Australia). The search did not reveal any documents with a literature review of the health effects of odour. Additional Google searches for recent literature reviews of odour-related health effects produced a similar lack of results.

This report explores the findings of over 500 peer-reviewed epidemiology and experimental studies assessing odour responses in humans. Chapter 2 provides background information on odours and the olfactory system, as well as a discussion of the techniques used for odour measurement. Chapter 3 summarizes the odour epidemiology studies, while Chapters 4 and 5 review the human experimental studies. Chapter 6 consolidates the evidence from all chapters and presents an overall evaluation of the impact of odours on health; limitations and research needs are also discussed.

Odour perception and responses can be influenced by individual social characteristics such as culture, age, gender, and disease status. These topics are discussed briefly in Chapter 2 (Olfaction Background Information); however, the differences in odour perception between sub-groups were not assessed in detail.

As a final note, responses to odours are heavily tied to past experiences, memory, and emotion, causing the physiological and psychological effects to vary greatly between individuals. This complicates any assessment of health effects induced by odours, and is an important caveat to keep in mind throughout this report.

2. Olfaction Background Information

2.1 What is Odour

Odour is the quality of a substance that is perceived by the sense of smell. Odours can be pleasant or unpleasant, intense or weak, familiar or unfamiliar, and can carry a distinct quality such as floral, minty, musky, or putrid. Environmental odours originate from many different sources; examples include livestock operations, agricultural sources, waste landfills, sewage/water treatment plants, power plants, refineries, industrial factories, lagoons, wildfires, and vehicles.

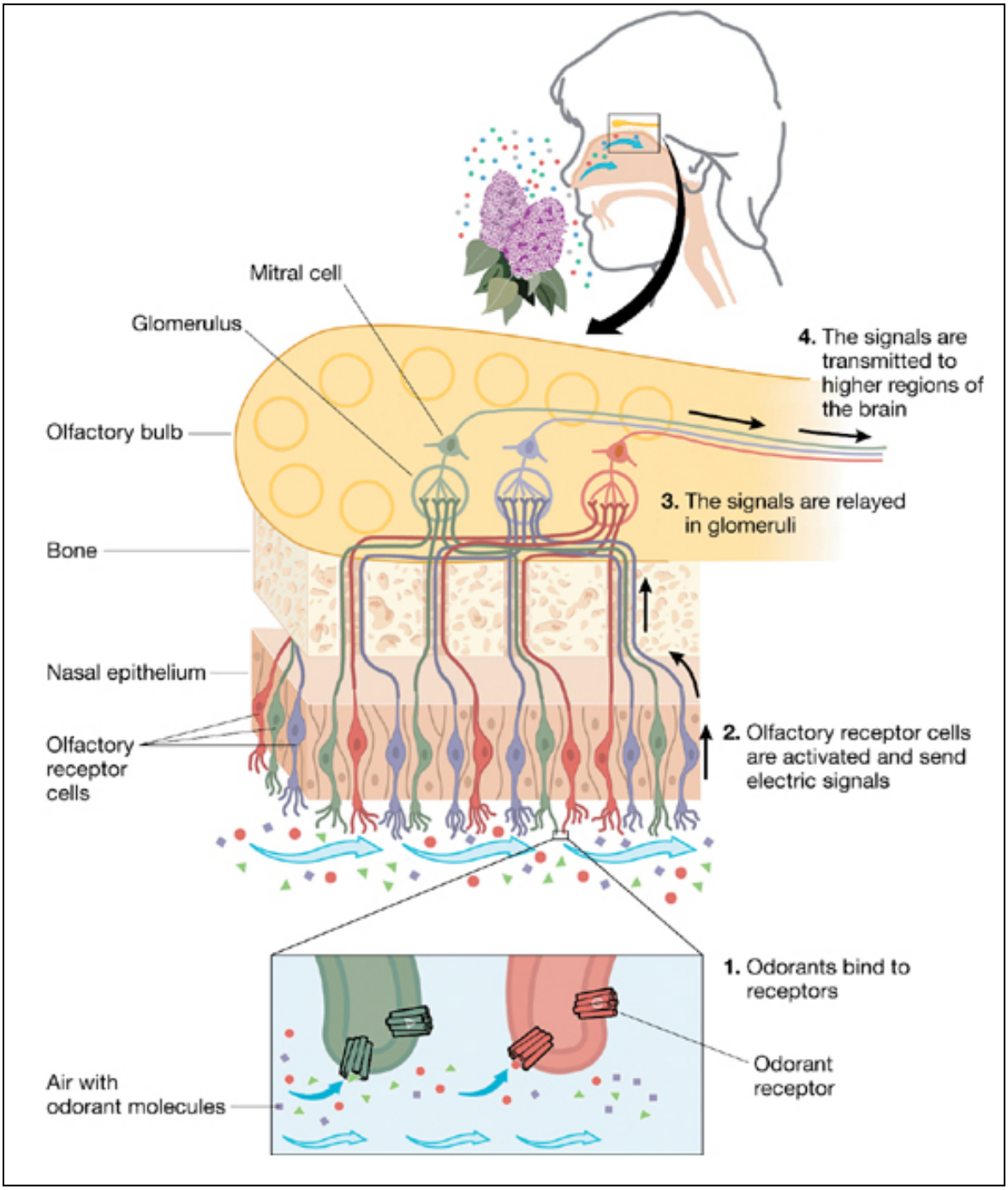
The substance that produces an odour is called an odorant. Odorants are volatile, hydrophobic molecules that are dissolved in the air and can activate the olfactory system. Odorants encompass a wide range of chemical compounds (acids, alcohols, aldehydes, amines, aromatics, sulphur compounds, etc.), and vary greatly in terms of size, structure, and functional groups (Schiffman et al., 2001; Malnic et al., 1999).

There are several commonly used odour terms encountered in the odour literature. These include odour quality, intensity, hedonicity (or hedonic tone), detection threshold, recognition threshold, and discrimination threshold. Odour quality refers to the general type of a smell (e.g., floral, musky, woody), while odour intensity and odour hedonicity are the perceived strength and pleasantness/ unpleasantness of an odour, respectively. The odour detection threshold refers to the level at which an odour is first detectable, and the recognition threshold is the level at which the odour quality can be identified. The discrimination threshold is the concentration at which one is able to differentiate between two odours.

2.2 Understanding the Olfactory System

The term olfaction refers to the sense of smell or the process of smelling an odorant. The basic anatomy of the nose and the process of detection of odour molecules has been well-defined (Figure 2-1). The main components of the olfactory system are the olfactory receptors, olfactory receptor neurons, glomeruli, mitral cells, and the olfactory bulb. Upon exposure to odorants, which can occur orthonasally (via the external nostrils) or retronasally (via the internal nares of the mouth), odorant molecules pass through the upper part of the nasal cavity lined by the olfactory epithelium (or nasal epithelium). Olfactory receptors located on olfactory receptor neurons in the mucosa of the epithelium bind to specific odorant molecules. There are several million receptor neurons in the human olfactory epithelium and ~350 receptor types, with each receptor neuron containing only one type of receptor (Malnic et al., 1999). Odorants can bind to one or more receptors, and receptors can bind to one or more odorants.

Figure 2-1: Process of olfaction (Rinaldi, 2007)



Odorant receptors are localized on olfactory sensory neurons, which occupy a small area in the upper part of the nasal epithelium. Every olfactory receptor cell expresses only one odorant receptor. On activation, signals from olfactory receptor cells are relayed in the glomeruli (micro-regions in the olfactory bulb). Receptor cells of the same type are randomly distributed in the nasal mucosa but converge on the same glomerulus. In the glomerulus, the receptor nerve endings excite mitral cells that forward the signal to higher regions of the brain. (Rinaldi, 2007)

The binding of an odorant to a receptor induces a conformation change, which initiates a sequence of events that converts the chemical signal into a neuronal signal. The neuronal signal is then transferred to the glomeruli in the olfactory bulb (Gottfried, 2010). Synaptic connections in the glomeruli allow transfer of the signal from the olfactory receptor neurons to the mitral cells, and then on to higher regions of the brain. Similar types of olfactory receptor neurons are randomly dispersed throughout 1 of 4 zones in the nasal epithelium, and axons from similar neurons converge at the same glomerulus. The combination of olfactory receptor neuron signals creates an 'odour map' in the glomerulus; the spatial and temporal 'odour map' allows the brain to decode and translate the neuronal signal as a distinct smell (Rinaldi, 2007; Shepherd, 2007; Malnic et al., 1999). This odour coding provides an explanation for the ability of the olfactory system to differentiate between an endless number of odours, odorants of similar structure, and varying concentrations of a single odorant.

2.2.1 Theories of the Odorant Structure–Odour Relationship

The mechanism in which an odorant molecule interacts with and activates an odorant receptor is, to date, not fully understood. Three theories for explaining the relationship between odorant structure and odour are the odotope theory, the vibrational theory, and the shape theory, with the odotope theory currently being the most widely accepted (Rinaldi, 2007; Rossiter, 1996). These theories are briefly described below:

(1) Shape theory: an early theory whereby the interaction between the odorant and receptor is based on a 'lock and key' mechanism: the odorant molecule fits into the receptor (Rossiter, 1996). The theory proposed that detection of smell is based on a combination of 7 basic primary odours, each with its own olfactory receptor that recognizes a particular shape of molecule (akin to color vision, where the observance of a spectrum of colours is based on 3 primary colours). However, the theory failed to explain how similar odorant molecules may be perceived as different smells and how different odorant molecules may be perceived as similar smells.

(2) Odotope theory (Weak-shape theory): a successor to the shape theory suggesting that olfactory receptors recognize a small part of an odorant molecule, such that each receptor can bind numerous molecules and each molecule can bind to numerous receptors (Rinaldi, 2007). Despite its wide acceptance, this theory does not explain how enantiomers (molecules with the same structure that are mirror images of each other) can have different smells.

(3) Vibration theory: suggests that odorant molecules are recognized by olfactory receptors based on their distinct vibrational pattern. The receptor becomes activated via inelastic electron tunneling when a molecule with the correct vibration frequency/pattern binds to the receptor. The theory offers a practical alternative to the theories based on molecular shape, but has not been supported in psychophysical studies in humans (Keller and Vosshall, 2004).

Though parts of each theory are plausible, none of the theories provide a consistently sound basis for predicting odour from an odorant molecule. It is possible that the mechanism involves a combination of both molecular shape and vibration; the flexibility of a molecule has also been suggested as a contributing factor (Brookes, 2010).

2.2.2 Cortical Processing

While the general regions of the brain involved in olfactory processing have been identified, the exact mechanism in which the brain decodes odour information remains poorly understood. Adding further difficulty is the fact that the brain areas involved may differ depending on odour properties (e.g., pleasantness or familiarity) or the task at hand (e.g., odour identification or discrimination). This represents an area of ongoing research, and only a basic introduction to cortical processing is presented here. Further discussion of neuronal responses to odours can be found in Chapter 5.

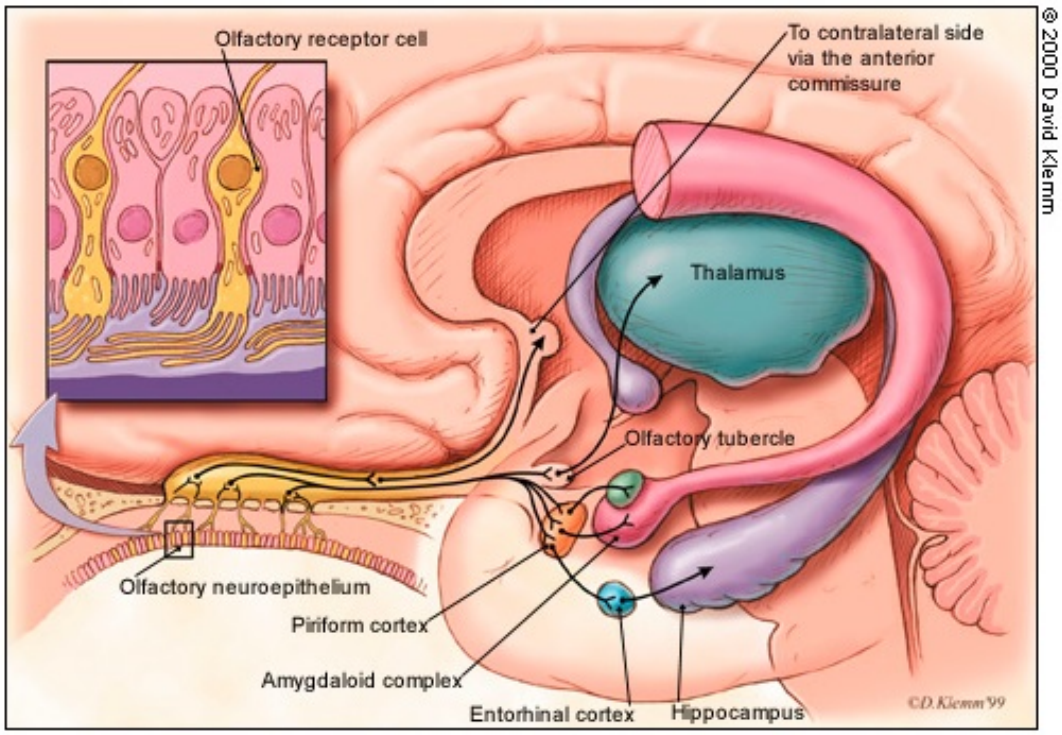
From the glomeruli in the olfactory bulb, neuronal signals are transferred to the brain via the olfactory tract which consists of bundles of axons of mitral cells (Gottfried, 2010; Haberly, 2001). Regions of the brain that receive direct input from the mitral cell axons make up the primary olfactory cortex (POC); the areas that make up the POC vary depending on the literature source, but mainly include the piriform cortex, anterior olfactory cortex, olfactory tubercle, amygdala, and rostral portions of the entorhinal cortex (Figure 2-2) (Wilson and Rennaker, 2010; Menini et al., 2004; Savic, 2001). Regions that receive neuronal input from the POC are considered the secondary olfactory cortex (SOC), and consist primarily of the orbitofrontal cortex (OFC), lateral entorhinal cortex, and insular cortex.

The piriform cortex and the OFC are the primary areas of the brain responsible for odour processing. The OFC receives sensory input from the piriform cortex, thalamus, amygdala, entorhinal cortex, and hippocampus to formulate the behavioral response to an odour. The involvement of a large portion of the limbic system (a group of brain structures associated with controlling emotion) reflects the high interconnectedness between smell and emotion, memory, and behavior (Gottfried, 2010; Wilson and Rennaker, 2010; Savic, 2005). This helps to explain why responses to odours are largely dependent on the perceived intensity, pleasantness, and familiarity of the odour as well as past experiences with the odour.

2.2.3 Olfactory and Trigeminal Odorants

In addition to olfactory neurons, the olfactory epithelium is innervated by trigeminal neurons. While the olfactory system is responsible for the smelling sensation of odorant molecules, the trigeminal system is responsible for sensations of pressure, pain, and temperature as well as responses to noxious stimuli. Odorants can be classified as pure olfactory, trigeminal, or mixed olfactory/ trigeminal odorants. Pure olfactory odorants (e.g., hydrogen sulphide (H_2S), phenylethyl alcohol, vanillin) stimulate only the olfactory neurons, and pure trigeminal odorants (e.g., carbon dioxide) stimulate trigeminal neurons; odorants activating only one system are referred to as unimodal.

Figure 2-2: Main areas of the brain involved in olfactory processing (Bromley, 2000)



Mixed olfactory/trigeminal odorants (or bimodal odorants) activate both the olfactory and trigeminal systems; the majority of odorants used in odour research are bimodal with varying strengths of trigeminal properties. The combination of olfactory and trigeminal properties explains why menthol, a bimodal odorant, produces a minty smell as well as a tingling or irritating sensation in the nose (Nagata et al., 2005). The olfactory and trigeminal processing systems exist independently, but appear to converge and interact during brain processing (Hummel et al., 2009a; Boyle et al., 2007b; Savic, 2001). For example, exposure to carbon dioxide (pure trigeminal) was found to activate both cortical somatosensory regions (primary and secondary somatosensory cortices) as well as olfactory processing regions (POC), suggesting a high inter-connectedness between the two systems (Hummel et al., 2009b). Further, olfactory/trigeminal mixtures have been found to produce activations in more brain regions than the sum of its components, including areas involved in cross-modal integration (Boyle et al., 2007a). This report focuses mainly on the effects of olfactory and bimodal odorants, with occasional discussion of trigeminal odorants.

2.2.4 Odour Mixtures

Odours in the environment are typically experienced as a complex mixture of multiple odorants. In general, humans are considered to have a limited ability for discriminating single components in a mixture (Livermore and Laing, 1998). The overall perceived odour is dependent on the number, type, and intensities of the odorants in the odour mixture, with some odorants dominating and others being masked. Livermore and Laing (1998) postulated that, from an evolutionary standpoint,

the limited ability of the olfactory system to identify individual odorants in a mixture may reflect a highly efficient neural encoding mechanism that simplifies complex multi-component environmental odours.

Though not a lot is known about the processing of odour mixtures, research with binary mixtures of odorants has suggested involvement at both the peripheral (receptor) and central (cortical) levels. At the receptor level, competitive and non-competitive interactions between individual odour components and olfactory neuron receptors result in a combination of suppression, hypoadditivity (response to mixture is lower than that induced by individual odorant at the same concentration), and synergy to both the magnitude and timing of a neuronal response (Su et al., 2011; Rospars et al., 2008; Duchamp-Viret et al., 2003; Laing et al., 1994). At the cortical level, activity responses in certain brain regions have been found to differ with binary mixtures in comparison to its single components. Boyle et al. (2009) demonstrated that processing of odour mixtures involves activation of more brain regions compared to single odorants, and specifically, that the lateral and anterior portions of the OFC are important in odour mixture processing. In a study of cortical responses to an unpleasant odorant, a pleasant odorant, and a mixture of the two, Grabenhorst et al. (2007) found both the unpleasant and pleasant aspects of the mixture to be represented separately in the brain. This suggests that, to some extent, there remains some separation in the cortical processing of the components of an odour mixture. Overall, these studies provide some interesting insight into the complexities of odour mixture processing; however, much about the topic remains largely unexplained.

2.2.5 Habituation

Habituation is the decrease in response to an odour following prolonged or repeated exposure. This process allows an organism to adjust to constant stimulations in the surrounding environment, while maintaining responsiveness to new odours or changes in odour concentration (Wilson, 2009; Dalton, 2000). Habituation can result in delayed reaction time for odour detection, reductions in perceived intensity of an odour, and reductions in odour-induced behavioral responses (Dalton and Wysocki, 1996). The extent of habituation is influenced by odour concentration, exposure duration, odorant physicochemical properties, and individual cognitive associations with the odour (Wilson, 2009; Kobayashi et al., 2008; Wang et al., 2002; Dalton, 2000).

The terms adaptation and habituation are often used interchangeably to describe reduced odour-induced responses. Generally, adaptation describes changes in peripheral processes, such as alterations in olfactory receptor responsiveness and odorant clearance (Wang et al., 2002; Dalton, 2000). Habituation, on the other hand, generally refers to changes in central processing, such as reduced glomerular responses and reduced cortical activity in certain regions of the brain. The exact mechanism of the habituation response is not clearly understood, but appears to be mediated by reductions in synaptic responses between the olfactory bulb and piriform cortex (Linster et al., 2009; Wilson, 2009; Wilson and Linster, 2008; Best et al., 2005). Habituation and adaptation of smell have also been referred to as olfactory fatigue.

A decrease in response to one odorant may affect the response to another odorant; this phenomenon is referred to as cross-adaptation (Pierce et al., 1996). The cross-adaptation response is similar to that of habituation; prolonged exposure to one odorant leads to reductions in perceived intensity and behavioral responses to another odorant. Hypotheses describing the basis for cross-adaptation tend to focus on the quality, structure, and functional groups of odorant pairs; for example, cross-adaptation has been found to occur between 3-methyl-2-hexenoic acid and the ethyl esters of 3-methyl-2-hexenoic acid (similar structures but different smells) and between trimethyl pyrazine and 2-propionyl-3-methyl furan (similar smells of bitter chocolate but different structures) (Pierce et al., 1995; Cain and Polak, 1992). However, cross-adapting odorant pairs are not always structurally or perceptually similar, suggesting the involvement of other unknown factors (Pierce et al., 1996). Recent research has indicated that the main underlying mechanism appears to be related to the degree of shared olfactory coding patterns between a pair of odorants (Gottfried et al., 2006).

2.2.6 Factors Influencing Odour Perception

Olfactory function and olfactory sensitivity can vary greatly between individuals. Factors such as age, gender, disease status, and culture can contribute to significant differences in odour perception. For example, women have generally been found to perform better than men on tests of olfactory threshold sensitivity, odour discrimination, and odour identification (Ferdenzi et al., 2011; Doty and Cameron, 2009; Doty et al., 1985). Similarly, olfactory function can differ between age groups. A loss of olfactory function is associated with aging, and elderly subjects typically perform poorer than younger adults on tests of odour sensitivity and odour identification (Murphy et al., 1994; Doty et al., 1984). Odour perception can also be influenced by certain diseases; for example, Parkinson's disease, Alzheimer's disease, and multiple sclerosis can impair the sense of smell (Bromley, 2000). Disorders such as environmental chemosensory responsivity, multiple chemical sensitivity, and idiopathic environmental intolerance can also influence odour perception (Kärnekull et al., 2011).

Age, gender, disease status, and culture, as well as individual past experience with an odour, may heavily influence odour-induced responses. The impacts of these factors on olfactory function are worthy of mention, but will not be addressed in detail in this report. In most experimental studies, subjects are asked to rate odours in terms of intensity and pleasantness prior to or following the session to help control for these differences.

2.3 Methods of Odour Measurement

Techniques for the measurement of odour concentration are either based on sensory measurements or chemical analyses, both of which are advantageous and disadvantageous in different ways. Sensory measurements (e.g., dynamic dilution olfactometry) provide a measure of overall odour exposure and are an indicator of what is perceived by the human nose; however, sensory measurements rely on the perceptions of a group of odour panelists and results may vary based on panelist selection. Chemical analyses (e.g., H_2S concentration) provide a quantitative estimate of levels of specific odorous chemicals, but give no indication of the total odour exposure.

Additionally, chemical analyses are not suitable for measurement of complex odour mixtures, as total odour level cannot be predicted by simply summing the individual odorous components.

Accurate measurement of environmental odours has proven difficult for several reasons. Firstly, odours are typically present as a diverse mixture of chemicals that may undergo rapid fluctuations over distance and time. This means that a single odour sample may not provide an accurate estimation of overall odour levels. Secondly, odour levels may be influenced by sampling techniques, instability of the odour samples following sampling, concentration decay, and presence of dust particles in the sample (Bockreis and Steinberg, 2005; van Harreveld, 2003; Bottcher, 2001; Schiffman et al., 2001). And thirdly, sensory and chemical odour measurements do not account for odour hedonic (pleasantness); assessments of hedonic tone must be performed separately.

A brief summary of the various odour measurement methods used in odour research are presented in the following sections. Refer to Brattoli et al. (2011) for a more detailed review of the measurement methods.

2.3.1 Sensory Measurements

Dynamic dilution olfactometry (DDO) is typically used for sensory measurements of complex mixtures of odour. Using an olfactometer to distribute gases, trained odour panelists smell diluted odour samples in order to determine the strength or intensity of an odour. DDO methods are suitable for estimating total odour level, but no information is determined about the components of the sample or the character of the odour (i.e., quality, pleasantness, pungency). DDO methods can be expensive and time-consuming, and are also limited in that determined thresholds are dependent on the odour sensitivities of the panelists.

The American Society of Testing and Materials (ASTM) has developed a standard methodology for determining the sensory threshold level of an odour sample titled '*E679-04 Standard Practice for Determination of Odor and Taste Thresholds By a Forced-Choice Ascending Concentration Series Method of Limits*' (ASTM, 2011; McGinley, 2002). Odour panelists are presented with 3 samples (1 odour sample, 2 odourless air samples) and asked to identify the odour sample; this is referred to as the 'triangular forced-choice' method. The panelist indicates whether the response was a guess, a detection (the selection smells different than the other 2), or a recognition (the selection smells like something). The method begins using sub-threshold odour levels and the process is repeated using successively higher odour concentrations (i.e. 'ascending concentration series'). The detection and recognition thresholds are determined from the responses of the panelists, and expressed as a dilution factor (dilution-to-threshold (D/T)) equivalent to the ratio of the volume of clean air to the volume of odorous air. Larger ratios indicate a stronger odorant.

A similar odour measurement method has also been developed by the European Committee for Standardization: *EN13725 Air quality - Determination of odour concentration by dynamic olfactometry* (McGinley and McGinley, 2001). This method is much the same as the ASTM E679 method, except that the EN13725 method indicates stricter specifications for operating equipment and panelist

selection. Further, the odour panelists may be presented with 2 samples (binary forced-choice: 1 odour sample, 1 odourless sample) instead of 3. The odour concentration is expressed in terms of European odour units (OU_E or OU_E/m^3), which is defined as "the amount of odorants that, when evaporated into 1 m^3 of neutral gas at standard conditions, elicits a physiological response from a panel (detection threshold) equivalent to that elicited by 1 European reference odour mass [123 µg *n*-butanol] evaporated in 1 m^3 of neutral gas at standard conditions" (Bockreis and Steinberg, 2005). Thus, the OU_E accounts for the variation in detection thresholds (for *n*-butanol) of the panelists.

An alternative ASTM standard '*E544-10 Standard Practices for Referencing Suprathreshold Odor Intensity'* is a methodology for determining the intensity of odours using an Odour Intensity Referencing Scale (ASTM, 1996-2011; McGinley, 2002). This method utilizes odour panelists/inspectors to compare the odour intensity of a sample to the odour intensities of a range of concentrations of a reference odorant, *n*-butanol. The intensity of the odour sample is expressed in parts per million (ppm) of *n*-butanol, with a larger value of indicating a stronger odorant.

For odour epidemiology studies, odour concentration is often determined in a manner similar to ASTM E679-04. The concentration is defined as the dilution level at which 50% of a panel of subjects cannot distinguish the odour from odourless air (Miedema and Ham, 1988). For example, if an odour diluted 10 times is just undetectable by 50% of the panel (i.e., half the group is no longer able to discriminate between the odour and odourless air), the odour concentration would be 10 OU/m^3.

A common cost-effective method for estimating odour levels in areas surrounding odour-emitting facilities is odour dispersion modeling. Modeling can be used to predict or estimate odour exposure levels at varying distances from an odour source under different atmospheric conditions. First, the relationship between emissions and odour perception/intensity is identified using an odour panel; the odour emission rate can then be determined based on chemical emissions from the odour source at any given time. Odour dispersion factors such as emission characteristics, stack height, meteorological conditions, wind speed and direction, season, and dust levels are then taken into account, and the resultant value provides an estimate of odour levels at a particular place and time (Yu et al., 2011; Janes et al., 2005; Schiffman et al., 2001).

2.3.2 Chemical Analyses

Quantification of individual odorous chemicals is a common approach for estimating odour exposure. Chemical analysis is most appropriate in cases where known single odorants are responsible for an odour, as opposed to diverse mixtures of odorants. The list of odorous compounds that may be measured is virtually endless; the most commonly measured include ammonia (NH_3), H_2S, sulphur dioxide (SO_2), mercaptans, methane (CH_4), volatile organic compounds (VOCs), and organic acids (e.g., propionic acid). H_2S and NH_3 are commonly used for odour regulation purposes (RWDI AIR Inc., 2005).

To put into perspective the difficulty of using chemical analyses for odour assessments, a recent study found over 400 different odorants emitted from swine facilities (Schiffman et al., 2001). Though levels of each individual odorant were low, the overall mixture of odorants produced extremely strong odour intensities. Thus, in cases of environmental odours such as those from swine facilities, sensory measurements and odour dispersion modeling are likely to provide better estimates of odour concentration than individual odorants.

2.3.3 Electronic Nose (E-Nose)

The electronic nose (E-Nose) is an analytical method that has the ability to objectively analyze and quantify odours (Brattoli et al., 2011). Briefly, the E-nose makes use of an array of chemical sensors and a data processing unit to detect odours in a manner that mimics the human nose. Odours are identified based on the pattern of response of the sensor array (i.e., chemical fingerprint) by comparing to the fingerprints of known samples.

The E-Nose is becoming increasingly popular for environmental monitoring of odours; with proper calibration, E-Noses have the ability to continuously detect the presence of odours in ambient air, estimate concentrations of odours, and attribute the odour to a specific odour source (Dentoni et al., 2012). Use of the E-Nose helps to overcome some of the limitations of sensory measurements (reliance on panelists, expensive) and chemical analyses (unsuitable for diverse mixtures).

2.4 FIDOL

The main contributing factors in triggering an odour-induced response are typically referred to as FIDOL: Frequency, Intensity, Duration, Offensiveness, and Location (Nicell, 2009). Frequency refers to how often the population is exposed to odour; Intensity refers to the strength of the odour; Duration refers to the length of time of the odour episode; Offensiveness/character encompasses the odour quality (type of odour) and hedonic tone; and Location represents the specified land use of the surrounding area and the tolerance of the community (residential/rural location, schools, hospitals). These 5 factors are often used collectively to evaluate the potential impact of odour on a population surrounding an odour source.

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3. Epidemiological Studies

3.1 Introduction

This chapter summarizes the epidemiological literature evaluating environmental odours and health responses. More than 50 studies (publication dates of 1975-2013) were found that examined the impacts of odours on communities located near odour-emitting facilities. The odours originated from a wide variety of sources, ranging from oil refineries and chemical plants to waste treatment centres and livestock operations. Most of the studies were conducted in Europe (mainly Germany, the Netherlands, and Scandinavia), while considerably fewer studies were conducted in Canada (petroleum and petrochemical plants in Ontario) or the United States (livestock facilities and landfills in North Carolina and Iowa; sludge application sites in North Carolina, South Carolina, and Virginia; pesticides, waste disposal sites, pulp mills and sewage treatment plants in California).

There are various methods used to estimate individual or community exposures to odour. For the most part, exposure has been determined by frequency/intensity of odour perception (by subjects or trained panelists), frequency/intensity of self-reported odour annoyance, residence distance to facility, or hedonic tone (i.e., pleasantness) of the odour (by subjects or trained panelists). Some studies use 2, 3, or 4 geographic zones to categorize exposure; the different zones represent areas with different levels of exposure, and are typically based on residence distance to the odour source and prevailing wind direction. Alternatively, an average odour concentration (measured in odour units per metre cubed (OU/m^3)) can be calculated using trained odour panelists, factory emission data, and odour dispersion modeling. Odour concentration is defined as the dilution level at which 50% of a panel of subjects cannot distinguish the odour from odourless air (Miedema and Ham, 1988). For example, if an odour diluted 10 times is just undetectable by 50% of the panel (i.e., half the group is no longer able to discriminate between the odour and odourless air), the odour concentration would be 10 OU/m^3. Further details about odour measurement techniques can be found in Section 2.3.

The main responses that have been evaluated in odour epidemiology studies include health symptoms (e.g., respiratory symptoms, nausea, headache, fatigue), physiological responses (e.g., blood pressure, lung function), odour annoyance, mood (e.g., stress, anxiety, depression), changes to daily activities, and coping mechanisms. Responses are typically self-reported via mail-in questionnaires, telephone interviews, or in-person interviews. The impacts of individual socio-economic factors such age, gender, race, occupation, and smoking status on reported health responses are often considered in the analyses. Most epidemiology studies focus on the health effects of chronic odour exposures rather than acute exposures.

There are several weaknesses and limitations that are common to the studies reviewed in this chapter. Firstly, many of the studies suffer from a weak exposure assessment, either by using subjective measures of exposure, evaluating odour levels at only one point in time, or not measuring

odour at all. Secondly, the majority of studies are cross-sectional in nature, with subjects being assessed only once by questionnaire or interview. Reporting bias is also an important limitation to consider, as most studies have relied on self-reported accounts of exposure and/or response. Furthermore, it is not always known if pollutant levels were below irritant thresholds; in which case, it is indiscernible if the outcomes observed are a result of exposure to odour itself or exposure to irritating pollutants. There are also a number of sample biases that may influence findings including selection bias (those that have a problem with the odour or industry are more likely to participate), selective migration (odour-sensitive individuals move away or live in areas of lower exposure), socio-economic differences between exposed and control communities, small sample sizes, and low participation rates. These weaknesses limit the applicability of epidemiology studies to the risk assessment of odour exposure; however, the studies are suitable for identifying common patterns among exposed communities and indicating potential links between odours and responses.

In the following chapter, studies are categorized by response (health symptoms and physiological responses, odour annoyance, and mood/coping/activity changes) and further by location of study. A tabulated summary of the odour epidemiology studies is provided in Appendix C. An evaluation of the quality of the studies was beyond the scope of this review; however, any apparent limitations were noted for each study.

3.2 Health Symptoms and Physiological Responses

Canada

In Canada, the effects of odours on health symptoms have been studied in residents living near a petroleum refinery in Oakville, ON. In a cross-sectional analysis, 391 adults underwent telephone interviews discussing background information, health symptoms, illnesses, odour perception and annoyance, and attitudes regarding the refinery (Taylor et al., 1997). Exposure to odours was determined by residence distance to the refinery (three zones) or self-reported frequency of odour perception. Compared to subjects who infrequently or never noticed odours, subjects who noticed odours frequently (>once per week) were 2–4 times more likely to report cardinal symptoms (cough, nausea, congestion, eye irritation, throat irritation, earache, skin rash; OR range: 1.84– 3.43), general symptoms (headache, sleep problems, dizziness, stomach pain, diarrhea, chest pain; OR range: 1.75–2.96), and other symptoms (back pain, bruising; OR range: 2.09–2.23). These subjects were also more likely to state that the symptoms were induced or worsened by the refinery odours. Symptoms were found to be 2–4 times more prevalent in subjects that were frequently bothered by the odours, compared to those infrequently bothered (OR range: 1.65–4.71). No significant associations were observed for wheeze, colds, nosebleeds, appetite loss, or dysuria.

The authors hypothesized that odour perception and annoyance sensitize residents to possible health effects, leading to increased symptom reporting and attributing symptoms to refinery emissions; however, they also realized that the association may occur in the reverse direction, such that experiencing symptoms may increase the likelihood that residents perceive and become annoyed by refinery odours. As odour exposure (as measured by residence distance to the refinery) was not

associated with symptoms, the evidence supports an indirect role of odours in symptom reporting, rather than a direct toxicological link.

In a follow-up study of the same area, Luginaah et al. (2002a, 2000) studied community changes in odour perception and health symptom reporting before and after implementation of an odour reduction plan. The initial survey of 391 adults was conducted in 1992 (Taylor et al., 1997), and the follow-up survey of 427 adults was conducted in 1997. Exposure determination and telephone interviews were as described above. There was no significant difference in health symptom reporting between zones for either year, nor did the health symptom reporting change between 1992 and 1997. The investigators concluded that zone of residence (as a measure of exposure) was not a strong predictor of health symptoms for nearby residents. In both years, the prevalence of several symptoms (cough, nausea, sinus/nose congestion, eye irritation, throat irritation, headaches, sleep problems, dizziness, stomach pain, diarrhea, chest pain) was significantly higher in subjects who perceived odours frequently and in subjects who were frequently annoyed. The investigators found symptom reporting to be strongly mediated by odour perception and odour annoyance.

Despite the implementation of odour reduction measures by the industry, no significant changes to symptom prevalence rates nor to the association between odour perception/annoyance and symptom reporting were found. The authors suggested that the persistence of symptom reporting points to the possibility that sensitive individuals in the community may be reporting health issues in the absence of harmful effects from the refinery. Reappraisal of odours is thus considered a complex process that involves personal and situational factors as well as changes in exposure.

United States

Several studies have been conducted in the United Stated investigating the health symptoms associated with exposure to odours from hazardous waste sites, paper mills, pesticide use, and livestock operations. Shusterman et al. (1991) examined the effect of odour perception and environmental worry on symptom prevalence in subjects residing near three hazardous waste sites in California. More than 2000 subjects answered questions regarding odour perception, environmental worry, and health issues by questionnaire, telephone interview, or personal interview. Odour exposure was defined as self-reported frequency of odour perception, and data from the three areas were pooled for the analysis. Symptom prevalence (headache, nausea, eye and throat irritation) was significantly associated with both frequency of odour perception (e.g., headache OR: 5.0, CI: 3.3–7.7) and degree of environmental worry (e.g., headache OR: 10.8, CI: 6.2–16.8). The strongest associations were found in subjects that perceived odours frequently and were very worried about environmental health (e.g., headache OR: 36.7, CI: 11.2–77.7). For nausea and throat irritation, no significant association was found with odour frequency in subjects with low environmental worry. The authors concluded that both odours and environmental worry play a role in health symptom complaints in residents living near hazardous waste sites.

Lipscomb et al. (1991) examined the impact of site remediation on health symptom reporting in a community located near a waste disposal site in Fullerton Hills, California. The community was first

assessed by the California Department of Health Services in a 1981 cross-sectional analysis, and site clean-up began in 1983 and 1984. The 1991 publication presented a follow-up analysis of the same areas assessed in the 1981 study. One-hundred ninety-three subjects were interviewed by telephone or in-person regarding demographics, odour perception, perceived environmental risk, and health symptoms. Exposure in the affected community was defined as high exposure or low exposure based on odour zones around the facility, and a non-exposed control community was also included. Reporting of several health symptoms (e.g., skin irritation, nausea, wheezing, loss of appetite, headache) was increased among the high-exposed group relative to the control group (crude OR range: 0.78 to 5.95; skin irritation OR: 4.97; CI: 1.82-13.63). Interestingly, toothache (included as a dummy symptom to assess reporting bias) showed the highest odds ratio (OR: 5.95, CI: 1.85-19.16). When the associations between exposure group and health symptoms were stratified by low, medium, or high environmental worry, results remained for the high worry group only. No association or a negative association was found for subjects with low environmental worry.

A subset of six symptoms (loss of appetite, fatigue, headache, skin irritation, stomach symptoms, wheezing) was used to compare the data from the 1981 and 1988 surveys. Reporting of the six symptoms was significantly increased in the high-exposure group in both 1981 and 1988. Symptom reporting for the 1988 survey was higher than in the 1981 survey, despite remediation efforts at the site and reduced odour exposures. Overall, the evidence suggests that symptom reporting in odour-exposed areas is mediated by environmental worry. Further research into the reasons for environmental worry suggested that worry caused symptom reporting rather than symptoms causing worry. Similar to the above study by Shusterman et al. (1991), it was concluded that both odour exposure and environmental worry are involved in health symptom reporting.

In Eureka, California, the relationship between odours and health symptoms was examined in 140 adults living near two pulp mills (Deane and Sanders, 1977). Subjects underwent interviews discussing presence of odours, attitudes, annoyance reactions, health symptoms, and socio-economic data. Estimation of odour exposure was based on residence distance to the pulp mills (3 zones: 1–2 miles, 2–3 miles, and >4 miles from facility). Measurements of odour frequency by trained panelists as well as measurements of methanethiol levels showed that odour exposure was highest in zone 1 and lowest in zone 2. Odour exposure did not positively correlate with most health symptoms (e.g., cough, shortness of breath, runny nose, nervousness, headache, nausea). A significantly higher prevalence of phlegm was found in zone 1 females relative to the other zones ($p<0.05$); however, this may have been influenced by the high percentage of female smokers in zone 1. Unexpectedly, some symptoms showed an inverse relationship with odour, including difficulty urinating, sleeplessness, sinus congestion, eye irritation, and runny nose. Reports of headache were significantly higher in annoyed subjects compared to subjects annoyed little to not at all ($p<0.05$); no significant differences between annoyance groups were found for any other symptoms. The authors considered the overall results to be inconclusive concerning the link between odours and health effects.

Ames and Stratton (1991) compared odour perception and health effects in subjects living near a pesticide-treated potato field in Dorris, CA. Questionnaires were distributed to all residents of

Dorris six weeks after the application of ethoprop to the potato field (main odorant: *n*-propyl mercaptan). 421 subjects answered questions discussing odour perception, health effects that occurred in the previous six weeks, and socio-demographic variables. Self-reported frequency/ intensity of odour perception and residence distance to the potato field were used as the exposure variables. The incidence of 15 health outcomes (e.g., headaches, asthma attacks, burning eyes, runny nose, and nausea) was significantly increased in subjects who perceived a strong odour compared to those who did not (OR range: 1.77–6.00). A unit increase in odour intensity (no odour, mild, strong, extremely strong) was associated with an increased risk of being highly symptomatic (OR=2.42). Also, a dose-response correlation was observed between the number of days strong odour was perceived and the total number of reported symptoms. Residence distance to the potato field did not show a significant relationship with health symptoms. *n*-Propyl mercaptan levels were not measured in the study; thus, it is not known if the observed health effects are due to odour itself or to toxic properties of the chemical.

In Iowa and North Carolina, Wing and Wolf (2000) and Thu et al. (1997) conducted cross-sectional analyses examining the health of subjects living near swine operations. Subjects were interviewed in-person about health symptoms, quality of life, and socio-demographic factors. Results from exposed adults living near a swine operation (Iowa: 18 adults; North Carolina: 105 adults) were compared to control subjects (Iowa: 18 adults; North Carolina: 50 adults). Thu et al. (1997) found higher frequencies of several health symptoms including respiratory symptoms (p=0.02), nausea/weakness/ dizziness/fainting (p=0.04), and headaches/plugged ears (p=0.06) in exposed subjects relative to control subjects. Frequency of reported symptoms did not correlate with residence distance from the swine facility. The authors noted that ammonia, dust, and endotoxins are typically present in the air downwind from swine facilities in Iowa; however, the levels are much lower than irritant thresholds. Wing and Wolf (2000) found that subjects living near a hog operation showed a significantly higher prevalence of mucous membrane irritation, runny nose, sore throat, excessive coughing, headaches, burning eyes, and diarrhea (p<0.05) compared to the control community. Subjects living near the cattle operation reported significantly more episodes of excessive coughing and heartburn (p<0.05). Reporting for many other health outcomes (e.g., shortness of breath, chest tightness, wheezing, heartburn, tearing eyes, dry skin, joint/muscle pain, tiredness, dizziness, blurred vision, and fever/chills) did not differ between exposed and control communities. Odour exposure was not measured in this study and it is not known if pollutant levels were below irritant thresholds.

Also in North Carolina, Schinasi et al. (2011) assessed odours, health symptoms, and lung function in 101 adults residing near hog operations. Twice-daily for two weeks, subjects rated the intensity of any present odours, answered health questionnaires, and performed lung function and blood pressure testing. The 12-hour average odour intensity level was also determined at a central location each neighborhood, as well as levels of H_2S, semi-volatile PM_{10}, $PM_{2.5}$, and endotoxin. Self-reported odour intensity was significantly associated with eye, nasal, throat irritation, and cough; these outcomes were also associated with 1-hour averages of H_2S and PM_{10}, though the correlations were not as strong. 12-hour average central odour levels correlated with difficulty breathing, burning eyes, and nasal irritation; some of these outcomes also correlated with $PM_{2.5}$, semi-volatile PM_{10}, and H_2S. No associations were found between 12-hour odour levels and other health symptoms (sore throat,

cough, wheezing, chest tightness, itching eyes, nausea, diarrhea, appetite, headache, dizziness, joint pain, fever) or changes in lung function. Health outcomes were not assessed in multi-pollutant models; it is not clear if the observed health effects are a result of odour exposure, co-pollutant exposure, or a combination of both.

In another study of the same subjects, Wing et al. (2013) evaluated the relationship between livestock odours and blood pressure. Increases in self-reported odour intensity were found to correlate with diastolic blood pressure (*t*-value=3.02) and, to a lesser extent, systolic blood pressure (*t*-value=0.86). The associations declined after adjustment for stress (*t*-value or *p*-value not given), and the authors suggested that stress may be a potential mediator of odour-related changes in blood pressure. H_2S also showed correlations with diastolic and systolic blood pressure; these correlations changed little after adjustment for stress.

Lowman et al. (2013) conducted a qualitative analysis aimed at understanding the health and quality of life in residents living near sludge application sites in North Carolina, South Carolina, and Virginia. Thirty-four subjects underwent open-ended in-person interviews discussing demographics, community history, common activities, experiences with sludge application near their home, and coping mechanisms or actions taken. From the interviews, the investigators identified common themes outlining the impact of sludge application on health responses and quality of life in these residents. Most respondents (30/34) described offensive odours related to sludge application; approximately half of the respondents (18/34) associated sludge application with acute health symptoms. The most commonly reported symptoms were eye, nose, and throat irritations and gastrointestinal symptoms (nausea, vomiting, diarrhea); other symptoms reported by more than one respondent include cough, difficulty breathing, sinus congestion or drainage, and skin infections or sores. The authors concluded that residents from 3 different states demonstrated similar health and environmental concerns regarding sewage sludge application, and further attention from scientists and public health officials is warranted. It is important to note that subjects were not a random sample of the population and an exposure assessment was not performed.

Avery et al. (2004) examined the effect of hog odour exposures on secretory immunoglobulin A in saliva in North Carolina adults. Twice-daily for two weeks, 15 subjects provided saliva samples as well as rated the intensity of any present odours. Subjects served as their own controls. For both the morning and evening samples, odour intensity inversely correlated with immunoglobulin A concentrations and secretion rates (modest *t*-values; *p*-values not given). The authors concluded that exposure to odours from hog operations have an effect on the functioning of the mucosal immune system. The sample size was very small and no odour was present for the majority of sampling points in the study.

In a similar study, Heaney et al. (2011) investigated the effect of landfill odours on the health and quality of life of nearby residents in North Carolina. Twice daily for 2 weeks, 23 adult subjects sat outdoors for 5 minutes and took note of odour intensity, mood states, and health symptoms. Notes on odours and daily activities for the previous 12-hour period were also recorded. Exposure was defined as subjects' perception of odour (yes/no), rating of odour intensity (none to very strong), or

community H_2S levels. For the 5-minute outdoor periods, perception of odour correlated with several health symptoms (mucosal irritation, upper respiratory symptoms, dizzy or lightheadedness, and general ill feeling; OR range: 1.9 to 5.3). No associations were found with ringing in the ears or gastrointestinal symptoms. For evaluations of H_2S and health responses, correlations tended to be positive but were highly imprecise. Overall, the authors concluded that odours from a landfill negatively impact the health of nearby residents. Similar to the study above, this analysis is limited by its small sample size and the absence of odour for the majority of the sampling periods.

Worldwide

The relationship between odour exposures and health symptoms has been investigated in a number of German studies. Steinheider (1999) and Steinheider et al. (1998) examined the health-related effects of odour exposures in residents living near a fertilizer plant in Nettetel or a pig rearing facility in Nörvenich. Exposure was measured as residence distance to the fertilizer plant in Nettetel (close, medium or remote distance), and odour frequency in Nörvenich (odour hours/year as determined by trained panelists). For both cities, adult subjects (Nettetel: 250; Nörvenich: 322) were interviewed in-person regarding odour annoyance, somatic symptoms, general health, and socio-demographics. Subjects living closer to the fertilizer plant reported more gastric symptoms (disgust, loss of appetite, vomiting, nausea, retching) and some general health symptoms (headache, breathing difficulties, cough, stomach and sleep disorders) than those living further away. Symptom reporting appeared to be mediated by both odour exposure and odour annoyance in these subjects. In Nörvenich, odour frequency had a small but significant effect on reporting of gastric symptoms and general health symptoms. After adjustment for odour annoyance, no association was found between odour exposure and symptoms; symptom reporting appeared to be mediated strictly by odour annoyance. The authors concluded that exposure to offensive odours (i.e., pig facility in Nörvenich) induces both annoyance reactions as well as symptom reporting, while in the case of exposure to moderate odour exposures (i.e., fertilizer plant in Nettetel), somatic symptoms are mediated by odour annoyance. Response rates were low (27–56%) and it is not known if pollutant levels were below irritant thresholds.

Also in Germany, Sucker et al. (2009, 2008) compared odour exposure and health symptoms in 1408 adults residing near various industrial odour sources (two pleasant: sweets production, rusk bakery; two neutral: textile production, seed oil production; two unpleasant: fat refinery, cast-iron factory) and 901 adults residing near livestock operations. Subjects underwent interviews regarding quality of life, odour perception, odour annoyance, health symptoms, and socio-demographic factors. Odour exposure was estimated using frequency of odour perception, intensity of odour, and hedonic tone of odour, as measured at multiple sites near each source by a group of trained panelists. For the industrial odours, frequency of odour exposure was associated with increased percentage of subjects with general health complaints (OR: 1.8, CI: 1.4–2.3; $p<0.001$); this association was greatly influenced by odour hedonic (OR: 3.2, CI: 2.0–5.0; $p<0.001$) and odour annoyance (OR: 1.7, CI: 1.6–1.8; $p<0.001$). For individual symptoms, significant correlations were found with difficulties falling asleep (OR: 1.6, CI: 1.0–2.5; $p<0.001$) and headache (OR: 1.8; CI: 1.1–3.1; $p<0.001$). Stronger correlations were found between odour hedonic and cough, breathing difficulties, stomach

disorders, and nose/eye irritation (OR range: 3.0–10.7; $p<0.01$). However, none of these results were significant when odour annoyance was included in the model. For the livestock operations, no significant correlations were found between health symptoms and odour frequency, odour intensity, or odour quality (i.e., poultry, pig). Annoyance from livestock odours was significantly associated with most symptoms (OR range: 1.3–1.4; $p<0.01$). Overall, the authors concluded that odour hedonic, but not odour intensity, has a strong influence on exposure-annoyance and exposure-symptom associations. Symptom reporting appears to be mediated mainly by odour annoyance. Response rates were quite low and varied between cities (18–43%).

Herr et al. (2009, 2003a,b) assessed the prevalence of unexplained health symptoms in subjects living near 3 composting sites in Germany compared to subjects living in control communities. In the first cross-sectional study, 496 adults living within 1.5 km of a composting site and 301 control adults responded to questionnaires discussing odour annoyance and somatic health complaints (Herr et al., 2003a). Residing near a composting site and frequency of odour annoyance were used as the exposure variables. Frequency of odour annoyance was higher in all exposed communities (80%, 90%, and 41%) compared to their respective controls (26%, 17%, and 12%). Nausea was found to be more frequently reported in the two communities reporting high rates of odour annoyance. Frequency of total number of reported somatic symptoms (e.g., headache and facial pain, lower back pain, nausea, joint pain, breathlessness) was higher in all exposed groups compared to their control groups, though this difference was only significant ($p<0.001$) for the community that was also exposed to airborne micro-organisms. Other than nausea, the investigators found that frequently-reported somatic symptoms were influenced little by odour annoyance.

In the second cross-sectional study, 356 adults living near a composting site and 142 control subjects were similarly assessed (Herr et al., 2009; Herr et al., 2003b). Odour annoyance was reported by 80% of subjects living within 500 m and 95% of subjects living within 200 m of the site, compared to 26% in the control community. Odour annoyance was associated with nausea, itching or stinging eyes, joint problems, muscular complaints, and impaired coordination (OR range: 1.84–10.40). No associations were found with respiratory outcomes. It is important to note that odour exposure levels were not measured in either of the above studies.

Radon et al. (2007, 2004) studied the effects of livestock odours on health of subjects in rural Germany. In the initial study, livestock odours and quality of life were examined in 3112 adults living near intensive livestock production facilities (Radon et al., 2004). Subjects responded to questionnaires discussing physical and emotional health, odours, and socio-demographics via mail. Self-reported intensity of odour annoyance was used as the exposure variable. Physical health scores (based on a survey of self-reported general health and ability to do physical activities) showed a significant inverse relationship with odour annoyance ($p<0.05$). In the second study, respiratory health was examined in subjects living near confined animal feeding operations (Radon et al., 2007). A total of 6937 adults responded to mail-in questionnaires discussing respiratory symptoms, animal feeding operations within 500 m of home, odours, and socio-demographics. A subset of 2571 subjects also underwent blood sampling and pulmonary function testing. Exposure was estimated as self-reported odour annoyance or the number of feeding operations within 500 m of the home.

Relative to subjects not annoyed at all, strongly annoyed subjects reported more wheezing, allergic rhinitis, and physician-diagnosed asthma (OR range: 1.81–2.96). No associations were found between odour annoyance and any of the physiological responses (bronchial hyper-responsiveness to metacholine, lung function, allergic sensitization). Subjects with >12 animal operations within 500m of their home showed increased prevalence of wheezing (OR: 2.45, 95% CI: 1.22–4.90) and decreased forced expiratory volume (OR: −7.4, 95% CI: −14.4 – −0.4) relative to subjects with less than 5 animal operations nearby; no associations were found with allergic rhinitis or specific sensitization. Overall, the investigators demonstrated that subjects living near feeding operations have decreased respiratory health; however, the cause of this change in respiratory health was not evaluated.

Odour exposures and health symptoms have also been evaluated in several other European countries. In the Netherlands, Cavalini (1994) and Cavalini et al. (1991) studied health symptoms in 2413 subjects living near sugar refineries, a tobacco plant, or a nursery of mushroom manure/cattle fodder plant. Five cross-sectional surveys were undertaken: two assessments of short-term (momentary) exposure to sugar refinery odours, and three assessments of long-term exposure (1971 through 1990) to either sugar refinery odours, tobacco plant odours, or manure/cattle fodder plant odours. Subjects responded to questionnaires discussing demographics, odour annoyance, and health via in-person interviews (short-term exposure) or mailed questionnaires (long-term exposure). An odour dispersion model using emission levels and meteorological conditions was used to estimate average odour exposure levels for each zip code in the research area; average odour concentrations ranged from 0 to 15 OU/m^3. Self-reported odour annoyance was also considered as an exposure variable. For all odour types, long-term odour concentrations correlated little with health complaints, while odour annoyance showed stronger associations with health complaints (r range: 0.23–0.68; $p<0.01$). In subjects who believe odours to be a threat to health, subjective health complaints increased with increasing odour concentration. For subjects not perceiving odour as a threat, health complaints showed no correlation with odour concentration. Additionally, both the high avoidance group (e.g., look for diversion, withdraw from situation) and the group low in comforting cognitions (e.g., stay calm and optimistic, assume problems will disappear) reported more general health complaints, and this occurred independently of odour concentration. Overall, the authors concluded that odour exposure does not directly cause reported health complaints; rather, annoyance is the intervening factor linking odour and health complaints.

In Finland, Aatamila et al. (2011) examined the impact of waste treatment odours on self-reported health symptoms in nearby residents. Five waste treatment facilities with large-scale composting plants were included in the study. Residents (1142 adults) living at various distances from a facility (3 zones: <1.5 km, 1.5 to <3km, and 3 to <5 km) were interviewed by telephone about their background, health symptoms in the previous year, and odour perception and annoyance. Odour exposure was estimated as residence distance to facility, self-reported frequency/intensity of odour perception, or self-reported odour annoyance. Elevated correlations were observed between odour perception and several health symptoms; the strongest associations were found with hoarseness/dry throat, headache, and diarrhea (OR range: 1.3–1.4). Odour annoyance showed the most consistent

relationship with symptoms; significant correlations were found with shortness of breath, eye irritation, hoarseness/dry throat, unusual tiredness, toothache, fever/shivering, joint pain and muscular pain (OR range: 1.4–2.0). Health symptoms did not correlate with zone of residence. The investigators concluded that high levels of odour annoyance exist in the proximity of large-scale waste treatment centres, and odour annoyance, rather than odour perception or residence distance to facility, appeared to be the most influential factor in self-reported health symptoms.

In Värnamo, Sweden, Claeson et al. (2013) assessed the interrelations between odours, perceived pollution, health risk perception, annoyance and health symptoms in 722 adults residing near a biofuel facility. Odour exposure was defined as 3 zones (low, medium, and high) based on emission data and postcode area. Subjects completed mailed questionnaires discussing demographics, odours, health, and risk perception. Exposure level did not directly correlate with health symptoms in the prior 3-month period; however, the investigators did observe an indirect relation between exposure level and health symptoms that was mediated by health risk perception ($p<0.01$). The authors concluded that perceptions of health risk are influential in predicting health symptoms in communities located near odorous sources.

In another Swedish study conducted in Stockholm, Engvall et al. (2001) assessed respiratory symptoms and building dampness or odour in multi-family dwellings. Subjects responded to mail-in questionnaires discussing respiratory symptoms and allergy, odour perception, building characteristics, and socio-demographics. Odour exposure was defined as self-reported perception of pungent, mouldy, musty, or stuffy odours. All types of odours showed significant relationships with cumulative incidence of asthma symptoms, current cough, and hay fever (OR range: 2.06–5.86). For subjects with hay fever without respiratory symptoms, the relationships were significant for pungent, musty, and stuffy odours, but not for mouldy odours (OR range: 1.86–2.10). Though a link was observed between odour perception and respiratory outcomes, the time course of these events was not determined. In other words, it was not established that exposure preceded the outcome.

Georgieff and Turnovska (1999) studied the effect of cellulose paper plant odours on the health status of nearby residents in Stamboliisky, Bulgaria. 374 subjects (>16 yrs) responded to questionnaires discussing odours, annoyance, health symptoms, and socio-demographic factors. Prevalence of odour perception and health outcomes was determined for the sample population in Stamboliisky; however, the results were not compared to any control population. A large portion of the subjects (89%) perceived an unpleasant odour near their home, and 19–54% of these subjects reported health symptoms (headache (27%), sleep disturbances (19%), nausea or vomiting (30%), and allergic reaction (54%)). 52% of subjects perceiving the odour reported that olfactory irritation led to decreased work capacity. This study is considered to be weak, as there was no control group, response rates were moderate (69%), and it was not clear if pollutant levels were below irritant thresholds.

One study was found investigating the health effects of odour exposure in China. Liu et al. (2007) assessed domestic renovation-related odour emissions and health symptoms in 198 subjects living in a house undergoing renovations in Tianjin, China. Subjects were interviewed in-person regarding

odours, health symptoms, and socio-demographics. Intensity of odour (weak, moderate, strong) as determined by the researcher was used as the exposure variable. Odour intensity showed a significant association with nausea (p=0.017) and unspecific discomforts (p=0.018). For example, subjects exposed to moderate or strong odours were more likely to report unspecific discomfort compared to those exposed to weak odours (OR: 4.05, 95% CI: 1.49–11.03). Odour was not associated with any other health symptoms (eye or nose irritation, dry throat, cough, rashes, fatigue, headache). Duration of odour exposure (i.e., average time spent at home) showed no association with symptoms. Results were adjusted for exposures to volatile organic carbons, but not other chemicals.

3.3 Odour Annoyance

Odour annoyance has been defined by Van Harreveld (2001) as "the complex of human reactions that occurs as a result of an immediate exposure to an ambient stressor (odour) that, once perceived, causes negative cognitive appraisal that requires a degree of coping". Annoyance is not a direct health effect of odour (i.e., an adverse effect causing detectable impairment of health (International Commission on Non-Ionizing Radiation Protection, 1998)), but rather an emotional response to a stimulus that may act as a mediator of health symptoms.

This section reviews the epidemiology studies evaluating the effect of odour exposure on annoyance; a summary of the studies is presented in Table 3-1. Most of the studies demonstrate an increase in frequency and/or intensity of odour annoyance with increasing odour exposure. Effects appear to be influenced by odour hedonic, with unpleasant odours inducing more annoyance than pleasant odours.

Table 3-1: Summary of epidemiology studies evaluating odour exposure and annoyance

Odour Source	Measure of Exposure[a]	Annoyance Response[b]	Reference
Canada			
Petroleum refinery (Ontario)	·Residence distance to source (3 zones) ·Odour frequency	·Significant gradients in frequent odour annoyance were found between the 3 zones of exposure for both the 1992 and 1997 surveys ($p<0.001$); ·After implementation of an odour reduction plan, percentage of subjects indicating they were bothered by the odour half the time to all of the time had decreased from 35% to 29%; ·Degree of annoyance was not associated with odour exposure	Luginaah et al, 2000; Taylor et al, 1997
Petrochemical area (Ontario)	·NO_2 concentration ·SO_2 concentration ·VOC concentrations	·Degree of annoyance greater in the higher exposure quartiles for all pollutants ($p<0.05$); ·Believing odours to have an adverse affect on health and a general dissatisfaction with the community also influenced odour annoyance	Atari et al, 2012, 2009
United States			
Pulp mills (California)	·Residence distance to source (3 zones) ·Odour frequency ·Methanethiol	·In the pilot study, significant gradients across the 3 zones of exposure were observed for degree and frequency of odour annoyance ($p<0.01$); ·In the follow-up study, degree of annoyance correlated with odour frequency and methanethiol levels, but not zone of exposure; ·Negative attitude towards the mill played a role in degree of annoyance	Deane et al, 1977; Jonsson et al, 1975
Sewage treatment plants (California)	·Reside near sewage treatment plant ·Odour perception ·H_2S concentration	· H_2S concentration, odour perception, and intensity of odour annoyance were higher in each area located near a plant, relative to its control area; ·When data from all areas were pooled, intensity of odour annoyance was higher in those living close to a sewage treatment plant ($p<0.001$) and those living in the area with the highest odour exposure ($p<0.001$)	Bruvold et al, 1983
Worldwide			
Odour-emitting facilities (Germany)	·Odour concentration	·Degree of odour annoyance was lowest in subjects living near a chocolate factory, moderate in subjects living near an insulation plant, and highest in those living near a brewery and a tar-oil refinery	Winneke and Kastka, 1987
Odour-emitting facilities (Germany)	·Odour frequency	·Degree of odour annoyance correlated with odour frequency (r range: 0.25–0.34; $p<0.001$)	Steinheider and Winneke, 1993
Odour-emitting facilities (Germany)	·Odour frequency ·Odour intensity ·Odour hedonicity	·Odour frequency correlated with percentage of seriously annoyed subjects (OR: 1.9, CI: 1.3–2.6; $p<0.001$); ·This association increased greatly with inclusion of odour hedonic in the model (OR: 17.6, CI: 6.7–46.5; $p<0.001$); ·Subjects living near the pleasant odours reported less odour annoyance than other subjects ($p<0.05$); ·Odour intensity was not associated with degree of annoyance	Sucker et al, 2008; Both et al, 2004;
Fertilizer plant (Germany)	·Residence distance to source (3 zones)	·Degree of annoyance increased significantly with increasing proximity to the fertilizer plant (residence distance explained ~61% of the variation in annoyance)	Steinheider, 1999; Steinheider et al, 1998
Pig rearing facility (Germany)	·Odour frequency	·Degree of annoyance increased significantly with frequency of odour perception (odour frequency explained ~17% of variation in annoyance)	
Odour-emitting facilities (Netherlands)	·Odour concentration	·Odour concentration correlated with the percent of annoyed or very annoyed subjects (r: 0.90); ·Exposure-annoyance relationships did not differ between sources	Miedema and Ham, 1988

[a] Measure of exposure: the factors that were used in each study to estimate individual or community exposure to odour. See Section 3-1 for a discussion of the various odour exposure assessment methods

[b] Annoyance response: the observed relationship between odour exposure and frequency of odour annoyance or degree of odour annoyance

Table 3-1: Summary of epidemiology studies evaluating odour exposure and annoyance (continued)

Odour Source	Measure of Exposure[a]	Annoyance Response[b]	Reference
Worldwide			
Odour-emitting facilities (Netherlands)	·Odour concentration ·Odour hedonicity	·The meta-analysis of 6 studies found log odour concentration to correlate with the percentage of highly annoyed subjects (*r*:0.889); ·The percentage of highly annoyed subjects was greater if the odour was unpleasant, and including an odour pleasantness score improved the accuracy of the model (*r*: 0.945)	Miedema et al, 2000
Odour-emitting facilities (Netherlands)	·Odour concentration	·Long-term concentration correlated with odour annoyance (product of annoyance intensity and frequency; *r* range: 0.24–0.36; $p<0.01$); ·Unpleasant odour caused more annoyance than pleasant odour, suggesting a role for odour hedonic in annoyance; ·Subjects perceiving odour as a health risk more likely to be annoyed; ·The authors suggested annoyance is a result of long term odour exposures	Cavalini et al, 1994; Cavalini 1991
Paper mill, Water treatment plant (Netherlands)	·Residence distance to source (2 zones)	·Degree of odour annoyance significantly higher in the inner zone relative to the outer zone ($p<0.001$)	van den Hazel and Waegemaekers, 1991
	·Odour frequency ·Odour concentration (3 zones)	·For rotten odour, annoyance correlated with odour exposure across the three zones, whether measured by odour frequency or odour concentration (*p*-values not given)	
Solid waste treatment facility (Italy)	·Residence distance to source (4 zones)	·The village nearest to the facility had a lower percentage of subjects who found the odour moderately to very irritating (~89% in the village nearest to source, compared to ~100% in the next 2 closest villages); ·The lower annoyance levels may have been related to the municipality receiving economic compensation for the presence of the facility	De Feo et al, 2013
Waste treatment centres with composting plant (Finland)	·Residence distance to source (3 zones)	·Proportion of subjects somewhat or very annoyed was higher in the inner zone (OR: 19, CI: 12–32) and middle zone (OR: 6.1, CI: 3.7–10), relative to the outer zone	Aatamila et al, 2010
	·Odour frequency	·Subjects perceiving odour at least weekly were more annoyed than subjects perceiving odour less than monthly (OR: 5, CI: 2.9–8.8)	
	·Odour intensity	·Annoyance was higher when intensity was very strong compared to mild/negligible (OR: 112, CI: 47–296)	
Petrochemical area (Sweden)	·Reside near petro-chemical area	·Proportion of annoyed/very annoyed was 20–27% in the exposed group and 2–4% in the control group; ·Subjects worried about health risk of air pollution more likely to be annoyed by odour	Axelsson et al, 2013
Biofuel facility (Sweden)	·3 zones of exposure (using emission data + dispersion models)	·Odour exposure level correlated with intensity of annoyance ($p<0.001$); ·Annoyance mediated by perceived pollution and perceived health risk	Claeson et al, 2013
Livestock facilities (Denmark)	·NH_3 concentration	·Prevalence of odour annoyance correlated with measured ($p<0.01$) and modeled ($p<0.05$) NH_3 concentration; ·Residential NH_3 levels were associated with moderate to extreme odour annoyance (OR=10.59, CI: 1.35–83.13)	Blanes-Vidal et al, 2012a,b
Landfills (Malaysia)	·Reside near landfill	·92% of respondents indicated they were bothered by odour (no control group)	Sakawi et al, 2011
Vegetable oil processing plant (Iran)	·Work near processing plant	·Odour annoyance was very high, with 41% selecting the highest level for degree of odour annoyance (no control group); ·Number of years at current workplace correlated with annoyance	Monazzam et al, 2012
Vegetable oil processing plant (Iran)	·Reside near processing plant	·Odour annoyance was very high, with 72% selecting the highest level for degree of odour annoyance (no control group)	Avishan et al, 2012

[a] Measure of exposure: the factors that were used in each study to estimate individual or community exposure to odour. See Section 3-1 for a discussion of the various odour exposure assessment methods

[b] Annoyance response: the observed relationship between odour exposure and frequency of odour annoyance or degree of odour annoyance

Canada

In Canada, the effect of odours on odour annoyance has been studied in residents of two areas – Oakville, ON (petroleum refinery) and Sarnia, ON (petrochemical plants). In Oakville, ON, Taylor et al. (1997) assessed the community health impacts of a Petro Canada petroleum refinery on local residents. The relationship between odour exposure and odour annoyance was studied in a cross-sectional baseline survey; 391 adults underwent telephone interviews discussing background information, health symptoms, illnesses, odour perception and annoyance, and attitudes regarding the refinery. Exposure to odours was determined by residence distance to the refinery (three zones) or self-reported frequency of odour perception. Odour annoyance was most common in the two zones closest to the refinery, and a significant gradient in frequent odour annoyance was found across the three zones (Zone 1 (closest to refinery): 51%, Zone 2: 27%, Zone 3: 10%; $p<0.0001$). Of subjects who perceived odours at least once per month (215 subjects, 151 of which lived in Zone 1), 52% were bothered by the odours all the time to half the time.

In a follow-up analysis of the same area, Luginaah et al. (2000) studied community changes in odour perception and annoyance before and after the implementation of an odour reduction plan. The initial survey of 391 adults was conducted in 1992 (Taylor et al., 1997), and the follow-up survey of 427 adults was conducted in 1997. Exposure determination and telephone interviews were as described above. In both surveys, significant zonal gradients were found for frequency of odour perception and odour annoyance ($p<0.00001$). Over the five-year period, a significant decrease in frequency of odour perception was observed for Zone 1 ($p<0.0016$), while Zones 2 or 3 showed non-significant decreases. Of subjects who perceived odours at least once per month, the percentage of subjects that were frequently annoyed by odours decreased (non-significantly) over the five years for all zones (Zone 1: 51–47%, Zone 2: 27–17%, Zone 3: 10–8%). The degree of annoyance ('a great deal' to 'not at all') did not differ between zones, and did not change over the five years.

Atari et al. (2012, 2009) evaluated the correlation between petrochemical emissions (NO_2, SO_2, and VOCs (measured as benzene, toluene, ethylbenzene, *o*-xylene and (*m*+*p*)-xylene (BTEX)) and odour annoyance in Sarnia, ON, with the primary goal being to determine if odour annoyance could be a suitable proxy measure for ambient pollution exposures. Subjects underwent telephone interviews discussing attitudes toward the local area, perceptions of air pollution, odour annoyance, occupational exposure, health symptoms, health conditions, coping, and socio-demographics. Individual exposures (at the postal code level) were calculated using land use regression models and pollutant concentrations measured at 39 sites across Sarnia. Exposure levels were categorized into quartiles for the analyses. Odour annoyance score (degree of annoyance) was found to be greater in the higher exposure quartiles, relative to the lowest quartiles, for all pollutants. For NO_2 and SO_2, adjusted odds ratios for the highest quartiles were 3.32 ($p<0.01$) and 3.92 ($p<0.01$), respectively. Odds ratios for the highest quartiles for benzene, toluene, and BTEX were 4.77 ($p<0.05$), 10.99 ($p<0.05$), and 10.93 ($p<0.05$), respectively. The authors also found that negative perceptions about the odours and the industry, such as believing odours to have an adverse affect on health or a

general dissatisfaction with the community, significantly impacted reported annoyance. They concluded that these factors are key modifiers of the relationship between exposure and annoyance.

United States

In Eureka, California, the relationship between odours and odour annoyance was examined in subjects living near two pulp mills (Deane and Sanders, 1977; Deane et al., 1977; Jonsson et al., 1975). In two surveys conducted in 1969 and 1971, 298 subjects underwent interviews discussing presence of odours, attitudes, annoyance reactions, health symptoms, and socio-economic data. Estimation of odour exposure was based on residence distance to the pulp mills (3 zones: 1–2 miles, 2–3 miles, and >4 miles from facility). Measurements of odour frequency by trained panelists as well as measurements of methanethiol levels confirmed that odour exposure was highest in Zone 1 and lowest in Zone 3 in 1969. However, the same pattern was not seen in 1971, as Zone 3 had odour concentrations similar to Zone 2. In the pilot study, investigators observed significant gradients across the three zones in odour perception ($p<0.01$), as well as in the degree and frequency of odour annoyance ($p<0.01$); for example, the percentage of subjects moderately to very annoyed by the odours was 50%, 31%, and 18% in Zones 1–3, respectively ($p<0.01$). The differences in annoyance across areas were not explained by differences in socio-economic factors; however, negative attitudes towards the pulp mill appeared to play a role in degree of annoyance. In the follow-up study, zone 1 had the greatest number of subjects who were annoyed by odours; however, Zones 2 and 3 no longer showed a distinct difference in odour annoyance. Of subjects who noticed odours, the percentage that were very bothered decreased in Zones 1 and 2, and increased in Zone 3. These differences matched the changes in odour exposure levels (odour frequency by trained panelists, methanethiol concentrations) seen across the two surveys.

In Pacifica and Novato, California, Bruvold et al. (1983) studied the association between odour perception and annoyance in 104 subjects living near sewage treatment plants and 102 subjects in control areas. Subjects were interviewed in-person regarding odour perception and annoyance, complaints and activity changes, and socio-economic factors. Exposure was defined as residence distance to the treatment plant or self-reported perception of odour. Levels of H_2S were also measured at multiple sites in each community; concentrations were highest in the exposed Pacifica area (1.7–5.7 ppb) and lowest in the control Novato area (<0.4 ppb). H_2S levels, odour perception, and degree of odour annoyance were found to be higher in each exposed community relative to its control community. H_2S levels, odour perception, and intensity of odour annoyance were higher in each exposed community relative to its control community. Degree of odour annoyance was significantly higher in those living close to a sewage treatment plant ($p<0.001$) and those living in Pacifica ($p<0.001$); associations were not significantly modified by socio-economic factors.

Worldwide

Several studies conducted in Germany have looked at the relationship between odours and odour annoyance. Odour sources have included livestock operations, composting sites, and several types of industrial plants, ranging from fertilizer plants to sugar refineries. In an early cross-sectional study, Winneke and Kastka (1987) examined odour annoyance in subjects residing near four industrial odour sources (chocolate factory, insulation plant, tar-oil refinery, brewery) in three German cities. Subjects were interviewed in-person regarding odour annoyance, odour-related health complaints, and socio-demographic characteristics. Average odour concentrations at varying distances from the sources were determined using trained panelists, and ranged from two to 25 OU/m^3 for the four sources. Degree of odour annoyance was highest in subjects living near the brewery and the tar-oil refinery, while those living near the insulation plant showed moderate annoyance. Annoyance was found to be much lower in subjects living near the chocolate factory, despite having similar odour concentrations as the other sources. These differences were not explained by variations in socio-economic factors, attitudes towards industry, or self-reported health. Odour annoyance as a function of distance to the plant was difficult to interpret and no clear pattern emerged. The authors concluded that different odour sources are related to varying levels of odour annoyance, and suggested that exposure-annoyance correlations be considered for homogeneous classes of sources. Possible daily or seasonal patterns in odour emissions were not accounted for, and response rates were not given in this study.

Steinheider and Winneke (1993) completed a cross-sectional study of five different odour sources (cast-iron factory, sugar refinery, iron/steel plant, sulphur chemical plant, oil refineries) in four German cities. A sample of 1539 adults underwent in-person interviews regarding odour annoyance, health symptoms, coping strategies, and socio-demographic factors. Response rates varied widely across the cities (31–88%).Odour frequency (odour hours/year) estimated at various points in each area by trained panelists was used as the exposure variable. Data for two odour sources (cast-iron factory, sugar refinery) were excluded due to lack of suitable exposure measurements, leaving the final sample size at 1000 adults from three cities. Odour frequency was found to be significantly associated with degree of odour annoyance in each city (r range: 0.25–0.34; $p<0.001$). Annoyance appeared to be modified by age, perceived health status, and coping strategy, but these factors did not significantly influence the odour frequency-odour annoyance association.

Similarly, Sucker et al. (2008) and Both et al. (2004) compared odour exposure and degree of odour annoyance in 1408 adult subjects living near industrial odour sources in Germany (two pleasant: sweets production, rusk bakery; two neutral: textile production, seed oil production; two unpleasant: fat refinery, cast-iron factory). Subjects underwent interviews regarding quality of life, odour perception, odour annoyance, health symptoms, and socio-demographic factors. Response rates were quite low and varied between cities (18–43%). Odour exposure was estimated using frequency of odour perception, intensity of odour, and hedonic tone of odour, as measured at multiple sites near each source by a group of trained panelists. A significant dose-response correlation was found between frequency of odour exposure and percentage of seriously annoyed subjects (OR: 1.9, CI:

1.3–2.6; $p<0.001$); this association was strongly influenced by inclusion of odour hedonic in the model (OR: 17.6, CI: 6.7–46.5; $p<0.001$). Subjects living near the pleasant odours (sweets, rusk) reported less odour annoyance compared to the other subjects ($p<0.05$). Odour intensity did not appear to have an effect on degree of annoyance. The authors concluded that pleasant odours have a lower annoyance potential than unpleasant or neutral odours.

Steinheider (1999) and Steinheider et al. (1998) examined the effect of odour exposures on odour annoyance in residents living near a fertilizer plant (Nettetel, Germany) or a pig rearing facility (Nörvenich, Germany). Exposure was measured as residence distance to the fertilizer plant in Nettetel (close, medium or remote distance), and odour frequency (odour hours/year as determined by trained panelists) in Nörvenich. For both cities, adult subjects (Nettetel: 250; Nörvenich: 322) were interviewed in-person regarding odour annoyance, somatic symptoms, general health, and socio-demographics. In Nettetel, degree of annoyance increased significantly with increasing proximity to the odour source (distance to source explained ~61% of the variation in annoyance). In Nörvenich, degree of annoyance increased significantly with odour frequency (odour frequency explained ~17% of variation in annoyance). Response rates were low (27–56%) and it is not known if pollutant levels were below irritant thresholds.

The Netherlands have also been the focus of several odour annoyance studies. An early study by Miedema and Ham (1988) evaluated odour annoyance in subjects living near three odour-emitting sources (oil extraction factory, pig farm, and wire coating). A total of 1253 adults underwent interviews discussing frequency of odour perception, odour annoyance, activity changes, and health issues. Average odour concentration was determined using odour panelists, factory emission data, and an odour dispersion model; the concentration ranged from 0.6 to 106 OU/m^3. Log of the one-hour average odour concentration was significantly associated with the percent of subjects who were annoyed or very annoyed (r: 0.90, with exclusion of the very low exposure values). Exposure-annoyance relationships did not differ between the three sources.

Miedema et al. (2000) conducted a meta-analysis study of odour annoyance using 6 previously-published Netherlands studies (five studies published in Dutch only; other study: Miedema et al. (1988)). Odour sources were 11 odour-emitting factories in the Netherlands (chemical, oil extraction, rendering plant, pig farm, sugar blending, grass drying, potato chips, wire coating, pastry, cacao, and tobacco). A total of 6276 subjects from the six studies (98 to 984 subjects per factory) were interviewed by mail, by telephone, or in person. Odour concentrations were estimated in the same manner as discussed above, and the one-hour averages ranged between ~0.15 and 100 OU/m^3. Odour hedonic for all sources was determined not in the original studies, but simultaneously at a later time point by a group of trained panelists. Using data from all studies combined, log odour concentration (one-hour average) correlated with the percentage of highly annoyed persons as a quadratic function (r: 0.889). The percentage of highly annoyed subjects was greater if the odour was unpleasant, and including an odour pleasantness score improved the accuracy of the model (r: 0.945). The authors concluded that odour hedonic plays an important role in odour annoyance, or alternatively, that factors confounded with odour hedonic are partly

responsible for the differences in annoyance. Response rates were low and varied widely across the studies (14–47%).

Cavalini (1994) and Cavalini et al. (1991) studied annoyance in 2413 subjects living near sugar refineries, a tobacco plant, or a nursery of mushroom manure/cattle fodder plant in two cities in the Netherlands. Five cross-sectional surveys were undertaken: two assessments of short-term (momentary) exposure to sugar refinery odours, and three assessments of long-term exposure (1971 through 1990) to either sugar refinery odours, tobacco plant odours, or manure/cattle fodder plant odours. Subjects responded to questionnaires discussing demographics, odour annoyance, and health via in-person interviews (short-term exposure) or mailed questionnaires (long-term exposure). An odour dispersion model using emission levels and meteorological conditions was used to estimate average odour exposure levels for each zip code in the research area; average odour concentrations ranged from 0 to 15 OU/m^3. For all odour types, annoyance (taken as a product of annoyance intensity and frequency) correlated with long-term odour concentrations (r range: 0.24–0.36; $p<0.01$). Despite tobacco and manure odorant concentrations (~0.2 OU/m^3) being lower than the sugar refinery odours (~3 OU/m^3), they caused the same or more annoyance than the sugar odours; this suggests that odour hedonic may play a role in annoyance. Age typically showed a negative correlation with odour annoyance (r range: -0.20 – -0.22; $p<0.001$).

The relationship between odour concentration and annoyance was stronger in subjects that perceived the odour as a threat to health. General coping strategies also appeared to modify the odour concentration-annoyance relationship. Subjects coping in a problem-oriented way (look for ways to solve the problem) reported annoyance more often than subjects coping in an emotion-oriented manner (regulating emotions caused by the problem). In the studies of short-term exposures to sugar odours, the relationship between odour and annoyance was similar or weaker (depending on the year of assessment) than the assessments of long-term exposure. Perceiving odour as a threat to health was the strongest predictor of annoyance in subjects of the short-term studies. The authors suggested that annoyance may be a phenomenon resulting from long term exposures.

In another Netherlands study, the relationship between odours and annoyance was assessed in a small town located near a paper mill and water treatment station (van den Hazel and Waegemaekers, 1991-1992). For two 6-week periods, 142 subjects kept diaries tracking odour perception and odour annoyance. Very little detail was given regarding the subjects (demographics, recruitment methods, participation rates, instructions for keeping diaries, etc). Exposure was defined by residence distance to paper mill (inner zone: <1.2 km; outer zone: >1.2 km), odour frequency (in three zones: 300m, 900m, and 1800m from odour source), and odour concentration calculated using emission data and dispersion modeling (also in three zones). Degree of odour annoyance was found to be significantly higher in the inner zone relative to the outer zone ($p<0.001$). For rotten odour (odour from the water treatment station), annoyance correlated with odour exposure across the three zones, whether measured by odour frequency or odour concentration (p-values not given). Wood odour did not

follow the same pattern; the authors stated that a masking of the wood odour by the rotten odour may have resulted in the lack of association.

In Southern Italy, De Feo et al. (2013) compared the changes in odour perception, annoyance, and attitudes toward industry before and after the closure of a solid waste facility. Cross-sectional analyses of residents of 4 villages were conducted in 2003 and 2009. Subjects underwent in-person interviews discussing socio-economic and demographic factors, opinions on environmental pollution, odour annoyance, concerns and attitudes towards the facility, and knowledge about the facility. In the 2003 survey, the village nearest to the facility showed an unexpectedly low awareness of local pollution (68% indicated there was pollution in their local environment, compared to 85-100% in the other 3 villages) and a lower percentage of subjects who found the odour moderately to very irritating (~89% in village 1 compared to 100% in villages 2 and 3). The nearest village also showed the lowest concerns about odour-associated health issues. The authors postulated that the lower concerns about local pollution and odour-related health issues, and the lower annoyance levels, in the nearest village were related to the municipality receiving economic compensation for the presence of the facility. The study also found that between 2003 and 2009, the percentage of subjects who thought there were odour issues in the area, who were very annoyed by odour, and who thought odour intensity had increased over the previous 2 years decreased for all villages. The facility closure had a greater impact on the closer villages than the further villages. The results are limited by the unsystematic method of sampling used in the study.

In a Finnish cross-sectional analysis, Aatamila et al. (2010) examined the impact of waste treatment odours on annoyance in nearby residents. Five waste treatment facilities with large-scale composting plants were included in the study. Residents living at various distances from a facility (1142 adults across three zones: <1.5 km, 1.5 to <3km, and 3 to <5 km) were interviewed by telephone about their background, health symptoms in the previous year, and odour perception and annoyance. Odour exposure was estimated as residence distance to facility or self-reported frequency/intensity of odour perception. Odour annoyance (proportion of subjects somewhat annoyed or very annoyed) was found to be higher in the innermost zone (OR: 19, CI: 12–32) and intermediate zone (OR: 6.1, CI: 3.7–10), relative to the outermost zone. Annoyance was also higher when odour intensity was very strong compared to mild/negligible (OR: 112, CI: 47–296, after adjustment for odour frequency). With regards to odour frequency; subjects perceiving odour at least weekly were more annoyed than subjects perceiving odour less than monthly (OR: 5, CI: 2.9–8.8, after adjustment for odour intensity). The investigators concluded that high levels of odour annoyance exist in the proximity of large-scale waste treatment centres; annoyance appeared to be more influenced by odour intensity than odour frequency.

In Stenungsund, Sweden, Axelsson et al. (2013) studied the occurrence of odour-induced annoyance, as well as worry about health effects, three times over a 14-year period in a community located near petrochemical industries. Cross-sectional analyses of subjects residing near the petrochemical area and in a control area were conducted in 1992, 1998, and 2006 (total of 4201 respondents). Subjects completed mail-in questionnaires discussing socio-demographics, odour-related annoyance (not

annoyed, annoyed, very annoyed), and worry about health effects from industrial air pollution. For the control area, the proportion of subjects who were annoyed/very annoyed by odour was low for all 3 surveys (2–4%). In the exposed areas, the proportion of annoyed/very annoyed was highest in 1992 (27%) and lower in 1998 (20%) and 2006 (20%). The authors indicated that the reduction in odour annoyance between 1992 and 1998 was likely a result of emission reduction measures that were undertaken in the mid-1990s. The proportion of subjects who were worried about health effects from industrial air pollution did not differ over the three surveys in the exposed group (48–50%). Subjects who were annoyed by vehicle exhaust or industrial noise or those who worried about health effects from air pollution were more likely to be annoyed by industrial odour; this indicates a possible vulnerable group for various environmental stressors. Numbers of years living in the home did not impact the results, suggesting that residents do not become accustomed to the odours over time.

Claeson et al. (2013) studied the interrelations between odours, perceived pollution, health risk perception, annoyance and health symptoms in 722 adults residing near a biofuel facility in Värnamo, Sweden. Odour exposure was defined as 3 zones (low, medium, and high) based on emission data and postcode area. Subjects completed mailed questionnaires discussing demographics, odours, health, and risk perception. Exposure level significantly correlated with intensity of odour annoyance ($p<0.001$), and this association was found to be mediated by perceived pollution ($p<0.001$) and perceived health risk ($p<0.001$). The authors concluded that perceptions of pollution and health risk are influential in predicting odour-induced annoyance.

A recent cross-sectional study conducted in Denmark aimed to determine if a measurable compound (ammonia (NH_3)) is related to odour annoyance in subjects living near livestock facilities (Blanes-Vidal et al., 2012a,b). NH_3 levels were estimated at central sites and at residences in 6 regions using emission data and dispersion models; additionally, NH_3 levels were measured at central sites in 5 of the 6 regions. Information on living conditions, demographics, and odour annoyance was collected from 180 residents using mailed questionnaires. Blanes-Vidal et al. (2012a) observed a correlation between prevalence of odour annoyance and measured NH_3 concentrations ($p<0.01$) and modeled NH_3 concentrations ($p<0.05$). Similarly, Blanes-Vidal et al. (2012b) demonstrated a significant association between estimated residential NH_3 exposure and moderate to extreme odour annoyance (adjusted OR=10.59, CI: 1.35–83.13, for each unit increase in Log_eNH_3 exposure). Overall, the authors concluded that NH_3 levels could serve as a marker for prevalence of odour annoyance in non-urban residential communities. It is important to note that exposure data were collected in 2008 and 2009, while questionnaires were administered in 2010 and 2011. Questionnaire response rates were low (38%).

In Malaysia, Sakawi et al. (2011) conducted a preliminary assessment of the impacts of landfill odours on nearby residents. One-hundred ninety subjects (16-75 yrs) living within 2 km of a landfill site were interviewed in person regarding socio-demographics, odour perception, odour annoyance, health, and quality of life. Odour was perceived by ~99% of respondents, with 74% classifying the odour as very strong. Most respondents indicated they were bothered by the odour (92%). Similar

cross-sectional studies conducted in Tehran, Iran assessed the impact of odours from a vegetable oil processing plant in nearby residential and non-industrial work areas (Avishan et al., 2012; Monazzam et al., 2012). Two-hundred eighty two residents (18-79 yrs) and 174 male non-industrial workers (17-75 yrs) were interviewed in person regarding socio-demographics, health issues, odour perception, odour annoyance, and activity/mood changes. For the residents, 95% of respondents perceived odour, with 83% classifying the odour as strong to unbearably strong. Odour annoyance was very high, with 72% selecting the highest level for degree of odour annoyance. For the non-industrial workers, 98% of respondents perceived odour, with 50% classifying the odour intensity as strong to unbearably strong and 78% classifying the hedonic tone as unpleasant to offensive. Odour annoyance was very high, with 41% selecting the highest level for degree of odour annoyance. Number of years at current workplace correlated with odour annoyance. All of the above studies were exploratory analyses of the impacts of odours, and did not compare the findings with a control group.

3.4 Mood, Coping, and Activity Changes

Canada

In Oakville, ON, two qualitative studies were found that assessed the impacts of a petroleum refinery on the everyday life residents. In the first study, a sample of 40 adults were interviewed in-person regarding odour perception and annoyance, coping mechanisms, health concerns, and attitudes towards the refinery (Taylor et al., 1997). The authors discussed three typical profiles for residents living near the refinery: (1) those who are frequently annoyed by odours and worried about possible health effects; (2) those who notice odours but are not very annoyed by them, with some concern about possible health effects; and (3) those who rarely notice odors and feel that the benefits of the refinery outweigh any concerns. Three hypotheses for the link between odour perception/annoyance and symptom reporting are supported: psychosomatic reaction to stress, reporting bias, and odour-mediated effects. The authors concluded that social and community factors play an important role in conditioning how residents perceive and respond to the refinery.

In the follow-up study, in-depth interviews were completed for 29 adults to evaluate coping strategies and community perceptions about the refinery before and after the implementation of an odour reduction plan (Luginaah et al., 2002b). While odour levels had been reduced over the five years, many residents perceived no change in odour and still expressed concern about the refinery, employing both action-focused and emotion-focused coping strategies in response to odours. The authors concluded that refinery intervention may have to move beyond the technological odour reduction measures to address the psychological and social concerns of residents.

United States

In North Carolina and Iowa, the effect of livestock odours on the moods and activities of nearby residents has been evaluated in a number of studies. Horton et al. (2009) and Wing et al. (2008)

quantified odour exposures and evaluated longitudinal relationships among malodour, airborne emissions, stress, negative mood, and changes to daily activities in 101 adults residing near 16 North Carolina hog operations. Twice-daily for two weeks, subjects rated the intensity of any present odours and answered mood and activity questionnaires. Levels of H_2S (concentration range: 0.01–90 ppb) and semi-volatile PM_{10} (concentration range: ~0–9.2 $\mu g/m^3$) were also measured at a central location in each neighborhood. Odours were found to bring about changes in the daily activities of subjects, including closing windows, avoiding sitting outside, cancelling plans to barbecue, not going for outdoor walks, not doing lawn work, and not washing the car. Overall, there was a 62% increase in the odds of activity change per one-unit increase in reported odour (on a 0–8 scale). The odds of reporting stress for a one-unit increase in odour was 1.81 (95% CI: 1.63–2.00), and for a four-unit increase in odour was 10.6 (CI not shown). Unit increases in odour were also associated with feeling nervous, gloomy, angry, and an inability to concentrate (OR range: 1.31–1.60). The investigators found that coping style, but not age or odour sensitivity, modified the association between odour and stress. H_2S and semi-volatile PM_{10} also showed associations with stress/annoyance and nervous/anxious outcomes (OR range: 1.10–1.18).

In earlier qualitative cross-sectional studies, the same research group explored perceptions of odour, emotional health, quality of life, and changes to daily activities in adults living near swine operations in North Carolina and Iowa (Tajik et al., 2008; Wing and Wolf, 2000; Thu et al., 1997). In the two earlier studies, results from odour-exposed adults (North Carolina: 105 adults; Iowa: 18 adults) were compared to control subjects (North Carolina: 50 adults; Iowa: 18 adults). Wing and Wolf (2000) found that subjects living near a North Carolina hog operation reported significantly lower quality of life, as measured by 'can't open windows' and 'can't go outside', compared to control subjects or subjects living near a cattle operation. For example, the percentage of subjects reporting they 'can't open windows' often was 14%, 8%, and 57% for the control, cattle, and hog groups, respectively. Thu et al. (1997) found no significant differences in reports of depression or anxiety in subjects residing near an Iowa swine facility compared to control subjects. In the third study, Tajik et al. (2008) assessed the impact of odour on daily activities in 49 adults living near North Carolina hog operations; no control group was used in the study. Subjects reported that hog odours limited activities such as cookouts, barbequing, family reunions, socializing with neighbors, gardening, working outside, playing, drying laundry outside, opening doors and windows, use of well water, and growing vegetables. Odour levels were not measured in any of the above studies.

Schiffman et al. (1995) compared the moods of 44 residents living near hog operations in North Carolina to 44 subjects living in control areas. Profile of Mood States (POMS) questionnaires were used to assess the moods of subjects in both groups; exposed subjects completed the questionnaire four times (when odours were present) while control subjects completed the questionnaire twice in two days. For every mood factor (e.g., tension, depression, anger, vigor, fatigue, and confusion) as well as the total mood disturbance score, subjects living near hog operations had significantly worse scores than the control group ($p<0.0001$). The authors concluded that odours from swine operations

have a negative impact on the moods of nearby residents. Odour levels were not measured in the study.

Also in North Carolina, Heaney et al. (2011) investigated the effect of landfill odours on the health and quality of life of nearby residents. Twice daily for 2 weeks, 23 adult subjects sat outdoors for 5 minutes and took note of odour intensity, mood states, and health symptoms. Notes on odours and daily activities for the previous 12-hour period were also recorded. Exposure was defined as subjects' perception of odour (yes/no), rating of odour intensity (none to very strong), or community H_2S levels. For the 12-hour periods prior to surveying, significant associations were observed between presence of odour and alteration of daily activities (OR: 9.0, CI: 3.5–23.5). Rating of odour intensity was associated with reports of doing things differently or with difficulty (OR: 3.3, CI: 1.9–5.6) and deciding not to do things because of landfill odour (OR: 2.9, CI: 1.7–4.7). For the 5-minute outdoor periods, perception of odour correlated with having a negative mood state (e.g., stressed, angry, gloomy) (OR: 5.2, CI: 2.8–9.6). Overall, the authors concluded that odours from a landfill negatively impact the health and quality of life of nearby residents. This study is limited by the small sample size and the absence of odour for the majority of the sampling periods.

Lowman et al. (2013) conducted a qualitative analysis aimed at understanding the health and quality of life in residents living near sludge application sites in North Carolina, South Carolina, and Virginia. Thirty-four subjects underwent open-ended in-person interviews discussing demographics, community history, common activities, experiences with sludge application near their home, and coping mechanisms or actions taken. From the interviews, the investigators identified common themes outlining the impact of sludge application on health responses and quality of life in these residents. Most respondents (30/34) described offensive odours related to sludge application; approximately half of the respondents (18/34) reported that sludge application led to unsettling emotions (anger, frustration, misery, fear, worry, anxiety, insecurity and helplessness). Respondents most commonly expressed anger related to a lack of information about the sludge application, a lack of concern by regulators and officials, and health impacts. Most respondents (26/34) indicated that sludge odour and other related nuisances interfered with their enjoyment of home, property and the outdoors. The authors concluded that residents from 3 different states demonstrated similar health and environmental concerns regarding sewage sludge application, and further attention from scientists and public health officials is warranted. It is important to note that subjects were not a random sample of the population and an exposure assessment was not performed.

In Pacifica and Novato, California, Bruvold et al. (1983) studied the association between odour perception and annoyance/activity changes in 104 subjects living near sewage treatment plants compared to 102 subjects in control areas. Subjects were interviewed in-person regarding odour perception and annoyance, complaints and activity changes, and socio-economic factors. Exposure was defined as residence distance to treatment plant or self-reported perception of odour. Levels of H_2S were also measured at multiple sites in each community; concentrations were highest in the exposed Pacifica area (1.7–5.7 ppb) and lowest in the control Novato area (<0.4 ppb). Subjects in the 2 exposed communities reported the highest number of odour-induced complaints. For

example, subjects reported that odours had an effect on children playing, having guests over, working outdoors, being forced indoors, temporarily leaving the neighborhood, considering moving, and having reduced property values. The number of complaints matched well with the number of subjects perceiving odours in each area.

Worldwide

Studies conducted in Europe have also looked at the impact of odours on mood and changes in activities. In rural Germany, Radon et al. (2004) studied odours and health in 3112 subjects living near livestock operations. Subjects responded to questionnaires discussing physical and emotional health, odours, and socio-demographics via mail. Self-reported intensity of odour annoyance was used as the exposure variable. Emotional health scores (based on a survey of self-reported depression, anxiety, feeling calm/peaceful, energy levels, or feeling downhearted) showed a significant inverse relationship with odour annoyance ($p<0.05$). The investigators concluded that subjects living near feeding operations may have a decreased quality of life, and suggested that this could be improved by better communication about health risks.

Miedema and Ham (1988) examined annoyance and odour-induced closing of windows in subjects living near three odour-emitting sources (oil extraction factory, pig farm, and wire coating) in the Netherlands. A total of 1253 adults underwent interviews discussing frequency of odour perception, odour annoyance, activity changes, and health issues. Average odour concentration was determined using odour panelists, factory emission data, and an odour dispersion model; the concentration ranged between 0.6 and 106 OU/m^3. Log of the one-hour average odour concentration correlated with closing of windows. No association was found between odour exposure and frequency of reporting odour-induced sleeping problems.

Georgieff and Turnovska (1999) studied the effect of cellulose paper plant odours on the emotional health of nearby residents in Stamboliisky, Bulgaria. 374 subjects (>16 yrs) responded to questionnaires discussing odours, annoyance, health symptoms, and socio-demographic factors. Prevalence of odour perception and emotional health outcomes was determined for the sample population in Stamboliisky; however, the results were not compared to any control population. A large portion of the subjects (89%) perceived an unpleasant odour near their home, and 90% of these subjects reported psycho-emotional symptoms (irritation, nervousness, depression). This study is considered to be weak as there was no control group, response rates were moderate (69%), and it was not clear if pollutant levels were below irritant thresholds.

In Malaysia, Sakawi et al. (2011) conducted a preliminary assessment of the impacts of landfill odours on nearby residents. One-hundred ninety subjects (16-75 yrs) living within 2 km of a landfill site were interviewed in person regarding socio-demographics, odour perception, odour annoyance, health, and quality of life. Odour was perceived by ~99% of respondents, with 74% classifying the odour as very strong. Most respondents felt the odour impacted their quality of life (84%) and/or felt the odour contributed to a health effect (81%). Thirteen per cent felt the odour was related to

corrosion of household utensils and equipment. Similar cross-sectional studies conducted in Tehran, Iran assessed the impact of odours from a vegetable oil processing plant in nearby residential and non-industrial work areas (Avishan et al., 2012; Monazzam et al., 2012). Two-hundred eighty two residents (18-79 yrs) and 174 male non-industrial workers (17-75 yrs) were interviewed in person regarding socio-demographics, health issues, odour perception, odour annoyance, and activity/mood changes. For the residents, 85% of respondents felt the odour often or always impacted their daily life and emotion. For the non-industrial workers, the odour negatively impacted their activity and emotion sometimes (31%), often (23%), or always (10%). The negative impact of odour on activity and emotion correlated with daily hours spent at work ($p<0.001$) and number of years at current workplace ($p<0.001$). All of the above studies were exploratory analyses of the impacts of odours, and did not compare the findings with a control group.

3.5 Summary

3.5.1 Health Symptoms and Physiological Responses

Residents of communities located near odour emitting facilities have been found to report a higher number of health symptoms compared to residents of control communities. Reported outcomes included respiratory symptoms, nausea, congestion, eye irritation, headache, dizziness, sleep problems, and diarrhea. These symptoms have been observed in response to odours from a range of sources including petroleum refineries, livestock operations, hazardous waste sites, municipal landfills, and industrial plants.

The method of estimating exposure to odours is an important factor of studies comparing odour and symptoms. Self-reported frequency of odour perception (a subjective measure) has been the exposure measure that most often demonstrated significant correlations with symptoms (Sucker et al., 2009, 2008; Luginaah et al., 2002a, 2000; Ames and Stratton, 1991; Shusterman et al., 1991). Contrarily, zone of residence or residence distance to the odour source (objective measures) have not typically been significant predictors of symptom reporting (Claeson et al., 2013; Aatamila et al., 2011; Luginaah et al., 2002a, 2000; Taylor et al., 1997; Thu et al., 1997; Ames and Stratton, 1991; Deane and Sanders, 1977). The use of subjective measures of exposure is a potential source of reporting bias and results should thus be interpreted with caution.

The effect of odour hedonic on symptom reporting has been considered in several German studies (Sucker et al., 2009, 2008; Steinheider, 1999; Steinheider et al., 1998). In assessments of the health effects induced by odours of varying pleasantness, unpleasant odours, such as those from a pig facility, a fat refinery, or a cast-iron factory, induced more symptom reporting than exposure to moderate or pleasant odours. These studies concluded that the relationship between odour exposure and health symptoms is greatly influenced by odour hedonic, perhaps more so than odour intensity.

One of the most consistent findings among the epidemiology studies is that symptom reporting is mediated by odour annoyance. Many studies have found odour annoyance to be a stronger predictor

of symptom reporting than odour perception, odour concentration, and residence distance to facility, or alternatively, that adjustment for odour annoyance in the statistical modeling significantly attenuates the association between odour exposure and symptoms (Aatamila et al., 2011; Herr et al., 2009, 2003a,b; Sucker et al., 2009, 2008; Radon et al., 2007; Luginaah et al., 2002a, 2000; Steinheider, 1999; Steinheider et al., 1998; Taylor et al., 1997). Environmental worry or perceiving odour as a threat to health also appears to play an important role in symptom reporting (Claeson et al., 2013; Cavalini, 1994; Cavalini et al., 1991; Lipscomb et al., 1991; Shusterman et al., 1991). The influence of personal attitudes in symptom reporting is further supported by Luginaah et al. (2002a, 2000) in their studies of Oakville, ON residents before and after implementation of an odour reduction plan. Following odour reduction measures by the nearby petroleum refinery, no significant changes were found in symptom prevalence rates or to the association between odour perception/annoyance and symptom reporting. Thus, individual and community attitudes towards an odour or industry appear to be an important factor in odour-induced health symptoms.

Only a few studies were found examining odours and physiological responses (lung function and blood pressure). Regarding lung function, decrements in forced expiratory volume correlated with the number of confined animal feeding operations near the home; however, no associations were found when self-reported odour annoyance or central odour levels were used as the exposure metric (Schinasi et al., 2011; Radon et al., 2007). With regards to blood pressure, one study demonstrated an association between self-reported odour intensity and diastolic blood pressure; this relationship may have been mediated by stress (Wing et al., 2013).

Schiffman and Williams (2005) and Schiffman et al. (2000) discuss three possible models that may explain the association between exposure to odours and health effects. First, symptoms occur as a result of the toxicological effects of the odorant; in other words, odorant levels are above irritant thresholds. Second, symptoms occur at odorant levels that are not irritating (odour detection threshold is below irritant threshold). The underlying mechanism for this model is not known, but likely involves psychosocial responses. Thirdly, the odorant may be a component of a mixture that contains a toxic co-pollutant. As most studies support odour annoyance as a mediating factor in symptom reporting, and residence distance to the odour source appears to be a poor predictor of symptom reporting, the second model is likely the most plausible in many cases. However, in most odour epidemiology studies, it is not clear if odorant/pollutant levels are below irritant thresholds, and thus, the first and third models are also possible.

3.5.2 Odour Annoyance

Odour annoyance is a commonly reported problem for residents living in the vicinity of odour-emitting facilities. As mentioned in Section 3.3, annoyance is not a direct health effect of exposure to odours, but rather an emotional response that may act as a mediator of health symptoms. According to the World Health Organization, the threshold level for community annoyance is defined as the concentration where 5% of the population experiences annoyance 2% of the time; odorant concentration, as well as psychological and socioeconomic factors, are considered to be influential

determinants of annoyance (World Health Organization, 2000). Several epidemiology studies have shown significant associations between odour exposure and odour annoyance, using a number of different measurement methods and a variety of odour sources. Self-reported odour annoyance has been defined both in terms of frequency (e.g., never annoyed, often annoyed) and intensity (e.g., not at all annoyed, very annoyed).

Frequency of odour annoyance was found to correlate inversely with zone of residence or residence distance to a facility in studies of petrochemical odours in Ontario and pulp mill odours in California (Luginaah et al., 2000; Taylor et al., 1997; Jonsson et al., 1975). Similar inverse correlations have been found between zone of residence/residence distance to source and degree of odour annoyance in studies of pulp mill odours and sewage treatment odours in California, waste treatment odours in Italy and Finland, petrochemical odours in Sweden, and fertilizer plant odours in Germany (Axelsson et al., 2013; Claeson et al., 2013; De Feo et al., 2013; Aatamila et al., 2010; Steinheider, 1999; Steinheider et al., 1998; Bruvold et al., 1983; Jonsson et al., 1975). Other industrial odours in Germany or petrochemical odours in Ontario showed no clear pattern between degree of annoyance and residence zone/residence distance to facility (Luginaah et al., 2000; Taylor et al., 1997; Winneke and Kastka, 1987).

Self-reported frequency and intensity of odour has also been used as a measure of exposure in odour annoyance studies. In an analysis of waste treatment odours in Finland, self-reported odour frequency and intensity both correlated with degree of annoyance, with odour intensity having a stronger impact (Aatamila et al., 2010). In studies of odours from a pig-rearing facility or a fertilizer plant in Germany, self-reported odour frequency, but not odour intensity, correlated with degree of annoyance (Sucker et al., 2008; Both et al., 2004). A few German studies have made use of trained panelists to estimate odour frequency (in odour hours/year) near various odour sources (oil refineries, iron/steel plant, sulphur chemical plant, pig rearing facility); odour frequency was found to correlate with degree of annoyance in all studies (Steinheider, 1999; Steinheider et al., 1998; Steinheider and Winneke, 1993).

Several studies conducted in the Netherlands have compared odour concentrations and odour annoyance with odours originating from a wide range of industrial sources (e.g., oil extraction, pig farm, sugar refineries, tobacco plants) (Miedema et al., 2000; Cavalini, 1994; Cavalini et al., 1991; Miedema and Ham, 1988). In all studies and for all odour types, odour concentrations were significantly associated with odour annoyance (either as percentage of highly annoyed subjects, or as the product of annoyance intensity and frequency). Degree of odour annoyance has also been linked to levels of odorous petrochemical compounds (NO_2, SO_2, and VOCs) in Sarnia, ON (Atari et al., 2012, 2009).

The influence of odour hedonic in exposure-annoyance relationships has been an important consideration in odour epidemiology. In studies assessing odours of varying pleasantness, degree of annoyance tended to be lowest with pleasant odours (e.g., chocolate factory, sweets production) and highest with unpleasant odours (e.g., tar-oil refinery, cast-iron factory) (Sucker et al., 2008; Both et

al., 2004; Miedema et al., 2000; Cavalini, 1994; Cavalini et al., 1991; Winneke and Kastka, 1987). Accounting for odour pleasantness in the statistical analyses often improved the strength of the observed exposure-annoyance relationship. These studies all came to the same conclusion - that odour hedonic plays an important role in odour annoyance.

Socio-economic factors such as age, gender, race, occupation, income, and smoking status may have an effect on odour annoyance, and most studies have considered the impact of these factors in their analyses. Other determinants of odour annoyance include perceiving odour as a threat to health, method of coping with the odour, and general dissatisfaction with the community (Axelsson et al., 2013; Claeson et al., 2013; Atari et al., 2012,2009; Cavalini, 1994; Cavalini et al., 1991). It has also been shown that residents of communities receiving financial compensation for presence of an odour source may report lower levels of annoyance (De Feo et al., 2013).

In summary, both the frequency and intensity of odour annoyance have been shown to increase with increasing odour exposure, regardless of the measure of exposure used (residence distance, self-reported odour exposure, odour frequency by trained panelists, or odour concentration). These associations have been observed in several locations in response to a wide range of odours. Odour hedonic appears to play a significant role in the exposure-annoyance association, with unpleasant odours inducing more annoyance than pleasant odours.

3.5.3 Mood, Coping, and Activity Changes

Studies assessing odours and changes in mood were conducted in areas surrounding livestock facilities or municipal waste sites in North Carolina and Germany. In North Carolina, three studies found negative moods (e.g., feeling stressed, nervous, gloomy, depression, anger, fatigue, confusion) to be more prevalent in subjects exposed to odour (Heaney et al., 2011; Horton et al., 2009; Schiffman et al., 1995), while another found no differences in reports of depression or anxiety between exposed and control groups (Thu et al., 1997). In rural Germany, degree of odour annoyance was found to correlate with decreased emotional health scores (based on self-reported depression, anxiety, feeling calm/peaceful, energy levels, and feeling downhearted) (Radon et al., 2004).

Several epidemiology studies have suggested that exposure to odours may lead to a lower quality of life (Heaney et al., 2011; Tajik et al., 2008; Wing et al., 2008; Wing and Wolf, 2000; Miedema and Ham, 1988; Bruvold et al., 1983). This effect has been measured in a number of ways, ranging from avoiding outdoor activities and keeping windows closed to temporarily leaving the neighborhood and having reduced property values. These changes were observed in areas located near livestock facilities or municipal waste sites in North Carolina, sewage treatment plants in California, and industrial sources in the Netherlands.

In summary, these studies have identified a list of common mood and activity complaints of residents living near odour-emitting facilities. It is important to keep in mind that reported changes

in mood and daily activities are subjective outcome measures, and may be influenced by personal attitudes toward the industry.

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4. Experimental Studies - Physiological Responses, Mood, and Task Performance

4.1 Introduction

The following chapter reviews experimental studies evaluating odour-induced physiological and psychological responses in humans. Commonly assessed outcomes include physiological arousal (e.g., heart rate, blood pressure), irritant symptoms (e.g., nausea, headache, and cough), mood, cognitive performance, and athletic performance.

Tabulated summaries of the studies assessing physiological responses and mood/task performance are provided in Appendices D and E, respectively. An evaluation of the quality of the studies was beyond the scope of the review. In order to limit the amount of data reviewed, studies assessing aromatherapy for medical purposes (e.g., aromatherapy treatments for medical conditions, use of aromatherapy to reduce pre-medical procedure anxiety) were not included.

Odour can be produced by an endless number of chemicals and chemical mixtures. Experimental studies utilize a wide variety of pleasant and unpleasant odours (refer to Appendix B for a description of odorants) over a range of concentrations; this makes it extremely difficult to compare and contrast results between studies. In addition, the majority of experimental studies expose subjects to a single odorant; this contrasts environmental exposures where odours are typically experienced as a complex mixture. It is important to consider that the response to single odorants may differ from the response to mixtures of odorants.

Odour research in humans utilizes a variety of experimental methodologies (e.g., variations in odorant delivery method, exposure time, measured response), which may contribute to some inconsistencies between studies. For example, exposure times may be extremely short (e.g., one inhalation or exposures of less than 10 seconds using an olfactometer), or relatively long (e.g., ambient room exposures of 10-90 minutes). Because odour-induced responses can differ with varying exposure times, it can be difficult to compare results between studies using short and long exposure times. Another concern with regards to duration of exposure is that the relatively short exposure times used in some experimental studies may limit the applicability of their findings to situations of repeated or prolonged environmental exposures.

Subject characteristics such as age, gender, and health status can significantly influence individual responses to odours. Responses can also vary based on past experiences and emotional association to an odour. Recent research suggests that in age groups with low odour semantic knowledge (children and seniors), odour hedonic can be predicted by the physicochemical properties of an odorant; this association was less marked in groups with high odour semantic knowledge (teenagers and young adults) (Joussain et al., 2011; Poncelet et al., 2010). Perceived pleasantness thus appears to be influenced by both odour learning and odorant physicochemical properties, which may translate into variations in odour-induced physiological and mood alterations. To help control for this, many

studies have subjects rate the intensity, pleasantness, and/or familiarity of the experimental odour prior to or following odour exposure.

A complex set of social factors are also involved in influencing an individual's response to an odour, including the social situation, culture, presence of other odorants, and the state of mind of the individual (Herz, 2002; Kirk-Smith and Booth, 1987). When an odour is experienced outside of its normal social context, the determinants of the odour response change, and may potentially lead to a different odour response. Thus, results achieved in controlled laboratory settings may not always accurately reflect a typical social response.

All the factors discussed above severely complicate the assessment of odour-induced changes in physiological and psychological outcomes. Identifying consistencies across studies and drawing concise conclusions is therefore an extremely challenging task. Though some conclusions can be made about odours in general, it appears that most odorants carry their own physiological, mood, and cognitive profiles.

4.2 Physiological Responses

The main outcomes of interest in studies of odour-induced physiological responses are arousal (heart rate (HR), heart rate variability (HRV), blood pressure (BP), skin conductance response (SCR)), irritant symptoms, and facial muscle activity. Physiological responses were quite varied for each outcome and definitive conclusions relating odours and responses were difficult to make. Effects appeared to be influenced by factors such as odour hedonic and intensity, chirality of odour molecules, odour arousal rating, and cognitive attitudes towards the odour.

4.2.1 Physiological Arousal

A large number of studies have evaluated physiological arousal outcomes in response to unpleasant and pleasant odour exposures. In hopes of simplifying the results, the data are presented in tabulated form in Table 4-1 (unpleasant odours) and Table 4-2 (pleasant odours). As heart rate was the most commonly measured outcome, the studies were separated based on their observed effect on heart rate. Within each subgroup, the studies are organized by increasing exposure time. The tables demonstrate the wide range of odours used in odour research, the variation in experimental exposure times, and the variation in physiological responses observed with different (or even the same) odours.

Heart rate

Odours have been shown to induce changes in heart rate (HR) or pulse rate, with varying effects based on odour hedonic. Unpleasant odours (e.g., limburger cheese, acetic acid, butyric acid, valeric acid, pyridine) were more likely to induce HR increases, while pleasant odours (e.g., phenylethyl alcohol, lavender, ethyl acetoacetate, jasmine tea, cedrol, citral, ylang-ylang) were more likely to induce HR decreases (Sayorwan et al., 2012; Delplanque et al., 2009; Li et al., 2007; Field et al., 2005;

Kuroda et al., 2005; Hongratanaworakit and Buchbauer, 2004; Dayawansa et al., 2003; Inoue et al., 2003; Bensafi et al., 2002b,c; Alaoui-Ismaïli et al., 1997b; Ehrlichman et al., 1997; Brauchli et al., 1995). Other studies showed no significant changes in HR in response to a variety of pleasant and unpleasant odours (swine odour, hydrogen sulphide (H_2S), rotten yeast, vanillin, isoamyl acetate, lemon, lavender, rosemary, peppermint, neroli, cineole, coconut, Citrus bergamia, green odour) (Peng et al., 2009; Kiecolt-Glaser et al., 2008; Oka et al., 2008; Shiina et al., 2008; Schiffman et al., 2005; Burnett et al., 2004; Campenni et al., 2004; Bartocci et al., 2001; Motomura et al., 2001; Simpson et al., 2001; Hermann et al., 2000; Romine et al., 1999; Schneider et al., 1999; Soussignan et al., 1999; Ehrlichman et al., 1997; Miltner et al., 1994; Redd et al., 1994).

Table 4-1: Summary of the effects of unpleasant odours on physiological arousal parameters

Unpleasant Odour	Exposure Time	HR	HRV	BP	RR	SCR	Reference
Yeast	≤1 sec	NC	-	-	-	-	Hermann 2000
Hospital detergents	10 sec	NC	-	-	NC	-	Bartocci 2001
Hydrogen sulphide	5 min	NC	-	-	-	NC	Miltner 1994
Swine odour	60 min	NC	-	NC	NC	-	Schiffman 2005
Isovaleric acid, Pyridine, Thiophenol	≤1 sec	↑	-	-	-	NC	Bensafi 2002b
Acetic acid, Butyric acid	≤1 sec	↑	-	-	-	↑	Alaoui-Ismaili 1997a
Limburger cheese, Valeric acid	13-30 sec	↑	-	-	-	-	Ehrlichman 1997
Valeric acid	30 sec	↑	-	-	-	↑	Brauchli 1995
Isovaleric acid	≤1 sec	-	-	-	↑	-	Masaoka 2005
Isobutyric acid, Pyridine	2 sec	-	-	-	-	↓	Banks 2012
Triethylamine	3 sec	-	-	-	-	↑	Brand and Jacquot 2001; Brand 2000
Several unpleasant odours	3-5 sec	-	-	-	-	↑	Royet 2003
Butyric acid, Skatole	6 sec	-	-	-	-	↑	Møller and Dijksterhuis, 2003

Abbreviations: DBP: diastolic BP; HR: heart rate; HRV: heart rate variability; NC: no change; PNS: parasympathetic nervous system; RR: respiratory rate; SBP: systolic blood pressure; SCR: skin conductance response; SNS: sympathetic nervous system; (-): not measured

Table 4-2: Summary of the effects of pleasant odours on physiological arousal parameters

Pleasant Odour	Exposure Time	HR	HRV	BP	RR	SCR	Reference
Ethyl acetoacetate, Lavender	≤1 sec	↓	-	-	-	↓	Alaoui-Ismaili 1997a
Citral	≤1 sec	↓	-	-	-	-	Li 2007
Phenylethyl alcohol	30 sec	↓	-	-	-	↓	Brauchli 1995
Lavender	2 min	↓	-	-	-	-	Field 2005
Jasmine tea, Lavender, (*R*)-(–)-Linalool	5-6 min	↓	↑ PNS NC SNS	-	-	-	Kuroda 2005; Inoue 2003
Cedrol	10 min	↓	↑ PNS ↓ SNS	↓ DBP ↓ SBP	↓	-	Dayawansa 2003
Lavender, Ylang-ylang	20 min	↓	-	↓ DBP ↓ SBP	NC	-	Sayorwan 2012; Hongratana-worakit and Buchbauer 2004
Sandalwood	20 min	↓ (pulse rate)	-	NC	-	↑	Heuberger 2006
Cineole, Isoamyl acetate, Menthol	≤1 sec	NC	-	-	-	NC	Bensafi 2002b
Vanilla	≤1 sec	NC	-	-	-	-	Hermann 2000
Coconut	13 sec	NC	-	-	-	-	Ehrlichman 1997
Lavender, Peppermint	1 min	NC	-	-	-	-	Simpson 2001
Lavender, Vanillin	5 min	NC	-	-	-	NC	Miltner 1994
Green odour, Lavender	10 min	NC	-	NC	-	-	Oka 2008; Romine 1999
Lavender, Neroli	11 min	NC	-	-	-	NC	Campenni 2004
Citrus bergamia	15 min	NC	↑ PNS ↓ SNS	NC			Peng 2009
alpha-santolol	20 min	NC (pulse rate)	-	NC	NC	NC	Heuberger 2006
Lavender	20-30 min	NC	-	NC	-	-	Shiina 2008; Motomura 2001
Lavender	40 min	NC	↑ PNS ↓ SNS	NC	-	-	Duan 2007
Lavender, Lemon	75 min	NC	-	NC	-	-	Kiecolt-Glaser 2008
(*S*)-(+)-Linalool	6 min	↑	↓ PNS ↑ SNS	-	-	-	Kuroda 2005
Rosemary	20 min	↑	-	↑ DBP ↑ SBP	↑	-	Sayorwan 2013
Coconut	45 min	↑	↓ PNS	-	-	-	Mezzacappa 2010
Laurel leaves	45 min	-	↑ SNS	-	-	-	Matsubara 2011
Jasmine, Lavender, Lemon, Orange, Peppermint, Rose	2.5-4 min	-	-	↓ DBP NC SBP	NC	-	Nagai 2000
Phenylethyl alcohol	≤1 sec	-	-	-	↓	-	Masaoka 2005
Bergamot, Citral, Muguet, Peach	2-6 sec	-	-	-	-	↑	Banks 2012; Møller and Dijksterhuis 2003
Lavender	10 min	-	-	-	-	↑	Howard and Hughes 2008

Abbreviations: DBP: diastolic BP; HR: heart rate; HRV: heart rate variability; NC: no change; PNS: parasympathetic nervous system; RR: respiratory rate; SBP: systolic blood pressure; SCR: skin conductance response; SNS: sympathetic nervous system; (-): not measured

The relationship between odour and HR or pulse rate may be influenced by the chirality of the odour molecules, as seen in studies of the pleasant odours linalool and carvone (Kuroda et al., 2005; Heuberger et al., 2001). (*S*)-(+)-Linalool was found to increase HR, while (*R*)-(–)-linalool was found to decrease HR; similarly, *R*-(–)-carvone increased pulse rate, while *S*-(+)-carvone had no effect.

Odour suggestion or individual experience may also have an impact on odour-induced HR changes. In a study of lavender and neroli odours, the suggestion that an odour was relaxing led to decreased HR, while the suggestion that an odour was stimulating led to increased HR; all HR changes were attributable to suggestion (Campenni et al., 2004). In studies of the dental odour eugenol, subjects who were fearful of the dentist showed increases in HR, while no changes were found in non-fearful subjects (Robin et al., 1999, 1998). Contrarily, in an assessment of 10 odours paired with positive, neutral, or negative names, no effect of odour naming (odour expectation) was found on HR (Djordjevic et al., 2008). Overall, it appears that expectations and suggestion may influence odour-induced HR responses, but not in all cases.

Heart rate variability

Heart rate variability (HRV) has been used in odour studies to assess changes in autonomic tone. Typically, changes in the frequency domain of HRV (LF (low frequency), HF (high frequency), LF/HF (low frequency to high frequency ratio)) are used as indicators of the balance of the sympathetic and parasympathetic nervous systems (Peng et al., 2009). Exposure to pleasant odours (cedrol, citrus bergamia, jasmine tea, lavender) has primarily been associated with increased HF, decreased LF, and/or decreased LF/HF, indicative of an increase in parasympathetic tone and/or a decrease in sympathetic tone (Peng et al., 2009; Duan et al., 2007; Kuroda et al., 2005; Dayawansa et al., 2003; Inoue et al., 2003). Contrarily, a pleasant odour considered to be a stimulant (laurel leaves) induced an increase in sympathetic tone (decreased HF, increased LF/HF) (Matsubara et al., 2011).

Similar to that observed with heart rate, the effect of odour on HRV may be influenced by chirality of the molecules. In an analysis of linalool odours, (*R*)-(–)-linalool increased parasympathetic nerve activity (increased HF), while (*S*)-(+)-linalool increased sympathetic and decreased parasympathetic activity (decreased HF, increased LF) (Kuroda et al., 2005). An individual's predilection towards an odour may have an impact on HRV changes as well. Inoue et al. (2003) found that a high intensity odour of jasmine tea led to an increase in parasympathetic HRV response in subjects who liked the odour, but an increase in sympathetic HRV response in those who disliked the odour. Similarly, a high intensity green tea odour induced an increase in parasympathetic activity in subjects who liked the odour, but not in those who disliked it (Oka et al., 2008).

Blood pressure

The results from studies assessing odour and blood pressure (BP) have been quite varied and are difficult to interpret. In studies of pleasant odours, carvone, limonene, rosemary, and sandalwood oil were found to induce BP increases, while Citrus bergamia, lemon, and alpha-santalol had no effect (Sayorwan et al., 2013; Peng et al., 2009; Kiecolt-Glaser et al., 2008; Duan et al., 2007; Heuberger et al., 2006, 2001). For lavender odour, one study observed decreases in systolic and diastolic BP while

two others showed found no significant effect (Sayorwan et al., 2012; Motomura et al., 2001; Romine et al., 1999). Shiina et al. (2008) also found no effect of lavender on BP, but did observe an increase in coronary circulation.

Nagai et al. (2000) found that exposure to a subject's most preferred odour (of 6 pleasant odours) attenuated handgrip exercise-induced increases in diastolic BP. Similarly, green odour (odour of green leaves) was found to weaken a cold-pressor induced BP increase (Oka et al., 2008).

With regards to unpleasant odours, asafoetida, cigarette ash, rotten egg, and skunk induced varied BP responses, and no clear pattern emerged between odour discomfort and BP (Asmus and Bell, 1999).

Respiratory rate

Most studies evaluating respiratory rate showed no significant changes in response to odours (carvone, limonene, lavender, jasmine, peppermint, *a*-santalol, sandalwood oil, ylang-ylang, diluted swine odour) (Sayorwan et al., 2012; Heuberger et al., 2006, 2001; Schiffman et al., 2005; Hongratanaworakit and Buchbauer, 2004; Nagai et al., 2000). One study observed an increase in respiratory rate with exposure to unpleasant odour (isovaleric acid) and a decrease in respiratory rate with pleasant odour (phenylethyl alcohol) (Masaoka et al., 2005). Dayawansa et al. (2003) also observed a decrease in respiratory rate with the pleasant odour cedrol, while Sayorwan et al. (2013) observed a respiratory rate increase with the stimulating odour rosemary. Contradicting responses were found in studies of newborns: respiratory rate increases were observed with odours of baby formula, vanillin, and butyric acid, while no changes were found in response to odours of a hospital detergent or adhesive remover (Bartocci et al., 2001; Soussignan et al., 1999, 1997).

Skin conductance response

Skin conductance response (SCR), or electrodermal response, is a measure of physiological arousal that varies based on the moisture of the skin. Higher SCRs indicate a more aroused state, while lower SCRs indicate a more relaxed state. Variations in SCRs have been observed following exposure to different odours, with odour hedonic appearing to be a main determinant of the response. Several studies have demonstrated that unpleasant odours produce an increase in SCRs (amplitude and duration) relative to pleasant odours (Delplanque et al., 2009, 2008; Royet et al., 2003; Brand and Jacquot, 2001; Brand et al., 2000; Alaoui-Ismaïli et al., 1997a,b; Brauchli et al., 1995). Examples of odour comparisons include triethylamine with isoamyl acetate, valeric acid with phenylethyl alcohol, a group of 48 pleasant and unpleasant odours, and a group of 126 food odours.

Other studies have shown no association between odour-induced SCR and odour pleasantness, nor with odour familiarity or intensity (e.g., menthol, pyridine, butyric acid, and citral odours) (Møller and Dijksterhuis, 2003; Bensafi et al., 2002b,c,d). Rather, odour arousal rating has been identified as a significant predictor of SCR. Other factors that may impact SCRs include the trigeminal properties of an odour (Jacquot et al., 2004; Brand and Jacquot, 2001), smelling a novel versus a repeated odour (Delplanque et al., 2009), anxiety (Krusemark and Li, 2012), and cognitive attitudes/expectations

towards an odour (Djordjevic et al., 2008; Howard and Hughes, 2008; Campenni et al., 2004; Robin et al., 1999, 1998; Van Toller et al., 1983).

Several other odours produced no significant change in SCR, including H_2S, vanillin, carvone, limonene, alpha-santalol, lavender, and neroli (Heuberger et al., 2006, 2001; Campenni et al., 2004; Miltner et al., 1994).

Other arousal outcomes

Other parameters of physiological arousal evaluated less frequently include skin blood flow, temperature, facial sebum secretion, pupil diameter, and blood oxygen saturation. Alaoui-Ismaili et al. (1997a,b) observed increases and decreases in skin blood flow following exposure to unpleasant odours (e.g., butyric acid, propionic acid) and pleasant odours (lavender, menthol), respectively. In studies evaluating skin/body temperature, rosemary odour induced an increase, lavender induced a decrease, and carvone, limonene, ylang-ylang, green odour, and swine odour had no effect (Sayorwan et al., 2013, 2012; Oka et al., 2008; Schiffman et al., 2005; Hongratanaworakit and Buchbauer, 2004; Heuberger et al., 2001). One other study showed no significant impact of lavender or rosemary odours on body temperature following an anxiety-provoking task (Burnett et al., 2004). Tanida et al. (2008) found a floral green fragrance (4 weeks of continuous exposure) to reduce facial sebum secretion during a stressful arithmetic task. With regards to pupillary changes, Schneider et al. (2009) demonstrated an increase in pupil diameter following exposure to carbon dioxide (CO_2), H_2S, lime, or phenylethyl alcohol; this response was influenced by odour intensity and quality (i.e., trigeminal or olfactory odour), but not odour hedonic. No odour-induced changes were found for blood oxygen saturation (Heuberger et al., 2006, 2001; Bartocci et al., 2001).

4.2.2 Irritant Symptoms

The effect of odours on reported general health symptoms has been examined by only a few research groups. Schiffman et al. (2005) found that subjects exposed to diluted swine odour for one hour reported more headaches, eye irritation, and nausea than subjects exposed to clean air; no differences were found for sore throat, nasal irritation/congestion, or cough. The authors noted that it was unclear if the increase in symptoms was due to the odours or to the combined exposure to irritant components (H_2S, ammonia, VOCs, particulates, and endotoxin).

In a study of furfurylmercaptan odours (coffee aroma), Pan et al. (2003) observed an increase in reports of dry nose, but not headache or skin moisture. Meanwhile, subjects exposed to baby powder or lemon odours were found to report a fewer number of health symptoms (fatigue, headache, pain, irritation of the eye, throat, nose, or skin) than control subjects; no differences in symptom reporting were found for the chocolate, lavender, or dimethyl sulphide odour groups (Knasko, 1995, 1992). Odour had no impact on symptom intensity in these two studies.

Cognitive influences and emotional biases have been shown to play a significant role in symptom reporting. In a study of butanol, isobornyl acetate, and methyl salicylate odours, subjects were given a healthful, harmful, or neutral odour bias prior to exposure (Dalton, 1999). For all odours, those

given a harmful odour bias reported more health symptoms (e.g., throat irritation, headache, nausea, bad taste) than subjects given a neutral or healthful odour bias. Similarly, in a group of women exposed to isobornyl acetate, those told the odour was harmful reported more symptoms than those told the odour was healthy or neutral (Laudien et al., 2008). These findings are further supported by Knasko et al. (1990), who found that suggestion of a harmful odour resulted in more reported symptoms than suggestion of a pleasant or neutral odour, despite no odour being used in the study. In another study by Knasko (1993), no effect of odour was found on reported health symptoms; however, subjects exposed to malodor stated retrospectively that they believed the odour had a negative influence on their health. All these studies concluded that health symptom reporting is highly mediated by cognitive variables and perceived health risks of the odour.

4.2.3 Facial Muscle Activity

Pleasant and unpleasant odours have been shown to significantly alter facial muscle activity and emotional facial expression. Increases in corrugator, zygomaticus, orbicularis oculi, levator, and nasalis muscle activities have been observed in response to unpleasant odours, while increases in zygomaticus and orbicularis oculi muscle activities have been found with pleasant odours (Armstrong et al., 2007; Bensafi et al., 2002d; Hermann et al., 2000; Jäncke and Kaufmann, 1994). More recently, Delplanque et al. (2009) have shown that frontalis muscle activity increases initially for novelty evaluation (new odour versus known odour), followed by an increase in corrugator and frontalis muscle activities for pleasantness evaluation. Odours have also been found to induce changes in facial displays in newborns (Soussignan et al., 1999, 1997). The results of these studies provide evidence to suggest that the pattern of facial muscle activity varies as a function of odour pleasantness.

Other studies have examined the effect of odours on startle reflex, as measured by orbicularis oculi activity of the left eye. Unpleasant odours (e.g., limburger cheese, cigar butt, H_2S, yeast) were found to increase startle reflex, while pleasant odours (e.g., coconut, orange oil, vanillin) typically decreased or caused no change to startle reflex (Hermann et al., 2000; Ehrlichman et al., 1997, 1995; Miltner et al., 1994). All studies concluded that, similar to other aversive stimuli, unpleasant odours can potentiate startle reflex.

4.2.4 Other Physiological Outcomes

Other clinical outcomes that have briefly been studied include blood and nasal inflammation, salivary or serum markers, and pulmonary function. Kiecolt-Glaser et al. (2008) observed a decrease in hypersensitivity to Candida (infectious agent) in response to lemon and lavender odours, but no changes to blood interleukin levels or salivary cortisol (stress hormone) levels. Trellakis et al. (2012) also demonstrated no effect of stimulating (grapefruit, fennel, pepper) or relaxing odours (lavender, patchouli, rose) on markers of blood inflammation (cytokines, neutrophil activity). Atsumi and Tonosaki (2007) found lavender and rosemary to be associated with an increase in free radical scavenging activity and a decrease in salivary cortisol levels. Overall, they concluded that lavender and rosemary odours help to protect the body from oxidative stress. Additionally, lavender odour was shown to reduce cortisol levels in serum (Shiina et al., 2008). Toda and Morimoto (2008) also

demonstrated a stress-relieving effect of lavender; levels of the salivary stress marker chromogranin A, but not salivary cortisol, were reduced following lavender exposure. In a study of swine odour, Schiffman et al. (2005) found increases in the percentage of epithelial cells and lymphocytic cells in nasal lavage, but no effect on salivary immunoglobulin A levels or any measures of pulmonary function. Regarding metabolic changes, Zhang et al. (2013) found repeated exposure to a pleasant aromatic odour (45 minutes per day for 10 days) to significantly alter metabolites in urine (e.g., carbohydrates, amino acids, tricarboxylic acid cycle metabolites).

4.3 Mood

Transient changes in mood in response to odour exposures are typically measured using the Profile of Mood States (POMS) survey (Campenni et al., 2004; Goel and Grasso, 2004; Schiffman et al., 1995b). Briefly, POMS is a self-reported questionnaire in which the subjects rate 65 feelings or emotions on a scale of 0 to 4; the 65 feelings are grouped into six primary mood categories: tension/anxiety, depression, confusion, anger, fatigue, and vigor. A higher score for a particular category indicates a stronger prevalence of that mood. Total mood scores are calculated by summing the scores for the first 5 categories and subtracting the score for vigor, with a higher total mood score indicating a more negative mood. The POMS survey has been a widely used standard test for more than 30 years and is considered to be a valid method for the assessment of mood (Nyenhuis et al., 1999). Other less commonly used surveys include visual analogue scales, bipolar mood scales, the State Trait Anxiety Inventory, the Positive and Negative Affect Scale, and the Self Assessment Manikin scale.

The relationship between odour and mood has proven to be extremely complex. Multiple external factors (e.g., odour intensity, pleasantness) and internal factors (e.g., emotional association, expectations) heavily influence odour-induced changes in mood, making comparisons between studies quite difficult. Tables 4-3 and 4-4 provide a summary of the observed effects on mood/ emotion in response to unpleasant and pleasant odours, respectively. The main consistent finding among the mood studies is, rather simply, that unpleasant odours induce more negative moods and pleasant odours induce more positive moods. Further conclusions beyond this basic finding are difficult to identify, owing to the variations in experimental methodology, types of odours used, and individual attitudes of the subjects.

For studies evaluating unpleasant odours, the most common responses are increased anger and disgust; this has been found with exposures to H_2S, yeast, pyridine, methyl methacrylate, and propionic acid (Reske et al., 2010; Seubert et al., 2009; Weber and Heuberger, 2008; Habel et al., 2007; Villemure et al., 2003; Alaoui-Ismaïli et al., 1997a; Ehrlichman et al., 1997). A study of 4 unpleasant odours (asafoetida, cigarette ash, rotten egg, skunk) found odour unpleasantness to correlate with discomfort and motivation to escape, but not with anger (Asmus and Bell, 1999). Decreases in happiness, pleasure, and calmness have also been observed in a number of studies (Reske et al., 2010; Seubert et al., 2009; Weber and Heuberger, 2008; Rotton, 1983). In contrast to these findings, the unpleasant odours isovaleric acid and skatole were not found to significantly impact mood (Knasko, 1993).

Table 4-3: Summary of the effects of unpleasant odours on mood and emotion

Effect on Mood	Unpleasant Odour	Exposure Time	Reference
Increased anger and disgust; More negative (less positive) mood	Acetic acid, Butyric acid, Hydrogen sulphide, Limburger cheese, Methyl methacrylate, Propionic acid, Pyridine, Yeast	1-13 sec	Reske 2010; Seubert 2009; Weber and Heuberger 2008; Villemure 2003; Vernet-Maury 1999; Alaoui-Ismaili 1997a; Ehrlichman 1997
	Hair perm product	3 min	Marchand and Arsenault 2002
	Ethyl mercaptan	15-30 min	Rotton 1983
	Dimethyl sulphide	unknown	Knasko 1992
Decreased calmness	Hydrogen sulphide	<5 sec	Weber and Heuberger 2008
Discomfort; Motivation to escape	Asafoetida, Cigarette ash, Rotten egg, Skunk	10-20 min	Asmus and Bell 1999
Decreased ratings of images	Hydrogen sulphide, Isobutyric acid, Pyridine, Rubber, Synthetic body odour, Valeric acid, Yeast, Several unpleasant odours	<5 sec	Banks 2012; Walla and Deecke 2010; Demattè 2007; Li 2007; Schneider 1999; Todrank 1995
	Ethyl mercaptan	15-30 min	Rotton 1983
Increased ratings of positive images	Hydrogen sulphide	1 sec	Walla and Deecke 2010
No effect on ratings of images	Ammonium sulphide	10-15 min	Cann and Ross 1989
No effect on mood	Isovaleric acid, Skatole; Swine odour	15-60 min	Schiffman 2005; Knasko 1993
	Hiba (conifer)	38-50 min	Hiruma 2002
	Fecal odour	unknown	Gilbert 1997

Table 4-4: Summary of the effects of pleasant odours on mood and emotion

Effect on Mood	Pleasant Odour	Exposure Time	Reference
Increased happiness; More positive (less negative) mood	Blooming plants, China rain, Coconut, Creamsicle, Ethyl acetoacetate, Lavender, Lemon meringue, Menthol, Mint, Vanillin, Violet, Several other pleasant odours	1-13 sec	Seubert 2009; Villemure and Bushnell 2009; Weber and Heuberger 2008; Villemure and Bushnell 2007; Villemure 2003; Vernet-Maury 1999; Alaoui-Ismaili 1997a; Ehrlichman 1997
	Almond, Baby oil, Floral fragrance, Jasmine tea, Lavender, Lemon, *R*-(–)-Linalool, Massage oil, PCK	1-6 min	Field 2005; Koruda 2005; Kim and Watanuki 2003; Marchand and Arsenault 2002; Diego 1998; Baron and Thomley 1994
	Baby powder, Chocolate, Lavender, Lemon, *R*-(+)-Limonene, Rosemary, *a*-Santolol	15-75 min	Sayorwan 2012; Kiecolt-Glaser 2008; Heuberger 2006; Moss 2003; Heuberger 2001; Knasko 1995
	Air fresheners, Apple, Chamomile, Cologne, Fragrances (various), Orange, Peppermint, Seawater	unknown	Schifferstein 2011; Barnham and Broughan 2002; Rétiveau 2004; Schiffman 1995a,b; Roberts and Williams 1992; Baron 1990
Increased calmness/relaxation	Blooming plants, Several pleasant odours	<5 sec	Weber and Heuberger 2008; Villemure 2003
	Lavender, Rosemary	2-3 min	Field 2005; Diego 1998
	Ylang-ylang	25 min	Moss 2008
	Chamomile	unknown	Moss 2006
Decreased calmness/relaxation	Peppermint	25 min	Moss 2008
Increased alertness	Blooming plants, Jasmine, Rose oil	<5 sec	Weber and Heuberger 2008
	Rosemary	3 min	Diego 1998
	R-(–)-Carvone, *R*-(+)-Limonene, Peppermint, Rosemary, *Salvia lavandulae-folia*, *Salvia officinalis* (sage), Ylang-ylang	20-30 min	Moss 2010, 2008, 2003; Hongratanaworakit and Buchbauer 2004; Heuberger 2001
Decreased alertness	Ylang-ylang	25 min	Moss 2008
	Chamomile	unknown	Moss 2006
Decreased daytime sleepiness	Peppermint	11 min	Norrish and Dwyer 2005
Increased willingness to help	Perfume	<5 sec	Guéguen 2001
	Floral fragrance, Lemon	5 min	Baron and Thomley 1994
	Bakery odours, Coffee odours	unknown	Guéguen 2012; Baron 1997
Increased ratings of images	Bergamot, Muguet, Phenylethyl alcohol, Several pleasant odours	<5 sec	Banks 2012; Walla and Deecke 2010; Todrank 1995
Decreased ratings of disgusting images	Phenylethyl alcohol	<5 sec	Walla and Deecke 2010
No effect on ratings of images	Floral mixture	<5 sec	Bensafi 2002a
	Cologne	10-15 min	Cann and Ross 1989
No effect on mood	Vanilla	<5 sec	Reske 2010
	Green odour, Lavender, Neroli	10-11 min	Oka 2008; Campenni 2004; Knasko 1993
	S-(+)-Carvone, Clove, Coconut, Lavender, Lemon, *S*-(–)-Limonene, Muguet, Peppermint, Sandalwood oil, Ylang-ylang	15-75 min	Mezzacappa 2010; Kiecolt-Glaser 2008; Heuberger 2006, 2001; Warm 1991; Ludvigson and Rottman 1989
	Fruity/floral fragrance, Lavender, Lemon	unknown	Gilbert 1997; Knasko 1992

For studies of pleasant odours, the most common responses were increased happiness and improved overall mood; this was found with exposure times ranging from < 1 second to 90 minutes (Sayorwan et al., 2012; Villemure et al., 2012, 2003; Seubert et al., 2009; Villemure and Bushnell, 2009, 2007; Weber and Heuberger, 2008; Field et al., 2005; Moss et al., 2003; Barnham and Broughan, 2002; Marchand and Arsenault, 2002; Diego et al., 1998; Alaoui-Ismaïli et al., 1997a; Ehrlichman et al., 1997; Knasko, 1995; Schiffman et al., 1995b,c; Baron and Thomley, 1994; Roberts and Williams, 1992). The pleasant odours used in these studies are typically floral, woody, and food scents (e.g., baby powder, chocolate, coconut, flowers, lavender, lemon, menthol, and vanillin). Contrarily, some studies found no change to overall mood in response to pleasant odours such as coffee, coconut, peppermint, lavender, lemon, hiba (conifer), or other fruity and floral odours (Mezzacappa et al., 2010; Campenni et al., 2004; Pan et al., 2003; Hiruma et al., 2002; Gilbert et al., 1997; Knasko, 1993, 1992; Warm et al., 1991).

For studies assessing both pleasant and unpleasant odours, a correlation between odour hedonicity and overall mood has often been observed, with pleasant odours inducing a more positive mood and unpleasant odours a more negative (or less positive) mood (Weber and Heuberger, 2008; Villemure et al., 2003; Marchand and Arsenault, 2002; Ehrlichman et al., 1997).

One research group utilized the overall pattern of autonomic responses (e.g., heart rate, skin conductance) as a means of objectively measuring changes in mood following odour exposure. Alaoui-Ismaili et al. (1997a,b) found that pleasant odours (menthol, vanillin) induced autonomic responses consistent with happiness and surprise, while unpleasant odours (methyl methacrylate, propionic acid) induced autonomic responses consistent with disgust and anger. Similar results were observed in a follow-up study by Vernet-Maury et al. (1999), where pleasant odours (lavender, ethyl acetoacetate) were associated with an autonomic response of happiness and unpleasant odours (butyric acid, acetic acid) with autonomic responses of anger and disgust. These studies provide objective evidence supporting the relationship between odour hedonic and mood.

Only one study was found that assessed the impact of environmental odorous mixtures on mood. Schiffman et al. (2005) exposed a sample of 48 adults to diluted swine odour for 60 minutes. Swine odour had no effect on total mood score or mood subscales (depression, anxiety, anger, vigor, fatigue, or confusion).

In a study concerned with environmental annoyance, subjects with low and high degrees of self-reported environmental annoyance were exposed to H_2S for 60 minutes (Winneke and Neuf, 1992). The effect of H_2S odour differed between the two groups: subjects with high self-reported environmental annoyance showed higher levels of odour-induced annoyance than subjects with low environmental annoyance. Additionally, this odour-induced annoyance correlated positively with self-reported dissatisfaction with perceived health, suggesting that odour-induced annoyance plays a role in overall health.

There is evidence to suggest that a harmful or healthful bias may influence odour-induced mood changes. In a study assessing the impact of odour suggestion, Knasko et al. (1990) told subjects they were being exposed to either a pleasant, unpleasant, or neutral odour, but no actual odour was present. Subjects in the pleasant bias group were found to be in a more pleasant mood than subjects in the neutral and unpleasant bias groups. Similar results were found by Laudien et al. (2008) in a study using isobornyl acetate, an odour considered to be malleable. Following exposure to the odour, subjects given a healthy bias were happier than subjects given a harmful or neutral bias. In another study of isobornyl acetate, intensity ratings differed between subjects given a healthful bias (intensity decreased over time) and those given a harmful bias (intensity increased over time) (Dalton, 1996). The role of cognition in odour-induced responses is also supported by the fact that the same odour can induce varying mood responses. For example, mood changes following exposure to odours of eugenol, camphor, and jasmine tea have been found to vary based on subjects' past experiences and their predilection or aversion towards the odour (Seubert et al., 2009; Inoue et al., 2003; Vernet-Maury et al., 1999; Alaoui-Ismaïli et al., 1997a). The results of these studies highlight the important role that cognitive biases play in emotional responses to odours.

Odours have been found to influence subjects' judgments of faces in photographs. For example, a group of female subjects rated male faces as less attractive when presented with an unpleasant odour (body odour or rubber) compared to pleasant odour (germanium or male fragrance) or no odour (Demattè et al., 2007). Similarly, other studies have found that subjects give lower or more negative ratings of faces following exposure to unpleasant odour (valeric acid, ethyl mercaptan, rotten yeast) (Li et al., 2007; Schneider et al., 1999; Rotton, 1983). In a study of repeated presentation of pleasant or unpleasant odours with a neutral photograph of a person of the opposite sex, subjects' preference ratings for the photograph shifted in the direction of odour pleasantness (i.e., unpleasant odour induced a lower face preference rating) (Todrank et al., 1995). Contrary to these studies, others have found no effect of pleasant odour (floral scent, cologne) or unpleasant odour (ammonium sulphide) on subjective judgments of faces (Bensafi et al., 2002a; Cann and Ross, 1989). Overall, these findings suggest that some odours may have an effect on social judgments and attitudes, likely by influencing an individual's affective reaction towards the social stimulus.

Odours may also influence emotion ratings in response to visual stimuli. Banks et al. (2012) studied the effect of pleasant (bergamot, muguet) and unpleasant odours (isobutyric acid, pyridine) on ratings of a range of visual stimuli (e.g., scared child, motorcycle, scenic mountain). Isobutyric acid or pyridine exposure resulted in a decrease in ratings of images compared to no odour; effects were strongest with pleasant and neutral images. Bergamot and muguet were found to increase the ratings of images, relative to unpleasant odour but not to air. Walla and Deecke (2010) also assessed the influence of pleasant odour (phenylethyl alcohol) and unpleasant odour (H_2S) on visually-induced emotion ratings. Flower pictures were rated as more positive and disgusting pictures rated as more negative when in the presence of phenylethyl alcohol and low-dose H_2S odours. Additionally, H_2S (high dose) led to a decrease in emotion rating when subjects were shown a picture of a baby. Overall, the authors concluded that there is a variable influence of odours on visually-induced emotion, which is dependent on the type and intensity of visual stimuli as well as the type of odour.

Several researchers have found that pleasant odours increase the willingness to help others. Baron and Thomley (1994) found pleasant floral or lemon odours to increase subjects' willingness to help the experimenter by serving as an uncompensated volunteer. In a study evaluating ambient shopping mall odours, help was offered more often to someone who needed change when in the presence of pleasant bakery or coffee odours (Baron, 1997). Similarly, another study of shopping mall odours demonstrated that help was offered more often to someone who dropped a glove when exposed to pleasant bakery odour (Guéguen, 2012). The same study group also found help to be offered more often to a young woman who dropped a glove if she was wearing perfume, compared to not wearing perfume (Guéguen, 2001). The above studies consistently demonstrate a positive influence of pleasant odours on willingness to help; this association may be partially mediated by positive affect.

4.4 Cognitive Performance

The effect of odours on cognitive function has been evaluated using a variety of mental and motor tasks. Subjects in these types of studies are typically exposed to ambient room odours for 3 min to 1 hour while performing memory tasks, recognition tasks, math tasks, lexical tasks (word recognition, word decoding), or motor reaction tasks. Studies often make use of the Cognitive Drug Research tests – a standardized battery of cognitive tests – to examine cognition.

Several unpleasant odours have been found to impair performance on cognitive tasks. Danuser et al. (2003) demonstrated an impairment of mental task performance (short-term memory task and reaction time) in response to the unpleasant odours ammonia and H_2S. Rotton (1983) found the malodour ethyl mercaptan to reduce performance on complex tasks (proofreading) but not simple tasks (arithmetic). Habel et al. (2007) observed a decrease in performance on a verbal working memory task in response to rotten yeast odours in 9 of 21 subjects. This effect was not related to subjects' ratings of unpleasantness or disgust, but rather to differences in neuronal processing (greater activations in emotion-related brain areas).

The pleasant odours lemon, floral fragrance, muguet, peppermint, cinnamon, hiba (conifer), powder fresh air freshener, and spiced apple air freshener have been shown to improve performance on vigilance tasks, memory tasks, word decoding tasks, typing tasks, reaction time tasks, and vibrotactile discrimination tasks (Ho and Spence, 2005; Zoladz and Raudenbush, 2005; Barker et al., 2003; Hiruma et al., 2002; Baron and Bronfen, 1994; Baron and Thomley, 1994; Warm et al., 1991). Odours of cinnamon and peppermint have also improved self-evaluated performance on a simulated driving task (Raudenbush et al., 2009). Effects of pleasant odour on performance may be mediated, at least partially, by positive mood or arousal of attention (Barker et al., 2003; Baron and Thomley, 1994).

Matsubara et al. (2011) compared the effects of low dose (more pleasant) and high dose (less pleasant) laural leaf odours on a visual discrimination vigilance task. The low dose exposure attenuated a decrease in vigilance at 20-30 minutes, while the high dose had no effect. The authors

suggested the observed effect with low-dose exposure may have been related to the higher rating for pleasantness and lower scores for negative emotions compared to the high-dose exposure.

Two research groups found exposure to pleasant odours (air fresheners, cineole, jasmine, menthol) to act as a distraction and impair performance on cognitive tests and slow motor reaction times (Gaygen and Hedge, 2009; Ilmberger et al., 2001). Additionally, Lorig et al. (1991) found Galaxolide fragrance to impair performance on a visual search task when the odour was undetectable, but not at above-threshold concentrations.

Several studies have compared the effects of pleasant, unpleasant, and neutral odours on task performance. Millot et al. (2002) demonstrated that both pleasant odour (lavender) and unpleasant odour (pyridine) significantly improved reaction times for simple sensory-motor tasks. In a comparison of H_2S (unpleasant) and eugenol (neutral) odour, H_2S was found to improve performance (reduce reaction time) for incongruent stimuli in the Stroop test (a word/colour processing task) while eugenol had no consistent effect (Finkelmeyer et al., 2010). In a visual task, Michael et al. (2005, 2003) found unpleasant odour (allyl isothiocyanate) to increase attentional capture (i.e., improve attention); this effect correlated with perceived (trigeminal) irritation from the odour. Contrarily, pleasant odour (phenylethyl alcohol) reduced attentional capture in the same task, an effect that appeared to be related to a reduction in arousal level. Donoso et al. (2008) assessed the effect of odorant stimuli (hexanal, honeydew) on visual working memory performance. Neither odour was associated with any significant change in performance; however, an increase in memory task errors was observed with exposure to the odour personally rated as unpleasant. The authors concluded that memory processes can be modulated by the subjective hedonic quality of an odour.

Studies of other pleasant (lemon, ylang-ylang, fruity/floral fragrance, menthone, pentylacetate) or unpleasant odours (isovaleric acid, skatole, fecal odour, swine odour) have shown no effect on task performance (math and verbal tasks, visual presentation task, digit deletion task, digit span test) (Ho and Spence, 2005; Schiffman et al., 2005; Danuser et al., 2003; Gilbert et al., 1997; Knasko, 1993).

The observed outcomes on cognition appear to be more related to the specific characteristics of an odour, rather than simply its pleasantness or unpleasantness. Moss et al. (2008, 2003) observed varying effects for the pleasant odours lavender (relaxing odour), ylang-ylang (relaxing odour), rosemary (alerting odour), and peppermint (alerting odour). Lavender impaired both memory and memory reaction times, ylang-ylang impaired memory but improved reaction times, and rosemary and peppermint improved overall quality of long-term memory but impaired reaction times. The same research group found that odours of two varieties of sage had different effects: *Salvia officinalis* improved quality of long-term memory and *Salvia lavandulaefolia* did not, despite both odours leading to increased alertness (Moss et al., 2010). Gould and Martin (2001) found bergamot (relaxing odour) to decrease performance on a visual vigilance task, while peppermint (alerting odour) had no effect. Diego et al. (1998) demonstrated that, for a math computational task, lavender improved speed and accuracy, while rosemary improved speed but not accuracy. These odour-specific effects on task

performance make it extremely difficult to draw any generalizations about odour exposure as a whole.

In looking specifically at lavender, an odour considered to have relaxing and sedating properties, effects on task performance are quite varied. Lavender was found to improve speed and accuracy performance on math tasks (Field et al., 2005; Diego et al., 1998), improve the reaction time for simple sensory-motor tasks (responses to visual or auditory stimulation) (Millot et al., 2002), and help to maintain attention on a vigilance task (Shimizu et al., 2008); contrarily, one study found lavender to impair overall memory and memory reaction times (Moss et al., 2003). The underlying mechanisms for these effects are not well understood; it has been suggested that lavender, as well as other odours affecting task performance, may act through psychological mechanisms (pleasure/ displeasure from the odour), pharmacological interactions, and/or olfactory-induced changes in neuronal activity (Moss et al., 2003; Sanders et al., 2002; Diego et al., 1998).

Heuberger and Ilmberger (2010) studied the interactive effects of odour exposure (1,8-cineole, jasmine, linalyl acetate, peppermint), subjective ratings of pleasantness, and mood/stress on performance on a vigilance task. Exposure to linalyl acetate was found to improve reaction times on the task; performance speed correlated with subjective ratings of odour pleasantness. Additionally, for 1,8-cineole and linalyl acetate odours, false alarms (errors) increased with ratings of odour pleasantness and relaxation. For peppermint, false alarms increased with higher ratings of odour intensity and lower ratings of stress. The authors concluded that subjective factors have a strong impact on odour-induced modulation of attentional functions.

4.5 Athletic Performance

Raudenbush et al. (2001) evaluated the impact of peppermint odour on athletic activity in collegiate athletes. Exposure to peppermint resulted in increased running speed, hand grip strength, and number of push-ups; no effect was found on skill-related tasks such as basketball free-throw shots. In a follow-up study, exposure to peppermint reduced perceived physical and temporal workload (easier and more slowly paced task), effort, and frustration during a walking/running task (Raudenbush et al., 2002). Peppermint odour also increased self-evaluations of performance and vigor, and reduced fatigue. No effects were found for jasmine or dimethyl sulphide odours. Overall, the authors concluded that peppermint odour can enhance physical performance but not overall skill; the effect on performance may be mediated by improved mood and motivation.

Contrary to these findings, exposure to odours of peppermint or peppermint plus ethanol did not impact running time or ratings of physical exertion in walking/running tasks (Pournemati et al., 2009; MacKenzie and Hedge, 2005).

Studies evaluating physiological parameters during exercise in athletes found no significant effects of odours (dimethyl sulphide, jasmine, peppermint, peppermint/ethanol mixture) on pulse/heart rate,

blood pressure, or respiratory physiological values (Pournemati et al., 2009; Raudenbush et al., 2002).

4.6 Pain, Sleep, and Appetite

This section reviews various other odour topics that are worthy of discussion but are not evaluated in detail in this report. Brief summaries of the effects of odours on pain perception, sleep, and taste/appetite are presented below. The studies discussed in this section were not included in the summary tables in Appendices D and E.

Perception of pain

Several studies have evaluated the impact of odour exposure on perception of pain, with some odours enhancing perception and others reducing perception. Pain perception is typically measured by subject ratings of pain intensity (no pain to intense pain) and/or pain hedonics (not unpleasant to most unpleasant).

With regards to enhancing pain perception, Martin (2006) found that exposure to either pleasant (lemon) or unpleasant (machine oil) odour increased the intensity of cold-induced pain. Villemure et al. (2003) found heat-induced pain unpleasantness to be higher in the presence of unpleasant odour (pyridine); no effects were found on pain intensity.

Regarding the potential analgesic effect of odour exposure, Marchand and Arsenault (2002) demonstrated that pleasant odours (primarily baby oil, massage oil, and almond extract) can lower heat-induced pain intensity and pain unpleasantness in women (but not men). Villemure and colleagues (2012, 2009) observed a reduction in heat-induced pain unpleasantness in response to pleasant food and floral odours; this analgesic effect was found to be mediated by changes in mood. Contrarily, others have shown no relationship between odour-induced mood and perception of pain, and suggested that different mechanisms are involved in odour-related changes in mood and pain perception (Villemure et al., 2003; Marchand and Arsenault, 2002).

Prescott and Wilkie (2007) found the pleasant and sweet odour of caramel to improve cold-induced pain tolerance (increase the duration of time a subject left their arm in cold water), compared to pleasant (aftershave) or unpleasant odour (civet). The positive effect on pain tolerance was found to be related to odour sweetness, rather than odour pleasantness. Ratings of pain intensity were not significantly impacted by any of the 3 odours in this study.

One study evaluating lavender and rosemary odours found that aromatherapy may not have a direct analgesic effect, but instead may retrospectively alter affective appraisal of a painful experience (Gedney et al., 2004).

Other studies demonstrated no significant impact of odours (green odour (green leaves), lavender, lemon) on ratings of pain intensity or unpleasantness for pain induced by hot/cold water (Kiecolt-

Glaser et al., 2008; Oka et al., 2008). However, Aou et al. (2005) noted an increase in pain perception threshold with exposure to green odour. Marchand and Arsenault (2002) found no effect of a range of neutral and unpleasant odours on pain perception.

Overall, the results regarding the effect of odour on perception of pain are quite varied, making it difficult to draw any major conclusions. Odour sweetness, odour pleasantness, and odour-induced changes in mood are potential factors that may influence the odour-pain relationship.

Sleep

Research regarding the effect of odours on sleep is varied and somewhat limited. The main consistent finding is that exposure to trigeminal odorants (CO_2) or combined trigeminal and olfactory odorants ($CO_2 + H_2S$) induces arousal during sleep (Heiser et al., 2012; Stuck et al., 2011, 2007; Grupp et al., 2008). In contrast, olfactory odorants (ammonium sulphide, artificial smoke, hydrogen sulphide, lavender, peppermint, pyridine, vanillin, vetiver oil) have not consistently lead to arousals during sleep, particularly in the deeper sleep stages (Heiser et al., 2012; Arzi et al., 2010; Grupp et al., 2008; Stuck et al., 2007; Carskadon and Herz, 2004).

Several odours (ammonium sulphide, lavender, vanillin, vetiver oil) were found to modify respiration during sleep; inhalation volume was decreased and exhalation volume was increased for several breaths after odour onset for both pleasant and unpleasant odours (Arzi et al., 2010). The investigators identified this change as a temporary respiratory rejection type response, and concluded that it is possible for odours to manipulate the respiratory system without inducing arousal.

Regarding the potential for odours to improve the quality of sleep, lavender odour was found to improve sleep quality, with more time being spent in both REM sleep and deep sleep (Torii, 1997). Another study of lavender odour demonstrated an increase in deep sleep and increased morning vigor following 30 minutes of pre-bedtime exposure (Goel et al., 2005). The authors concluded that lavender acts as a mild sedative and promotes deep sleep.

Exposure to peppermint odour for 30 minutes before bedtime had varied effects based on individual odour perception (Goel and Lao, 2006). Subjects rating peppermint as very intense had more total sleep than subjects rating peppermint as moderately intense. Additionally, those rating peppermint as sedating took longer to reach slow-wave sleep.

Raudenbush et al. (2003) found that exposure to jasmine odour continuously during sleep led to greater sleep efficiency and reduced sleep movement. Lower levels of anxiety and vigor were reported upon wakening; increases in afternoon alertness and cognitive performance were also observed. For lavender odour, a decrease in vigor upon awakening was observed, but no other significant effects on sleep were found.

Recently, exposure to a stimulating odour (Thesaron®) for 6 hours during sleep was found to suppress secretion of cortisol, a hormone related to stress (Hasegawa-Ohira et al., 2013). The authors attributed this effect to suppression of the hypothalamus-pituitary-adrenal system.

Schredl et al. (2009) demonstrated that olfactory stimuli can significantly impact the emotional tone of dreams. Unpleasant odour (H_2S) yielded dreams with more negative tones, while pleasant odour (phenylethyl alcohol) yielded dreams with more positive tones. Odours did not significantly affect dream content.

Sleep problems have been reported in several epidemiology studies of communities exposed to industrial or agricultural odours (see Chapter 3). The experimental data presented above demonstrate an ability of odours to influence sleep quality, emotional tone of dreams, the respiratory system, and stress hormone levels; however, these findings are insufficient to support or disclaim the epidemiological association between odours and sleep problems.

Taste/Appetite

It is generally recognized that food odours can stimulate appetite and enhance or alter the flavour of foods. Studies of various taste-smell combinations have found that odours can enhance or suppress the perceived sweetness, saltiness, or sourness of a tastant, an effect considered to be odorant and tastant specific (Prescott, 2012; Djordjevic et al., 2004). For example, odours of strawberry and lemon were found to enhance the sweetness of a sweet solution, but suppress perceived saltiness. Similarly, caramel odour was found to enhance sweetness, but suppress sourness. Level of enhancement of a particular taste by an odorant has been shown to correlate with perceived similarity or congruency of the odorant-tastant pair; the perceived congruency is dependent on prior associations with the odorant-tastant pair (Prescott, 2012).

With regards to odours and appetite, a recent study demonstrated that food odours increase general appetite, while non-food odours decrease general appetite (Ramaekers et al., 2013). Additionally, savoury odours were found to stimulate appetite for savory foods and decrease appetite for sweet foods; the reverse was observed for sweet odours (increase appetite for sweet foods, decrease appetite for savoury foods). Other studies have also found food-related odours to stimulate salivation, insulin release, and gastric acid secretion (Yeomans, 2006). In studies evaluating the use of odours in dieting, exposure to the pleasant odours of peppermint, banana, and green apple led to reduced hunger levels, reduced appetite, and weight loss (Reed et al., 2008; Mayer et al., 1999; Hirsch and Gomez, 1995). Recently, two studies found a non-food odorant (jasmine) or neutral unfamiliar odorant (menthyl acetate) to lower cravings for chocolate and other highly desired foods (Kemps and Tiggemann, 2013; Kemps et al., 2012).

Regarding the effects of environmental odours or unpleasant odours on appetite, very little data were found. In epidemiology studies, loss of appetite has been reported in response to some environmental odours (waste disposal site, fertilizer plant, pig farm), but not others (petroleum, hog odour) (Chapter 3). While it is generally accepted and often stated in the literature that unpleasant

odours lead to loss of appetite (ASHRAE, 2009; Schiffman et al., 1995a; Miner, 1981), there were no human experimental data found to support this.

4.7 Summary

This chapter summarizes the effects of odours on physiological and psychological responses in humans. The evidence indicates that odours can have a significant impact on physiological outcomes, irritant symptoms, mood, and cognition (task performance); however, this is not true for all odours in all situations. Responses appear to be odorant-specific and are heavily influenced by individual factors.

Understanding the effects of odours on physiological and psychological health is complicated by the wide variety of odours used and the lack of consistency across studies. Different odours lead to different outcomes and responses are often contradicting. The effect of an odour cannot always be predicted by its quality, hedonic, intensity, or familiarity, and it is likely that a combination of these factors, as well as personal characteristics and past experience, are involved in producing a response.

With regards to physiological outcomes, arousal parameters (HR, HRV, BP, respiratory rate, skin conductance) have been shown to be altered during odour exposure, though not in all cases. Odour characteristics (hedonic, intensity, chirality) and individual cognitive attitudes toward an odour have been identified as playing important roles in these responses. For irritant symptoms, results were contradictory and unclear. Some studies observed an increase in symptoms following odour exposure (headaches, eye irritation, nausea, dry eye), while other studies showed no change or a decrease in reported symptoms. Symptom reporting appeared to be highly mediated by cognitive variables and perceived health risks of the odour. This was demonstrated in multiple studies that gave subjects a healthful, harmful or neutral bias prior to odour exposure. Those told the odour was harmful were more likely to report irritant symptoms such as throat irritation, headache, nausea, and bad taste.

The primary conclusion from studies of odour and mood is that pleasant odours induce more positive moods (mainly increased happiness and improved overall mood) and unpleasant odours induce more negative moods (mainly increased anger and disgust). These results were observed with both subjective measures (self-reports) and objective measures (autonomic measurements) of mood. Further conclusions beyond this basic finding were difficult to identify, primarily due to variations in experimental methodology, the wide variety of odours used, and the influence of individual factors in mood responses. Similar to the results of irritant symptoms, odour-induced changes in mood were found to be influenced by individual biases towards an odour. Subjects given a healthy bias towards an odour tended to be in a more pleasant mood than those given a harmful bias.

For studies assessing the effect of odours on cognitive task performance, the results have been quite varied. Both pleasant and unpleasant odours were shown to improve or impair performance on memory and recognition tasks, math tasks, lexical tasks (word recognition, word decoding), and

motor reaction tasks. A number of studies also showed no effect of odours on task performance. The lack of consistency across studies makes it extremely difficult to draw any definitive conclusions about odours as a whole, and suggests that the impact of odours on task performance is odorant-specific. The observed effects of odour on task performance may be related, at least partially, to positive or negative affect.

With regards to the influence of odours on athletic performance, peppermint was the odour most often evaluated. Two studies found peppermint odour to enhance physical performance (e.g., increase running speed, reduce perceived effort), but not overall skill; the positive effect on performance was thought to be mediated by improved mood and motivation. Contrarily, two other studies did not find any impact of peppermint odour on athletic performance.

One experimental study was found that directly assessed the physiological or psychological effects of environmental odours. Schiffman et al. (2005) observed an increase in reports of headaches, eye irritation, and nausea in subjects exposed to diluted swine odour for 1 hour compared to control subjects. No significant differences were found for sore throat, nasal irritation, cough, HR, BP, respiratory rate, body temperature, pulmonary function, mood, or attention. This study is perhaps the most relevant in terms of identifying potential adverse effects from environmental odours; however, the results may have been confounded by the presence of irritant components in the odour sample.

Four hypotheses have been proposed to explain the mechanism in which odours exert psychodynamic effects (Johnson, 2011; Herz, 2009; Jellinek, 1997). Briefly, these include: (i) a quasi-pharmacological mechanism, in which odorants enter the bloodstream following inhalation and impact neural or hormonal activity; (ii) a hedonically-driven mechanism, in which effects are dictated by the perceived pleasure or displeasure from an odour; (iii) a purely psychological (placebo) mechanism, where effects on cognition are mediated by prior beliefs/expectancies about an odour; and (iv) a contextual (semantic) mechanism, where odorants exert specific effects because their odour has previously been associated with a particular stimulus/mood/behavior. All hypotheses carry supporting and opposing arguments and evidence, and none are able to fully explain the mechanism of odour-induced responses [see Johnson (2011) and Herz (2009) for detailed reviews]. Johnson (2011) concluded that the pharmacological properties of odour can influence cognition; however, these effects can also be influenced by odour-induced changes in mood, expectancy of cognitive effects, and contextual associations with the odour. Jellinek (1997) indicated that it is likely the mechanisms are not clearly separated, but rather come into play jointly to influence a response.

Two general conclusions can be drawn from the studies in this chapter. Firstly, the relationship between odours and physiological or psychological health is extremely complex and influenced by a wide variety of odour characteristics (e.g., hedonicity, familiarity) and individual factors (e.g., subjective expectations, personal experience, culture). Secondly, specific odours appear to have their own cognitive and mood profiles; this is evidenced by the varied results produced by odours of similar quality or hedonicity.

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5. Experimental Studies - Brain Responses

5.1 Introduction

Identifying the pattern of odour-induced brain activity is an integral part of understanding the human response to odours. The measurement and localization of neuronal activity helps to improve our knowledge of how the brain and body responds to odours of different quality, intensity, familiarity, and hedonicity. There are two main approaches for measuring neuronal activity: hemodynamic techniques that measure changes in regional cerebral blood flow (rCBF), and electromagnetic techniques that measure changes in olfactory event-related potentials (OERPs) (Cabeza and Nyberg, 2000). Hemodynamic techniques are typically used to identify regions of the brain involved in an olfactory response, while electromagnetic techniques are generally used to investigate changes in the timing of an olfactory response. For both techniques, brain activity is typically measured during exposure to pulses of odorant stimuli ranging from 200 ms to 1 second.

While studies of neuronal activity have helped to advance our knowledge in the study of olfaction, discrepancies between studies make it difficult to compare and contrast the results. The lack of standard experimental and analytical techniques, ambiguity in the description of activity location (coordinate x,y,z locations (voxels) vs Brodmann areas vs general terms describing broad areas), and the wide variety of brain areas examined all contribute to the difficulty in making comparisons. Discrepancies between studies may also be caused by methodological differences (e.g., varying exposure times, sniffing vs non-sniffing), temporal issues (e.g., varying rates of habituation in the region of interest), and the strong influence of individual past experience on odour responses (Royet and Plailly, 2004; Sobel et al., 2000). Further, interpretation of neuronal activity data is extremely complex and can require subjective judgments. Despite these problems, several advancements have been made in identifying the areas of the brain activated by odorants with different qualities and during different olfactory tasks (i.e., hedonic judgments, intensity ratings, discrimination tasks).

The main cortical regions involved with odorant processing are termed the primary olfactory cortex (POC; includes primarily the piriform cortex, anterior olfactory cortex, olfactory tubercle, amygdala, and the entorhinal cortex) and the secondary olfactory cortex (SOC; includes the orbitofrontal cortex (OFC), lateral entorhinal cortex, and insular cortex). The following section provides a very high level summary of the key findings of neuronal responses induced by exposure to odours, mainly in these cortical regions. The intention of the summary is not to provide a detailed description of odour processing, but rather to offer a brief overview of the regions of the brain activated during different aspects of olfaction. For a basic introduction to cortical processing of odours, refer to Section 2.2.2.

5.2 Hemodynamic Techniques

The hemodynamic techniques used in olfactory studies are functional magnetic resonance imaging (fMRI) and, to a lesser degree, positron emission tomography (PET) and near-infrared spectroscopy (NIRS). The fMRI technique estimates neuronal activity using blood oxygen level-dependant (BOLD) contrasts, a measure of oxygen metabolism relative to rCBF and regional cerebral blood volume (Di Salle et al., 1999; Kim and Ugurbil, 1997). The method is non-invasive, non-radioactive, has relatively high spatial resolution, and has improved temporal resolution over PET (Royet and Plailly, 2004; Savic, 2002b; Zald and Pardo, 2000). The primary drawbacks are its susceptibility to movement and noise artifacts and difficulty compensating for the variation in magnetic permeability between brain tissue, bone, and air (Savic, 2002a,b; Zald and Pardo, 2000).

In PET, a radioactive tracer is injected into the bloodstream and radioactivity is measured in different areas of the brain using a scanner; a region with a higher radioactive signal indicates a region of increased blood flow and thus, increased neuronal activity (Cabeza and Nyberg, 2000, 1997). PET benefits from a high spatial resolution, the ability to simultaneously visualize neuronal activity across multiple regions, and better access to areas of the brain that are difficult to image using other techniques (Royet and Plailly, 2004; Zald and Pardo, 2000). Weaknesses of PET include poor temporal resolution, low signal to noise ratio (especially during shorter scans), and the safety limit on the number of scans a subject can undergo due to radiation exposure.

With NIRS, hemodynamic activity is measured based on changes in oxy-hemoglobin, deoxy-hemoglobin, and total hemoglobin in the region of interest (Kokan et al., 2011). A higher concentration of oxygenated hemoglobin is considered to reflect higher neuronal activity. NIRS has been used in only a handful of olfactory studies, primarily in assessments of newborn subjects.

The main topics of interest for this section are the changing levels of activity in the human brain during odour perception, and more specifically, the differences that occur when using odours with varying intensity, hedonicity and familiarity properties. A number of studies have also examined the impact of paying attention versus not paying attention to an odour. A tabulated summary of all studies is provided in Appendix F. For a description of the odorants used in these studies, refer to Appendix B.

5.2.1 Summary of fMRI and PET Data

Perception

More than 20 different brain regions have been noted as showing increased activity in response to perception of an odour (Table 5-1a). The activated regions have ranged from known olfactory-related areas such as the OFC and amygdala, to lesser-mentioned areas such as the claustrum and substantia nigra. The patterns of odour-induced activity vary greatly between studies; this is likely a result of differences in the odorants used, the experimental methodology, image resolution, data analysis techniques, and brain region terminology. The areas that most commonly demonstrated

activation during odour perception are the amygdala, piriform cortex, OFC, and insular cortex (Savic, 2005; Sobel et al., 1998; Zald and Pardo, 1997; Zatorre et al., 1992). Involvement of these areas was confirmed in a recent meta-analysis of 45 fMRI and PET studies (Seubert et al., 2013).

Recent studies have used fMRI analyses to assess the functional connectivity of different brain regions during olfaction. Nigri et al. (2013) found that olfactory information is scattered by the amygdala and piriform cortex (both had high afferent connectivity (i.e., connecting towards)) and then gathered and integrated in the medial OFC (had high efferent connectivity (i.e., connecting outwards)). Karunanayaka et al. (2013) demonstrated several parallel neural networks involved in olfaction; these included: I) bilateral parietal-occipital association cortices, II) bilateral striatum, III) bilateral primary olfactory cortex, IV) bilateral dorsolateral prefrontal cortex, and V) bilateral polar and rostral prefrontal cortex. Networks II and III were considered to be directly related to primary olfactory sensory-perceptual processing as well influencing downstream effects associated with affective learning, memory, and motivation/reward. Networks I, IV, and V were considered to be related to the higher order cognitive processing of olfactory information (in the parietal, occipital and prefrontal cortices).

Hedonicity

Odour hedonicity refers to the perceived pleasantness or unpleasantness of an odour. Most studies assessing brain activity induced by odours of varying hedonicity have found that pleasant and unpleasant odours activate different regions of the brain (Garcia-Gonzalez et al., 2011; Reske et al., 2010; Grabenhorst et al., 2007; Zelano et al., 2007; Popp et al., 2004; Gottfried and Dolan, 2003; Rolls et al., 2003; Royet et al., 2003; Gottfried et al., 2002; Savic et al., 2002). Table 5-1b presents a list of brain regions activated in response to pleasant and unpleasant odours. Regions typically found to respond to pleasant odours include the frontal gyrus, left superior temporal gyrus, right parietal cortex, and regions of the OFC (Garcia-Gonzalez et al., 2011; Reske et al., 2010; Popp et al., 2004; Gottfried and Dolan, 2003). Recent studies have identified a correlation between hedonicity ratings and activity in the OFC (Grabenhorst et al., 2007; Rolls et al., 2003). Brain areas found to be activated by unpleasant odours include the piriform cortex, OFC, amygdala, superior temporal gyrus, precentral gyrus, cingulate cortex, and the insula (Garcia-Gonzalez et al., 2011; Reske et al., 2010; Bensafi et al., 2007; Zelano et al., 2007; Popp et al., 2004; Gottfried and Dolan, 2003; Schneider et al., 1999). Activity in the mid and lateral-OFC and the left amygdala has been found to negatively correlate with hedonicity ratings (Grabenhorst et al., 2007; Rolls et al., 2003; Zald, 2003; Zald and Pardo, 1997).

Regions of brain activity may vary based on an individual's preference for an odour. In a study of phenylethyl alcohol and undecalone, subjects perceiving an odour as unpleasant showed more activity in the left middle OFC and right lateral OFC, while those perceiving an odour as pleasant showed more activity in the right anterior cingulate cortex (Katata et al., 2009).

Table 5-1: Regions of the brain activated during different aspects of olfaction (measured by fMRI): (a) passive perception of odours; (b) pleasant or unpleasant odours; (c) olfactory tasks

	Regions Activated	References
a. Perception	amygdala, caudate nucleus, cerebellum, cingulate cortex, claustrum, cuneus, entorhinal cortex, frontal cortex, hippocampus, hypothalamus, insula, occipital cortex, OFC, parahippocampal gyrus, parietal cortex, perisylvian region, piriform cortex, precentral gyrus, putamen, substantia nigra, supplemental motor area, temporal gyrus, thalamus, tubercle	Karunanayaka et al., 2013; Nigri et al., 2013; Hummel et al., 2012, 2005; Kjelvik et al., 2012; Katata et al., 2009; Ciumas et al., 2008; Lombion et al., 2008; Plailly et al., 2008; Djordjevic et al., 2005; Osterbauer et al., 2005; Porter et al., 2005; Wang et al., 2005; Gottfried and Dolan, 2003; Kareken et al., 2003; Rolls et al., 2003; Royet et al., 2003; Gottfried et al., 2002; Bengtsson et al., 2001; Kobal and Kettenmann, 2000; Qureshy et al., 2000; Savic and Gulyas, 2000; Savic et al., 2000; Sobel et al., 2000, 1998; Levy et al., 1999, 1997; Yousem et al., 1999a, 1999b, 1997;Koizuka et al., 1994; Zatorre et al., 1992
b. Hedonicity	*Pleasant odours*: amygdala, frontal gyrus, insula, occipital cortex, OFC, parietal cortex, piriform cortex, temporal gyrus	Krusemark and Li, 2012; Garcia-Gonzalez et al., 2011; Reske et al., 2010; Bensafi et al., 2008, 2007; Vaidya et al., 2007; Zelano et al., 2007; Winston et al., 2005; Popp et al., 2004; Gottfried and Dolan, 2003; Heining et al., 2003; Rolls et al., 2003; Wicker et al., 2003; Gottfried et al., 2002; Savic et al., 2002; Zald et al., 1998; Zald and Pardo, 1997
	Unpleasant odours: amygdala, cerebellum, cingulate gyrus, claustrum, frontal gyrus, hippocampus, hypothalamus, insula, lingual gyrus, motor areas, occipital cortex, OFC, parietal lobule, precentral gyrus, piriform cortex, pons/medulla, putamen, striatum, temporal gyrus, thalamus	
c. Olfactory Tasks	*Hedonicity judgment*: amygdala, cerebellum, cingulate cortex, claustrum, hippocampus, hypothalamus, insula, lateral sulcus, lingual gyrus, occipital cortex, OFC, parietal cortex, piriform cortex, prefrontal cortex, temporal gyrus	Rolls et al., 2010, 2008; Plailly et al., 2007; Kareken et al., 2003; Royet et al., 2003; Royet et al., 2001, 2000; Savic et al., 2000; Zatorre et al., 2000
	Intensity judgment: cerebellum, frontal gyrus insula, occipital cortex, OFC, prefrontal cortex, premotor cortex	
	Discrimination task: brainstem, Broca's area, caudate nucleus, cerebellum, cingulate cortex, frontopolar gyrus, subiculum-hippocampus, insula, OFC, prefrontal cortex, temporal gyrus, thalamus	
	Identification task: Broca's area, frontal gyrus, insula	

There are some inconsistencies in the findings of hedonicity studies making it difficult to draw concise conclusions about the impact of odour hedonic on cortical activity. However, the regions that appear to be most involved in hedonic responses are the amygdala and the OFC.

The amygdala is part of the limbic system (a group of brain structures associated with controlling emotion) and is considered to play a role in sensory-related emotional processing and memory (Zald, 2003). Recent research has indicated a role for the amygdala in the cognitive response to aversive odours. For instance, activity in the amygdala has been found to correlate with subjects' aversiveness ratings of odorants (Zald and Pardo, 2000, 1997). Interestingly, Krusemark and Li (2012) demonstrated a correlation between subjects' ratings of personal anxiety and malodour-induced functional connectivity between the piriform cortex and the amygdala. This suggests that the perceptual network in anxious individuals may have a hyper-sensitivity to olfactory threat.

Some studies have also observed an increase in activity in the amygdala with pleasant odours (Gottfried et al., 2002; Bengtsson et al., 2001; Royet et al., 2000), while others have not (Zald and Pardo, 2000; Zatorre et al., 1992). Recently, Winston et al. (2005) found that the response of the amygdala involves both the intensity and hedonic aspects of an odour. This is in contrast to the findings of Anderson et al. (2003), who found that the amygdala responds to changes in odour intensity but not valence.

Overall, these results support a role for the amygdala in the emotional processing of an odour; however, a definitive function has not yet been determined. It has been suggested that the amygdala is either directly involved in the processing of emotionally-relevant odours, or is indirectly involved by facilitating the transmittance of a neuronal signal into an emotional response (Zald and Pardo, 1997).

With regards to the role of the OFC, activity increases have been observed during exposure to unpleasant odour (Reske et al., 2010; Grabenhorst et al., 2007; Popp et al., 2004), pleasant odour (Djordjevic et al., 2005; Wang et al., 2005), or both unpleasant and pleasant odours (Ishimaru et al., 2004; Royet et al., 2000). Anderson et al. (2003) demonstrated that different regions of the OFC are activated by odours of varying hedonicity; increased activity was observed in the medio-rostral OFC with pleasant odours, and the left lateral OFC with unpleasant odours. A high correlation between odour-induced activity in the left OFC and the left amygdala has been observed with aversive odours, suggesting a strong connectivity between the amygdala and the OFC during olfaction (Royet and Plailly, 2004; Zald and Pardo, 1997). Stronger activities in the left OFC and left amygdala induced by hedonic odours provide evidence for the dominance of the left hemisphere of the brain in olfactory emotional processing (Royet et al., 2003). Specific regions of the OFC have also shown activation during sniffing of a pleasant odour or when making hedonic judgments (Rolls et al., 2010, 2008; Grabenhorst and Rolls, 2009; Kareken et al., 2004; Royet et al., 2003, 2001, 2000). Though the findings across studies are not always consistent, the main conclusion that can be taken from the above results is that the OFC plays some role in the assessment of the emotional quality of an odour.

Intensity

Odour intensity refers to the perceived strength of an odour. Odours of different intensities can have varying pleasantness ratings, can be perceived as different odours, and may induce different odour responses. Grabenhorst et al. (2007) reported that intensity ratings correlate with activity in primary olfactory areas such as the piriform cortex and the anterior insula. Similarly, positive correlations between odour intensity and piriform cortex activity were found in other studies (Winston et al., 2005; Anderson et al., 2003; Rolls et al., 2003). Activity levels in the amygdala, hippocampus, and entorhinal cortex have also been shown to correlate with intensity ratings (Anderson et al., 2003; Rolls et al., 2003; Zald and Pardo, 2000).

Evidence for a relationship between odour intensity and OFC activity has been contradicting. Winston et al. (2005) found intensity ratings to correlate with OFC activity; however, Grabenhorst et al. (2007) and Rolls et al. (2003) found no relationship between intensity and OFC activity.

Familiarity

Studies comparing activations induced by odours of varying familiarities have generally found that familiar and unfamiliar odorants activate different cortical pathways (Kjelvik et al., 2012; Ciumas et al., 2008; Savic and Berglund, 2004; Royet et al., 2001, 1999). Savic and Berglund (2004) observed activations in the piriform cortex, amygdala, and cingulate cortex in response to both familiar and unfamiliar odorants, with additional activations in the left frontal cortex, the right parahippocampus, and the left parietal cortex by familiar odorants. They summarized that, in addition to the expected olfactory activations, familiar odorants appear to activate regions of the brain associated with memory and language. Royet et al. (2001, 1999) studied brain activity while subjects performed familiarity judgments of 32 odorants. Increases in activity were found in the right OFC, frontal gyrus, subcallosus gyrus, left inferior and superior frontal gyri, and anterior cingulate gyrus. Activations of the right OFC were considered the result of a comparison being made between the present odour and stored odour information, thus reflecting a type of olfactory memory. Kjelvik et al. (2012) assessed brain activations in response to odours that were identifiable and non-identifiable by the subjects. The investigators found the entorhinal cortex and hippocampus to be involved specifically in odour identification, while the piriform cortex and OFC are involved in both smelling and odour identification. Herz et al. (2004) compared brain responses evoked by emotionally-meaningful familiar perfumes and neutral non-familiar perfumes. They reported increases in activity in the amygdala and hippocampal regions during exposures to perfumes that had a positive emotional valence, relative to the neutral perfume.

Olfactory tasks

Several research groups have looked at the differences in activation during olfactory tasks such as odour discrimination, odour identification, or judgments of hedonicity or intensity (Table 5-1c). Activated regions during olfactory tasks typically reflect olfactory processes as well as task-specific

brain functions. Studies assessing subjects during hedonicity judgments have found increases in a wide variety of brain regions, with the insula and the OFC being the most common (Rolls et al., 2008; Royet et al., 2003, 2001, 2000; Zatorre et al., 2000). The lateral OFC is considered to be involved in the conscious assessment of pleasant and unpleasant odorants (Porter et al., 2005). Judgments of odour intensity seem to recruit a smaller number of areas than hedonicity judgments. This may be due to intensity judgments being a less complex task that does not involve working memory, thereby recruiting fewer brain regions (Savic et al., 2000).

Karekan et al. (2003) studied brain activations during an odour identification task; increases in activity were noted in the Broca's area, left inferior frontal gyrus, posterior insula, and left anterior insula. Activity in the left inferior frontal gyrus was considered to represent semantic associations. Studies of odour discrimination tasks have observed increased activity in the insula, frontopolar gyrus, frontal gyrus, hippocampus, temporal gyrus, and Broca's area (Plailly et al., 2007; Kareken et al., 2003; Savic et al., 2000). The involvement of the hippocampus and the frontal lobe are thought to reflect working memory and semantic associations during odour discrimination.

Paying attention to an odour (attend condition) versus being distracted from an odour (non-attend condition) has also been shown to influence odour-induced brain activity. Attending to an odour has been associated with activations in the right OFC, frontal piriform cortex and olfactory tubercle, while inattentive odour detection has been found to activate the cingulate cortex and central posterior OFC (Sabri et al., 2005; Zelano et al., 2005). Zelano et al. (2005) also noted that the activity increases in the piriform cortex and tubercle occurred in anticipation of the odour task, prior to odour exposure; they suggested that this response may reflect a mechanism preparing the olfactory bulb for odour presentation.

In a study assessing the impact of odour warnings, Murata et al. (2007) found that subjects given prior warning showed activation increases in the putamen, insula, amygdala, and inferior frontal gyrus in response to an unpleasant odour. When no warnings were given, activity increased in the putamen, anterior cingulate cortex, entorhinal cortex, and inferior frontal gyrus. The authors suggested that putamen/insula activation in the expected condition may be a result of focus/concentration or expectation, while cingulate cortex activation in the unexpected condition may be due to lack of expectation or difficulty recognizing an unexpected odour.

Stress-inducing tasks

Tanida et al. (2008) evaluated the impact of continuous exposure to a floral green fragrance on activity in the prefrontal cortex while under stress. Following 4 weeks of exposure, subjects showed a shift in the dominant side of prefrontal cortex activity (from right side to left side) during a stress-inducing arithmetic task. This change in prefrontal cortex activity was associated with a reduction in facial sebum secretion (in subjects who showed right-dominant prefrontal cortex activity and hypersecretion of sebum prior to odour exposure), an effect thought to be mediated by reduced

activity of the hypothalamic-pituitary-adrenal axis. The authors concluded that the mechanism of fragrance effects on systemic response to mental stress may involve the prefrontal cortex.

Pain modulation

Two recent studies evaluated the impact of odours on neural responses during heat-induced pain. Villemure and Bushnell (2009) found pleasant odours to reduce pain-related neural activity in the anterior cingulate cortex, medial thalamus, and primary and secondary somatosensory cortices. The effect of odour on pain unpleasantness was found to be mediated by mood, and activity in the lateral inferior frontal cortex correlated with the mood-related pain modulation. In the follow-up analysis of the same dataset, activity in the left and right ventral striatum was found to correlate with the amount of pain reduction during pleasant odour exposure (Villemure et al., 2012). Further, ventral striatum activity negatively covaried with activity in the medial thalamus and dorsal anterior cingulate cortex, two areas thought to be involved in perception of pain unpleasantness. Overall, the authors concluded that the ventral striatum is involved in the analgesic effect of positive mood changes induced by pleasant odours on pain unpleasantness.

Imagined vs real odours

Studies comparing brain activity induced by real odours and imagined odours have generally found that the two conditions induce similar patterns of activity. Bensafi et al. (2007) found that imagined odours produced a similar activity pattern to real odours in the primary olfactory cortex and the insular cortex. Levy et al. (1999) showed similar patterns of activity for real and imagined odours in the frontal cortex and temporal cortex. In both studies, activity increases were generally greater with real odours than imagined odours. These results suggest that imagined and real perception of odours may involve similar neural pathways.

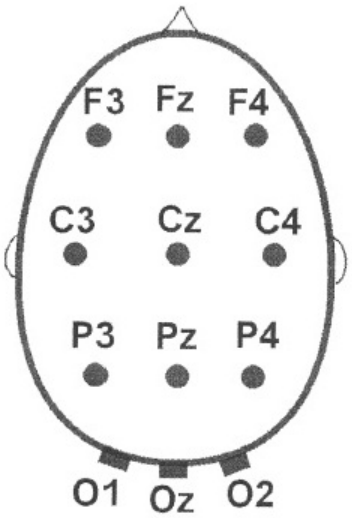
5.3 Electromagnetic Techniques

The two types of electromagnetic techniques used in olfactory studies are electroencephalography (EEG) and magnetoencephalography (MEG), with EEG being the most common. Both techniques assess neuronal activity in the brain: EEG measures electric potential differences, while MEG measures the magnetic field produced by the same electrical activity (Hämäläinen et al., 1993).

For EEG, electrical activity is recorded using electrodes placed at specific locations on the scalp; Figure 5-1 displays the locations of 12 common electrode sites (Stenberg et al., 2000). In studies of olfaction, up to 80 electrode sites have been used, though most studies focus on the 3 midline sites Fz (frontal), Cz (central), and Pz (parietal). The measured outcome of EEG is referred to as an olfactory event-related potential (OERP) or a chemosensory event-related potential, which reflect voltage fluctuations in the scalp. A typical chemosensory event-related potential consists of a series of peaks of negative polarity (N1, N2) and positive polarity (P1, P2, P3a (or P3-1), P3b (or P3-2)) (Figure 5-2). These peaks may also be named N100, N200, P300, etc., in reference to the time (in

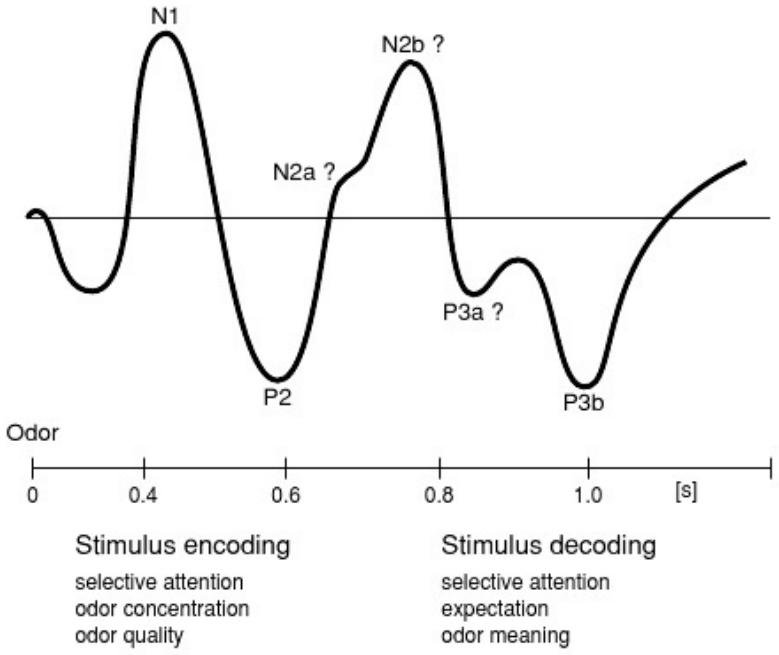
milliseconds) at which the peaks occur following stimulus onset. Three main pieces of information can be derived from the analysis of event-related potentials: speed of odour processing (peak latencies), strength of the response (peak amplitudes), and location of activity (distribution across scalp) (Pause, 2002). Changes in the amplitudes and latencies of peaks in response to different odours can be helpful in identifying the cortical regions and mechanisms involved in odour processing, as well as the inter- and intra-individual differences in odour perception. Differences in EEG recording conditions, odour exposure conditions, and sample group can contribute to variations in OERPs (Boesveldt et al., 2009). It is important to also note that there is some inconsistency in the identification and naming of peaks, which can complicate comparisons across studies (Rombaux et al., 2006; Pause and Krauel, 2000).

Figure 5-1: Schematic diagram of electroencephalography (EEG) electrode positions (Stenberg et al., 2000)



F=frontal; C=central; P=parietal; O=occipital; z=midline sites.

Figure 5-2: Chemosensory event-related potential components and their relation to stimulus encoding and decoding (Pause, 2002)



In the less-commonly used MEG technique, a neuromagnetometer placed around a subject's head is used to measure weak magnetic fields produced by neuronal current (Hämäläinen et al., 1993). Through detection of magnetic fields at multiple cortical sites, researchers can localize the areas of the brain activated by an odour. The measured outcome in MEG is referred to as an olfactory event-related field (OERF); changes in OERF magnitudes and latencies can be used to identify areas of increased activity following odour exposure.

EEG and MEG techniques are objective, non-invasive, and offer extremely high temporal resolution (milliseconds) (Wendel et al., 2009). EEG is sensitive to neuronal activity in the sulci and gyri (grooves on the surface of the brain), while MEG is sensitive to neuronal activity in the sulci only (Okada et al., 1999). MEG offers improved spatial resolution over EEG; however, it can be difficult to detect activity in deeper brain regions such as the piriform and olfactory cortices (Rolls et al., 2010; Miyanari et al., 2006).

The following section provides a review of the findings from human EEG and MEG olfactory studies. A tabulated summary of these studies can be found in Appendix G.

5.3.1 Summary of Electroencephalography (EEG) Data

Temporal changes

The most consistent finding among studies assessing EEG temporal changes is that odour concentration (or intensity) is associated with shorter peak latencies of the early peaks N1 and P2. This effect has been observed with odours typically perceived as pleasant (amyl acetate, citral, linalool, menthol, mint, phenylethyl alcohol, and vanillin) (Poncelet et al., 2010; Covington et al., 1999; Tateyama et al., 1998; Pause et al., 1997, 1996). For the later peaks (P3a, P3b), most studies have shown no association between odour concentration and peak latencies (Covington et al., 1999; Pause et al., 1997,1996).

Two studies were found directly comparing peak latencies for pleasant and unpleasant odours. Croy et al. (2013) observed shorter N1 and P2 peak latencies with unpleasant odour (hydrogen sulphide (H_2S) compared to pleasant odour (PEA, peach). Contrarily, Masago et al. (2001) found that peak latencies did not differ for unpleasant (eugenol) and pleasant odour (limonene). With regards to varying durations of exposure, no effect of odour duration on peak latencies was found for odours of amyl acetate, H_2S, or phenylethyl alcohol (Frasnelli et al., 2006; Wang et al., 2002).

The timing of OERPs may be influenced by an individual's bias towards an odour. In a study of isobornyl acetate, Laudien et al. (2008) found that peak latencies were influenced by a healthy or harmful bias towards the odour. N1, P2, and P3b latencies differed between bias groups: compared to subjects given a neutral bias, subjects told the odour was a healthy extract had decreased latencies, while those told the odour was hazardous had increased latencies. Bulsing et al. (2010, 2007) also observed an effect of bias on peak latencies in studies of H_2S and phenylethyl alcohol odours. For both odours, subjects in the painful expectancy condition had decreased N1 latencies compared to subjects in the non-painful condition. All studies concluded that negative odour expectancies/biases can impact early odour processing.

Attending to an odour has also been shown to modulate the timing of OERPs. In two studies assessing odours of limonene (pleasant) and eugenol (unpleasant), latencies of all peaks (N1, P2, N2, P3) were shorter in the attend condition relative to the non-attend condition (Masago et al., 2001; Krauel et al., 1998). Similarly, peak latencies were found to be shorter when subjects performed an intensity judgment of the pleasant odour amyl acetate (Geisler and Murphy, 2000). Krauel et al. (1998) suggested that the shorter peak latencies represent a more efficient transduction of olfactory signals during attentive odour exposure. In contrast to these studies, Pause et al. (1997) found that paying attention to pleasant odour had no effect on OERP latencies.

Amplitude changes

Several studies have shown that OERP amplitudes can be influenced by odour concentration. Higher odour concentrations have been associated with increases in P1 amplitude in response to toluene (Prah and Benignus, 1992), P2 amplitude in response to H_2S and butanol (Stuck et al., 2006;

Lorig et al., 1996, 1993), and all peak amplitudes in response to vanillin (Tateyama et al., 1998). Additionally, in a study of the pleasant odour citral, Pause et al. (1996) demonstrated that amplitudes of early OERP peaks (N1, P2) are impacted by odour concentration, but late peaks (P3a, P3b) are not. Contrarily, studies of the pleasant odours amyl acetate, linalool, and menthol showed no association between odour concentration and OERP peak amplitudes (Covington et al., 1999; Pause et al., 1997). Pause et al. (1997) suggested that odours of different concentrations encode qualitatively different stimuli rather than stronger or weaker neuronal responses.

In a comparison of odours of varying hedonicity, unpleasant odour (H_2S) produced higher P2 amplitudes than pleasant odours (phenylethyl alcohol, peach) (Croy et al., 2013). The increase in P2 amplitude attenuated with repeated exposure to H_2S, and the authors suggested this may be related to a reduced emotional salience and subsequent decrease in attention towards the odour.

The late positive peak P3 is considered to reflect subjective or emotional processing of odours. Masago et al. (2001) found the pleasant odour limonene to produce greater P3 amplitude than the unpleasant odour eugenol. Contrarily, Lundström et al. (2006b) found that individual hedonicity ratings of androstenone negatively correlated with P3 amplitude. Paying attention to an odour can also impact P3 peaks. P3 amplitude was greater in the attend condition relative to the non-attend condition for the pleasant odours amyl acetate, limonene, linalool, and menthol, and the unpleasant odour eugenol (Masago et al., 2001; Geisler and Murphy, 2000; Krauel et al., 1998; Pause et al., 1997). Pause et al. (1997, 1996) concluded that early OERP components are modulated by exogenous odour properties (concentration), while late OERP components are modulated by subjective odour significance.

Three studies have examined the influence of individual bias towards an odour on OERP amplitudes. Laudien et al. (2008) found that OERP peak amplitudes were not influenced by a healthy or harmful bias towards the odour isobornyl acetate. Similarly, Bulsing et al. (2007) found no effect of painful versus non-painful expectations of an odour on OERP amplitudes. In a follow-up study, Bulsing et al. (2010) demonstrated N1 and P3 peak amplitude increases for subjects expecting a painful stimulus compared to subjects expecting a non-painful stimulus.

Distribution of activity

The distribution of odour-induced cortical activity has been discussed in more detail in the introduction of Section 5.2.1 (Summary of fMRI and PET Data). The fMRI method offers improved spatial resolution and thus is more suited for discussions of activity location than EEG. This section will instead briefly discuss the timing of cortical activity in different regions, and also touch on the relationship between location of EEG activity and changes in mood.

A recent study by Lascano et al. (2010) utilized EEG to assess the temporal sequence of activation in different areas of the brain. Four distinct steps in odour processing occurring between 200 and 1000 ms following the odour stimulus were identified: (1) ipsilateral activation of mesial and lateral temporal cortex (amygdala, parahippo-campal gyrus, superior temporal gyrus, and insula) (~250-350

ms); (2) contralateral activation of mesial areas (~350-550 ms); (3) activation of lateral temporal areas (~550-600 ms); (4) activation of middle and inferior frontal gyrus (~600-850 ms). They concluded that odours are processed first ipsilaterally to the stimulated nostril, followed by activation in both hemispheres.

Diego et al. (1998) assessed the effect of the aromatherapeutic agents lavender, a relaxant, and rosemary, a stimulant, on EEG activity and mood. They found that lavender increased alpha and beta 2 activity in the frontal area, which was related to an increase in drowsiness. Further, rosemary led to decreased alpha activity in the frontal area, which was related to increased alertness. This study provides electrophysiological support for the theory that aromas can lead to psychological and physiological changes. In follow-up studies, Field et al. (2005) and Sanders et al. (2002) examined frontal EEG asymmetry in response to rosemary and lavender. Lavender, but not rosemary, was found to increase left frontal EEG activity relative to right frontal EEG activity. The authors stated that, as greater relative left frontal EEG activity has been found to be an indicator of positive mood, the studies support the notion that lavender odour may have antidepressant properties. These findings are further supported by Kline et al. (2000), who found that vanillin (pleasant odour), but not valerian (unpleasant odour), induced greater relative left frontal EEG activity.

5.3.2 Summary of Magnetoencephalography (MEG) Data

The few olfactory MEG studies that have been conducted have reported odour-induced activity in several cortical regions - the superior temporal plane, superior temporal sulcus, parainsular cortex, insular cortex, orbitofrontal sulcus, and Sylvian fissure regions (Kobal and Kettenmann, 2000; Tonoike et al., 1998; Kettenmann et al., 1997, 1996; Sakuma et al., 1997). Kettenmann et al. (1997) noted activity in the left insular area in response to pleasant but not unpleasant odour, suggesting a possible role for odour hedonic in this region. Further, Miyanari et al. (2006) reported odour-induced activity in broad areas across the frontal and parietal lobes, with processing of strong and weak odours occurring in different areas (left hemisphere for strong, right hemisphere for weak).

In a series of MEG studies, Walla et al. (2008, 2005, 2003a,b, 2002) assessed changes in brain activity during odour exposure and word or face encoding. They found that simultaneous processing of olfactory information with visual word or facial information leads to a competition for cortical resources. The neurophysiological result was a decrease in early MEG activity at ~300 to 500 ms (relative to odour exposure with no word or facial information) reflecting the competition for higher cognitive resources between the two sensory systems. The behavioral result was poorer performance on subsequent recognition of words/faces, reflecting an impairment during word or face encoding in the presence of odour. Overall, the authors concluded that odour processing involves similar cognitive functions as face/word encoding, and that odours can have a strong influence on higher cognitive functions. This finding is further supported by Boesveldt et al. (2009), who found that odour exposure induced an MEG activity pattern similar to that produced by cognitive tasks.

5.4 Summary

One of the main points that can be taken from this chapter is that the effect of odours on brain activity is extremely complex. Using fMRI to localize brain activity, more than 30 different regions have been indicated as being involved in some aspect of olfaction. Regions of activity have included known olfactory areas such as the OFC and amygdala, as well as areas generally considered to be outside the olfactory system (e.g., lingual gyrus, pons/medulla), possibly relating to task-specific brain functions. The pattern of neuronal activity can be influenced by a wide variety of factors, such as odour characteristics (e.g., intensity, hedonicity), the task at-hand (e.g., paying attention to an odour, odour identification), subjective association with an odour (e.g., familiarity, emotional association), and pre-conceived expectations about an odour. Differences in study design, type of odorant used, and data interpretation can also contribute to variations in calculated activity patterns.

With regards to hedonicity, fMRI studies of pleasant and unpleasant odours have been shown to induce activity in similar or different regions of the brain, depending on the particular study. The lack of consistency across studies makes it difficult to draw any definitive conclusions regarding how pleasant or unpleasant odours affect the brain. There appears to be a complex array of factors that are involved in the response to odour hedonic, such as type of odour (e.g., food vs floral), familiarity, and situational context. The OFC and the amygdala are often found to be activated by both pleasant and unpleasant odours, and are considered to play a strong role in emotional processing. Additionally, the involvement of many of the structures of the limbic system (e.g., amygdala, hippocampus, cingulate gyrus) helps to explain the emotional response to a hedonic odour. Unpleasant odours appear to recruit a larger number of brain regions than pleasant odours, which may reflect a fight or flight reaction to odours considered to be threatening. It has also been shown that subjects with anxiety have a neural hyper-sensitivity to unpleasant odour in the amygdala.

The key conclusion from the electromagnetic studies is that the timing and strength of an OERP can be altered by odour concentration, hedonicity, odour bias/expectation, and paying attention to an odour. In general, early peaks (N1, P2) are thought to reflect stimulus encoding processes as well as cognitive processing, and are influenced by odour concentration, odour quality, and the level of attention and expectations of the subjects. Late peaks (N2, P3) are thought to reflect cognitive and emotional processing of the odour (stimulus decoding), and are influenced by individual cognitive associations with an odour as well as the level of attention of the subjects.

At present, the clinical application of odour-induced neuronal activity studies is rather limited. While the temporal and spatial characteristics of neuronal activity have been assessed in detail, the relationships between these changes and health responses are poorly understood. Some studies have suggested that odour-induced alterations in neuronal activity can be linked to certain behaviors/ responses. For example, increases in relative left frontal EEG activity (induced by pleasant odour) are considered an indicator of positive mood. Additionally, lavender-induced increases in frontal activity have been linked to drowsiness, while rosemary-induced decreases in frontal activity have

been linked to alertness. It has also been demonstrated that a shift in the dominant side of stress-induced prefrontal cortex activity (from the right side to the left side) is associated with reduced facial sebum secretion, an effect thought to be mediated by the hypothalamic–pituitary–adrenal axis. Further, odour-induced modulation of pain was found to be related to changes in activity in the ventral striatum, medial thalamus, and anterior cingulate cortex. While these studies provide insight into the link between neural activity and behaviors/responses, studies of this nature are few in number and additional research in this area is needed before further conclusions can be drawn.

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6. Overall Evaluation

The aim of Chapter 6 is to summarize information from all prior chapters and provide an overall evaluation of the evidence. The chapter discusses the epidemiology and experimental findings regarding the association between odours and health, the potential mechanisms for odour-induced health effects, and current knowledge gaps.

6.1 Summary of Findings

6.1.1 Epidemiological Studies

Several epidemiology studies have demonstrated an association between exposure to odours and odour annoyance. This has been observed with a variety of odour sources (petrochemical plants, pulp mills, sewage/waste treatment plants, fertilizer plants, pig-rearing facilities) in several countries around the world. A number of different methods for estimating odour exposure have been used: zone of residence/residence distance to facility, self-reported frequency/intensity of odour, trained panelists estimating odour frequency, and direct measures of odour concentration. Regardless of the measure of exposure used, odours were typically found to correlate with frequency and intensity of odour annoyance. Studies assessing the influence of odour hedonic on this relationship demonstrated that degree of annoyance is lowest with pleasant odours and highest with unpleasant odours; odour hedonic is thus considered to play an important role in odour-induced annoyance.

Residents of communities located near odour-emitting facilities have been found to report a higher number of health symptoms compared to residents of control communities. Reported symptoms included cough, nausea, congestion, eye irritation, headache, dizziness, sleep problems, diarrhea, chest pain, and respiratory symptoms; these symptoms have been observed in response to odours from petroleum refineries, livestock operations, hazardous waste sites, and industrial plants. The measure of exposure most often showing significant correlations is self-reported frequency of odour perception (a subjective measure). Contrarily, zone of residence or residence distance to facility (an objective measure) has not typically been a significant predictor of symptoms. The use of subjective measures of exposure is a potential source of reporting bias and results should be interpreted with caution.

The relationship between odour exposure and health symptoms appears to be greatly influenced by odour hedonic, perhaps more so than odour intensity. In studies assessing odour hedonic, exposure to unpleasant odours such as those from a pig facility, a fat refinery, or a cast-iron factory, were found to induce more symptom reporting than exposure to moderate or pleasant odours.

A consistent finding among the epidemiology studies is that symptom reporting is mediated by odour annoyance. Many studies have found odour annoyance to be a stronger predictor of symptom reporting than odour perception, odour concentration, and residence distance to facility, or alternatively, that adjustment for odour annoyance in the statistical modeling significantly attenuates

the association between odour exposure and symptoms. The relationship between odour annoyance and symptom reporting may also be influenced by individual or community attitudes towards an odour, environmental worry, or perceiving odour as a threat to health.

Odours from livestock facilities, sewage treatments plants, and industrial sources have also been associated with negative moods (e.g., stress, gloom, depression, anger, fatigue), as well as lower quality of life (as measured by outcomes such as avoiding outdoor activities, keeping windows closed, temporarily leaving the neighborhood, and having reduced property values).

6.1.2 Experimental Studies - Physiological Responses, Mood, and Performance

The experimental findings demonstrate that odours can significantly impact physiological outcomes, irritant symptoms, mood, and cognition (task performance); however, this is not true for all odours in all situations. Responses appear to be odorant-specific and are also heavily influenced by individual factors and experimental methods.

Odours were found to have a significant influence on physiological arousal parameters (heart rate, blood pressure, respiratory rate, skin conductance) and reporting of irritant symptoms (headaches, eye irritation, nausea, dry eye) in several studies. However, contradictory or null findings to these results were also found. For studies of odour and mood, pleasant odours tended to induce more positive moods (mainly increased happiness and improved overall mood) and unpleasant odours tended to induce more negative moods (mainly increased anger and disgust). Due to the variation in responses, any further conclusions beyond this basic finding were difficult to identify.

A common finding among the experimental studies of physiological outcomes, symptoms, and mood is that odour-induced responses are impacted by individual cognitive attitudes towards an odour. Several studies demonstrated that subjects given a harmful bias towards an odour were more likely to report irritant symptoms than those given a healthful bias. Similarly, subjects given a healthful bias towards tended to be in a more pleasant mood than those given a harmful bias.

Varied results have been found with studies assessing odours and cognition function (task performance). Both pleasant and unpleasant odours were shown to improve or impair performance on memory and recognition tasks, math tasks, lexical tasks (word recognition, word decoding), and motor reaction tasks. Other studies found odours to have no effect on task performance. This lack of consistency across studies suggests that the impact of odours on task performance may be odorant-specific.

Four mechanisms have been proposed as plausible explanations for the influence of odours on mood, cognition, physiology, and behavior: (i) a quasi-pharmacological interaction between odorants and the central nervous system and hormonal system; (ii) a hedonically-driven mechanism, in which effects are dictated by the perceived pleasure or displeasure from an odour; (iii) a psychological (placebo) mechanism based on prior beliefs and expectations about an odour; and (iv) a semantic mechanism based on previous personal experiences with an odour (Johnson, 2011; Jellinek, 1997).

Additionally, odours may alter mood and cognition by acting as a distracter to the task-at-hand. All these factors have the potential to influence experimental results, and can complicate the difficult task of understanding odour-induced responses.

The relationship between odours and physiological or psychological responses is extremely complex and influenced by a wide variety of odour characteristics (e.g., hedonicity, familiarity) and individual factors (e.g., subjective expectations, personal experience with an odour). Different odours induce different responses, and odours appear to have their own cognitive and mood profiles.

6.1.3 Experimental Studies - Brain Responses

In studies localizing odour-induced brain activity, more than 30 different regions have been indicated as being involved in some aspect of olfaction. The pattern of neuronal activity can be influenced by a wide variety of factors, such as odour characteristics (e.g., intensity, hedonicity), the task at-hand (e.g., paying attention to an odour, odour identification), subjective association with an odour (e.g., familiarity, emotional association), and pre-conceived expectations about an odour.

With regards to hedonicity, different studies show varied brain responses following exposure to pleasant and unpleasant odours. The lack of consistency across studies makes it extremely difficult to draw any definitive conclusions regarding how pleasant or unpleasant odours affect the brain. There appears to be a complex array of factors that are involved in the response to odour hedonic, such as type of odour (e.g., food vs floral), familiarity, and situational context. The orbitofrontal cortex and the amygdala are often found to be activated by both pleasant and unpleasant odours, and are considered to play a strong role in emotional processing. Additionally, the involvement of many of the structures of the limbic system (e.g., amygdala, hippocampus, cingulate gyrus) helps to explain the emotional response to a hedonic odour. Unpleasant odours appear to recruit a larger number of brain regions than pleasant odours, which may reflect a fight or flight reaction to odours considered to be threatening.

At present, the clinical application of odour-induced neuronal activity studies is rather limited, and the link between changes in activity and health is poorly understood. Some studies have suggested that odour-induced increases in neuronal activity can be linked to certain behaviors; for example, changes in odour-induced frontal lobe activity have been linked to changes in mood, drowsiness, and alertness. However, studies of this nature are few in number and additional research in this area is needed before further conclusions can be drawn.

6.1.4 Experimental Support for Epidemiological Findings

Epidemiological studies often find that exposure to environmental odours is associated with increases in reported symptoms (cough, nausea, congestion, eye irritation, headache, dizziness, sleep problems, diarrhea, chest pain, and/or respiratory symptoms), with unpleasant odours inducing more symptoms than pleasant odours. Only one experimental study was found that directly assessed the health effects of a typical environmental odour. Schiffman et al. (2005) demonstrated that

subjects exposed to diluted swine odour for one hour reported more headaches, eye irritation, and nausea than subjects exposed to clean air; no differences were found for sore throat, nasal irritation/ congestion, or cough. This study is perhaps the most relevant in terms of identifying potential adverse effects from environmental odours; however, the results may have been confounded by the presence of irritant components in the odour sample. Overall results from other experimental studies assessing odour-induced health symptoms were generally inconclusive: coffee odours induced an increase in reports of dry nose, but not headache or skin moisture (Pan et al., 2003), lemon and baby powder odours induced fewer reported symptoms than controls (Knasko, 1995, 1992), and pleasant (lemon, ylang) and unpleasant odours (isovaleric acid, skatole) had no effect on reported symptoms (Knasko, 1993).

One of the main findings from the epidemiological studies is that symptom reporting is mediated or influenced by factors such as annoyance, individual or community attitudes towards an odour, environmental worry, or perceiving odour as a threat to health. Experimental studies of odour-induced health symptoms have also demonstrated that individual beliefs about odour can influence symptom reporting. In studies where subjects are given a healthful, harmful, or neutral odour bias prior to exposure, those given a harmful bias reported more health symptoms following odour exposure than those given a healthful or neutral bias (Laudien et al., 2008; Dalton, 1999). Further, Knasko et al. (1990) demonstrated that, despite no odour being used in the study, suggestion of a harmful odour induces more symptom reporting than suggestion of a pleasant or neutral odour.

Winneke and Neuf (1992) compared odour-induced annoyance in subjects pre-classified as having low or high degrees of environmental annoyance. They demonstrated that subjects with a higher degree of self-reported environmental annoyance show higher H_2S-induced annoyance, and the H_2S-induced annoyance correlated with dissatisfaction with perceived health. This study supports the idea that personality traits can influence odour-induced responses.

With regards to mood, epidemiology studies have shown that exposures to environmental odours from livestock facilities, sewage treatments plants, and industrial sources are associated with negative mood (stress, gloom, depression, anger, fatigue). This finding is supported by experimental studies assessing mood: unpleasant odours have consistently been associated with increases in negative mood, particularly anger and disgust.

6.2 Mechanisms of Odour-induced Irritant Responses

Three models have been proposed to explain the relationship between odour and irritant qualities of an odorant: odour threshold is well above the irritant threshold, odour threshold is at or near the irritant threshold, and odour threshold is well below the irritant threshold (Figure 6-1) (Shusterman, 2001). Depending on the particular chemical(s) involved and their odorant and irritant qualities, odours either play a central role or a bystander role. Three assumptions have been made for development of these explanatory models: (i) the focus is on olfaction and sensory irritation, disregarding potential toxicological effects such as carcinogenesis or teratogenesis; (ii) the term

'threshold' was used without regard for experimental methodologies or testing conditions; and (iii) exposure duration was disregarded (Shusterman, 2001).

Based on these models, three paradigms for explaining the association between odours and health have been proposed: (1) Odours are at or above irritant thresholds; (2) Exposure to a co-pollutant in an odorous mixture; and (3) Odours are below irritant thresholds (Schiffman and Williams, 2005; Schiffman et al., 2000).

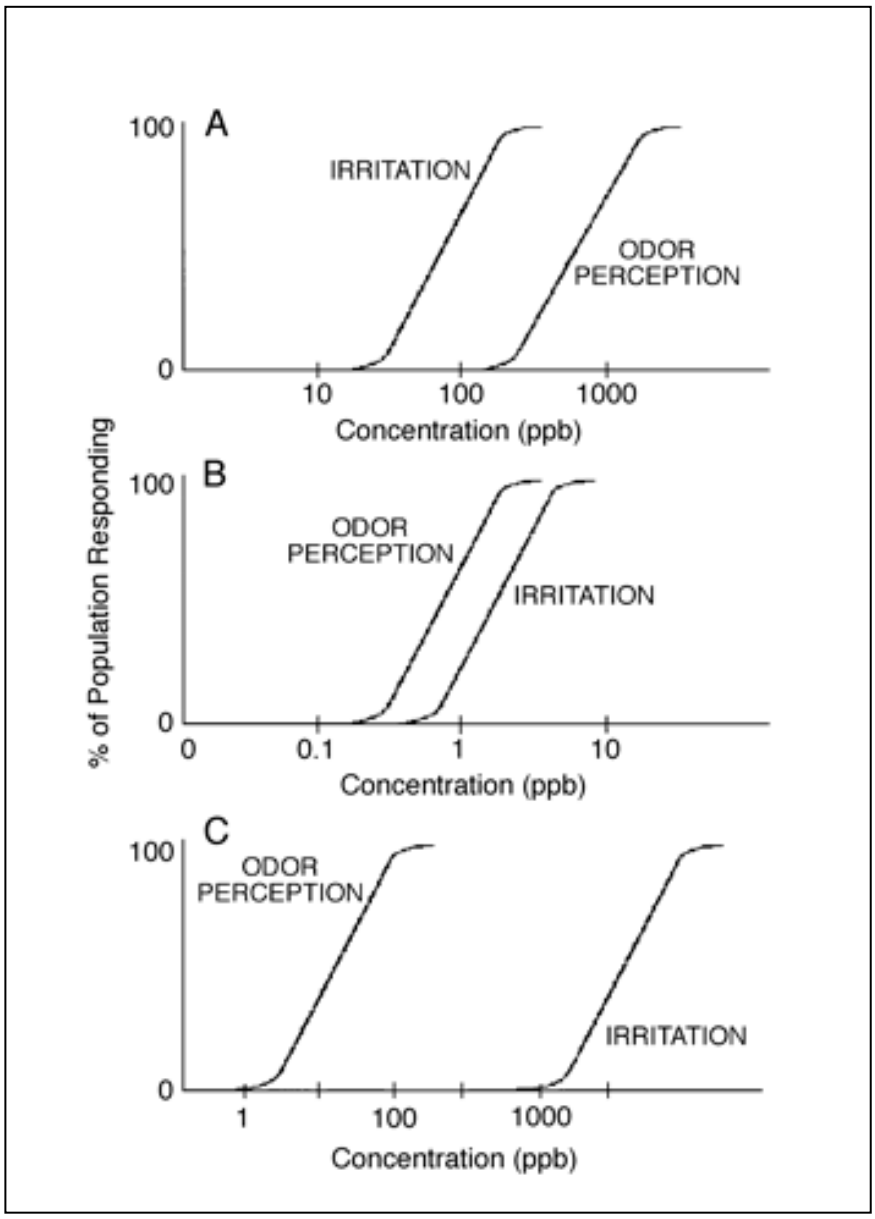
6.2.1 Odours are At or Above Irritant Thresholds

In this mechanism, health symptoms occur as a result of the direct toxicological effects of the odorant (Schiffman and Williams, 2005; Shusterman, 2001; Schiffman et al., 2000). Odorant concentrations are at or above irritant thresholds as well as above the odour detection threshold. The two thresholds are typically within an order of magnitude (3 to 10 times) of each other (Figure 6-1b). The sensory irritation can be due to a single odorant above its irritant threshold, the additive effect of mixtures of low concentrations of odorants (e.g., volatile organic compounds), or combined weak trigeminal and strong olfactory stimulation (Schiffman et al., 2000). The odour and irritant sensations occur simultaneously, and the resulting health symptoms are more likely due to irritation than to the odour sensation. In this paradigm, odour is simply serving as an exposure marker. Examples of odorants with irritant thresholds within an order of magnitude of their detection thresholds include ammonia, chlorine, menthol, alcohol, and phosphine (Smeets et al., 2007; Shusterman, 2001; Schiffman et al., 2000).

6.2.2 Exposure to Co-Pollutants

In this paradigm, the odorant may be a component of a mixture that contains a toxic co-pollutant. For example, environmental odour mixtures can contain odourless co-pollutants such as carbon dioxide (CO_2) and nitrogen dioxide (NO_2), particulate matter, and endotoxins (Schiffman and Williams, 2005). In cases of health complaints reported by residents living near odour-emitting facilities, it is possible that co-pollutants are responsible for the observed health effects, with odour serving as a marker of exposure. However, very few odour epidemiology studies assessed this possibility. For example, Schinasi et al. (2011) found that hog odours, as well as hydrogen sulphide and particulate matter, correlated with increased reports of irritant symptoms; yet, it is not clear whether the odours or the co-pollutants (or both) were responsible for the observed health effects.

Figure 6-1: Cumulative population dose-response curve for olfactory and irritant effects of odorants



(a) a potent irritant compound (odour threshold is well above irritant threshold); (b) an intermediate potency irritant compound (odour threshold is at or near irritant threshold); (c) a weakly irritant/potent odorant compound (odour threshold is well below irritant threshold). (Shusterman, 2001).

If exposure to co-pollutants were a contributing factor in odour-induced health effects, residence distance to an odour-emitting facility might be expected to be a significant predictor of health complaints. However, in most epidemiology studies, residence distance to the facility was often a poor predictor of odour-induced health complaints.

Experimental support for this mechanism was also sparse. In one toxicology study assessing the health impact of swine odour, subjects exposed to diluted swine odour reported more headaches, eye irritation, and nausea than control subjects; the authors indicated, however, that the effects of odours could not be separated from the effects of co-pollutants in the mixture (e.g., particulates, endotoxins) (Schiffman et al., 2005). No other experimental studies were found that assessed the effects of complex mixtures of environmental odours.

Despite the lack of research in this area, the possibility that co-pollutants may play a role in odour-induced health effects remains an important factor to consider in odour research.

6.2.3 Odours are Below Irritant Thresholds

In this paradigm, health symptoms occur at odorant levels that are detectable but not irritating (odour detection threshold is below irritant threshold, Figure 6-1c). The mechanisms in which odours induce adverse health effects are not well understood; it is not clear if the odour-induced effects are the result of a direct biological process or an indirect psychological response based on past experiences and expectations. In most cases, the observed health effects of odours cannot be explained by classical toxicological mechanisms (Shusterman, 1992). Examples of odorants with odour thresholds well below irritant thresholds include hydrogen sulphide, isopropanol, phenylethyl alcohol, 1-butanol, organic amines, and mercaptans (Smeets and Dalton, 2002; Shusterman, 2001). For example, health complaints are often reported with exposure to H_2S at levels above the odour threshold (0.5 to 30 ppb) but well below the irritant threshold (2.5 to 20 ppm) (Schiffman and Williams, 2005).

Possible mechanisms for odour-induced health effects occurring under this paradigm include physiological changes, mood changes and stress, cognitive bias and expectations, and learned or conditioned associations (Schiffman and Williams, 2005; Schiffman et al., 2000; Shusterman, 1992).

6.2.3.1 Physiological Responses to Odours

Some researchers have suggested that odours may induce adverse health effects via changes in breathing patterns (Schiffman and Williams, 2005; Schiffman et al., 2000). However, evidence from studies assessing odour-induced changes to lung function or respiratory rate has been inconclusive. Experimental studies examining the effect of odours on respiratory rate have shown mixed results, with most studies showing no association (Heuberger et al., 2006, 2001; Nagai et al., 2000). In particular, no changes to respiratory rate were found in a study of subjects exposed to diluted swine odour (Schiffman et al., 2005). In one epidemiology study that measured breathing parameters, odours from industrial hog operations were not associated with changes in lung function (Schinasi et

al., 2011). Based on these data, odours do not appear to have a significant impact on breathing parameters. However, only a few studies have assessed this, and factors such as the timing of response and the measured respiratory outcome may have contributed to the null findings.

A large number of studies have demonstrated that odours can induce changes in brain activity. It is possible that these observed neuronal changes may be an initiating step in odour-induced health effects; however, research assessing the link between odour-induced activity changes and clinical health outcomes was limited. Some studies have suggested that odour-induced changes in neuronal activity can be linked to certain behaviors; for example, changes in frontal EEG activity have been linked to drowsiness, alertness, or having a more positive mood (Field et al., 2005; Sanders et al., 2002; Diego et al., 1998). The clinical significance of odour-induced neuronal activity changes represents a relatively new area of study, and, at present, is not well understood.

6.2.3.2 Changes in Mood and Stress

Unpleasant or annoying environmental odours may result in negative mood, 'environmental worry', or 'environmental stress' (i.e., perceiving the odour as a health risk), which in turn, may result in stress-related illnesses. Stress has been linked to physiological changes such as elevated blood pressure, immune suppression, muscle tension, and alterations to epinephrine and norepinephrine levels (Schiffman et al., 2000); subsequently, these changes may cause observable health symptoms including headache, nausea, fatigue, mood disturbances, and cardiovascular effects (Dimsdale, 2008; Shusterman, 1992; Shusterman et al., 1991; DeLongis et al., 1988). The role of stress in odour-induced responses is supported in epidemiology and experimental studies indicating odour annoyance or environmental annoyance as a mediating factor.

6.2.3.3 Cognitive Bias and Expectations

Several experimental studies have demonstrated that odour-induced health effects are mediated by cognitive biases and perceived health risks or expectations of the odour. Subjects with a negative or harmful bias are more likely to show negative health responses; this has been observed with subjective outcomes such as self-reported health symptoms or mood changes (Laudien et al., 2008; Dalton, 1999; Knasko et al., 1990), as well as objective outcomes such as skin conductance responses (Djordjevic et al., 2008; Howard and Hughes, 2008; Campenni et al., 2004). Further, studies of neuronal activity have shown that processing of odours occurs earlier in subjects with a negative bias towards the odour (Bulsing et al., 2010, 2007; Laudien et al., 2008).

In epidemiology studies, attitudes toward an odour-emitting facility have been found to significantly influence reporting of odour-induced annoyance and heath symptoms, where those with a negative bias are more likely to report symptoms (Cavalini, 1994; Cavalini et al., 1991; Shusterman et al., 1991). Additionally, no change to symptom reporting was found before and after odour reduction measures were introduced for a petroleum refinery (Luginaah et al., 2002, 2000). Overall, these studies emphasize the important role of individual and community attitudes towards an odour or industry in odour-induced health responses.

6.2.3.4 Learned Associations

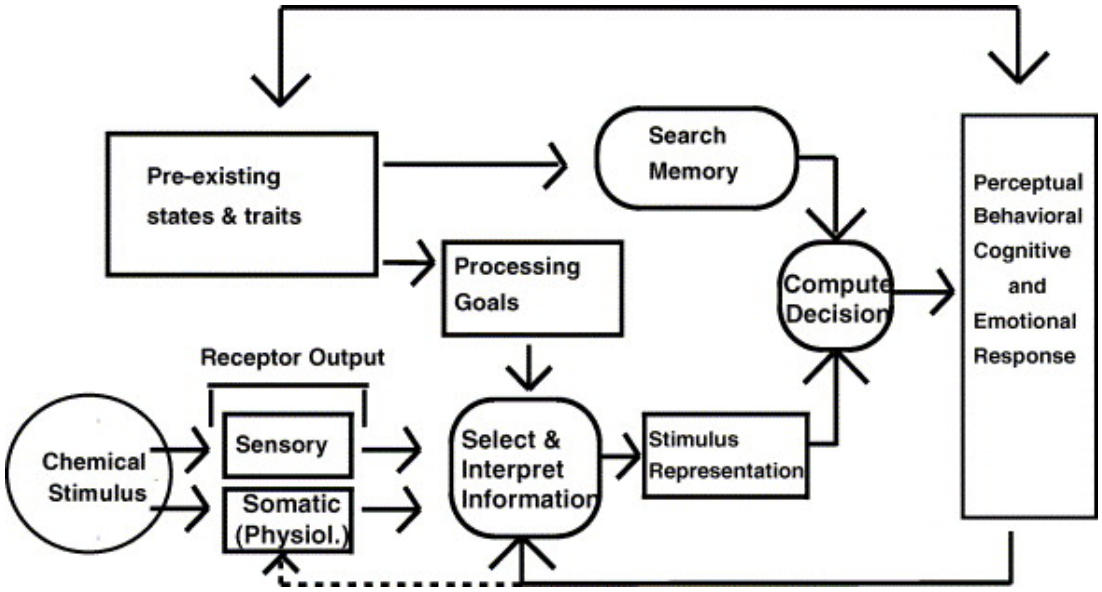
Another possible explanation for the presence of health symptoms in response to odours may be through a phenomenon called symptom learning (or Pavlovian conditioning) (Van den Bergh et al., 2001). Symptoms may be learned through combined exposure to an odour and a toxic chemical that induces adverse health effects. Subsequent exposure to the odour, or other odours, may then induce health symptoms, even in the absence of the toxic component (Devriese et al., 2000). This learning paradigm is considered to be a possible explanation for multiple chemical sensitivity and chemical intolerance (Leer et al., 2011; Otto and Giardino, 2001). The occurrence of learned symptoms has been observed in several studies in response to a number of different odours (ammonia, butyric acid, acetic acid) paired with toxic CO_2 stimuli, as well as in case studies of occupational exposures (Devriese et al., 2006, 2000; Van Diest et al., 2006; Winters et al., 2003; Van den Bergh et al., 1999, 1998, 1997, 1995; Shusterman et al., 1988). Responses have typically been more pronounced with unpleasant odours than with neutral odours. A learned response may be influenced by individual factors (e.g., negative affect) (Van den Bergh et al., 2004, 2002; Devriese et al., 2000), odour pleasantness (Winters et al., 2003), or memory of previous experiences (Van den Bergh et al., 1999, 1998). Further research has also shown that 'learned symptoms' may increase when subjects are given prior warning about chemical pollution (Devriese et al., 2004; Winters et al., 2003).

Similar to odour-induced health symptoms, a Pavlovian conditioning paradigm may also exist for odour-induced changes in mood. When an odour is associated with a negative or stressful event, the odour experienced again later may trigger negative emotions (Zucco et al., 2009; Epple and Herz, 1999; Kirk-Smith et al., 1983). This type of odour learning has been observed primarily with neutral odours, with and without the subjects' awareness of the presence of an odour. Likewise, an odour associated with a positive event may later trigger positive emotions, as has been observed with children in the presence of strawberry or peppermint (Chu, 2008).

6.2.4 Information Processing Model

Smeets and Dalton (2005) proposed a model for chemosensory responses that incorporates both bottom-up processes (reflecting responses driven by the stimulus) and top-down processes (reflecting the cognitive or perceptual processing of the stimulus) (Figure 6-2). The model presents a presumed sequence of events that occurs when a chemosensory stimulus (odour) is encountered. There is a flow of information occurring from the external environment to the brain, as well as a flow of information in the opposite direction representing cognitive responses to the stimulus. The model reflects the parallel processing that occurs between the bottom-up and top-down processes, and highlights the role of pre-existing knowledge and personality traits in odour-induced responses.

Figure 6-2: Information-processing model of chemosensory perception



The boxes denote states or constructs, octagons/circles denote processes. Bottom-up processing indicated mostly, but not exclusively, by arrows pointing right or up. Top-down processing indicated mostly, but not exclusively, by arrows pointing left and down. (Smeets and Dalton, 2005).

6.3 Summary and Limitations/Research Needs

The association between odours and health has proven to be extremely complex. The evidence demonstrates that all odours are not of equal consequence; a wide range of responses can be induced by different odorants and the health impacts of odours are often odorant-specific. Studies have shown that odour-induced responses are heavily influenced by odour characteristics (e.g., hedonicity, familiarity) as well as individual factors (e.g., past experience, cognitive bias).

Several mechanisms for odour-induced health effects have been proposed. For odours that are at or above irritant thresholds, classical toxicological mechanisms likely apply. For odorants at levels below their irritant thresholds, the mechanism for health effects is not fully understood. Factors such as individual personality, biases and expectations, changes to mood and stress, and learned associations all appear to play some role in odour-induced responses.

There are a number of limitations and research needs that were noted throughout the development of this report. The main limitations associated with epidemiological research are the weak exposure assessments and the use of subjective measures for exposures and/or outcomes. The main limitations associated with human experimental studies are the lack of standardized exposure methods (type of odorant, odorant delivery method), the difficulty in conducting blinded experiments (as subjects are often aware of the presence of odour), and the influence of individual predilections and individual past experience on odour-induced responses.

Odour epidemiological research would benefit from:

- improved exposure assessments; more objective and consistent/standardized assessments of exposure would help to limit bias and improve comparability between studies.
- additional measurements of co-pollutants to allow differentiation of odour-related effects from toxic or irritant effects.
- more prospective studies evaluating community health responses before and after introduction of an odour-emitting facility, or before and after implementation of an odour reduction plan.

For human experimental studies, there is a need for:

- more consistency in terms of odour exposure (concentration, method of odorant delivery, exposure time) to allow for generalizations of the effects of odours.
- evaluations of repeated exposures to odours (i.e., over multiple days).
- more studies assessing physiological and psychological responses simultaneously; correlating objective physiological responses with subjective mood/behavior responses would provide more meaningfulness to the physiological data (Herz, 2009).
- further research into the clinical application of odour-induced neuronal activity (understanding the link between brain activity changes and behavioral/physiological responses)
- more experimental studies directly evaluating the physiological or psychological effects of complex environmental odours.

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Appendix A: Glossary

Amygdala – almond-shaped structure located in the medial temporal lobe of the brain. The amygdala is part of the limbic system and is considered to play a role in sensory-related emotional processing and memory.

Bimodal odorant – an odorant that activates both the olfactory and trigeminal systems. Odorants that activate only one system are referred to as unimodal odorants.

Cingulate cortex – a ring-like brain structure located in the center fold of the neocortex (outer layer of the cerebral hemispheres). The cingulate cortex is considered part of the limbic system and plays a vital role in emotion and behavior.

Contralateral – referring to the opposite side of the body.

Detection threshold – the concentration at which an odour is first detectable.

Dilution-to-threshold ratio (D/T) – the number of dilutions required to make an odour non-detectable. Calculated as the volume of odorless air to the volume of odorous air.

Discrimination threshold – the concentration at which two odours can be differentiated.

Dynamic dilution olfactometry (DDO) – a method of determining odour concentration where a panel of human subjects is presented with dilutions of an odour sample. Odour concentration is determined as the dilution level at which 50% of the panel cannot distinguish the odour from odorless air.

Electroencephalography (EEG) – measurement of electrical activity in the brain; electrodes attached to the scalp are used to measure electrical potentials.

Entorhinal cortex – a brain structure located in the medial temporal lobe. Involved in memory and navigation.

Functional magnetic resonance imaging (fMRI) – a neuroimaging technique for measuring activity levels in the brain. fMRI makes use of blood oxygen level-dependant (BOLD) contrasts to localize changes in blood flow and blood volume in response to metabolic demand.

Glomerulus (glomeruli) – a spherical structure in the olfactory bulb where olfactory receptor neurons and mitral cells form synaptic connections.

Gyrus (gyri) – an elevated convolution on the surface of a cerebral hemisphere caused by the infolding of the cerebral cortex. Adjacent gyri are separated by sulci (grooves).

Habituation – the decrease in sensation of or response to an odour following prolonged or repeated exposure.

Hedonicity (or hedonic tone) – the perceived pleasantness or unpleasantness of an odour. Typically assessed using a numerical or descriptive scale ranging from extremely unpleasant to neutral to extremely pleasant.

Hippocampus – a brain structure located in the medial temporal lobe. The hippocampus is considered part of the limbic system and is involved in memory, organization, and spatial navigation. It is also thought to be important for connecting emotions and senses to memories.

Insula (Insular cortex) – a brain structure located between the temporal lobe and frontal lobe. The insula is thought to be involved in processes such as emotion, perception, motor control, self-awareness, cognitive functioning, and interpersonal experience.

Ipsilateral – referring to the same side of the body.

Limbic system – a group of brain structures involved with controlling emotion. Involved in olfaction, emotion, behavior, motivation, memory, and autonomic functions.

Magnetoencephalography (MEG) – measurement of magnetic activity in the brain; magnetometer coils placed on the scalp are used to measure magnetic fields produced by neuronal electrical activity.

Mitral cell – a nerve cell in the olfactory bulb. Mitral cells extend from the glomeruli in the olfactory bulb to structures of the primary olfactory cortex.

Odorant – a substance that produces a smell. Odorants are volatile, hydrophobic molecules that are dissolved in the air and can activate the olfactory system.

Odour intensity – the perceived strength of an odour.

Odour quality – a description of the general type of smell of an odour (e.g., floral, musky, woody, fruity).

Odour unit (OU or OU/m^3) – a measurement of odour concentration defined as the dilution level at which 50% of a panel of subjects cannot distinguish the odour from odourless air. For example, if an odour diluted 10 times is just undetectable by 50% of the panel (i.e., half the group is no longer able to discriminate between the odour and odourless air), the odour concentration would be 10 OU/m^3.

Odour unit (European) (OU$_E$ or OU$_E$/m^3) – a measurement of odour concentration defined as the amount of odorants that, when evaporated into 1 m^3 of neutral gas at standard conditions, elicits a physiological response from a panel (detection threshold) equivalent to that elicited by 1 European reference odour mass [123 µg *n*-butanol] evaporated in 1 m^3 of neutral gas at standard conditions. Through the use of *n*-butanol as a reference odour, the OU$_E$ accounts for variation in detection thresholds of the panelists.

Olfaction – the sense of smell; the act of smelling.

Olfactometer – a dilution instrument used for measuring the intensity or strength of an odour. The instrument mixes an odour sample with odour-free air at specific ratios, and the diluted odour is then presented to a panel of human assessors.

Olfactory bulb– a brain structure located just above the nasal cavity. The olfactory bulb transmits olfactory neuronal signals to the brain, and represents the first site of processing of olfactory information.

Olfactory odorant – an odorant that activates olfactory neurons. Pure olfactory odorants (e.g., hydrogen sulphide) stimulate only the olfactory system, while mixed bimodal odorants (e.g., menthol) activate both the olfactory and trigeminal systems.

Olfactory receptor neuron – an olfactory receptor cell that extends from the nasal epithelium to the olfactory bulb. Olfactory receptor neurons are activated by odorants, and the signal is transmitted to higher brain regions.

Olfactory tubercle – a component of the primary olfactory cortex. Involved in processing olfactory information.

Orbitofrontal cortex (OFC) – a prefontal cortex located in the frontal lobe of the brain. Thought to be involved in processes such as decision-making, judgments, emotion/mood, and sensory integration.

Orthonasal - a pathway of odour exposure occurring via the external nares (nostrils).

Piriform cortex – a component of the primary olfactory cortex. Involved in processing olfactory information.

Positron emission tomography (PET) – a neuroimaging technique that measures activity levels in the brain. In PET, a radioactive tracer is injected into the subject's bloodstream and radioactivity is measured in using a scanner; a region with a higher radioactive signal indicates a region of increased blood flow and thus, increased neuronal activity.

Primary olfactory cortex (POC) – refers to regions of the brain that receive direct neuronal input from mitral cell axons extending from the glomeruli in the olfactory bulb. Includes several brain structures including the piriform cortex, anterior olfactory cortex, olfactory tubercle, amygdala, and rostral portions of the entorhinal cortex.

Putamen– a brain structure located at the base of the forebrain. Involved in learning and regulating motor activity.

Recognition threshold – the odour concentration at which odour quality can be identified.

Retronasal – a pathway of odour exposure occurring via the internal nares of the mouth.

Secondary olfactory cortex (SOC) – refers to regions of the brain that receive neuronal input from the primary olfactory cortex. Includes several brain structures including the orbitofrontal cortex, lateral entorhinal cortex, and insular cortex.

Skin conductance response (SCR) – a measure of physiological arousal that varies based on the moisture of the skin. Higher SCRs indicate more moisture (sweat) and a more aroused state, while lower SCRs indicate less moisture and a more relaxed state. Also referred to as electrodermal response.

Sulcus (sulci) – a furrow or groove on the surface of a cerebral hemisphere caused by the infolding of the cerebral cortex. Separates adjacent gyri on the surface of the brain.

Trigeminal odorant – an odorant that activates trigeminal neurons. Pure trigeminal odorants (e.g., carbon dioxide) stimulate only the trigeminal system, while mixed bimodal odorants (e.g., menthol) activate both the olfactory and trigeminal systems.

Unimodal odorant – an odorant that activates either the olfactory system or the trigeminal system, but not both. Odorants that activate both systems are referred to as bimodal odorants.

Voxel – a volumetric pixel; represents a particular coordinate in three dimensional space. A voxel represents a specific location in the brain in fMRI analyses.

Appendix B: List of odorants used in odour research

Odorant [IUPAC name (pure compounds)]	Common name	Hedonicity* (commonly)	Descriptors and other information
Acetic acid [Ethanoic acid]	Vinegar	Unpleasant	Pungent; CASRN: 64-19-7
Acetophenone [1-Phenylethanone]	-	Neutral	Almond, fruity, floral (hawthorne-like); CASRN: 98-86-2
Aftershave	-	Pleasant	Many varieties used
Air fresheners	-	Pleasant	Many varieties used
Alinamin and Alinamin-F; Alinamin-F [N-[(4-amino-2-methylpyrimidin-5-yl)methyl]-N-{(1E)-4-hydroxy-1-methyl-2-[(tetrahydrofuran-2-ylmethyl)disulfanyl]but-1-en-1-yl}formamide]	Garlic	Neutral - unpleasant	Both compounds have the same medicinal properties, but Alinamin is a stronger odorant. Following intravenous injection, subjects will smell a garlic-odour in their expired breath; Alinamin-F CASRN: 804-30-8
Allyl isothiocyanate [3-Isothiocyanato-1-propene]	Synthetic mustard oil	Unpleasant	Strong mustard, horseradish. Strong trigeminal odorant; CASRN: 57-06-7
Almond	-	Pleasant - Neutral	Nutty
Ammonia [Azane]	-	Unpleasant	Pungent, sharp; CASRN: 7664-41-7
Ammonium sulphide [Ammonium sulphide]	Stink bomb	Unpleasant	Rotten egg smell; CASRN: 12135-76-1
Amyl acetate [Pentyl acetate]	Banana	Pleasant	Fresh, fruity (banana-like, pear-like); CASRN: 628-63-7; very similar odour to isoamyl acetate; CASRN: 628-63-7
Androstenone [(5S,8R,9S,10S,13R,14S)-10,13-Dimethyl-1,2,4,5,6,7,8,9,11,12,14,15-dodecahydrocyclopenta[a]phenanthren-3-one]	-	Varied	Urinous and sweaty, or woody and floral. Exhibits a range of pleasantness between individuals; CASRN: 18339-16-7
Anethol [(*E*)-1-Methoxy-4-(1-propenyl)benzene]	Licorice	Pleasant - Neutral	Sweet, anise, licorice; CASRN: 104-46-1
Anisole [Methoxybenzene]	-	Neutral	Ethereal, anise; CASRN: 100-66-3
Apple	-	Pleasant	Fruity
Apricot	-	Pleasant	Fruity
Asafoetida	Devil's dung	Unpleasant	Strong, pungent, sulphurous
Aurantiol [Methyl 2-[(7-hydroxy-3,7-dimethyloctylidene)amino]benzoate]	-	Pleasant - Neutral	Floral, orange flower, Linden blossom; CASRN: 89-43-0
Baby oil	-	Pleasant - Neutral	-
Baby powder	-	Pleasant	-
Baghdad water lily	-	Pleasant	Sweet, floral
Bangalol [(E)-2-Ethyl-4-(2,2,3-trimethyl-1-cyclopent-3-enyl)but-2-en-1-ol]	Sandalrome	Pleasant	Floral, woody (sandalwood-like); CASRN: 28219-61-6
Basil	-	Pleasant	Herbal, green, sweet, spice, woody
Benzaldehyde [Benzaldehyde]	-	Pleasant	Bitter almond odour; CASRN: 100-52-7
Bergamot	-	Pleasant	Orange, flowery, citrus
Birch tar	-	Unpleasant	Smoky, burnt, wood, leathery

*Hedonicity rating refers to the pleasantness perceived by the majority of the population. Actual pleasantness ratings may differ between individuals. IUPAC: International Union of Pure and Applied Chemistry. CASRN: Chemistry Abstract Services Registration Number.

Appendix B: List of odorants used in odour research (continued)

Odorant [IUPAC name (pure compounds)]	Common name	Hedonicity* (commonly)	Descriptors and other information
Blue cheese	-	Unpleasant	Strong, stinky cheese
Body odour	-	Unpleasant	-
n-butanol [Butan-1-ol]	-	Unpleasant	Medicinal, slight whiskey; CASRN: 71-36-3
Butter	-	Pleasant - Neutral	-
Butyl acetate [Butyl acetate]	-	Pleasant	Fruity, sweet, banana; CASRN: 123-86-4
Butyl isobutyrate [butyl 2-methylpropanoate]	-	Pleasant	Fruity, green, sweet, tropical; CASRN: 97-87-0
Butyric acid [butanoic acid]	-	Unpleasant	Sharp, cheesy, rancid butter; CASRN: 107-92-6
Camphor [1,7,7,-Trimethylbicyclo[2.2.1]heptan-2-one]	-	Neutral	Strong, aromatic; CASRN: 76-22-2
Caproic acid [hexanoic acid]	-	Unpleasant	Fatty, cheesy, waxy, sweat-like; CASRN: 142-62-1
Caramel	-	Pleasant - Neutral	-
Carbon dioxide [Carbon dioxide]	-	Odorless	Pure trigeminal odorant; CASRN: 124-38-9
Carrot seed oil	-	Pleasant	Herbaceous, earthy, fruity, spicy
R-(–)-Carvone [(5R)-2-Methyl-5-(1-methylethenyl)-2-cyclohexenone]	-	Pleasant	Smells like spearmint; CASRN: 6485-40-1
S-(+)-Carvone [(5S)-2-Methyl-5-(1-methylethenyl)-2-cyclohexenone]	-	Pleasant - Neutral	Pungent, anise-like. Smells like caraway; CASRN: 2244-16-8
Cedar(wood) oil	-	Pleasant	Woody, cedar. Similar to pencil shavings
Cedrol [(1S,2R,5S,7R,8R)-2,6,6,8-tetramethyltricyclo[5.3.1.01,5]undecan-8-ol]	-	Pleasant	Woody, cedar. A component of cedarwood oil; CASRN: 77-53-2
Chamomile oil	-	Pleasant	Sweet-herbal, floral
China rain	-	Pleasant	Floral, rose petals, green
Chocolate	-	Pleasant	-
Cigar butt	-	Unpleasant	-
Cigarette ash	-	Unpleasant	-
1-8 Cineole [1,3,3-Trimethyl-2-oxabicyclo[2,2,2]octane]	Eucalyptol, Eucalyptus	Pleasant	Fresh camphor-like smell; CASRN: 470-82-6
Cinnamon	-	Pleasant	-
Citral [3,7-dimethylocta-2,6-dienal]	Lemonal	Pleasant	Lemon; CASRN: 5392-40-5
Citralva [3,7-dimethylocta-2,6-dienenitrile]	-	Pleasant	Lemon-orange; CASRN: 5146-66-7
Citrus bergamia	-	Pleasant	Orange, citrus
Citronellol [3,7-Dimethyloct-6-en-1-ol]	-	Pleasant	Lemon floral, rose, green; CASRN: 106-22-9
Civet	-	Unpleasant	Animal fecal/urine odour
Clementine	-	Pleasant	Citrus, sweet
Cloves	-	Pleasant	-

*Hedonicity rating refers to the pleasantness perceived by the majority of the population. Actual pleasantness ratings may differ between individuals. IUPAC: International Union of Pure and Applied Chemistry. CASRN: Chemistry Abstract Services Registration Number.

Appendix B: List of odorants used in odour research (continued)

Odorant [IUPAC name (pure compounds)]	Common name	Hedonicity* (commonly)	Descriptors and other information
Coconut	-	Pleasant	-
Coffee	-	Pleasant	-
Cologne	-	Pleasant	Many varieties used
Conifer	-	Pleasant	-
Creamsicle	-	Pleasant	-
Cumin (seed) oil	-	Neutral	-
Cyclodecanone [Cyclodecanone]	-	Neutral	No information found; CASRN: 1502-06-3
Diacetyl [Butane-2,3-dione]	-	Unpleasant	Pungent, milk, butter; CASRN: 431-03-8
Dimethyl sulphide [methylthiomethane]	-	Unpleasant	Cabbage, vegetable, sulphurous; CASRN: 75-18-3
Douglas fir	-	Pleasant	-
Durian	-	Unpleasant	Characteristic overpowering odour, variously considered as fragrant or offensive
Estragon	Tarragon	Pleasant	Anise-like, spicy
Ethanethiol [Ethanethiol]	Ethyl mercaptan	Unpleasant	Onion, leek. Added to butane and propane fuels as a warning agent; CASRN: 75-08-1
Ethyl acetoacetate [Ethyl 3-oxobutanoate]	-	Pleasant	Sweet, ethereal, green apples; CASRN:
Eucalyptus (Eucalyptol) [see camphor]	-	Pleasant	Fresh camphor-like smell; CASRN:
Eugenol [4-Allyl-2-methoxyphenol]	-	Varied	Spicy, clove-like. Characteristic dentistry odour; CASRN:
Farnesol [(2E,6E)-3,7,11-trimethyldodeca-2,6,10-trien-1-ol]	-	Pleasant	Green, floral; CASRN: 4602-84-0.
Fecal odour	-	Unpleasant	-
Fennel	-	Pleasant	Aniseed-like
Fir needle oil	-	Pleasant	Fresh, balsam, woody
Fish	-	Unpleasant	-
Fish sauce	-	Unpleasant	-
Furfurylmercaptan [Furan-2-ylmethanethiol]	-	Pleasant	Roasted coffee; CASRN: 98-02-2
Galaxolide fragrance [4,6,6,7,8,8-Hexamethyl-1,3,4,6,7,8-hexahydrocyclopenta[g]isochromene]	-	Pleasant	Musky; CASRN: 1222-05-5
Galbanum	-	Unpleasant	Strong, pungent, balsamic
Garlic	-	Unpleasant	-
Geraniol [(trans)-3,7-Dimethyl-2,6-octadien-1-ol]	-	Pleasant	Floral, rose-like; CASRN: 106-24-1
Geranium	-	Pleasant	Floral, leafy, earthy, green
Geranyl acetate [3,7-Dimethyl-2,6-octadien-1-yl acetate]	-	Pleasant	Floral, fruity rose; CASRN: 105-87-3
Grapefruit	-	Pleasant	-

*Hedonicity rating refers to the pleasantness perceived by the majority of the population. Actual pleasantness ratings may differ between individuals. IUPAC: International Union of Pure and Applied Chemistry. CASRN: Chemistry Abstract Services Registration Number.

Appendix B: List of odorants used in odour research (continued)

Odorant [IUPAC name (pure compounds)]	Common name	Hedonicity* (commonly)	Descriptors and other information
Grass oil	-	Pleasant	-
Green odour	-	Pleasant	A mixture of 2*E*-hexenal and 3*Z*-hexenol; odour of green leaves
Green tea	-	Pleasant	-
Guaiacol [2-methoxyphenol]	-	Neutral - Unpleasant	Pungent, smoky, sweet, medicinal; CASRN: 90-05-1
Heliotropine [1,3-Benzodioxole-5-carbaldehyde]	Piperonal	Neutral	Floral, sweet, vanillin, cherry; CASRN: 120-57-0
2-Heptanol [Heptan-2-ol]	-	Neutral	Earthy, oily, woody, fruity, green; CASRN: 543-49-7
2-Heptanone [Heptan-2-one]	-	Neutral	Fruity (banana-like), spicy (cinnamon-like), cheesy; CASRN: 110-43-0
Hexanal [Hexanal]	-	Varied	Fresh green grass, green type odour; CASRN: 66-25-1
Hexanoic acid [Hexanoic acid]	Caproic acid	Unpleasant	Fatty, cheesy, waxy, sweat-like; CASRN: 142-62-1
cis-3-Hexenol [(Z)-Hex-3-en-1-ol]	Leaf alcohol 3*Z*-hexenol	Pleasant	Fresh, green grass; CASRN: 928-96-1
Hiba (*Thujopsis dolabrata*)	Conifer	Pleasant	Forest-like
Honey	-	Pleasant	-
Honeydew	-	Varied	-
Hydrogen sulphide [Hydrogen sulphide]	Sour gas	Unpleasant	Rotten egg smell; CASRN: 7783-06-4
Indole [Indole]	-	Unpleasant	Fecal odour (high concentrations). Floral odour (low concentrations); CASRN: 120-72-9
α-Ionone [(3E)-4-(2,6,6-Trimethylcyclohex-2-en-1-yl)but-3-en-2-one]	-	Pleasant - Neutral	Berry, violet, woody; CASRN: 127-41-3
Isoamyl acetate [3-methylbut-1-yl ethanoate]	Banana	Pleasant	Fresh, fruity (banana-like, pear-like); CASRN: 123-92-2; very similar odour to amyl acetate
Isobornyl acetate [(1*R*,4*S*,6*R*)-1,7,7-trimethyl-6-bicyclo[2.2.1]heptanyl] acetate]	-	Varied	Camphor, herbal, woody, pine. Considered as perceptually malleable; CASRN: 125-12-2
Isobutyric acid [2-Methylpropanoic acid]	-	Unpleasant	Sweat-like; CASRN: 79-31-2
Isovaleric acid [3-Methylbutanoic acid]	-	Unpleasant	Strong, pungent, cheesy, sweaty; CASRN: 503-74-2
Jasmine	-	Pleasant	Floral
Juniper berry	-	Pleasant	Fresh, herbal, coniferous, berry
Laurus nobilis L.	Laurel	Pleasant	Sweet, bay leaf
Lavender	-	Pleasant	-
Leather	-	Unpleasant	-
Lemon	-	Pleasant	-

*Hedonicity rating refers to the pleasantness perceived by the majority of the population. Actual pleasantness ratings may differ between individuals. IUPAC: International Union of Pure and Applied Chemistry. CASRN: Chemistry Abstract Services Registration Number.

Appendix B: List of odorants used in odour research (continued)

Odorant [IUPAC name (pure compounds)]	Common name	Hedonicity* (commonly)	Descriptors and other information
Lemon meringue	-	Pleasant	-
Lilac	-	Pleasant	-
Limburger cheese	-	Unpleasant	Described as smelling like human feet
Lime	-	Pleasant	-
R-(+)-Limonene [(4R)-1-Methyl-4-(1-methylethenyl)-cyclohexene]	-	Pleasant - Neutral	Fresh, citrus. Smells like orange; CASRN: 5989-27-5
S-(–)-Limonene [(4S)-1-Methyl-4-(1-methylethenyl)-cyclohexene]	-	Pleasant - Neutral	Harsh, turpentine-like, pine-like. Smells like lemon; CASRN: 5989-54-8
R-(–)-Linalool [(3R)-3,7-dimethylocta-1,6-dien-3-ol]	Licareol	Pleasant	Woody, lavender-like; CASRN: 126-91-0
S-(+)-Linalool [(3S)-3,7-dimethylocta-1,6-dien-3-ol]	Coriandrol	Pleasant	Sweet, floral, petitgrain-like; CASRN: 126-90-9
Linalyl acetate [3,7-Dimethylocta-1,6-dien-3-yl acetate]	Bergamiol	Pleasant	Floral, lavender, bergamot, fruity; CASRN: 115-95-7
Linden blossom	-	Pleasant	Floral, honey, lemon
Linen oil	-	Pleasant	Smells like freshly washed linen
Linseed oil	Flaxseed oil	Pleasant	Described as bland, nutty
Mackerel brine	-	Unpleasant	Rancid fish
Massage oil	-	Pleasant - Neutral	-
Melonal [2,6-dimethylhept-5-enal]	Melon heptenal	Unpleasant	Powerful, green-citrus, melon; CASRN: 106-72-9
Menthol [(1R,2S,5R)-2-Isopropyl-5-methylcyclohexanol]	-	Pleasant	Minty; CASRN: 89-78-1
Menthone [(2S,5R)-2-Isopropyl-5-methylcyclohexanone]	-	Pleasant	Minty; CASRN: 14073-97-3
2-Mercaptoethanol [2-Sulfanylethan-1-ol]	Thioglycol	Unpleasant	Rotten egg odour; CASRN: 60-24-2
Methanethiol [Methanethiol]	Methyl mercaptan	Unpleasant	Rotten cabbage; CASRN: 74-93-1
Methyl cedryl ketone [1-(3*R*,3a*R*,7*R*,8a*S*)-2,3,4,7,8,8a-Hexahydro-3,6,8,8-tetramethyl-1H-3a,7-methanoazulen-5-yl ethanone]	-	Pleasant	Rich, woody, musky; CASRN: 32388-55-9
Methyl-cyclopentenolone [3-Methylcyclopentane-1,2-dione]	Cyclotene	Pleasant	Nutty, sweet, maple, licorice; CASRN: 765-70-8
Methyl methacrylate [Methyl 2-methylpropenoate]	MMA	Unpleasant	Sharp, acrid, fruity; CASRN: 80-62-6
Methyl salicylate [Methyl 2-hydroxybenzoate]	Oil of wintergreen	Pleasant	Sweet, wintergreen, minty; CASRN: 119-36-8
2-Methyl-3-sulfanyl-butan-1-ol [2-Methyl-3-sulfanyl-butan-1-ol]	2M3M	Unpleasant	Sulphurous, sweat, raw onion; CASRN: 227456-33-9
4-Methylpentanoic acid [4-Methylpentanoic acid]	Isocaproic acid; 4-Methylvaleric	Unpleasant	Pungent, cheese-like; CASRN: 646-07-1

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Appendix B: List of odorants used in odour research (continued)

Odorant [IUPAC name (pure compounds)]	Common name	Hedonicity* (commonly)	Descriptors and other information
	acid		
Mint	-	Pleasant	-
Mouthwash	-	Pleasant	-
Muguet	Lily of the valley	Pleasant	Floral, lily, sweet, green
Neomidil	-	Pleasant	A detergent with a disinfectant smell
Neroli	-	Pleasant	Sweet, honey, orange blossom
S-(–)-nicotine [(S)-3-[1-Methylpyrrolidin-2-yl]pyridine]	-	Varied	CASRN: 54-11-5
Nonanal [Nonanal]	-	Pleasant	Floral, citrus, orange, fatty; CASRN: 124-19-6
Octanol	-	Unpleasant	Sharp, fatty-citrus; 89 possible isomers
1-Octen-3-ol [1-Octen-3-ol]	Octenol	Unpleasant	Green moldy, mushroom, meaty; CASRN: 3391-86-4
Olive oil (virgin)	-	Varied	-
Onion	-	Unpleasant	-
Orange	-	Pleasant	-
para-Cresol [4-Methylphenol]	*p*-Cresol	Unpleasant	Pig odour; CASRN: 106-44-5
Paraffin oil	Kerosene	Unpleasant	Fuel
Parmesan cheese	-	Neutral - Unpleasant	-
Patchouli	-	Pleasant	Earthy, woody, minty, balsamic
PCK	Japanese Cypress	Pleasant	Woody (like a Japanese forest), sweet
Peach	-	Pleasant	-
Pepper	-	Neutral	-
Peppermint	-	Pleasant	-
Perfumes		Pleasant	Many varieties used
Phenylethyl alcohol [2-Phenylethanol]	Rose; PEA	Neutral-Pleasant	CASRN: 60-12-8
2-Phenylpropionaldehyde [2-Phenylpropanal]	-	Neutral-Pleasant	Fresh, tart, green leafy-floral (hyacinth-like); CASRN: 93-53-8
Pine	-	Pleasant	Fresh, green
Pineapple	-	Pleasant	-
Propionic acid [Propionic acid]	-	Unpleasant	Pungent, sour, vinegar-like; CASRN: 79-09-4
Pumpkin	-	Pleasant	-
Pyridine [Pyridine]	-	Unpleasant	Fishy, sour; CASRN: 110-86-1
Raspberry	-	Pleasant	-
Remove®	-	Pleasant	An adhesive remover with a slight ether-like odour
Roquefort cheese	Blue cheese	Unpleasant	Pungent, stinky
Rose	-	Pleasant	-
Rose oxide	-	Pleasant - Neutral	Floral

*Hedonicity rating refers to the pleasantness perceived by the majority of the population. Actual pleasantness ratings may differ between individuals. IUPAC: International Union of Pure and Applied Chemistry. CASRN: Chemistry Abstract Services Registration Number.

Appendix B: List of odorants used in odour research (continued)

Odorant [IUPAC name (pure compounds)]	Common name	Hedonicity* (commonly)	Descriptors and other information
Rosemary	-	Pleasant	-
Rotten egg	-	Unpleasant	Sulphurous
Rubber	-	Unpleasant	-
Salvia lavandulaefolia	Sage	Pleasant	-
Salvia officinalis	Sage	Pleasant	-
Sandalwood oil	-	Pleasant	Woody, herbal, spicy
α-Santolol [(Z)-5-(2,3-Dimethyltricyclol[2.2.1.02,6]hept-3-yl)-2-methylpent-2-en-1-ol]	-	Pleasant	Woody, sandalwood. Main component of sandalwood oil; CASRN: 115-71-9
Sesame oil	-	Neutral	Faint, nutty
Skatole [3-methylindole]	-	Unpleasant	Strong, fecal odour; CASRN: 83-34-1
Skunk	-	Unpleasant	Strong, foul odour
Soy sauce	-	Neutral	-
Spearmint	-	Pleasant	-
Strawberry	-	Pleasant	-
Swine air	-	Unpleasant	Components included: hydrogen sulphide, ammonia, particulates, endotoxin
Thesaron®	-	Pleasant	Fruity, floral, rose
Thiophene [Thiophene]	-	Unpleasant	Benzene-like, gasoline-like; CASRN: 110-02-1
Thiophenol [Thiophenol]	Phenyl mercaptan	Unpleasant	Phenolic, sulphurous, rubbery; CASRN: 108-98-5
Thymol [2-isopropyl-5-methylphenol]	-	Pleasant	Thyme-like, herbal, phenolic, medicinal; CASRN: 89-83-8
Toluene [Methylbenzene]	Toluol	Neutral - Unpleasant	Sweet, pungent, benzene-like. Characteristic smell of paint-thinners; CASRN: 108-88-3
Tomato	-	Pleasant	-
Triethylamine [Triethylamine]	-	Unpleasant	Fishy, ammonia-like; CASRN: 121-44-8
Trimethylamine [Trimethylamine]	-	Unpleasant	Fishy, ammonia-like; CASRN: 75-50-3
γ-Undecalactone [5-Heptyloxolan-2one]	Peach aldehyde	Pleasant	Fruity, sweet, peachy; CASRN: 104-67-6
Undecanol [Undecan-1-ol]	-	Pleasant	Lemon, floral, sweet; CASRN: 112-42-5
Valerian	-	Unpleasant	Described as smelling like dirty feet. The odour is due to presence of isovaleric acid
Valeric acid [Pentanoic acid]	Pentanoic acid	Unpleasant	Putrid, rancid, cheesy, sweaty; CASRN: 109-52-4
Vanillin [4-Hydroxy-3-methoxybenzaldehyde]	Vanilla, vanilla bean	Pleasant	CASRN: 121-33-5
Vetiver acetate [4,8-Dimethyl-2-propan-2-ylidene-3,3a,4,5,6,8a-hexahydro-1H-azulen-6-yl) acetate]	-	Pleasant	Woody; CASRN: 117-98-6
Violet	-	Pleasant	-
Whiskey	-	Neutral	-

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Appendix B: List of odorants used in odour research (continued)

Odorant [IUPAC name (pure compounds)]	Common name	Hedonicity* (commonly)	Descriptors and other information
White sapphire	-	Pleasant	Green, floral
Wood workers glue	-	Neutral	-
Yeast (rotten yeast)	-	Unpleasant	Foul, disgusting
Ylang-ylang	-	Pleasant	Sweet, floral, woody

*Hedonicity rating refers to the pleasantness perceived by the majority of the population. Actual pleasantness ratings may differ between individuals. IUPAC: International Union of Pure and Applied Chemistry. CASRN: Chemistry Abstract Services Registration Number.

Appendix C: Summary of odour epidemiology studies

Reference	Study Date / Study Type	Odour Source and Location	Sample Size and Source Population	Measure of Exposure	Outcome	Study Findings
2013 Axelsson et al.	1992-2006 --- Longitudinal / Cross-sectional	Petrochemical area in Stenungsund, Sweden	764 (1992), 855 (1998), and 554 (2006) adults (18-75 yrs) living near petrochemical area 854 (1992), 976 (1998), and 198 (2006) adults (18-75 yrs) living in a control area	Reside near petrochemical area	Odour annoyance	For the control area, the proportion of subjects who were annoyed/very annoyed by odour was low for all 3 surveys (2–4%). In the exposed areas, the proportion of annoyed/very annoyed was highest in 1992 (27%) and lower in 1998 (20%) and 2006 (20%). The authors indicated that the reduction in odour annoyance between 1992 and 1998 was likely a result of emission reduction measures that were undertaken in the mid-1990s. The proportion of subjects who were worried about health effects from industrial air pollution did not differ over the three surveys in the exposed group (48–50%). Compared to males, females were more annoyed (OR: 1.44, 95% CI: 1.05–1.96) and more worried about health effects (OR: 1.92, 95% CI: 1.48–2.49). Subjects who were annoyed by vehicle exhaust or industrial noise or those who worried about health effects from air pollution were also more likely to be annoyed by industrial odour; this indicates a possible vulnerable group for various environmental stressors. Numbers of years living in the home did not impact the results, suggesting that residents do not become accustomed to the odours over time.
2013 Claeson et al.	Study dates not stated --- Cross-sectional	Biofuel facility in Värnamo, Sweden	722 adults (18–75 yrs) living in Värnamo, Sweden	Odorous pollution (3 zones)	Odour annoyance Health symptoms	Exposure level correlated with increases in perceived pollution (p<0.001), health risk perception (p<0.001), and intensity of odour annoyance (p<0.001). Exposure level did not correlate with health symptoms in the prior 3-month period. The investigators found that odour-related annoyance and health symptoms were not directly influenced by odorous pollution; rather, annoyance and health symptoms were mediated by perceived pollution and perceived health risk.
2013 De Feo et al.	2003 and 2009 --- Longitudinal / Cross-sectional	Municipal solid waste facility in Campania, Southern Italy	2003: 204 adults (>18 yrs) living in 4 villages near facility 2009: 200 adults (>18 yrs) living in 4 villages near facility	Residence distance to facility (4 zones)	Odour Annoyance	In 2003, the village nearest to the facility showed an unexpectedly low awareness of local pollution (68% indicated there was pollution in their local environment, compared to 85-100% in the other 3 villages) and a lower percentage of subjects who found the odour moderately to very irritating (~89% in village 1 compared to 100% in villages 2 and 3). The nearest village also showed the lowest concerns about odour-associated health issues. The authors postulated that the lower concern about local pollution and odour-related health issues, and the lower annoyance levels, were related to the municipality receiving economic compensation for the presence of the facility. Between 2003 and 2009, the percentage of subjects who thought there were odour issues in the area, who were very annoyed by odour, and who thought odour intensity had increased over the previous 2 years decreased for all villages. The facility closure had a greater impact on the closer villages than the further villages. Limitations: sampling bias (unsystematic method of sampling), potential recall bias.

CI: confidence interval; H_2S: hydrogen sulphide; NO_2: nitrogen dioxide; OR: odds ratio; ou/m^3: odour units per metre cubed; ppb: parts per billion; PM_{10}: particulate matter of ≤10 μm diameter; SO_2: sulphur dioxide

Appendix C: Summary of odour epidemiology studies (continued)

Reference	Study Date / Study Type	Odour Source and Location	Sample Size and Source Population	Measure of Exposure	Outcome	Study Findings
2013 Lowman et al.	2009-2011 --- Qualitative	Treated sewage sludge applied to land in North Carolina, South Carolina, and Virginia	34 adults (35-83 yrs) living within 1 mile of a sludge application site	Perception of odour (by subjects)	Health symptoms Mood Activity changes	Most respondents (30/34) described offensive odours related to sludge application. Approximately half (18/34) associated sludge application with acute health symptoms. The most commonly reported symptoms were eye, nose, and throat irritations and gastrointestinal symptoms (nausea, vomiting, diarrhea); other symptoms reported by more than one respondent include cough, difficulty breathing, sinus congestion or drainage, and skin infections or sores. Approximately half of the respondents (18/34) reported that sludge application in their neighborhood led to unsettling emotions (anger, frustration, misery, fear, worry, anxiety, insecurity and helplessness). Respondents most commonly expressed anger related to a lack of information about the sludge application, a lack of concern by regulators and officials, and health impacts. Most respondents (26/34) indicated that sludge odour and other related nuisances interfered with their enjoyment of home, property and the outdoors. The authors concluded that residents from 3 different states demonstrated similar health and environmental concerns regarding sewage sludge application, and further attention from scientists and public health officials is warranted.
2013 Wing et al. 2011 Schinasi et al.	2003-2005 --- Longitudinal	Industrial hog operations in 16 North Carolina communities	101 adults (>18 yrs) living within 1.5 miles of an industrial hog operation (same subjects as 2009 Horton and 2008 Wing)	Intensity of odour (by subjects) Intensity of odour (central location) H_2S (12-hr avg: 0.25 ppb) Semivolatile PM_{10} (12-hr avg: 3.9 $\mu g/m^3$)	Health symptoms Lung function Blood Pressure	Self-reported odour intensity was significantly associated with eye, nasal, throat irritation, and cough. Significant associations were also found with 1-hour averages of H_2S and PM_{10}, though the correlations were not as strong. 12-hour average central odour levels were associated with difficulty breathing, burning eyes, and nasal irritation; some of these outcomes also correlated with $PM_{2.5}$, semi-volatile PM_{10}, and H_2S. No associations were found between 12-hour odour levels and other health symptoms (sore throat, cough, wheezing, chest tightness, itching eyes, nausea, diarrhea, appetite, headache, dizziness, joint pain, fever) or changes in lung function. Increases in self-reported odour intensity correlated with diastolic blood pressure and, to a lesser extent, systolic blood pressure. The associations declined after adjustment for stress, and the authors suggested that stress may be a potential mediator of odour-related changes in blood pressure. Health outcomes were not assessed in multi-pollutant models; it is not clear if the observed health effects are a result of odour exposure, co-pollutant exposure, or a combination of both.

CI: confidence interval; H_2S: hydrogen sulphide; NO_2: nitrogen dioxide; OR: odds ratio; ou/m^3: odour units per metre cubed; ppb: parts per billion; PM_{10}: particulate matter of ≤10 μm diameter; SO_2: sulphur dioxide

Appendix C: Summary of odour epidemiology studies (continued)

Reference	Study Date / Study Type	Odour Source and Location	Sample Size and Source Population	Measure of Exposure	Outcome	Study Findings
2012, 2009 Atari et al.	2005 --- Cross-sectional	Petrochemical area in Sarnia, Ontario	774 adults (>18 yrs) living in Sarnia, Ontario	NO_2 and SO_2 (24-hr avg: NO_2: 13.82 ppb; SO_2: 3.17 ppb) VOCs (24-hr avg: BTEX tot: 3.71 µg/m³)	Odour annoyance	Odour annoyance score (degree of annoyance) was found to be greater in the higher exposure quartiles, relative to the lowest quartiles, for all pollutants. For NO_2 and SO_2, adjusted odds ratios for the highest quartiles were 3.32 ($p<0.01$) and 3.92 ($p<0.01$), respectively. Odds ratios for the highest quartiles for benzene, toluene, and BTEX were 4.77 ($p<0.05$), 10.99 ($p<0.05$), and 10.93 ($p<0.05$), respectively. Believing odours to have an adverse affect on health and a general dissatisfaction with the community were also important determinants of annoyance.
2012 Avishan et al.	2010 --- Cross-sectional	Vegetable oil processing plant in Tehran, Iran	282 adults (18–79 yrs) living near processing plant	Reside near processing plant	Odour annoyance	95% of respondents perceived odour, with 83% classifying the odour as strong to unbearably strong. Odour annoyance was very high, with 72% selecting the highest level for degree of odour annoyance. Most respondents (85%) felt the odour often or always impacted on their daily life and emotion.
2012a, 2012b Blanes-Vidal et al.	2008-2011 --- Cross-sectional	Livestock facilities in 6 non-urban areas in Denmark	180 adults (>18 yrs) living in the 6 regions	Ammonia (NH_3) (central sites) (avg concentration range: 0.16–1.34 µg/m³) NH_3 (modeled concentration using emission data and a dispersion model) (avg concentration range: 0.14–5.05 µg/m³)	Odour annoyance	In the first analysis, estimated residential NH_3 exposure was found to be associated with moderate to extreme odour annoyance (adjusted OR=10.59, CI: 1.35–83.13, for each unit increase in Log_eNH_3 exposure). In the second analysis, prevalence of odour annoyance correlated with measured NH_3 concentrations ($p<0.01$) as well as modeled NH_3 concentrations ($p<0.05$). The authors concluded that local NH_3 levels could serve as a marker for prevalence of odour annoyance in non-urban residential communities.
2012 Monazzam et al.	2011 --- Cross-sectional	Vegetable oil processing plant in Tehran, Iran	174 men (17–75 yrs) working near processing plant	Work near processing plant	Odour annoyance Activity changes	98% of respondents perceived odour, with 50% classifying the odour intensity as strong to unbearably strong and 78% classifying the hedonic tone as unpleasant to offensive. Odour annoyance was very high, with 41% selecting the highest level for degree of odour annoyance. Number of years at current workplace correlated with odour annoyance. Several workers indicated the odour negatively impacted their activity and emotion sometimes (31%), often (23%), or always (10%). The negative impact of odour on activity and emotion correlated with daily hours spent at work ($p<0.001$) and number of years at current workplace ($p<0.001$).

CI: confidence interval; H_2S: hydrogen sulphide; NO_2: nitrogen dioxide; OR: odds ratio; ou/m³: odour units per metre cubed; ppb: parts per billion; PM_{10}: particulate matter of ≤10 µm diameter; SO_2: sulphur dioxide

Appendix C: Summary of odour epidemiology studies (continued)

Reference	Study Date / Study Type	Odour Source and Location	Sample Size and Source Population	Measure of Exposure	Outcome	Study Findings
2011, 2010 Aatamila et al.	2006 --- Cross-sectional	5 waste treatment centres (with a large-scale composting plant) in 5 cities in Finland	1142 adults (25–64 yrs) living within 5 km of a waste treatment centre	Residence distance to facility (3 zones) Intensity of odour (by subjects) Frequency of odour perception (by subjects)	Odour annoyance Health symptoms	Odour annoyance (proportion of subjects somewhat annoyed or very annoyed) was higher in the innermost zone (OR: 19, CI: 12–32) and intermediate zone (OR: 6.1, CI: 3.7–10), relative to the outermost zone. Odour annoyance was also higher when odour intensity was very strong compared to mild/negligible (OR: 112, CI: 47–296, after adjustment for odour frequency). With regards to odour frequency; subjects perceiving odour at least weekly were more annoyed than subjects perceiving odour less than monthly (OR: 5, CI: 2.9–8.8, after adjustment for odour intensity). Correlations were observed between odour perception and several health symptoms; the strongest associations were found with hoarseness/dry throat, headache, and diarrhea (OR range: 1.3 to 1.4). Odour annoyance showed the most consistent relationship with symptoms; significant correlations were found with shortness of breath, eye irritation, hoarseness/dry throat, unusual tiredness, toothache, fever/shivering, joint pain and muscular pain (OR range: 1.4 to 2.0). Health symptoms did not correlate with zone of residence. The investigators concluded that high levels of odour annoyance exist in the proximity of large-scale waste treatment centres; annoyance appeared to be more influenced by odour intensity than odour frequency. Odour annoyance, rather than odour perception or residence distance to facility, appeared to be the most influential factor in self-reported health symptoms.
2011 Heaney et al.	2009 --- Longitudinal	Municipal solid waste landfill in Orange County, North Carolina	23 adults (>18 yrs) living within 0.75 miles of the landfill	Perception of odour (by subjects) Intensity of odour (by subjects) H_2S (1-hr avg: 0.22 ppb)	Health symptoms Mood Activity changes	For the 12-hour periods prior to data collection, significant associations were observed between presence of odour and alteration of daily activities (OR: 9.0, CI: 3.5–23.5). Rating of odour intensity was associated with reports of doing things differently or with difficulty (OR: 3.3, CI: 1.9–5.6) and deciding not to do things because of landfill odour (OR: 2.9, CI: 1.7–4.7). For the 5-minute outdoor periods, perception of odour correlated with negative mood states (OR: 5.2, CI: 2.8–9.6) and several health symptoms (mucosal irritation, upper respiratory symptoms, dizzy or lightheadedness, and general ill feeling; OR range: 1.9 to 5.3). No associations were found with positive mood states, ringing in the ears, or gastrointestinal symptoms. For evaluations of H_2S and health responses, correlations tended to be positive but were highly imprecise.

CI: confidence interval; H_2S: hydrogen sulphide; NO_2: nitrogen dioxide; OR: odds ratio; ou/m^3: odour units per metre cubed; ppb: parts per billion; PM_{10}: particulate matter of ≤10 μm diameter; SO_2: sulphur dioxide

Appendix C: Summary of odour epidemiology studies (continued)

Reference	Study Date / Study Type	Odour Source and Location	Sample Size and Source Population	Measure of Exposure	Outcome	Study Findings
2011 Sakawi et al.	2010 ---------- Cross-sectional	Landfills in Malaysia	190 subjects (16–75 yrs) living near a landfill site	Reside within 2 km of landfill	Odour annoyance Quality of life	Odour was perceived by ~99% of respondents, with 74% indicating the odour was very strong. Most respondents indicated they were bothered by the odour (92%), felt the odour impacted their quality of life (84%), and/or felt the odour contributed to a health effect (81%). 13% felt the odour was related to corrosion of household utensils and equipment.
2009 Horton et al. 2008 Wing et al.	2003-2005 ---------- Longitudinal	Industrial hog operations in 16 North Carolina communities	101 adults (>18 yrs) living within 1.5 miles of an industrial hog operation (same subjects as 2013 Wing and 2011 Schinasi)	Intensity of odour (by subjects) H_2S (concentrationrange: 0.01–90 ppb) Semi-volatile PM_{10} (concentrationrange: ~0–9.2 $\mu g/m^3$)	Mood Activity changes	Odours were found to bring about changes in the daily activities of subjects, including closing windows, avoiding sitting outside, cancelling plans to barbecue, not going for outdoor walks, not doing lawn work, and not washing the car. Overall, there was a 62% increase in the odds of activity change per 1-unit increase in reported odour (on a 0-to-8 scale). The odds of reporting stress for a 1-unit increase in odour was 1.81 (CI: 1.63–2.00), and for a 4-unit increase in odour was 10.6 (CI not shown). Unit increases in odour were also associated with feeling nervous, gloomy, angry, and an inability to concentrate (OR range: 1.31 to 1.60). The investigators found that coping style, but not age or odour sensitivity, modified the association between odour and stress. H_2S and semi-volatile PM_{10} also showed associations with stress/annoyance and nervous/ anxious outcomes (OR range: 1.10 to 1.18).

CI: confidence interval; H_2S: hydrogen sulphide; NO_2: nitrogen dioxide; OR: odds ratio; ou/m^3: odour units per metre cubed; ppb: parts per billion; PM_{10}: particulate matter of ≤10 μm diameter; SO_2: sulphur dioxide

Appendix C: Summary of odour epidemiology studies (continued)

Reference	Study Date / Study Type	Odour Source and Location	Sample Size and Source Population	Measure of Exposure	Outcome	Study Findings
2009, 2008 Sucker et al. 2004 Both et al.	1999-2001 (industrial) 2003-2006 (livestock) ---------- Cross-sectional	6 odour-emitting plants in 2 German states (2 pleasant - sweets production, rusk bakery; 2 neutral - textile production, seed oil production; 2 unpleasant - fat refinery, cast iron production) (industrial) 11 livestock operations in 5 German states (livestock)	1408 adults (>18 yrs) of residential areas in vicinity of plants (industrial) 901 adults (>18 yrs) of residential areas in vicinity of plants (livestock)	Frequency of odour perception (by subjects and trained panelists) Intensity of odour (by subjects and trained panelists) Hedonic tone of odour (by subjects and trained panelists)	Odour annoyance Health symptoms	A significant dose-response correlation was found between frequency of industrial odour exposure and percentage of seriously annoyed subjects (OR: 1.9, CI: 1.3–2.6; $p<0.001$); this association was strongly influenced by inclusion of odour hedonic in the model (OR: 17.6, CI: 6.7–46.5; $p<0.001$). Subjects living near the pleasant odours (sweets, rusk) reported less odour annoyance compared to the other subjects ($p<0.05$). Odour intensity did not appear to have an effect on degree of annoyance. Frequency of odour exposure was associated with increased percentage of subjects with general health complaints (OR: 1.8, CI: 1.4–2.3; $p<0.001$); this association was greatly influenced by odour hedonic (OR: 3.2, CI: 2.0–5.0; $p<0.001$) and odour annoyance (OR: 1.7, CI: 1.6–1.8; $p<0.001$). Significant correlations were found between frequency of industrial odour exposure and difficulties falling asleep (OR: 1.6, CI: 1.0–2.5; $p<0.001$) and headache (OR: 1.8; CI: 1.1–3.1; $p<0.001$). Stronger correlations were found between odour hedonic and cough, breathing difficulties, stomach disorders, and nose/eye irritation (OR range: 3.0 to 10.7; $p<0.01$). However, none of these results were significant when odour annoyance was included in the model. For the livestock operations, no significant correlations were found between odour frequency, odour intensity, odour quality (i.e., poultry, pig) and health symptoms. Annoyance from livestock odours was significantly associated with most symptoms (OR range: 1.3 to 1.4; $p<0.01$). Overall, the authors concluded that odour hedonic, but not odour intensity, has a strong influence on exposure-annoyance and exposure-symptom associations. Symptom reporting appears to be mediated mainly by odour annoyance.
2008 Tajik et al.	2002, 2004-2005 ---------- Cross-sectional	Industrial hog operations in 16 North Carolina communities	49 adults (>18 yrs) living within 1.5 miles of a hog operation	Reside near hog operation	Activity changes	Subjects reported that hog odours limited activities such as cookouts, barbequing, family reunions, socializing with neighbors, gardening, working outside, playing, drying laundry outside, opening doors and windows, use of well water, and growing vegetables.
2007 Liu et al.	2004 ---------- Cross-sectional	Domestic renovations in Tianjin, China	198 subjects living in a house undergoing renovations	Intensity of odour (by researcher)	Health symptoms	Odour intensity showed a significant association with nausea ($p=0.017$) and unspecific discomforts ($p=0.018$). For example, subjects exposed to moderate or strong odours were more likely to report unspecific discomfort compared to those exposed to weak odours (OR: 4.05, CI: 1.49–11.03). Odour was not associated with any other health symptoms (eye or nose irritation, dry throat, cough, rashes, fatigue, headache). Duration of odour exposure (i.e., average time spent at home) showed no association with symptoms.

CI: confidence interval; H_2S: hydrogen sulphide; NO_2: nitrogen dioxide; OR: odds ratio; ou/m^3: odour units per metre cubed; ppb: parts per billion; PM_{10}: particulate matter of ≤10 μm diameter; SO_2: sulphur dioxide

Appendix C: Summary of odour epidemiology studies (continued)

Reference	Study Date / Study Type	Odour Source and Location	Sample Size and Source Population	Measure of Exposure	Outcome	Study Findings
2007 Radon et al.	2002-2004 --- Cross-sectional	Confined animal feeding operations in 4 rural northwestern German towns	6937 adults (18–45 yrs) living near animal feeding operation (questionnaires) Subset of 2571 adults (18–45 yrs) living near animal feeding operation (clinical testing)	Intensity of odour annoyance (by subjects) Number of animal feeding operations within 500 m	Health symptoms Clinical outcomes	Relative to subjects not annoyed at all, strongly annoyed subjects reported more wheezing, allergic rhinitis, and physician-diagnosed asthma (OR range: 1.81 to 2.96). No associations were found between odour annoyance and any of the clinical outcomes (bronchial hyper-responsiveness to metacholine, forced expiratory volume, allergic sensitization). Subjects with >12 animal operations within 500m of their home showed increased prevalence of wheezing (OR: 2.45, CI: 1.22–4.90) and decreased forced expiratory volume (OR: -7.4, CI: -14.4 – -0.4) relative to subjects with less than 5 animal operations nearby; no associations were found with allergic rhinitis or specific sensitization.
2004 Avery et al.	Study dates not stated --- Longitudinal	7 hog operations in North Carolina	15 adults (33–77 yrs) living within 2.4 km of an intensive hog operation	Intensity of odour (by subjects)	Clinical outcomes	For both the morning and evening samples, odour intensity inversely correlated with immunoglobulin A concentrations and secretion rates (modest *t*-values; *p*-values not given). The authors concluded that exposure to odours from hog operations have an effect on the functioning of the mucosal immune system.
2004 Radon et al.	Study dates not stated --- Cross-sectional	Intensive livestock production facilities in rural Northern Germany	3112 adults (18–44 yrs) living near a livestock facility	Intensity of odour annoyance (by subjects)	Health symptoms Mood	Emotional health scores (based on a survey of self-reported depression, anxiety, feeling calm/peaceful, energy levels, or feeling downhearted) showed an inverse relationship with odour annoyance ($p<0.05$). A similar inverse correlation was found with physical health scores (based on a survey of general health and ability to do physical activities) ($p<0.05$). The investigators concluded that subjects living near livestock facilities may have a decreased quality of life, and suggested that this could be improved by better communication about health risks.
2003a Herr et al.	Study dates not stated --- Cross-sectional	3 composting sites in Germany	496 adults (>18 yrs) living within 1.5 km of a composting site 301 adults (>18 yrs) living in a control area	Reside near composting site Frequency of odour annoyance (by subjects)	Health symptoms	Frequency of odour annoyance was higher in all exposed communities (80%, 90%, and 41%) compared to their respective controls (26%, 17%, and 12%). Nausea was found to be more frequently reported in the two communities reporting high rates of odour annoyance. Frequency of total number of reported somatic symptoms (e.g., headache and facial pain, lower back pain, nausea, joint pain, breathlessness) was higher in all exposed groups compared to their control groups, though this difference was only significant ($p<0.001$) for the community that was also exposed to airborne micro-organisms. Other than nausea, the investigators found that frequently-reported somatic symptoms were influenced little by odour annoyance.

CI: confidence interval; H_2S: hydrogen sulphide; NO_2: nitrogen dioxide; OR: odds ratio; ou/m^3: odour units per metre cubed; ppb: parts per billion; PM_{10}: particulate matter of ≤10 μm diameter; SO_2: sulphur dioxide

Appendix C: Summary of odour epidemiology studies (continued)

Reference	Study Date / Study Type	Odour Source and Location	Sample Size and Source Population	Measure of Exposure	Outcome	Study Findings
2003b Herr et al. (also 2009 Herr et al.)	1997 ---------- Cross-sectional	Composting site in Germany	214 subjects (age not stated) living within 500 m of composting site 142 subjects (age not stated) living in a control area	Reside near composting site Frequency of odour annoyance (by subjects)	Health symptoms	Odour annoyance was reported by 80% of subjects living within 500 m and 95% of subjects living within 200 m of the site, compared to 26% in the control community. Odour annoyance was associated with nausea, itching or stinging eyes, joint problems, muscular complaints, and impaired coordination (OR range: 1.84 to 10.40). No associations were found with respiratory outcomes. Odour annoyance did not appear to influence the relationship between airborne microorganisms and irritant airway complaints.

CI: confidence interval; H_2S: hydrogen sulphide; NO_2: nitrogen dioxide; OR: odds ratio; ou/m^3: odour units per metre cubed; ppb: parts per billion; PM_{10}: particulate matter of ≤10 μm diameter; SO_2: sulphur dioxide

Appendix C: Summary of odour epidemiology studies (continued)

Reference	Study Date / Study Type	Odour Source and Location	Sample Size and Source Population	Measure of Exposure	Outcome	Study Findings
2002a, 2002b, 2000 Luginaah et al.	1992 and 1997 --- Longitudinal / Cross-sectional	Petroleum refinery in Oakville, Ontario	1997: 427 adults (>18 yrs) living near refinery 1992: 391 adults (>18 yrs) living near refinery (see 1997 Taylor)	Residence distance to facility (3 zones) Frequency of odour perception (by subjects)	Odour annoyance Health Symptoms Coping	Significant zonal gradients for frequency of odour perception and odour annoyance were found in both surveys, with more frequent reporting for zone 1 and least frequent for zone 3. The change in odour perception over the 5 years was significant for zone 1 (p<0.0016); very frequent reporting decreased from 42 to 26%, while the percentage of subjects perceiving odours less frequently or not at all showed corresponding increases. The percentage of subjects that were annoyed by odours all the time to half the time decreased from 35 to 29% over the 5 years. There was no significant difference in health symptom reporting between zones for either year, nor did the health symptom reporting change between 1992 and 1997. The investigators concluded that zone of residence (as a measure of exposure) was not a strong predictor of health symptoms for nearby residents. In both years, the prevalence of several symptoms (cough, nausea, sinus/nose congestion, eye irritation, throat irritation, headaches, sleep problems, dizziness, stomach pain, diarrhea, chest pain) was significantly higher in subjects who perceived odours frequently and in subjects who were frequently annoyed. The investigators found symptom reporting to be strongly mediated by odour perception and odour annoyance. Despite the implementation of odour reduction measures by the industry, no significant changes were found to symptom prevalence rates or to the association between odour perception/annoyance and symptom reporting. The authors suggested that the persistence of symptom reporting points to the possibility that sensitive individuals in the community may be reporting health issues in the absence of harmful effects from the refinery. Reappraisal of odours is thus considered a complex process that involves personal and situational factors as well as changes in exposure. In-depth interviews were completed for a subset of 29 subjects to assess the role of coping and community perceptions about the refinery. While odour levels had been reduced over the 5 years, many residents perceived no change in odour and still expressed concern about the refinery, employing both action-focused and emotion-focused coping strategies in response to odours. The authors concluded that refinery intervention may have to move beyond the technological odour reduction measures to address the psychological and social concerns of residents.

CI: confidence interval; H_2S: hydrogen sulphide; NO_2: nitrogen dioxide; OR: odds ratio; ou/m^3: odour units per metre cubed; ppb: parts per billion; PM_{10}: particulate matter of ≤10 μm diameter; SO_2: sulphur dioxide

Appendix C: Summary of odour epidemiology studies (continued)

Reference	Study Date / Study Type	Odour Source and Location	Sample Size and Source Population	Measure of Exposure	Outcome	Study Findings
2001 Engvall et al.	1992-1993 --- Cross-sectional	Multi-family building in Stockholm, Sweden	3241 subjects (>18 yrs) living in multi-family buildings	Odour perception (by subjects)	Health symptoms	All types of odours (pungent, musty, stuffy, mouldy) showed significant relationships with cumulative incidence of asthma symptoms, current cough, and hay fever (OR range: 2.06 to 5.86). For subjects with hay fever only (i.e., without respiratory symptoms), the relationships remained significant for pungent, musty and stuffy odours, but not for mouldy odours (OR range: 1.86 to 2.10).
2000 Miedema et al.	1984-1996 --- Meta-analysis of 6 cross-sectional studies	11 odour-emitting factories in the Netherlands (oil extraction, chemical, rendering plant, pig farm, sugar blending, grass drying, potato chips, wire coating, pastry, cacao, tobacco)	6276 subjects (>13 yrs or >18 yrs) living near a factory (98 to 984 subjects per factory)	Average odour concentrationusing trained panelists, factory emission data, and a dispersion model (concentrationrange: ~0.15–100 OU/m^3) Hedonic tone of odour (by trained panelists)	Odour annoyance	Using data from all studies combined, log odour concentration correlated with the percentage of highly annoyed persons as a quadratic function (*r*: 0.889). Including an odour pleasantness score improved the accuracy of the model (*r*: 0.945); the percentage of highly annoyed subjects was greater if the odour was unpleasant. The authors concluded that odour hedonic is an important factor in odour annoyance, or alternatively, that factors confounded with odour hedonic are partly responsible for the differences in annoyance.
2000 Wing and Wolf	1999 --- Cross-sectional	Cattle or hog operations in North Carolina	105 adults (>18 yrs) living within 2 miles of a cattle/hog operation 50 adults (>18 yrs) living in a control area	Reside near cattle or hog operation	Health symptoms Activity changes	Subjects living near the hog operation reported significantly lower quality of life, as measured by *'can't open windows'* and *'can't go outside'*, compared to control subjects and subjects living near the cattle operations. For example, the percentage of subjects reporting they *'can't open windows'* often was 14%, 8%, and 57% for the control, cattle, and hog groups, respectively. Subjects living near a hog operation reported a higher prevalence of mucous membrane irritation, runny nose, sore throat, excessive coughing, headaches, burning eyes, and diarrhea ($p<0.05$) compared to the control community. Subjects living near the cattle operation reported significantly more episodes of excessive coughing and heartburn ($p<0.05$). Reporting for many other health outcomes (e.g., shortness of breath, chest tightness, wheezing, heartburn, tearing eyes, dry skin, tiredness, joint/muscle pain, dizziness, blurred vision, and fever/chills) did not differ between exposed and control communities.
1999 Georgieff and Turnovska	Study dates not stated --- Cross-sectional	Cellulose paper plant in Stamboliisky, Bulgaria	374 adults (>16 yrs) living in Stamboliisky	Reside in Stamboliisky	Health symptoms Mood	89% of subjects perceived an unpleasant odour near their home. Psycho-emotional symptoms (irritation, nervousness, depression) were present in 90% of those perceiving the smell. A smaller percentage of subjects (19-54%) reported other symptoms such as headache (27%), sleep disturbances (19%), nausea or vomiting (30%), and allergic reaction (54%). 52% of subjects perceiving the odour reported that olfactory irritation led to decreased work capacity.

CI: confidence interval; H_2S: hydrogen sulphide; NO_2: nitrogen dioxide; OR: odds ratio; ou/m^3: odour units per metre cubed; ppb: parts per billion; PM_{10}: particulate matter of ≤10 μm diameter; SO_2: sulphur dioxide

Appendix C: Summary of odour epidemiology studies (continued)

Reference	Study Date / Study Type	Odour Source and Location	Sample Size and Source Population	Measure of Exposure	Outcome	Study Findings
1999 Steinheider 1998 Steinheider et al.	1992-1993 ---------- Cross-sectional	Odour-emitting sources in 2 German cities (Nettetel: fertilizer plant) (Nörvenich: pig rearing facility)	Nettetel: 250 adults (>18 yrs) living up to 3.5 km from facility Nörvenich: 322 adults (>18 yrs) living up to 7 km from facility	Nettetel: Residence distance to facility (3 zones) Nörvenich: Odour frequency (odour hours/year) by trained panelists	Odour annoyance Health symptoms	In Nettetel, degree of annoyance increased significantly with increasing proximity to the odour source (distance to source explained ~61% of the variation in annoyance). Subjects living closer to the plant reported more gastric symptoms (disgust, loss of appetite, vomiting, nausea, retching) and some general health symptoms (headache, breathing difficulties, cough, stomach and sleep disorders) than those living further away. Symptom reporting appeared to be mediated by both odour exposure and odour annoyance in these subjects. In Nörvenich, degree of annoyance increased significantly with odour frequency (odour frequency explained ~17% of variation in annoyance). Odour frequency had a small but significant effect on reporting of gastric symptoms and general health symptoms. After adjustment for odour annoyance, no association was found between odour exposure and symptoms; symptom reporting appeared to be mediated strictly by odour annoyance. The authors concluded that exposure to offensive odours (i.e., pig facility in Nörvenich) induces both annoyance reactions as well as symptom reporting, while in the case of exposure to moderate odour exposures (i.e., fertilizer plant in Nettetel), somatic symptoms are mediated by odour annoyance.

CI: confidence interval; H_2S: hydrogen sulphide; NO_2: nitrogen dioxide; OR: odds ratio; ou/m^3: odour units per metre cubed; ppb: parts per billion; PM_{10}: particulate matter of ≤10 μm diameter; SO_2: sulphur dioxide

Appendix C: Summary of odour epidemiology studies (continued)

Reference	Study Date / Study Type	Odour Source and Location	Sample Size and Source Population	Measure of Exposure	Outcome	Study Findings
1997 Taylor et al.	1992 (baseline survey) --- Cross-sectional	Petroleum refinery in Oakville, Ontario	391 adults (age not stated) living near refinery (baseline survey)	Residence distance to facility (3 zones) Frequency of odour perception (by subjects)	Odour annoyance Health symptoms	Odour annoyance was most common in the two zones closest to the refinery; a significant gradient in odour annoyance was found across the three zones (p<0.0001).Compared to those who infrequently or never noticed odours, subjects who noticed odours frequently (>once per week) were 2 to 4 times more likely to report cardinal symptoms (cough, nausea, congestion, eye irritation, throat irritation, earache, skin rash; OR range: 1.84 to 3.43), general symptoms (headache, sleep problems, dizziness, stomach pain, diarrhea, chest pain; OR range: 1.75 to 2.96), and other symptoms (back pain, bruising; OR range: 2.09 to 2.23). These subjects were also more likely to state that the symptoms were induced or worsened by the refinery odours. Symptoms were found to be 2 to 4 times more prevalent in subjects that were frequently bothered by the odours, compared to those infrequently bothered (OR range: 1.65 to 4.71). No significant associations were observed for wheeze, colds, nosebleeds, appetite loss, or dysuria. The authors hypothesized that odour perception and annoyance sensitize residents to possible health effects, leading to increased symptom reporting and attributing symptoms to refinery emissions; however, they also realized that the association may occur in the reverse direction, such that experiencing symptoms may increase the likelihood that residents perceive and become annoyed by refinery odours. As residence distance to the refinery and frequency of odour perception were not associated with symptoms, the evidence supports an indirect role of odours in symptom reporting, rather than a direct toxicological link. Follow-up studies of this population have been published by Luginaah *et al.* (2000, 2002a, 2002b).
1997 Taylor et al. (cont'd)	1994 (follow-up interview) --- Cross-sectional	Petroleum refinery in Oakville, Ontario	40 adults (age not stated) living near refinery (follow-up interview)	Residence distance to facility (3 zones)	Mood Activity changes	The authors discuss 3 typical profiles for residents living near the refinery: (1) those who are frequently annoyed by odours and worried about possible health effects; (2) those who notice odours but are not very annoyed by them, with some concern about possible health effects; and (3) those who rarely notice odors and feel that the benefits of the refinery outweigh any concerns. Three hypotheses for the link between odour perception/annoyance and symptom reporting are supported: psychosomatic reaction to stress, reporting bias, and odour-mediated effects. The authors concluded that social and community factors play an important role in conditioning how residents perceive and respond to the refinery.

CI: confidence interval; H_2S: hydrogen sulphide; NO_2: nitrogen dioxide; OR: odds ratio; ou/m^3: odour units per metre cubed; ppb: parts per billion; PM_{10}: particulate matter of ≤10 μm diameter; SO_2: sulphur dioxide

Appendix C: Summary of odour epidemiology studies (continued)

Reference	Study Date / Study Type	Odour Source and Location	Sample Size and Source Population	Measure of Exposure	Outcome	Study Findings
1997 Thu et al.	Study dates not stated --- Cross-sectional	Large-scale swine production facility in Iowa	18 adults (avg age: 47 yrs) living within 2 miles of a swine facility 18 adults (avg age: 47 yrs) living in a control area	Reside near swine facility	Health symptoms Mood	Compared to control subjects, the exposed group reported higher frequencies of several health symptoms including respiratory symptoms (p=0.02), nausea/weakness/dizziness/fainting (p=0.04), and headaches/plugged ears (p=0.06). Frequency of reported symptoms did not correlate with residence distance from the swine facility. No significant differences were found for depression or anxiety. The authors noted that while ammonia, dust, and endotoxin are typically present in the air downwind from swine facilities in Iowa, the levels are much lower than those previously associated with any known illness.
1995 Schiffman et al.	Study dates not stated --- Cross-sectional	Hog operations in North Carolina	44 adults (avg age: 52 yrs) living near hog operation 44 adults (avg age: 52 yrs) living in a control area	Reside near hog operation	Mood	For every mood factor (e.g., tension, depression, anger, vigor, fatigue, and confusion) as well as the total mood disturbance score, subjects living near hog operations had significantly worse scores than the control group (p<0.0001). The authors concluded that odours from swine operations have a negative impact on the moods of nearby residents.
1994 Cavalini 1991 Cavalini et al.	1988-1990 (subject interviews) 1971-1990 (odour exposure calculation) --- Cross-sectional	Odour-emitting sources in 2 cities in the Netherlands (Groningen: 2 sugar refineries) (sugar) (Groningen: tobacco plant) (tobacco) (Gennep: nursery of mushroom manure and a cattle fodder plant (manure)	511 subjects (sugar - short term exposure) 1033 subjects (sugar - long term exposure) 216 subjects (tobacco - long term exposure) 653 subjects (manure - long term exposure)	Average odour concentration using factory emission data and a dispersion model (concentrationrange: 0–15 OU/m^3)	Odour annoyance Health symptoms	For all odour types, long-term concentrations correlated with annoyance (taken as a product of annoyance intensity and frequency; r range: 0.24–0.36; p<0.01), and odour annoyance tended to correlate with health complaints (r range: 0.23–0.68; p<0.01). Age typically showed a negative correlation with odour annoyance (r range: –0.20 – –0.22; p<0.001). Despite tobacco and manure odorant concentrations (~0.2 OU/m^3) being lower than the sugar refinery odours (~3 OU/m^3), they caused the same or more annoyance than the sugar odours; this suggests that odour hedonic plays a role in annoyance. The relationship between odour concentration and odour annoyance or general health complaints was stronger in subjects that perceived the odour as a threat to health. Additionally, general coping strategies appeared to modify the relationship between odour concentration and annoyance. Subjects coping in a problem-oriented way (look for ways to solve the problem) reported annoyance more often than subjects coping in an emotion-oriented manner (regulating emotions caused by the problem). In the studies of short-term exposures to sugar odours, the relation between odour and annoyance was similar or weaker (depending on the year of assessment) than the assessments of long-term exposure. Perceiving odour as a threat to health was the strongest predictor of annoyance in these subjects. The authors suggested that annoyance may be a phenomenon resulting from long term exposures.

CI: confidence interval; H_2S: hydrogen sulphide; NO_2: nitrogen dioxide; OR: odds ratio; ou/m^3: odour units per metre cubed; ppb: parts per billion; PM_{10}: particulate matter of ≤10 μm diameter; SO_2: sulphur dioxide

Appendix C: Summary of odour epidemiology studies (continued)

Reference	Study Date / Study Type	Odour Source and Location	Sample Size and Source Population	Measure of Exposure	Outcome	Study Findings
1993 Steinheider and Winneke	1989-1990 --- Cross-sectional	Odour-emitting sources in 4 German cities (Brühl: cast-iron, sugar) (Dortmund: iron/steel) (Duisburg: sulphur chemical plant) (Rodenkirchen: several oil refineries)	Brühl: 539 adults Dortmund: 400 adults Duisburg: 400 adults Rodenkirchen: 200 adults	Odour frequency (odour hours/year) by trained panelists	Odour annoyance	Brühl was excluded from the analysis due to lack of exposure measurements during the period in which the refinery was operating. In the remaining 3 cities, odour frequency was significantly associated with degree of odour annoyance (*r* range: 0.25–0.34; $p<0.001$). Annoyance appeared to be modified by age, perceived health status, and coping strategy, but these factors did not significantly influence the odour frequency-odour annoyance association.
1991 Ames and Stratton	Study dates not stated --- Cross-sectional	Potato field treated with the pesticide Ethoprop (Mocap®) in Dorris, California (the main odorant was *N*-propyl mercaptan)	421 subjects (all ages) living within 1 km of potato field	Frequency of odour perception (by subjects) Intensity of odour (by subjects) Residence distance to potato field (4 zones)	Health symptoms	The incidence of 15 health outcomes (e.g., headaches, asthma attacks, burning eyes, runny nose, nausea, etc.) was significantly increased in subjects who perceived a strong odour compared to those who did not (OR range: 1.77 to 6.00). A unit increase in odour intensity (no odour, mild, strong, extremely strong) was associated with an increased risk of being highly symptomatic (OR=2.42). Also, a dose-response correlation was observed between the number of days strong odour was perceived and the total number of reported symptoms. Residence distance to the potato field did not show a significant relationship with health symptoms. *N*-propyl mercaptan levels were not measured in the study; thus, it is not known if the observed health effects are due to odour itself or to toxic properties of the chemical.

CI: confidence interval; H_2S: hydrogen sulphide; NO_2: nitrogen dioxide; OR: odds ratio; ou/m^3: odour units per metre cubed; ppb: parts per billion; PM_{10}: particulate matter of ≤10 μm diameter; SO_2: sulphur dioxide

Appendix C: Summary of odour epidemiology studies (continued)

Reference	Study Date / Study Type	Odour Source and Location	Sample Size and Source Population	Measure of Exposure	Outcome	Study Findings
1991 Lipscomb	1981; 1988 --- Cross-sectional / Longitudinal	Waste disposal site (inactive) in Fullerton Hills, California	123 adults (>22 yrs) living near waste disposal site 70 adults (>22 yrs) living in a control area	Reside near waste disposal site (2 zones)	Health symptoms	Reporting of several health symptoms (e.g., skin irritation, nausea, wheezing, loss of appetite, headache) was increased among the high-exposed group relative to the control group (crude OR range: 0.78 to 5.95; skin irritation OR: 4.97; CI: 1.82–13.63). Interestingly, toothache (included as a dummy symptom to assess reporting bias) showed the highest odds ratio (OR: 5.95, CI: 1.85–19.16). When the associations between exposure group and health symptoms were stratified by low, medium, or high environmental worry, results remained for the high worry group only. No association or a negative association was found for subjects with low environmental worry. A subset of six symptoms was used to compare the data from the 1981 and 1988 surveys. Reporting of the six symptoms was significantly increased in the high-exposure group in both 1981 and 1988. Symptom reporting for the 1988 survey was higher than in the 1981 survey, despite remediation efforts at the site and reduced odour exposures. Overall, the evidence suggests that symptom reporting is associated with perceived environmental risk. Further research into the reasons for environmental worry suggested that worry caused symptom reporting rather than symptoms causing worry. Environmental data showed contaminants to be below toxicological thresholds.
1991 Shusterman et al.	1983-1987 --- Cross-sectional	3 hazardous wastes sites in California (Fullerton: acid petroleum sludge) (Monterey Park: municipal and sewage waste, paint/petroleum sludge) (Del Amo/Montrose: DDT, synthetic rubber)	Fullerton: 670 adults Monterey Park: 514 adults Del Amo/Montrose: 856 adults	Frequency of odour perception (by subjects)	Health symptoms	Using pooled data from the three areas, symptom prevalence (headache, nausea, eye and throat irritation) was significantly associated with both frequency of odour perception (headache OR: 5.0, CI: 3.3–7.7) and degree of environmental worry (headache OR: 10.8, CI: 6.2–16.8). The strongest associations were found in subjects that perceived odours frequently and were very worried about environmental health (headache OR: 36.7, CI: 11.2–77.7). For nausea and throat irritation, no significant association was found with odour frequency in subjects with low environmental worry.

CI: confidence interval; H_2S: hydrogen sulphide; NO_2: nitrogen dioxide; OR: odds ratio; ou/m^3: odour units per metre cubed; ppb: parts per billion; PM_{10}: particulate matter of ≤10 μm diameter; SO_2: sulphur dioxide

Appendix C: Summary of odour epidemiology studies (continued)

Reference	Study Date / Study Type	Odour Source and Location	Sample Size and Source Population	Measure of Exposure	Outcome	Study Findings
1991 van den Hazel and Waege-maekers	Study dates not stated --- Longitudinal	Paper mill and water treatment plant in the Netherlands	142 subjects living near paper mill and water treatment plant	Residence distance to paper mill (2 zones) Frequency of odour perception (3 zones) (by trained panelists) Average odour concentration using emission data and a dispersion model (concentration not given)	Odour annoyance	Degree of odour annoyance was found to be significantly higher in the inner zone relative to the outer zone (p<0.001). For rotten odour, annoyance correlated with odour exposure across the three zones, whether measured by odour frequency or odour concentration (p-values not given). Wood odour did not follow the same pattern; the authors stated that a masking of the wood odour by the rotten odour may have resulted in the lack of association.
1988 Miedema and Ham	1984-1985 --- Cross-sectional	Odour-emitting sources in 3 cities in the Netherlands (Rotterdam: oil extraction factory) (Tiel: pig farm) (Venlo: electric wire coating factory)	Rotterdam: 353 adults Tiel: 172 adults Venlo: 728 adults	Average odour concentration using odour panelists, factory emission data, and a dispersion model (concentrationrange: 0.6–106 OU/m^3)	Odour annoyance Mood Activity changes	Odour concentration (1-hour average) was significantly associated with the percent of subjects who were annoyed or very annoyed (r: 0.90, with exclusion of the very low exposure values). Exposure-annoyance relationships did not differ between the three sources. Odour concentration also correlated with odour-induced closing of windows. No association was found between odour exposure and frequency of reporting odour-induced sleeping problems.
1987 Winneke and Kastka	Study dates not stated --- Cross-sectional	Odour-emitting sources in 3 German cities (Aachen: chocolate factory) (Cologne: insulation plant) (Duisburg: tar-oil refinery; brewery)	Aachen: 108 subjects Cologne: 108 subjects Duisburg: 97 subjects (brewery) 270 subjects (tar-oil refinery)	Average odour concentration using trained panelists (concentrationrange: 2–25 OU/m^3) Residence distance to facility (4 zones)	Odour annoyance	Degree of odour annoyance was lowest in subjects living near the chocolate factory compared to the other sources, despite similar odour concentrations. Annoyance was highest in those living near the brewery and the tar-oil refinery, while those living near the insulation plant showed moderate annoyance. These differences were not explained by variations in socio-economic factors, attitudes towards industry, or self-reported health. Odour annoyance as a function of distance to the plant was difficult to interpret and no clear pattern emerged. The authors concluded that different odour sources are related to varying levels of odour annoyance, and suggested that exposure-annoyance correlations be considered for homogeneous classes of sources.

CI: confidence interval; H_2S: hydrogen sulphide; NO_2: nitrogen dioxide; OR: odds ratio; ou/m^3: odour units per metre cubed; ppb: parts per billion; PM_{10}: particulate matter of ≤10 μm diameter; SO_2: sulphur dioxide

Appendix C: Summary of odour epidemiology studies (continued)

Reference	Study Date / Study Type	Odour Source and Location	Sample Size and Source Population	Measure of Exposure	Outcome	Study Findings
1983 Bruvold et al.	1980 --- Cross-sectional	Sewage treatment plants in Novato and Pacifica, California	Pacifica: 54 adults residing near treatment plant 54 control adults Novato: 50 adults residing near treatment plant 48 control adults	Reside near sewage treatment plant Odour perception (yes/no; by subjects) H_2S concentration (range:<0.4-5.7 ppb)	Odour annoyance Activity changes	H_2S levels, odour perception, and intensity of odour annoyance were higher in each area located near a plant, relative to its control area. When data from all areas were pooled, intensity of odour annoyance was higher in those living close to a sewage treatment plant (p<0.001) and those living in the area with the highest odour exposure (p<0.001); associations were not modified by socio-economic factors. Subjects in the 2 exposed communities reported the highest number of odour-induced complaints regarding quality of life. For example, subjects reported that odours had an effect on children playing, having guests over, working outdoors, being forced indoors, temporarily leaving the neighbourhood, considering moving, and having reduced property values. The number of complaints matched well with the number of subjects perceiving odours in each area.
1977 Deane and Sanders 1977 Deane et al. 1975 Jonsson et al.	1969 (pilot study) 1971 (second study) --- Cross-sectional	2 pulp mills in Eureka, California	158 adults living near pulp mills (pilot study) 140 new adults living near pulp mills (second study)	Residence distance to pulp mills (3 zones) Frequency of odour perception (by trained panelists) Methanethiol concentration (range: ~0-22 ppb)	Odour annoyance Health symptoms	In the pilot study, investigators observed significant gradients across the 3 zones in odour perception (p<0.01), as well as in the degree and frequency of odour annoyance (p<0.01); for example, the percentage of subjects moderately to very annoyed by the odours was 50%, 31%, and 18% in zones 1 to 3, respectively (p<0.01). The differences in annoyance across areas were not explained by socio-economic differences; however, negative attitudes towards the pulp mill appeared to play a role in degree of annoyance. In the follow-up study, zone 1 had the greatest number of annoyed subjects; however, zones 2 and 3 no longer showed a distinct difference in odour annoyance. Of subjects who noticed odours, the percentage that were very bothered decreased in zones 1 and 2, and increased in zone 3. These differences matched the changes in odour exposure levels (odour frequency, methanethiol levels) seen across the 2 surveys. Based on 1971 data, prevalence of phlegm was higher in zone 1 females relative to the other zones (p<0.05); however, this may have been influenced by the high percentage of female smokers in zone 1. Odour exposure did not positively correlate with any other health symptoms (e.g., cough, shortness of breath, runny nose, headache, nausea). Unexpectedly, some symptoms showed an inverse relationship with odour, including sleeplessness, difficulty urinating, sinus congestion, eye irritation, and runny nose. Reports of headache were higher in annoyed subjects compared to subjects annoyed little to not at all (p<0.05); no significant differences between annoyance groups were found for other symptoms. The authors considered the overall results to be inconclusive concerning the link between odours and health effects.

CI: confidence interval; H_2S: hydrogen sulphide; NO_2: nitrogen dioxide; OR: odds ratio; ou/m^3: odour units per metre cubed; ppb: parts per billion; PM_{10}: particulate matter of ≤10 μm diameter; SO_2: sulphur dioxide

Appendix D: Summary of physiological responses and health symptoms

Reference	Odour Type and Concentration	Exposure (sniff/non-sniffing) (BR/MR-L/MR-R)	Population Group (age)	Study Findings
2013 Sayorwan et al.	Rosemary oil (10% v/v)	20 min (non-sniffing; BR)	20 healthy adults (18-28 y; mean: 21 y)	·↑ systolic and diastolic BP, HR, and respiratory rate; ↓ skin temperature
2013 Zhang et al.	Essential oil from 4 aromatic plants (*Lavandula angustifolia, Salvia sclarea Lavandula, Santalum album, Citrus sinensis*)	45 min per day for 10 days (ambient room odour; BR)	31 female university students (mean: 20 y)	· odour induced significant metabolic changes in urine (↑ levels of arginine, homocysteine, and betaine, ↓ levels of alcohols, carbohydrates, and organic acids; also, tricarboxylic acid cycle metabolites and gut microbial metabolites were significantly altered)
2012 Banks et al.	Bergamot (100%), Isobutyric acid (50%), Muguet (90%), Pyridine (2.5%)	2 s (non-sniffing; BR)	16 female university students (19-33 y)	· pleasant odour (bergamot, muguet): ↑ SCR compared to the unpleasant odours (isobutyric acid, pyridine) · when paired with unpleasant images, pleasant odour ↓ SCR and unpleasant odour ↑ SCR
2012 Krusemark and Li	Acetophenone (0.00015-5%), Anisole (0.0005-5%), Eugenol (0.001-5%), Guaiacol (0.0005-5%), Trimethylamine (0.00005-0.00025%), Valeric acid (0.0005%), Mixtures of above odorants	2 s (sniff; BR)	14 healthy adults (18-28 y; mean: 21 y)	· unpleasant mixtures compared to neutral mixtures: correlation between subject anxiety ratings after the task and SCR induced by unpleasant odour (suggesting that anxiety heightened the emotional arousal induced by malodour) · no effect on respiratory parameters
2012 Sayorwan et al.	Lavender oil (10% v/v)	20 min (non-sniffing; BR)	20 healthy adults (18-35 y; mean: 23 y)	·↓ systolic and diastolic BP, HR, and skin temperature; no effect on respiratory rate
2012 Trellakis et al.	Fennel, Grapefruit, Lavender, Patchouli, Pepper, Rose essential oils (below threshold)	30 min (ambient room odour; BR)	32 healthy adults (20-45 y; mean: 29 y)	· odours had no effect on blood inflammatory markers (neutrophil activity, cytokines) · the authors concluded that short-term subconscious exposure to stimulating or relaxing odour had no relevant effect on immune function
2011 Matsubara et al.	*Laurus nobilis* L. leaves	45 min (non-sniffing; BR)	9 male university students (20-23 y)	· low dose *L. nobilis*: ↓ HRV R-R interval at 10-30 min and slightly ↑ LF/HF HRV at 20-30 min · high dose *L. nobilis*: ↓ HRV R-R interval at 10-30 min and slightly ↓ HF HRV at 25 min · results suggest an elevation of cardiovascular function (sympathetic activation) for both doses
2010 Mezzacappa et al.	Coconut extract	45 min (non-sniffing; BR)	32 healthy adults (mean: 33 y)	·↑ HR and ↓ HRV (root mean square of successive differences of R-R interval), suggestive of ↓ parasympathetic activity · coconut attenuated a stress-induced increase in HR and diastolic BP

BP: blood pressure; BR: birhinal; HF: high frequency (HRV component); HR: heart rate; HRV: heart rate variability; IL: interleukin; LF: low frequency (HRV component); min: minutes; MR-L: monorhinal left side; MR-R: monorhinal right side; ms: milliseconds; PEA: phenylethyl alcohol; ppb: parts per billion; ppm: parts per million; ppt: parts per trillion; s: seconds; SCR: skin conductance response; v/v: volume per volume; y: years

Appendix D: Summary of physiological responses and health symptoms (continued)

Reference	Odour Type and Concentration	Exposure (sniff/non-sniffing) (BR/MR-L/MR-R)	Population Group (age)	Study Findings
2009 Delplanque et al.	16 pairs of pleasant odours and 16 pairs of unpleasant odours (e.g., Amyl acetate, Basil, Body odour, Geraniol, Honey, Isovaleric acid, Lavender, Leather, Lime, Melanol, Octanol, Peach, Pineapple, Sulfox) (concentration not stated)	2 s (non-sniffing; BR)	18 university students (mean: 27 y)	· novelty and pleasantness appraisal processes are organized in a sequential fashion: earliest effects on facial muscles and HR occurred in response to novelty detection, while later effects on facial muscles and HR occurred in response to pleasantness evaluation · unpleasant odours and novel odours showed stronger SCRs than pleasant odours and repeated odours, respectively
2009 Peng et al.	*Citrus bergamia* oil (75× dilution)	15 min (non-sniffing; BR)	114 university students (18-25 y; mean: 20 y)	· odour ↑ HF HRV, ↓ LF HRV, and ↓ LF/HF HRV (increased parasympathetic tone, decreased sympathetic tone) · no change to HR, systolic or diastolic BP, or HRV time domain
2009 Schneider et al.	Carbon dioxide (40% and 60% v/v), Hydrogen sulphide (4 ppm), Lime (20% v/v), PEA (20% and 40% v/v)	500 ms (non-sniffing; BR)	21 healthy adults (18-35 y; mean 25 y)	· olfactory and trigeminal odours ↑ pupillary diameter · response latencies decreased with increasing odour intensity; response amplitudes differed with odour quality (largest for trigeminal odour (CO_2)) · pupillary response did not differ with odour hedonic
2009 Yamaguchi et al.	Citrus aurantium oil (bitter orange), Lavender oil (1% and 3% wt/wt)	10 min (non-sniffing; BR)	15 healthy women (20-24 y; Mean: 21 y)	· citrus, lavender (1%): ↓ salivary amylase · citrus, lavender (1% and 3%): non-significant ↓ in salivary cortisol and non-significant ↑ in salivary dehydroepiandrosterone (stress hormones)
2008 Delplanque et al.	48 odorants (e.g., Amyl acetate, Basil, Durian, Geraniol, Honey, Isobutyric acid, Isovaleric acid, Lavender, Leather, Lime, Skunk, Sulfox) (concentration not stated)	2 s (non-sniffing; BR)	18 university students (mean: 27 y)	· odour familiarity and pleasantness were negatively correlated with SCR; this effect was more significant in response to unpleasant than pleasant odours · odour familiarity, pleasantness or intensity did not correlate with latency of SCR or respiratory amplitude
2008 Djordjevic et al.	Almond extract, Carrot seed oil, Citral, Fir needle oil, Geraniol, Isoamyl acetate, Juniper berry, Parmesan cheese (all pure); Cumin oil (1%), Indole (1%) (odours were paired with positive, neutral, or negative names)	2 s (sniffing; BR)	30 university students (18-29 y; mean: 21 y)	· odours carrying positive or negative names ↑ SCR compared to odours with neutral names (this effect was not seen with odourless stimuli) · odour names had no effect on HR
2008 Howard and Hughes	Lavender	2 inhalations, then 10 min near sample vial (sniffing; BR)	96 female university students (mean: 21 y)	· odours had no effect on SCR · significant effect of suggestion/expectancy: subjects told that the odour would increase anxiety had ↓ SCR (↑ resistance), while those told the odour was relaxing had ↑ SCR (↓ resistance)
2008 Kiecolt-Glaser et al.	Lavender, Lemon (pure essential oil)	1.25 hr (non-sniffing; BR)	56 healthy adults (18-43 y; mean 24 y)	· odours did not significantly alter HR, BP, blood IL-6 or IL-10, salivary cortisol, or skin barrier repair following tape stripping · lemon and lavender led to ↓ hypersensitivity to Candida relative to no odour · elevated norepinephrine levels following cold pressor stress were maintained in subjects exposed to lemon odour

BP: blood pressure; BR: birhinal; HF: high frequency (HRV component); HR: heart rate; HRV: heart rate variability; IL: interleukin; LF: low frequency (HRV component); min: minutes; MR-L: monorhinal left side; MR-R: monorhinal right side; ms: milliseconds; PEA: phenylethyl alcohol; ppb: parts per billion; ppm: parts per million; ppt: parts per trillion; s: seconds; SCR: skin conductance response; v/v: volume per volume; y: years

Appendix D: Summary of physiological responses and health symptoms (continued)

Reference	Odour Type and Concentration	Exposure (sniff/non-sniffing) (BR/MR-L/MR-R)	Population Group (age)	Study Findings
2008 Laudien et al.	Isobornyl acetate (9.3% v/v)	300 ms (non-sniffing; BR)	45 healthy women (18-46 y; mean: 23 y)	· subjects told the odour was harmful reported more irritant symptoms (throat irritation, unclear vision, eye irritation, drowsiness, sleepiness, dazedness, bad taste) than subjects told the odour was healthy or neutral
2008 Oka et al.	Green odour (0.03% v/v; mixture of 2*E*-hexenal and 3*Z*-hexenol)	10 min (non-sniffing; BR)	19 healthy adults (21-48 y; mean: 33 y)	· non-stressful conditions: no effect on BP, HR, or skin temperature · stressful conditions: odour attenuated the cold pressor-induced ↑ in systolic and diastolic BP and improved the recovery of skin temperature; thus, green odour demonstrated anti-stress effects
2008 Shiina et al.	Lavender oil	30 min (ambient room odour; BR)	30 healthy men (24-40 y; mean: 34 y)	·↑ coronary circulation, no effect on BP or HR ·↓ serum cortisol (stress hormone)
2008 Tanida et al.	Fragrance (floral green)	Continuous exposure for 4 weeks	31 female college students (mean: 22 y)	· after 4 weeks continuous exposure, subjects had ↓ facial sebum secretion and non-significant ↓ in HR · these effects were thought the be mediated by a shift in the dominant side of stress-induced prefrontal cortex activity (from right side to left side) and subsequent activation of the hypothalamic–pituitary–adrenal axis
2008 Toda and Morimoto	Lavender oil	10 min (non-sniffing; BR)	30 university students (21-26 y)	· lavender induced a stress-relieving effect; levels of the salivary stress marker chromogranin A, but not salivary cortisol, were reduced after lavender exposure
2007 Armstrong et al.	Butyl isobutyrate, Triethylamine (concentrations used were those which produced max muscle activity for each child; range: 0.08-2.65 mol/L), Carvone (0.266 mol/L), *cis*-3-hexenol (0.034 mol/L)	5 s (non-sniffing; BR)	34 healthy children (6-9 y)	· the zygomatic and levator labii facial muscles show different activity changes in response to pleasant and unpleasant odours · odours ↑ activity in the zygomaticus; no discrimination between odour hedonic · the unpleasant odour (triethylamine) produced higher activity in the levator labii muscles than the other pleasant odours
2007 Atsumi and Tonosaki	Lavender oil, Rosemary oil (10× and 1000× dilutions)	5 min (non-sniffing; BR)	22 healthy adults (mean: 23 y)	· lavender (1000x dilution) and rosemary (10x dilution) ↑ salivary free radical scavenging activity · lavender and rosemary ↓ salivary cortisol (stress hormone) levels · no significant changes for salivary α-amylase or secretory immunoglobulin A · the authors concluded that lavender and rosemary odours help to protect the body from oxidative stress
2007 Duan et al.	Lavender fragrance (concentration not stated)	40 min (non-sniffing; BR)	10 healthy women (20-27 y; mean: 23)	· odour ↑ HF HRV and ↓ LF/HF HRV (increased parasympathetic tone, decreased sympathetic tone) · no change to HR, systolic BP, diastolic BP or mean BP

BP: blood pressure; BR: birhinal; HF: high frequency (HRV component); HR: heart rate; HRV: heart rate variability; IL: interleukin; LF: low frequency (HRV component); min: minutes; MR-L: monorhinal left side; MR-R: monorhinal right side; ms: milliseconds; PEA: phenylethyl alcohol; ppb: parts per billion; ppm: parts per million; ppt: parts per trillion; s: seconds; SCR: skin conductance response; v/v: volume per volume; y: years

Appendix D: Summary of physiological responses and health symptoms (continued)

Reference	Odour Type and Concentration	Exposure (sniff/non-sniffing) (BR/MR-L/MR-R)	Population Group (age)	Study Findings
2007 Li et al.	Anisole (720 ppt), Citral (3600 ppt), Valeric acid (7.5 ppt) (all included subjects considered the citral odorant to be pleasant)	1 inhalation (sniff; BR)	17 university students (17-27 y)	· citral ↓ HR and valeric acid ↑ HR ; anisole did not significantly affect HR · odour hedonic had a significant impact on HR; this effect was independent of odour awareness
2006 Heuberger et al.	*a*-Santalol, East Indian Sandalwood oil (~2.5-3.5 mg of odorant via nebulizer for each subject)	20 min (non-sniffing; BR)	36 healthy adults (mean: 24 y)	· sandalwood oil: ↑ pulse rate, skin conductance, and systolic BP · alpha-santalol: no change to any physiological arousal parameters (blood-oxygen saturation, respiration rate, eye-blink rate, BP, pulse rate, skin conductance, or surface electromyogram) · differences in arousal level appeared to be related to differences in perceived odour quality
2005 Field et al.	Lavender (fragrance in cleansing gel)	2 min (non-sniffing; BR)	11 healthy adults (age not stated)	· ↓ HR during exposure (relaxation)
2005 Kuroda et al.	Jasmine tea (20× dilution of 1 min steep of 25 g tea), Lavender oil (1 μL/L)	6 min (non-sniffing; BR)	12 healthy adults (21-36 y)	· both odours ↓ HR and ↑ HF HRV for more than 40 min (increased parasympathetic activity) · no effect found on LF HRV (sympathetic activity)
	(*R*)-(–)-Linalool (0.03 ppm), (*S*)-(+)-Linalool (0.03 ppm)	6 min (non-sniffing; BR)	12 healthy adults (21-36 y)	· (*R*)-(–)-linalool ↓ HR and ↑ HF HRV (increased parasympathetic activity); no change to LF HRV (sympathetic activity) · (*S*)-(+)-linalool ↑ HR, ↓ HF HRV, and ↑ LF HRV (increased sympathetic, decreased parasympathetic activity) · (*R*)-(–)-linalool (a component of jasmine tea) mimicked the effects of jasmine tea and lavender odours, while (*S*)-(+)-linalool did not
2005 Masaoka et al.	Isovaleric acid, PEA (individual odour detection and recognition thresholds used)	1 inhalation (non-sniffing; BR)	17 healthy men (mean: 32 y)	· pleasant odour (PEA): ↓ respiratory rate · unpleasant odour (isovaleric acid): ↑ respiratory rate · these changes not due to metabolic demand
2005 Schiffman et al.	Diluted swine air (57-fold greater than odour threshold) (components: H_2S (24 ppb), ammonia (817 ppb), total suspended particulates (0.0241 mg/m^3), endotoxin (7.40 units/m^3))	1 hr (ambient room odour; BR)	48 healthy adults (19-49 y; mean: 26)	· swine odour ↑ reports of headaches, eye irritation, and nausea, but not sore throat, nasal irritation/congestion, or cough · swine odour ↑ % of epithelial cells and lymphocytic cells in nasal lavage, but not any other measures of nasal inflammation or salivary immunoglobulin A · no change found in HR, BP, respiratory rate, body temperature, or pulmonary function
2004 Burnett et al.	Lavender, Rosemary	10 min (ambient room odour; BR)	73 university students (18-30 y)	· odour did not impact HR or body temperature following an anxiety-provoking task

BP: blood pressure; BR: birhinal; HF: high frequency (HRV component); HR: heart rate; HRV: heart rate variability; IL: interleukin; LF: low frequency (HRV component); min: minutes; MR-L: monorhinal left side; MR-R: monorhinal right side; ms: milliseconds; PEA: phenylethyl alcohol; ppb: parts per billion; ppm: parts per million; ppt: parts per trillion; s: seconds; SCR: skin conductance response; v/v: volume per volume; y: years

Appendix D: Summary of physiological responses and health symptoms (continued)

Reference	Odour Type and Concentration	Exposure (sniff/non-sniffing) (BR/MR-L/MR-R)	Population Group (age)	Study Findings
2004 Campenni et al.	Lavender, Neroli (concentration not stated)	11 min (ambient room odour; BR)	90 healthy women (mean: 20 y)	· odours had no significant effect on HR or SCR · the suggestion that an odour was relaxing led to ↓ HR and SCR, while suggesting that an odour was stimulating led to ↑ HR and SCR (all changes attributable to suggestion)
2004 Hongratana-worakit and Buchbauer	Ylang-ylang oil	20 min (ambient room odour; BR)	24 healthy subjects (age not stated)	·↓ systolic BP, diastolic BP, and pulse rate · no effect on breathing rate or skin temperature · breathing rate correlated with subjects ratings of attentiveness, while pulse rate negatively correlated with attentiveness
2004 Jacquot et al.	Butanol, PEA, Pyridine (concentration range: 0 to 25 dilutions (6×10^{-6} % to 100% v/v))	5 s (non-sniffing; BR)	30 healthy women (20-32 y; mean: 24 y)	· for all odorants, psychophysical odour thresholds (ability to differentiate between odour and control) were lower than self-evaluated thresholds (self-evaluation for certainty of odour choice) · bimodal odours (butanol, pyridine) showed lower psychophysiological thresholds (based on SCR) than psychophysical and self-evaluated thresholds · bimodal odours (butanol, pyridine) produced SCR at lower concentrations than the non-trigeminal odour (PEA) · unconscious odour detection may be due to trigeminal component of odours
2003 Danuser et al.	Ammonia, Hydrogen sulphide, Menthone, Pentylacetate (two intensities used: threshold or double the threshold for each subject)	2 min (non-sniffing; BR)	12 healthy adults (20-36 y; mean: 25 y)	· at threshold: no effect of odours on mean inspiration flow · at double threshold: unpleasant odours (ammonia, H_2S) induced a ↓ in mean inspiration flow; pleasant odours had no effect
2003 Dayawansa et al.	Cedrol (extract from cedar wood oil) (14.2 µg/L)	10 min (non-sniffing; BR)	26 healthy adults (mean: 24 y)	· odour ↓ HR, diastolic BP, systolic BP, and respiratory rate · odour ↑ HF HRV, ↓ LF HRV, and ↓ LF/HF HRV · overall, cedrol ↑ parasympathetic and ↓ sympathetic activity
2003 Inoue et al.	Chinese green tea, Jasmine tea (high-intensity: 1 min steep of 25 g tea; low-intensity: 20× dilution)	5 min (non-sniffing; BR)	8 healthy Japanese adults (21-36 y; mean: 25 y)	· jasmine tea (low dose): ↓ HR and ↑ HF HRV (↑ parasympathetic activity; induced a sedative effect) · jasmine tea (high dose): ↑ parasympathetic activity in subjects who liked the odour; ↑ sympathetic activity in those who disliked the odour · green tea (high dose): ↑ parasympathetic activity in subjects with a predilection for the odour
2003 Møller and Dijksterhuis	Butyric acid, Citral, Peach, Skatole (concentration not stated; all odours of similar intensity)	6 s (non-sniffing; BR)	14 healthy adults (21-38 y; mean: 26 y)	· all odours induced ↑ SCR, though at varying rates; responses were larger on right hand than the left hand · no relationship found between SCR and odour familiarity or pleasantness · SCR latencies were ~3 s and did not differ between odours and control
2003 Pan et al.	Furfurylmercaptan (coffee aroma) (concentration not stated)	80 min (ambient room odour; BR)	9 healthy adults (mean: 26 y)	· odour exposure ↑ symptoms of dry nose but not headache, skin moisture, or nasal dimensions · general well-being worsened with odour exposure

BP: blood pressure; BR: birhinal; HF: high frequency (HRV component); HR: heart rate; HRV: heart rate variability; IL: interleukin; LF: low frequency (HRV component); min: minutes; MR-L: monorhinal left side; MR-R: monorhinal right side; ms: milliseconds; PEA: phenylethyl alcohol; ppb: parts per billion; ppm: parts per million; ppt: parts per trillion; s: seconds; SCR: skin conductance response; v/v: volume per volume; y: years

Appendix D: Summary of physiological responses and health symptoms (continued)

Reference	Odour Type and Concentration	Exposure (sniff/non-sniffing) (BR/MR-L/MR-R)	Population Group (age)	Study Findings
2003 Royet et al.	126 odorants with varying hedonicity (e.g., Butyric acid, Cinnamon, Lavender, Lemon, Lilac, Mint, Onion, Pepper, Raspberry, Pine, Rose, Tobacco) (1-10% v/v)	3-5 s (non-sniffing; BR)	28 healthy adults (20-30 y)	· unpleasant odours induced ↑ SCR compared to pleasant odours
2002b Bensafi et al.	Cineole, Isoamyl acetate, Isovaleric acid, Menthol, Pyridine, Thiophenol (concentration not stated)	1 inhalation (~1 s) (sniff; MR-R or MR-L)	18 university students (mean: 27 y)	· unpleasant odours associated with ↑ HR; pleasant odours had no effect · no change to skin conductance
2002c Bensafi et al.	Cineole, Isoamyl acetate, Isovaleric acid, Menthol, Pyridine, Thiophenol (concentration range: 1.5-60 mmol/L)	1 inhalation (~1 s) (sniff; MR-R)	12 university students (mean: 26 y)	· odour arousal correlated with SCR · pleasantness negatively correlated with HR · no other significant associations found between odour arousal/pleasantness/ familiarity/intensity and skin conductance or HR
2002d Bensafi et al.	Apple, Butter, Caramel, Chocolate, Coconut, Coffee, Fish, Garlic, Onion, Roquefort cheese, Tomato, Vanilla (1/100 dilution for all odours)	1 inhalation (~1 s) (sniff; MR-R or MR-L)	12 university students (mean: 22 y)	· odour arousal, but not odour pleasantness or intensity, correlated with ↑ SCR · unpleasant odours associated with ↑ facial corrugator muscle activity compared to pleasant odours; also, odours judged as disgusting led to ↑ corrugator muscle activity than odours inducing joy or no emotion · odour intensity or arousal rating did not correlate with muscle activity
2002 Haze et al.	Estragon oil, Fennel oil, Grapefruit oil, Patchouli oil, Pepper oil, Rose oil (2% wt/wt)	3-7 min (non-sniffing; BR)	43 healthy women (22-25 y)	· estragon, fennel, grapefruit, pepper: ↑ sympathetic activity (measured as low frequency amplitude of systolic BP) · patchouli, rose oil: ↓ sympathetic activity · pepper ↑ plasma adrenaline; rose ↓ plasma adrenaline
2001 Bartocci et al.	Neomidil (a detergent), Remove® (adhesive remover)	10 s (non-sniffing; BR)	20 pre-term newborns (0-35 days)	· no change to HR, respiratory rate, or arterial oxygen saturation
2001 Brand and Jacquot	Allyl isothiocyanate (strong trigeminal), Isoamyl acetate, PEA (weak trigeminal), Triethylamine (concentration not stated, but odours were of similar intensities)	3 s (non-sniffing; BR, MR-R, or MR-L)	30 subjects (age not stated)	· unpleasant odour (triethylamine) showed ↑ SCR relative to pleasant odour (isoamyl acetate) · strong trigeminal odour showed ↑ SCR relative to weak trigeminal odour
2001 Heuberger et al.	*S*-(+)-Carvone, *R*-(–)-Carvone, *R*-(+)-Limonene, *S*-(–)-Limonene (~50-175 mg of odorant via nebulizer for each subject)	30 min (non-sniffing; BR)	20 healthy adults (18-36 y; mean: 24 y)	· *R*-(+)-limonene and *S*-(–)-limonene both ↑ systolic BP · *S*-(+)-carvone and *R*-(–)-carvone both ↑ diastolic BP; *S*-(+)-carvone also ↑ systolic BP, and *R*-(–)-carvone also ↑ pulse rate · no change to skin temperature, SCR, respiratory rate, blood oxygen saturation · effects of odours impacted by subjective odour evaluation and chirality of odour molecules
2001 Motomura et al.	Lavender oil	20 min (non-sniffing; BR)	42 university students (mean: 21 y)	· no effect of odour on HR, diastolic BP, or systolic BP

BP: blood pressure; BR: birhinal; HF: high frequency (HRV component); HR: heart rate; HRV: heart rate variability; IL: interleukin; LF: low frequency (HRV component); min: minutes; MR-L: monorhinal left side; MR-R: monorhinal right side; ms: milliseconds; PEA: phenylethyl alcohol; ppb: parts per billion; ppm: parts per million; ppt: parts per trillion; s: seconds; SCR: skin conductance response; v/v: volume per volume; y: years

Appendix D: Summary of physiological responses and health symptoms (continued)

Reference	Odour Type and Concentration	Exposure (sniff/non-sniffing) (BR/MR-L/MR-R)	Population Group (age)	Study Findings
2001 Simpson et al.	Lavender oil, Peppermint oil	1 min (non-sniffing; BR)	8 college students (mean: 22 y)	· no significant effect on respiratory parameters or HR during exercise (walking) · ratings of perceived exertion were slightly lower (non-significantly) in both odour conditions compared to control
2000 Brand et al.	Isoamyl acetate (25% v/v), Triethylamine (25% v/v)	3 s (non-sniffing; BR, MR-R, or MR-L)	30 university students (20-25 y)	· unpleasant odour (triethylamine): ↑ SCR relative to pleasant odour · pleasant odour (isoamyl acetate): ↑ SCR after birhinal exposure relative to monorhinal exposure; no differences found with the unpleasant odour
2000 Hermann et al.	Vanilla (concentration not stated), Yeast (0.2 g/mL)	500 ms (non-sniffing; BR)	30 healthy men (17-39 y; mean: 26 y)	· unpleasant odour (yeast): ↑ blink magnitude (startle reflex), ↑ activity of left and right corrugator muscles and left zygomaticus muscles; no change to HR · pleasant odour (vanilla): no change to blink magnitude (startle reflex), facial muscle activity, or HR
2000 Nagai et al.	Jasmine, Lavender, Lemon, Orange, Peppermint, Rose (all 1/1000 dilutions) (subjects chose their most preferred odour)	2.5-4 min (ambient room odour; BR)	26 university students (18-24 y)	· odours attenuated handgrip exercise-induced increase in diastolic BP · odours had no effect on systolic BP, respiratory rate, or finger pulse wave during handgrip exercises
1999 Asmus and Bell	Asafoetida, Cigarette ash, Rotten egg, Skunk (concentration not stated)	~10-20 min (ambient room odour; BR)	240 university students (age not stated)	· BP differed across odour groups, but no pattern found between odour discomfort and BP
1999 Dalton	Butanol, Isobornyl acetate, Methyl salicylate (concentration not stated)	20 min (ambient room odour; BR)	180 healthy adults (18-45 y; mean: 32 y)	· subjects given a harmful odour bias reported more intense odour and irritation and more health symptoms than subjects given a neutral or healthful odour bias · response to ambient odours may be determined more by perceived exposure risk and cognitive associations rather than a direct effect of odour
1999, 1998 Robin et al.	Eugenol (0.15% v/v), Menthol (1% v/v), Methyl methacrylate (0.015% v/v), Propionic acid (0.015% v/v), Vanillin (1% v/v)	5 s (non-sniffing; BR)	44 university students (20-28 y; mean: 25 y)	· eugenol: ↑ autonomic changes in subjects with a fear of the dentist (longer skin resistance response, primarily C-form skin potential responses, tachycardia) · eugenol can induce different emotional states (based on the pattern of autonomic responses) depending on a subject's dental experience · eugenol induced an autonomic response associated with negative emotions (fear, anger, disgust) in subjects fearful of the dentist, and an autonomic response of positive emotions (happiness, surprise) in non-fearful subjects · vanillin was associated with autonomic response of happiness; propionic acid associated with autonomic response of anger and disgust · autonomic responses to odours other than eugenol did not differ between fearful and non-fearful subjects
1999 Romine et al.	Lavender oil	10 min (ambient room odour; BR)	20 male university students (age not stated)	· no significant effect on cardiovascular parameters (HR, diastolic BP, systolic BP, mean arterial pressure, pulse pressure) during recovery from exercise (2 min brisk walking)

BP: blood pressure; BR: birhinal; HF: high frequency (HRV component); HR: heart rate; HRV: heart rate variability; IL: interleukin; LF: low frequency (HRV component); min: minutes; MR-L: monorhinal left side; MR-R: monorhinal right side; ms: milliseconds; PEA: phenylethyl alcohol; ppb: parts per billion; ppm: parts per million; ppt: parts per trillion; s: seconds; SCR: skin conductance response; v/v: volume per volume; y: years

Appendix D: Summary of physiological responses and health symptoms (continued)

Reference	Odour Type and Concentration	Exposure (sniff/non-sniffing) (BR/MR-L/MR-R)	Population Group (age)	Study Findings
1999 Soussignan et al.	Protein hydrolysate formula, Regular formula (familiar and unfamiliar), Vanillin (0.31% v/v) (odour intensity of the formulas was judged to be the same as the intensity of vanillin)	10 s (non-sniffing; BR)	14 healthy newborns (58-129 hrs)	· odours ↑ respiratory rate relative to no odour; this effect did not differ between pre-feeding and post-feeding conditions · no main effect of odours on HR · post-feeding: odours from familiar formulas induced ↑ HR change and facial disgust actions relative to odours from unfamiliar formulas
1997a Alaoui-Ismaili et al.	Acetic acid (1/1000 dilution), Butyric acid (1/1000), Camphor (1/100), Ethyl acetoacetate (1/100), Lavender (1/100)	1 inhalation (unclear) (non-sniffing; BR)	15 university students (22-28 y; mean: 25 y)	· unpleasant odour (acetic acid, butyric acid): long duration of SCR, ↑ skin blood flow, and ↑ HR · pleasant odour (lavender, ethyl acetoacetate): short duration of SCR, ↓ skin blood flow, and ↓ HR · pleasant (camphor): response between that of pleasant and unpleasant odour
1997b Alaoui-Ismaili et al.	Eugenol (0.5% v/v), Menthol (1% v/v), Methyl methacrylate (0.015% v/v), Propionic acid (0.015% v/v), Vanillin (1% v/v)	60s or 1 inhalation? (non-sniffing; BR)	44 university students (22-28 y; mean: 25 y)	· unpleasant odour (methyl methacrylate, propionic acid): long-duration responses in skin resistance, ↑ skin blood flow, ↑ instantaneous HR variation · pleasant odour (menthol, vanillin): short-duration responses in skin resistance, ↓ skin blood flow, ↓ instantaneous HR variation · eugenol: varied responses
1997 Ehrlichman et al.	Coconut (100% v/v), Limburger cheese (4 grams)	~13s (sniff; MR-R or MR-L)	80 university students (age not stated)	· cheese: ↑ blink magnitude (startle reflex), ↑ HR relative to no odour · coconut: ↓ blink magnitude (startle reflex), no difference in HR relative to no odour
1997 Soussignan et al.	Amniotic fluid, Breast milk, Butyric acid, Formula milks, Vanillin (concentration not stated)	10s (non-sniffing; BR)	46 healthy newborns (46-124 hrs)	· odours ↑ respiratory rate and induced changes in facial displays · some evidence to suggest that neonates can discriminate between pleasant and unpleasant odours, though not to the same extent as adults
1995 Brauchli et al.	PEA (76 ppb), Valeric acid (23 ppb)	30s (non-sniffing; BR)	4 healthy men (mean: 24 y)	· valeric acid: ↑ HR and ↑ SCR (non-significant) · PEA: ↓ HR and ↓ SCR (non-significant)
1995 Ehrlichman et al.	Baghdad water lily (20%), Butyric acid (30%), Coconut (pure), Douglas fir (20%), Isovaleric acid (5%), Limburger cheese (8.5 grams), Muguet (20%), Orange oil (pure), Smoked cigar butt, Thiophene (1%), Vanilla bean (20%), Vitamin B pills crushed	~13s (sniff; BR)	52 university students (age not stated)	· unpleasant odours: ↑ blink magnitude (startle reflex) relative to no odour · pleasant odours: no difference in blink magnitude relative to no odour
1995 Knasko	Baby powder, Chocolate (concentration not stated)	~15 min (ambient room odour; BR)	90 healthy adults (18-35 y)	· subjects exposed to baby powder reported fewer health symptoms (throat/eye/skin/nose irritation, headache, fatigue) than those exposed to no odour; symptoms did not differ between chocolate and no odour groups · subjects exposed to chocolate reported less hunger than those exposed to no odour; no significant difference in thirst symptoms was found between groups

BP: blood pressure; BR: birhinal; HF: high frequency (HRV component); HR: heart rate; HRV: heart rate variability; IL: interleukin; LF: low frequency (HRV component); min: minutes; MR-L: monorhinal left side; MR-R: monorhinal right side; ms: milliseconds; PEA: phenylethyl alcohol; ppb: parts per billion; ppm: parts per million; ppt: parts per trillion; s: seconds; SCR: skin conductance response; v/v: volume per volume; y: years

Appendix D: Summary of physiological responses and health symptoms (continued)

Reference	Odour Type and Concentration	Exposure (sniff/non-sniffing) (BR/MR-L/MR-R)	Population Group (age)	Study Findings
1994 Jäncke and Kaufmann	Butanol (1/1000 and 1/10 dilutions), PEA (1/1000 and pure) Pyridine (1/2000 and 1/10)	30 s (sniff; BR) (in private)	20 healthy adults (21-35 y)	· ↑ activity in orbicularis oculi, levator, and nasalis muscles in response to high concentrations of pyridine and butanol (unpleasant odours) · pleasant odours did not induce 'smiling' muscle activity · facial muscle activity did not correlate with odour hedonic rating
		30 s (sniff; BR) (in private or in front of investigator)	20 healthy men (20-29 y)	· in front of an audience: subjects showed ↑ zygomaticus and orbicularis oculi muscle activity when smelling pleasant odours (indicative of a smile), and ↑ nasalis muscle activity (indicative of disgust) when smelling unpleasant odours (compared to subjects smelling odours in private) · the authors concluded that facial responses to odours are more a function of social communication than pure reflex
1994 Miltner et al.	Hydrogen sulphide (10 ppm), Vanillin (2 ppm)	5 min (non-sniffing; MR-R or MR-L)	16 healthy adults (23-43 y; mean: 31 y)	· H_2S ↑ startle reflex amplitude (significant) and vanillin ↓ startle-reflex amplitude (non-significant), relative to no odour · odours had no effect on HR or SCR
1994 Warren et al.	Acetic acid (3.2-99.9 ppm), Amyl acetate (1.3-41.6 ppm), PEA (0.7-21 ppm)	10 s (non-sniffing; BR)	10 adults (age not stated)	· tidal volume showed an inverse correlation with ratings of nasal irritation · decreases in tidal volume were strongest for acetic acid and weakest for PEA
1993 Knasko	Isovaleric acid (0.5%), Lemon (100%), Skatole (0.5%), Ylang (10%)	15 min (ambient room odour; BR)	90 healthy adults (18-35 y)	· pleasant or unpleasant odour had no effect on number or intensity of reported symptoms (e.g., headache, eye irritation) · subjects exposed to malodor stated retrospectively that they believed the odour had a negative influence on their health
1992 Knasko	Dimethyl sulphide, Lavender, Lemon (concentration not stated)	time not stated (non-sniffing, ambient room odour; BR)	94 healthy adults (18-35 y)	· subjects exposed to lemon reported fewer symptoms (throat/eye/skin irritation, headache, other pain) compared to control sessions or to subjects exposed to dimethyl sulphide · odour had no significant effect on health symptom intensity
1990 Knasko et al.	No odours used; subjects were merely told they were being exposed to a pleasant, unpleasant, or neutral odour	15 min (non-sniffing; BR)	90 healthy adults (18-35 y)	· subjects in the unpleasant odour group reported significantly higher total number of symptoms (throat/eye/skin irritation, headache, backache, other pain) than subjects in the pleasant or neutral odour groups · no difference in hunger or thirst symptoms
1983 Van Toller et al.	Androstanone (0.6 mg/mL), Aurantiol (20% v/v)	< 25 s (non-sniffing; BR)	36 adults (age not stated)	· androstanone: ↑ SCR amplitude relative to aurantiol · those who perceived androstanone as pleasant showed faster SCR recovery times to both odours relative to those perceiving androstanone as unpleasant

BP: blood pressure; BR: birhinal; HF: high frequency (HRV component); HR: heart rate; HRV: heart rate variability; IL: interleukin; LF: low frequency (HRV component); min: minutes; MR-L: monorhinal left side; MR-R: monorhinal right side; ms: milliseconds; PEA: phenylethyl alcohol; ppb: parts per billion; ppm: parts per million; ppt: parts per trillion; s: seconds; SCR: skin conductance response; v/v: volume per volume; y: years

Appendix E: Summary of changes in mood and task performance

Reference	Odour Type and Concentration	Exposure (sniff/non-sniffing) (BR/MR-L/MR-R)	Population (age)	Study Findings
2013 Buissonnière-Ariza et al.	Fish odour (25%), Strawberry (10%)	500 ms (sniff; BR)	36 healthy adults (18-35 y; mean 24 y)	· subjects with high-trait anxiety had faster response times in the odour detection task for both the pleasant and unpleasant odour · the authors concluded that anxious subjects were faster at detecting odors than low anxiety subjects, regardless of odour hedonicity or subjective experience
2013 Sayorwan et al.	Rosemary oil (10% v/v)	20 min (non-sniffing; BR)	20 healthy adults (18-28 y; mean: 21 y)	·↑ active and fresh emotions ·↓ drowsy feelings
2012 Banks et al.	Bergamot (100%), Isobutyric acid (50%), Muguet (90%), Pyridine (2.5%)	2 s (non-sniffing; BR)	16 female university students (19-33 y)	· pleasant odour (bergamot, muguet): ↑ in ratings of images compared to unpleasant odour; no effect on ratings of images compared to air · unpleasant odour (isobutyric acid, pyridine): ↓ in ratings of images compared to control; effects were strongest with pleasant and neutral images
2012 Guéguen	Bakery pastry odours	not known (ambient odour in shopping mall)	400 adults (~20-50 y)	· help was offered more often to a man/woman who dropped a glove when in the presence of bakery odour, compared to no odour (pleasant odour ↑ helping behavior)
2012 Sayorwan et al.	Lavender oil (10% v/v)	20 min (non-sniffing; BR)	20 healthy adults (18-35 y; mean: 23 y)	·↑ pleasant emotions (good, active, fresh, and relaxed) ·↓ bad and drowsy feelings
2012 Villemure et al.; 2009 Villemure and Bushnell	China rain floral scent, Creamsicle, Lemon meringue, Violet (all 0.3% and 3% v/v); Mint (0.5% and 5% v/v); Pyridine (0.1% and 1% v/v) (most pleasant/unpleasant odour chosen by subject)	5 s (non-sniffing; BR)	14 healthy adults (18-28 y; mean: 23 y)	· pleasant odour: ↑ positive mood and ↑ calmness · pleasant odour: ↓ heat-induced pain unpleasantness (but not pain intensity); this effect occurred independent of attentional focus · effect of odour on pain unpleasantness was mediated by mood
2011 Matsubara et al.	*Laurus nobilis* L. (laurel) leaves	45 min (non-sniffing; BR)	9 male university students (20-23 y)	· low dose *L. nobilis*: attenuated a decrease in performance at 20-30 minutes on a visual discrimination vigilance task; emotion scores did not differ from control · high dose *L. nobilis*: no significant effect on vigilance task performance · high dose *L. nobilis*: higher scores for negative emotions (stormy, danger, unpleasant, acrid)
2011 Schifferstein et al.	Orange, Peppermint, Seawater	not known (ambient room odour; BR)	849 adults (age not stated)	· all odours ↑ dancing activity and improved evaluation of the evening and music at a nightclub · all odours ↑ self-reported cheerfulness; the effects of odours on the evaluation of the evening were found to be partly mediated by cheerfulness · no effect on other mood outcomes (quiet–active and independent–dependent)

BR: birhinal; H_2S: hydrogen sulphide; min: minutes; MR-L: monorhinal left side; MR-R: monorhinal right side; ms: milliseconds; PEA: phenylethyl alcohol; ppb: parts per billion; ppm: parts per million; ppt: parts per trillion; s: seconds; SZ: schizophrenia; v/v: volume per volume; wt/wt: weight per weight; y: years

Appendix E: Summary of changes in mood and task performance (continued)

Reference	Odour Type and Concentration	Exposure (sniff/non-sniffing) (BR/MR-L/MR-R)	Population (age)	Study Findings
2010 Finkelmeyer et al.	Eugenol (concentration not stated), Hydrogen sulphide (~9 ppm)	24 s (ambient room odour; BR)	25 healthy adults (22-58 y; mean 32 y)	· unpleasant odour (H_2S) resulted in reduced (improved) reaction times for incongruent stimuli in the Stroop test (a word/colour processing task) · neutral odour (eugenol) had no consistent effect on Stroop test reaction times · improved cognitive processing in the task appeared to be facilitated by an odour-induced negative emotional state
2010 Heuberger and Ilmberger	1,8-Cineole (5 and 20 µL), Jasmine absolute ether (20 and 50 µL), Linalyl acetate(5 and 20 µL), Peppermint oil (20 µL)	15 min (non-sniffing; BR)	240 healthy adults (16-66 y; mean: 32 y)	· linalyl acetate: improved reaction times on vigilance task; performance speed correlated with subjective ratings of odour pleasantness · cineole (low dose): false alarms (reaction without stimulus) increased linearly with ratings of odour unpleasantness and odour arousal · cineole, linalyl acetate (high dose): false alarms increased with ratings of odour pleasantness and relaxation · peppermint: false alarms increased with higher ratings of odour intensity and lower ratings of stress · the authors concluded that subjective factors have a strong impact on odour-induced modulation of attentional functions
2010 Mezzacappa et al.	Coconut extract	45 min (non-sniffing; BR)	32 healthy adults (mean: 33 y)	· no significant effect on mood scores
2010 Moss et al.	*Salvia lavandulaefolia*, *Salvia officinalis* (sage) (concentration not stated)	25 min (ambient room odour; BR)	135 university students (mean: ~22 y)	· *S. officinalis*: improved performance on tests assessing quality of memory; this occurred with long term memory but not working memory · *S. lavandulaefolia*: no significant effect on cognitive performance tests (results were typically between those of the control group and the *S. officinalis* group) · both odours ↑ alertness score; no effect on calmness or contentedness
2010 Reske et al.	Rotten yeast (0.1 g/mL), Vanilla (0.05 g/mL)	2 s (non-sniffing; MR-R)	15 healthy women (21-47 y)	· unpleasant odour (yeast) yielded increased ratings for disgust and lower ratings of happiness relative to air or vanilla · ratings for disgust and happiness did not differ for vanilla and air
2010 Walla and Deecke	Hydrogen sulphide (3 ppm and 0.03 ppm), PEA (100% and 5%)	1 s (non-sniffing; MR-R)	10 adults (mean: 24 y)	· H_2S (3ppm): ↓ in subjective emotion rating when shown a picture of a baby · PEA (5%, 100%) and H_2S (0.03 ppm): ↑ in subjective emotion rating when subjects shown a picture of a flower · PEA (5%, 100%) and H_2S (0.03 ppm): ↑ in negative valence emotion rating when subjects shown a disgusting picture
2009 Gaygen and Hedge	GoodAire air freshener (blend of lavender, tea tree, and eucalyptus; total volatile organic compound conc: 3.16 mg/m^3 (1376 ppb))	15-18 min (ambient room odour; BR)	28 healthy adults (18-26 y; mean: 21 y)	· no overall effect of pleasant odour on word recognition performance · significant order effect: subjects exposed to odour in the second session but not the first session had lower accuracy performance in the second session; the authors concluded that odour served as a distraction in the second session

BR: birhinal; H_2S: hydrogen sulphide; min: minutes; MR-L: monorhinal left side; MR-R: monorhinal right side; ms: milliseconds; PEA: phenylethyl alcohol; ppb: parts per billion; ppm: parts per million; ppt: parts per trillion; s: seconds; SZ: schizophrenia; v/v: volume per volume; wt/wt: weight per weight; y: years

Appendix E: Summary of changes in mood and task performance (continued)

Reference	Odour Type and Concentration	Exposure (sniff/non-sniffing) (BR/MR-L/MR-R)	Population (age)	Study Findings
2009 Pournemati et al.	Peppermint, Mixture of peppermint and ethanol (concentration not stated)	12-14 min (odour strip under nose; BR)	36 female athletes (mean: 21 y)	· odours had no significant effect on physiological measures during exercise (heart rate, oxygen consumption, minute ventilation, respiratory exchange ratio)
2009 Raudenbush et al.	Cinnamon oil, Peppermint oil	30 s (every 15 min for 2 hr) (non-sniffing; BR)	25 subjects (mean: 20 y)	· cinnamon, peppermint: ↓ temporal workload during simulated driving task (faster perceived testing session time); no effect on mental or physical workload · cinnamon, peppermint: ↑ alertness and ↓ frustration during driving task · peppermint: also ↓ anxiety and fatigue · no effect on ratings of anger, vigor, confusion, or depression
2009 Seubert et al.	Eugenol (1% v/v), Hydrogen sulphide (20 ppm), Vanillin (0.1 g/ml)	1.5 s (non-sniffing; MR-R)	25 healthy adults (mean: 28 y)	· unpleasant odour (H_2S): induced more anger and disgust, and less happiness · pleasant odour (vanillin): induced more happiness and less sadness · no significant differences were found for surprise or fear · eugenol: mood responses were variable and differed between men and women (eugenol induced more positive and less negative emotions in women than men)
2008 Donoso et al.	Hexanal (0.5%), Honeydew (11%)	8 s (non-sniffing; BR)	80 university students (17-30 y)	· odour had no significant differences from air on a visual working memory task · task performance was influenced by subject's perceived hedonic values: odours classified as unpleasant correlated with ↑ errors in the memory task (no effect on reaction time)
2008 Howard and Hughes	Lavender oil	2 inhalations, then 10 min near sample vial (sniffing; BR)	96 female university students (mean: 21 y)	· lavender had no effect on self-reported anxiety
2008 Kiecolt-Glaser et al.	Lavender, Lemon (pure essential oil)	1.25 hr (non-sniffing; BR)	56 healthy adults (18-43 y; mean 24 y)	· lemon oil: ↑ positive mood scores compared to lavender or no odour; the increase did not differ significantly from baseline scores · effect of lavender odour on mood did not differ from control · odour had no effect on arousal ratings or pain
2008 Laudien et al.	Isobornyl acetate (9.3% v/v)	300 ms (non-sniffing; BR)	45 healthy women (18-46 y; mean: 23 y)	· subjects in the healthy bias group were happier than subjects in the harmful or neutral groups; subjects in the healthy or harmful bias groups were more aroused than the neutral group · subjects in the harmful bias group judged the odour to be less pleasant than the other groups · odour familiarity, intensity, or thresholds did not differ between bias groups
2008 Moss et al.	Peppermint oil, Ylang-ylang oil (concentration not stated)	25 min (ambient room odour; BR)	144 healthy adults (mean: 24 y)	· ylang-ylang: impaired working memory performance, improved reaction times in memory and attention · peppermint: improved memory quality, working memory and secondary memory factors, slowed reaction times for memory · ylang-ylang: ↑ calmness and ↓ alertness mood scores · peppermint: ↓ calmness and small ↑ in alertness mood scores

BR: birhinal; H_2S: hydrogen sulphide; min: minutes; MR-L: monorhinal left side; MR-R: monorhinal right side; ms: milliseconds; PEA: phenylethyl alcohol; ppb: parts per billion; ppm: parts per million; ppt: parts per trillion; s: seconds; SZ: schizophrenia; v/v: volume per volume; wt/wt: weight per weight; y: years

Appendix E: Summary of changes in mood and task performance (continued)

Reference	Odour Type and Concentration	Exposure (sniff/non-sniffing) (BR/MR-L/MR-R)	Population (age)	Study Findings
2008 Oka et al.	Green odour (0.03% v/v; mixture of 2*E*-hexenal and 3*Z*-hexenol)	10 min (non-sniffing; BR)	19 healthy adults (21-48 y; mean: 33 y)	· odour had no effect on mood scores (tension, anxiety, depression, anger-hostility, confusion, fatigue, vigor) or cold pressor-induced pain
2008 Shimizu et al.	Eucalyptus, Lavender, Linalyl acetate, l-Menthol	30 min (non-sniffing; BR)	1548 healthy men (20-24 y)	· lavender attenuated a decrease in performance on a vigilance task (attention was maintained over time) · other odours had no significant effect on vigilance task performance
2008 Tubaldi et al.	Almond (1% v/v), Apple (0.75% v/v), Orange (7% v/v), Strawberry (3% v/v)	3 s (non-sniffing; BR)	49 healthy adults (mean: 22 y)	· odour ↑ the alertness (as measured by reaching duration) in one experiment but not the other · the authors concluded that odours can induce motor actions that interfere with those programmed for a reaching movement
2008 Weber and Heuberger	Blooming plants (e.g., *Brassicaceae, Caprifoliaceae, Liliaceae, Oleaceae, Paeoniceae, Rosaceae, Rutaceae*)	3 sniffs (sniff; BR)	32 healthy adults (mean: 24 y)	· in an outdoor odorous garden setting, pleasant plant odours ↑ ratings of alertness, mood, and calmness
	Hydrogen sulphide (2.5 mg/mL sodium sulphide), Jasmine absolute (2 µl/mL), Rose oil (2 µl/mL), Vanillin (1 mg/mL)			· unpleasant odour (H_2S): ↓ ratings of mood and calmness · pleasant odour (jasmine, rose oil): ↑ alertness; no effect on calmness or other mood scores
2007 Demattè et al.	Geranium (1.0% v/v), Male fragrance (0.5% v/v), Rubber (1.2% v/v), Synthetic body odour (0.33% v/v) (all odours had the same intensity)	1.5 s (non-sniffing; BR)	16 female university students (20-34 y)	· unpleasant odour significantly influenced judgments of facial attractiveness: male faces were rated as less attractive when presented with an unpleasant odour (body odour, rubber) compared to pleasant odour (germanium, male fragrance) or no odour
2007 Habel et al.	Rotten yeast	3 s (non-sniffing; MR-R)	21 healthy men (mean: 31 y)	· ↓ performance on a verbal working memory task in 9 of 21 subjects · no effect of odour on a selective attention memory task · ratings of unpleasantness/disgust were similar in all subjects
2007 Li et al.	Anisole (720 ppt), Citral (3600 ppt), Valeric acid (7.5 ppt) (all included subjects considered the citral odorant to be pleasant)	1 inhalation (sniff; BR)	31 university students (17-27 y)	· in subjects unaware of an odour, faces were rated less likeable after unpleasant odour (valeric acid) compared to pleasant odour or no odour · in subjects that were aware of an odour, hedonic had no effect on face ratings
2007 Villemure and Bushnell	4,16-androstadien-3-one (250 µM), 19 pleasant odorants (e.g., Apple, Apricot, Green tea, Lemon meringue, Pumpkin, Mint, Rose: 0.5–10% v/v)	6 s (non-sniffing; BR)	48 healthy adults (18-31 y)	· non-pain condition: pleasant odorants improved mood for all subjects; androstadienone improved mood in women only · these effects did not persist when pain (phasic heat) was introduced · pain intensity ratings were ↑ in the presence of androstadienone in women · pleasant odours did not attenuate pain-induced unpleasantness
2006 Demattè et al.	Animal odour (10% v/v), Lemon (10% v/v)	~3 s (non-sniffing; BR)	17 university students (18-35 y; mean: 22 y)	· fabric was rated as feeling softer when presented with pleasant odour (lemon) compared to unpleasant odour (animal); neither the pleasant nor unpleasant odour condition responses differed significantly from the no odour condition

BR: birhinal; H_2S: hydrogen sulphide; min: minutes; MR-L: monorhinal left side; MR-R: monorhinal right side; ms: milliseconds; PEA: phenylethyl alcohol; ppb: parts per billion; ppm: parts per million; ppt: parts per trillion; s: seconds; SZ: schizophrenia; v/v: volume per volume; wt/wt: weight per weight; y: years

Appendix E: Summary of changes in mood and task performance (continued)

Reference	Odour Type and Concentration	Exposure (sniff/non-sniffing) (BR/MR-L/MR-R)	Population (age)	Study Findings
	Animal odour, Lavender (odours had the same intensity)	time not stated (non-sniffing; BR)	40 university students (18-49 y; mean: 22 y)	· fabric was rated as feeling rougher when it carried an unpleasant odour (animal) compared to a pleasant odour (lavender) or no odour; no differences were found between the pleasant odour and no odour fabrics · overall, the authors concluded that a cross-modal interaction exists between olfaction and touch
2006 Heuberger et al.	alpha-Santalol, East Indian Sandalwood oil (~2.5-3.5 mg of odorant via nebulizer for each subject)	20 min (non-sniffing; BR)	36 healthy adults (mean: 24 y)	· alpha-Santalol: ↑ mood and attention · sandalwood oil: no change to mood or arousal · differences in arousal level appeared to be related to differences in perceived odour quality
2006 Moss et al.	Roman chamomile essential oil (concentration not stated)	time not stated (ambient room odour; BR)	80 healthy adults (mean: 22 y)	· odour ↓ alertness and ↑ calmness; no change to contentedness · odour ↓ scores on accuracy of attention test; no significant changes to other cognitive test scores (in subjects not given any expectation about the odour) · effects of odour were impacted by expectancy: the sedative effects were greater in subjects who were told the odour had sedative properties · expectancies of odour can influence its impact on mood and cognition
2005 Aou et al.	Green odour (concentration not stated)	time not stated (no info provided)	no info provided	· no effect on reaction times in visual discrimination tasks ·↑ threshold of pain perception
2005 Field et al.	Lavender (fragrance in cleansing gel)	2 min (non-sniffing; BR)	11 healthy adults (age not stated)	·↓ anxiety, ↑ relaxation, and ↓ depressed mood score · improved performance on math computation task
2005 Ho and Spence	Peppermint (10% v/v)	35 s (non-sniffing; BR)	16 healthy adults (18-35 y; mean: 25 y)	· peppermint improved performance in a difficult vibrotactile discrimination task; no effect on easy vibrotactile discrimination task · peppermint had no effect on a rapid serial visual presentation task
2005 Holland et al.	Citrus scent from all-purpose cleaner	time not stated (ambient room odour; BR)	50 university students (age not stated)	· in a lexical decision task, subjects exposed to citrus cleaner odour responded faster to cleaning-related words than to control words; results did not differ based on awareness of the odour · citrus odour had no effect on response times for non-cleaning-related words
			56 university students (age not stated)	· subjects exposed to citrus cleaner odour more frequently listed a cleaning activity as an activity they were planning to do later in the day
			22 university students (age not stated)	· subjects exposed to citrus odour more frequently listed a cleaning activity as an activity they were planning to do later in the day · overall, the authors concluded that presence of a typical cleaner scent enhanced the accessibility of the behavior concept of cleaning

BR: birhinal; H_2S: hydrogen sulphide; min: minutes; MR-L: monorhinal left side; MR-R: monorhinal right side; ms: milliseconds; PEA: phenylethyl alcohol; ppb: parts per billion; ppm: parts per million; ppt: parts per trillion; s: seconds; SZ: schizophrenia; v/v: volume per volume; wt/wt: weight per weight; y: years

Appendix E: Summary of changes in mood and task performance (continued)

Reference	Odour Type and Concentration	Exposure (sniff/non-sniffing) (BR/MR-L/MR-R)	Population (age)	Study Findings
2005 Kuroda et al.	Jasmine tea (20-fold dilution of 1 min steep of 25g tea), Lavender oil (1 μL/L)	6 min (non-sniffing; BR)	12 healthy adults (21-36 y)	· odours ↓ some negative mood scores (tension, anxiety, depression, anger, hostility), but not others (fatigue or confusion) · odours ↑ the positive mood score (vigor), but the change was not significant
	(*R*)-(–)-Linalool (0.03 ppm), (*S*)-(+)-Linalool (0.03 ppm)	6 min (non-sniffing; BR)	12 healthy adults (21-36 y)	· (*R*)-(–)-linalool ↓ some negative mood scores (tension, anxiety, depression, anger, hostility), but not others (fatigue or confusion) · (*S*)-(+)-linalool ↑ tension, anxiety, depression, anger, and hostility and tended to ↓ the positive mood score (vigor)
2005 MacKenzie and Hedge	Peppermint oil (1/20 dilution)	~1.5 min (non-sniffing; BR)	18 university students (18-25 y; mean: 20 y)	· running performance (run time) was not impacted by peppermint odour or expectancy condition (negative, neutral, positive expectancy)
2005 Michael et al.	Allyl isothiocyanate (mustard oil), PEA	~7 min (non-sniffing; BR)	47 healthy females (mean: 22 y)	· PEA: attenuated attentional capture in response to visual stimuli · PEA: caused a general slowing in the speed of information processing, which correlated with a reduction in arousal level · allyl isothiocyanate: ↑ amplitude and time course of attentional capture
2005 Norrish and Dwyer	Peppermint oil	11 min (non-sniffing; MR-L)	20 university students (mean: 23 y)	· reduced daytime sleepiness (measured by pupillary fatigue oscillations) when sitting in a dark room
2005 Sakamoto et al.	Lavender oil, Jasmine oil	30 min (4 times in workday) (ambient room odour; BR)	36 male university students (mean: 24 y)	· lavender: improved work performance in afternoon sessions when subjects showed the most fatigue · jasmine: no effect on work performance
2005 Schiffman et al.	Diluted swine air (57-fold greater than odour threshold) (components: H_2S (24 ppb), ammonia (817 ppb), total suspended particulates (0.0241 mg/m^3), endotoxin (7.40 units/m^3))	1 hr (ambient room odour; BR)	48 healthy adults (19-49 y; mean: 26 y)	· swine odour had no effect on total mood score or mood subscales (depression, anxiety, anger, vigor, fatigue, confusion) · swine odour had no effect on attention or memory (digit span test)
2005 Zoladz and Raudenbush	Cinnamon, Jasmine, Peppermint (concentration not stated)	~45 min (non-sniffing; BR)	39 young adults (mean: 18 y)	· cinnamon: ↑ scores for tasks related to attentional processes, virtual recognition memory, working memory, and visual-motor response speed · peppermint: reduced task-related decline in vigor · jasmine, peppermint: ↓ fatigue
2004 Burnett et al.	Lavender oil, Rosemary oil	10 min (ambient room odour; BR)	73 university students (18-30 y)	· rosemary: ↑ tension-anxiety and confusion-bewilderment; over-stimulation with rosemary may have caused the task to feel more challenging · lavender: ↑ scores for vigor-activity (possibly mediated by positive affect) · both odours: ↓ fatigue
2004 Campenni et al.	Lavender, Neroli (concentration not stated)	11 min (ambient room odour; BR)	90 healthy women (mean: 20 y)	· odours had no effect on total mood score or mood subscales (tension, depression, anger, vigor, fatigue, confusion)

BR: birhinal; H_2S: hydrogen sulphide; min: minutes; MR-L: monorhinal left side; MR-R: monorhinal right side; ms: milliseconds; PEA: phenylethyl alcohol; ppb: parts per billion; ppm: parts per million; ppt: parts per trillion; s: seconds; SZ: schizophrenia; v/v: volume per volume; wt/wt: weight per weight; y: years

Appendix E: Summary of changes in mood and task performance (continued)

Reference	Odour Type and Concentration	Exposure (sniff/non-sniffing) (BR/MR-L/MR-R)	Population (age)	Study Findings
2004 Goel and Grasso	5 different blends lavender oil (with varying intensities of lavender)	2 s (non-sniffing; BR)	169 college students (mean: 19 y)	· lavender was associated with sedative effects (↑ fatigue, ↑ confusion, ↓ vigor); contrarily, lavender also ↑ tension · in depressed subjects, lavender also ↑ anger
2004 Hongratana-worakit and Buchbauer	Ylang-ylang oil	20 min (ambient room odour; BR)	24 healthy subjects (age not stated)	·↑ attentiveness and alertness · no effect on scores for calmness, relaxation, mood, or vigor
2004 Rétiveau et al.	3 commercial fragrances (Bergamot/juniper, Eucalyptus/spearmint, Vanilla/lavender)	1 fragrance per day	58 healthy women (18-55 y)	· all 3 fragrances were associated with a more positive affect than control (e.g., lower ratings for fatigue–inertia, anger–hostility, and confusion–bewilderment) · all 3 fragrances elicited different mood patterns, which varied over time
2003 Barker et al.	Peppermint (concentration not stated)	time not stated (ambient room odour; BR)	26 university students (mean: 19 y)	· improved speed and accuracy on the typing task and improved alphabetization · no effect on typing duration or memorization · the authors concluded that peppermint odour may promote a general arousal of attention, which may lead to increased focus and performance
2003 Bensafi et al.	Acetophenone, Butanol, Cineole, Cyclodecanone, Heptanone, Isoamyl acetate (all 1/100 dilution); Isovaleric acid, Pyridine, Thiophenol (all 1/6250 dilution); Limonene (1/62.5 dilution), Menthol (30mg/mL), Thymol (15mg/mL)	1 inhalation (~1s) (sniff; MR-R or MR-L)	64 university students (mean: 22 y)	· during the pleasantness assessment task, unpleasant odours were processed more rapidly than neutral or pleasant odours · processing time did not differ between odour hedonics for the detection, intensity, or familiarity tasks
2003 Danuser et al.	Ammonia, Hydrogen sulphide, Menthone, Pentyl acetate (two intensities used: threshold or double the threshold for each subject)	2 min (non-sniffing; BR)	12 healthy adults (20-36 y; mean: 25 y)	· at threshold: no effect of odours on mental task performance (short-term memory task, reaction time) · at double threshold: unpleasant odours (ammonia, H_2S) impaired mental task performance; pleasant odours had no effect
2003 Inoue et al.	Chinese green tea, Jasmine tea (high-intensity: 1 min steep of 25g tea; low-intensity: 20-fold dilution)	5 min (non-sniffing; BR)	8 healthy Japanese adults (21-36 y; mean: 25 y)	· in subjects with tea odour predilection, high-intensity odours induced a ↓ in most negative mood scores (anxiety, tension, depression, anger, hostility, fatigue, confusion) · in subjects with tea odour antipathy, high-intensity odours induced ↑ negative mood scores · for low-intensity odours, negative mood scores ↓ in subjects with tea predilection or antipathy
2003 Kim and Watanuki	PCK (components from Japanese cypress; 150x and 500x dilution), 2-mercaptoethanol (150x and 300x dilution)	1 min (non-sniffing; BR)	12 male university students (22-26 y)	· pleasant (PCK): 150x, but not 500x dilution, ↑ favorable and pleasant emotion · unpleasant (2-mercaptoethanol): 150x and 500x dilutions ↑ summated rating of relaxing, dislike, anxiety, irritated, sleepy, unpleasant, pleasant, and calming

BR: birhinal; H_2S: hydrogen sulphide; min: minutes; MR-L: monorhinal left side; MR-R: monorhinal right side; ms: milliseconds; PEA: phenylethyl alcohol; ppb: parts per billion; ppm: parts per million; ppt: parts per trillion; s: seconds; SZ: schizophrenia; v/v: volume per volume; wt/wt: weight per weight; y: years

Appendix E: Summary of changes in mood and task performance (continued)

Reference	Odour Type and Concentration	Exposure (sniff/non-sniffing) (BR/MR-L/MR-R)	Population (age)	Study Findings
2003 Michael et al.	Allyl isothiocyanate (mustard oil), PEA	~2 min (non-sniffing; BR)	47 healthy females (mean: 22y)	· both odours modulated the attentional system's responsiveness in a visual task · allyl isothiocyanate: ↑ the amplitude of attentional effects caused by the visual stimuli (improved attention) · PEA: ↓ the amplitude of attentional effects caused by the visual stimuli · irritating properties of odours correlated with amplitude of attentional capture
2003 Moss et al.	Lavender oil, Rosemary oil (concentration not stated)	25 min (ambient room odour; BR)	144 healthy adults (mean: 25 y)	· lavender: impaired working memory performance, slowed reaction times for memory and attention · rosemary: improved memory quality and secondary memory factors, slowed reaction times for memory · both odours ↑ mood score for contentedness; rosemary also ↑ alertness score
2003 Pan et al.	Furfurylmercaptan (coffee aroma) (concentration not stated)	80 min (ambient room odour; BR)	9 healthy adults (mean: 26 y)	· odour ↑ sleepiness, concentration difficulty, and stress · odour exposure was not associated with changes in the mood-scale test or distraction (addition test)
2003 Villemure et al.	Food, floral, greenery, or woody odour (most pleasant odour chosen by subject); Pyridine (unpleasant odour chosen by all subjects) (0.1–3% v/v)	4 s (non-sniffing; BR)	15 healthy adults (18-34 y)	· pleasant odour induced a positive mood and a calm state, while unpleasant odour induced a negative mood, and mild anxiety; these effects did not differ between the attend and non-attend conditions · unpleasant odour induced disgust, which was stronger in the attend condition · pain unpleasantness, but not pain intensity, was higher with unpleasant odour than with pleasant odour · the effect of odour on pain was found to occur indirectly of changes in mood
2002 Barnham and Broughan	Apple, Thai fish sauce (concentration not stated, but odours were of similar intensities)	time not stated (ambient room odour; BR)	40 children (2-11 y)	· children were rated as happier in the pleasant odour condition (apple) compared to the unpleasant (fish sauce) or no odour conditions · odour had no effect on the amount of time spent playing with playdough
2002a Bensafi et al.	Floral mixture (1/1000 dilution)	5 s (unclear) (non-sniffing; BR)	15 female university students (mean: 20 y)	· in an affective face evaluation task, odour had no effect on subjective face judgment or task response time
2002 Hiruma et al.	Hiba (*Thujopsis dolabrata*; a conifer)	38-50 min (ambient room odour; BR)	16 female adults (19-22 y)	· hiba: improved response time for a reaction time task · odour had no effect on depression scores
2002 Marchand and Arsenault	Aftershave, Almond extract, Baby oil, Massage oil, Orange water, Perm product (hair), Vanilla extract, White vinegar, Zonalin (dentistry product) (concentration not stated)	3 min (non-sniffing; BR)	40 healthy adults (18-25 y)	· individual ratings of odour pleasantness correlated with mood (unpleasant odours associated with negative mood and pleasant odours with positive mood) · compared to neutral odours, pleasant odours led to reduced pain perception in women only

BR: birhinal; H_2S: hydrogen sulphide; min: minutes; MR-L: monorhinal left side; MR-R: monorhinal right side; ms: milliseconds; PEA: phenylethyl alcohol; ppb: parts per billion; ppm: parts per million; ppt: parts per trillion; s: seconds; SZ: schizophrenia; v/v: volume per volume; wt/wt: weight per weight; y: years

Appendix E: Summary of changes in mood and task performance (continued)

Reference	Odour Type and Concentration	Exposure (sniff/non-sniffing) (BR/MR-L/MR-R)	Population (age)	Study Findings
2002 Millot et al.	Lavender, Pyridine (concentration not stated, but levels were judged to be of similar intensities)	5 min (ambient room odour; BR)	99 female university students(age not stated)	· compared to no odour, both pleasant and unpleasant odours significantly improved the reaction time for simple sensory-motor tasks (responses to visual or auditory stimulation)
2002 Raudenbush et al.	Dimethyl sulphide, Jasmine, Peppermint (concentration not stated)	15 min (ambient room odour; BR)	40 adult athletes (mean: 20 y)	· peppermint: ↓ perceived physical/temporal workload (easier and more slowly paced), ↓effort, ↓ frustration, ↑ performance self-evaluations, ↑ vigor, ↓ fatigue · dimethyl sulphide, jasmine: no major effects · odours had no effect on physiological measures (pulse, BP, oxygen saturation)
2001 Gould and Martin	Bergamot, Peppermint	20 min (ambient room odour; BR)	54 university students (mean: 25 y)	· relaxing odour (bergamot): ↓ performance on a visual vigilance task · stimulating odour (peppermint): no effect on visual vigilance task performance · odours had no effect of self-reported feelings of alertness
2001 Guéguen	Perfume	a few seconds (walking behind a woman)	160 adults (~30-50 y)	· help was offered more often to a young woman who dropped a glove if she was wearing perfume, compared to not wearing a perfume (perfume ↑ helping behavior)
2001 Heuberger et al.	*S*-(+)-Carvone, *R*-(–)-Carvone, *R*-(+)-Limonene, *S*-(–)-Limonene (~50-175 mg of odorant via nebulizer for each subject)	30 min (non-sniffing; BR)	20 healthy adults (18-36 y; mean: 24 y)	· *R*-(+)-limonene: ↑ alertness, restlessness, and cheerfulness · *S*-(–)-limonene: no effect · *R*-(–)-carvone: ↑ alertness and restlessness; *S*-(+)-carvone had no effect · effects of odours impacted by subjective odour evaluation and chirality of odour molecules
2001 Ilmberger et al.	1,8-Cineole (10 or 100 µL), Jasmine (100 µL), (1*R*,2*S*,5*R*)-(−)-Menthol (50% w/v), Peppermint (44% w/v), Ylang-ylang (10 µL)	~25 min (non-sniffing; BR)	190 healthy adults (16-67 y)	· overall, reaction times did not differ significantly between exposure and control groups · however, motor reaction times improved between first and second trials for control groups but not the exposed groups; the authors suggested that exposed subjects may have been distracted by the odour · reaction times varied with subjective ratings of odours, suggesting a psychological component of odour-induced performance changes
2001 Millot and Brand	Lavender, Pyridine (concentration not stated)	time not stated (ambient room odour; BR)	18 university students (mean: 22 y)	· voice pitch was higher with pleasant ambient odour compared to unpleasant odour (possibly reflecting happiness) · the authors concluded that odour hedonic can influence the vocal acoustic characteristics of emotion
2001 Motomura et al.	Lavender oil	20 min (ambient room odour; BR)	42 university students (mean: 21 y)	· under stressful condition: lavender significantly lowered stress scores · lavender attenuated a stress-induced decrease in arousal
2001 Raudenbush et al.	Peppermint (concentration not stated)	time not stated (odour strip under nose; BR)	40 adult athletes (mean: 20 y)	·↑ running speed, hand grip strength, and number of push-ups · no effect on skill-related tasks (basketball free-throw shots) · the authors concluded that odour may enhance athletic performance

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Appendix E: Summary of changes in mood and task performance (continued)

Reference	Odour Type and Concentration	Exposure (sniff/non-sniffing) (BR/MR-L/MR-R)	Population (age)	Study Findings
1999 Asmus and Bell	Asafoetida, Cigarette ash, Rotten egg, Skunk (concentration not stated)	~10-20 min (ambient room odour; BR)	240 university students (age not stated)	· negative affect (odour discomfort) and motivation to escape ↑ with odour unpleasantness; no associations found between odour and anger or arousal · negative affect was predicted by anger and motivation to escape
1999 Chen and Haviland-Jones	Underarm odours from 6 groups of people (prepubertal girls, prepubertal boys, college women, college men, older women, and older men)	<2 min (sniff; BR)	308 university students (17-29 y; mean: 19 y)	· some underarm odours induced a small but significant reduction in depressive mood scores (improved mood) · odours perceived as unpleasant were as likely to have an uplifting effect on depressive mood as pleasantly-perceived odours
1999 Schneider et al.	Rotten yeast (0.2 g/mL)	3 s (non-sniffing; MR-R)	24 males (12 with social phobia) (18-45 y)	· neutral faces were rated as more negative when paired with malodour
1999 Vernet-Maury et al.	Acetic acid (1/1000 dilution), Butyric acid (1/1000), Camphor (1/100), Ethyl acetoacetate (1/100), Lavender (1/100)	1 inhalation? (non-sniffing; BR)	15 healthy adults (22-28 y; mean: 25 y)	· subjects' hedonic evaluation correlated with autonomic estimation of basic emotions; lavender and ethyl acetoacetate induced an autonomic response associated with happiness, camphor a response of happiness, surprise, or sadness, and butyric and acetic acid a response of anger and disgust
1998 Diego et al.	Lavender (10%), Rosemary (10%)	3 min (non-sniffing; BR)	40 adults (mean: 31 y)	· lavender group: reported feeling more relaxed, had less depressed mood scores, and performed math tasks more quickly and accurately · rosemary group: reported feeling more relaxed and alert, had lower anxiety scores, and performed math tasks more quickly but not more accurately
1997a Alaoui-Ismaili et al.	Eugenol (0.5% v/v), Menthol (1% v/v), Methyl methacrylate (0.015% v/v), Propionic acid (0.015% v/v), Vanillin (1% v/v)	1 inhalation (unclear) (non-sniffing; BR)	44 university students (22-28 y; mean: 25 y)	· unpleasant: induced autonomic response consistent with disgust and anger · pleasant: induced autonomic response consistent with happiness and surprise · eugenol: varied responses (all emotions seen: anger, disgust, happiness, surprise, fear, sadness)
1997 Baron	Pleasant odours at a shopping mall (bakery, coffee)	not known (ambient odour in shopping mall)	116 adults (age not stated)	· help was offered more often to someone who needed change when in the presence of pleasant odour, compared to no odour (pleasant odour ↑ helping behavior) · those exposed to pleasant odour reported higher levels of positive affect · the effect of pleasant odour on helping may be partially mediated by positive affect (positive mood)
1997 Ehrlichman et al.	Coconut (100% v/v), Limburger cheese (4 grams)	~13 s (sniff; MR-R or MR-L)	80 university students (age not stated)	· coconut odour induced a more positive mood, while limburger cheese induced a more negative mood · no differences found for arousal ratings
1997 Gilbert et al.	Fecal odour, Fruity/floral fragrance (concentration not stated)	time not stated (ambient room odour; BR)	80 adults (mean: 24 y)	· odours had no effect on mood scores or task performance · there was significant effect of odour suggestion on digit deletion task performance: women performed better and men performed worse on the task when told there an odour present compared to those not told about the odour

BR: birhinal; H_2S: hydrogen sulphide; min: minutes; MR-L: monorhinal left side; MR-R: monorhinal right side; ms: milliseconds; PEA: phenylethyl alcohol; ppb: parts per billion; ppm: parts per million; ppt: parts per trillion; s: seconds; SZ: schizophrenia; v/v: volume per volume; wt/wt: weight per weight; y: years

Appendix E: Summary of changes in mood and task performance (continued)

Reference	Odour Type and Concentration	Exposure (sniff/non-sniffing) (BR/MR-L/MR-R)	Population (age)	Study Findings
1996 Dalton	Acetic acid (2% v/v), Amyl acetate (2% v/v), Benzaldehyde (2% v/v), Butanol (5% v/v), Citralva (10% v/v), Isobornyl acetate (10% v/v), Methyl salicylate (20% v/v), PEA (5% v/v), Vanillin (3% wt/v)	duration based on task completion (sniff; BR)	60 adults (mean: 37 y)	· amyl acetate and isobornyl acetate were ranked differently based on the instructions given (rank odours from least to most healthy, or least to most hazardous), indicating an influence of instructional context on odour perception · some odorants were considered as healthy (vanillin, methyl salicylate) or hazardous (acetic acid, butanol) regardless of instructions
	Isobornyl acetate (concentration not stated, but was rated as moderate)	20 min (ambient room odour; BR)	45 healthy adults (18-62 y; mean: 35 y)	· intensity ratings differed between subjects given a healthful bias (intensity ↓ over time) and those given a harmful bias (intensity ↑ over time) · post-exposure thresholds were higher for isobornyl acetate and lower for citralva; effects did not differ between bias conditions · intensity judgments, but not threshold sensitivity, appear to be influenced by bias conditions
1995 Knasko	Baby powder, Chocolate (concentration not stated)	~15 min (ambient room odour; BR)	90 healthy adults (18-35 y)	· subjects exposed to odour were in a significantly more pleasant mood than those exposed to no odour · chocolate: reported ↑ arousal compared to no odour
1995a Schiffman et al.	5 different fruit/floral fragrances (concentration not stated; subjects sprayed fragrances on themselves as desired)	time not stated (mood survey filled out twice/day)	56 healthy women (46-60 y; mean: 54 y)	· improved mood scores for tension/anxiety, depression, confusion, anger, fatigue, vigor, and total mood score · effects of the fragrance on mood were stronger in subjects that liked the particular fragrance
1995b Schiffman et al.	5 different colognes (concentration not stated; subjects sprayed fragrances on themselves as desired)	time not stated (mood survey filled out twice/day)	60 healthy men (40-55 y; mean: 45 y)	· improved mood scores for tension/anxiety, depression, confusion, anger, fatigue, vigor, and total mood score
1995 Todrank et al.	11 'people-related' odours (e.g., lotions, musty, shampoos, soaps, sweaty); 12 'non-human' odours (e.g., citronellol, conifer, lavender, mouthwash)	2 sniffs (sniffing; BR)	72 university students (19-29 y)	· repeated presentation of pleasant/unpleasant odour with a neutral photograph of a person of the opposite sex shifted the preference rating for the photo in the direction of odour pleasantness (i.e., unpleasant odour, lower preference rating)
1994 Baron and Bronfen	Air fresheners (Glade Powder Fresh, Glade Spiced Apple, others) (concentration not stated)	10-15 min (ambient room odour; BR)	137 university students (age not stated)	· subjects exposed to pleasant odours had improved performance in word tasks and showed an ↑ willingness to help a coworker compared to the control group · the effect of pleasant odours on task performance may be mediated by positive affect
1994 Baron and Thomley	Floral fragrance, Lemon fragrance (concentration not stated)	5 min (ambient room odour; BR)	96 university students (age not stated)	· odours ↑ positive mood scores (positive affect) · odours ↑ performance on an anagram task (under low and moderate stress) and ↑ willingness to help the experimenter · effects of pleasant odour on performance and helping may be mediated, at least partially, by positive affect
1993 Knasko	Isovaleric acid (0.5%), Lemon (100%), Skatole (0.5%), Ylang-ylang (10%)	15 min (ambient room odour; BR)	90 healthy adults (18-35 y)	· pleasant or unpleasant odour had no effect on task performance (simple and complex math and verbal tasks) · odour (pleasant or unpleasant) had no effect on mood

BR: birhinal; H_2S: hydrogen sulphide; min: minutes; MR-L: monorhinal left side; MR-R: monorhinal right side; ms: milliseconds; PEA: phenylethyl alcohol; ppb: parts per billion; ppm: parts per million; ppt: parts per trillion; s: seconds; SZ: schizophrenia; v/v: volume per volume; wt/wt: weight per weight; y: years

Appendix E: Summary of changes in mood and task performance (continued)

Reference	Odour Type and Concentration	Exposure (sniff/non-sniffing) (BR/MR-L/MR-R)	Population (age)	Study Findings
1992 Knasko	Dimethyl sulphide, Lavender, Lemon (concentration not stated)	time not stated (ambient room odour; BR)	94 healthy adults (18-35 y; mean: 23 y)	· dimethyl sulphide tended to lower mood ratings; pleasant odours had no effect · no differences in control, arousal, or creativity performance between groups · individual odour expectations and cognitive associations may impact the effect of odours on mood
1992 Roberts and Williams	Chamomile oil (concentration not stated)	time not stated (no details given)	22 subjects (mean: 28 y)	· chamomile oil induced more positive mood ratings · this effect may have been mediated by longer latency of imagery
1992 Winneke and Neuf	Hydrogen sulphide (50 or 150 ppm)	60 min (ambient room odour; BR)	119 healthy adults (18-76 y; mean: 45 y)	· H_2S showed a dose-response correlation with annoyance; subjects with high self-reported environmental annoyance showed higher levels of odour-induced annoyance than subjects with low environmental annoyance · odour-induced annoyance positively correlated with self-reported dissatisfaction with perceived health, and negatively correlated with age
1991 Lorig et al.	Galaxolide fragrance (80%, 20%, and 5% v/v)	10 s (non-sniffing; BR)	12 university students (18-21 y)	· time to complete a visual search task was increased in the undetectable odour condition (5% v/v) compared to no odour · no significant differences in visual search task with higher odour levels
1991 Warm et al.	Muguet (0.13 ppm), Peppermint (0.05 ppm)	periodic 30 s whiffs over 40 min (non-sniffing; BR)	36 healthy subjects (18-30 y)	· pleasant odour (muguet, peppermint): ↑ performance on a vigilance task · odours had no effect on self-reports of stress (workload) or mood scores
1990 Baron	5 Perfumes/Colognes, Sesame oil, Sting-Eze, Soy sauce, WD-40 oil, Wood workers glue (concentration not stated)	1 inhalation (sniff; BR)	80 university students (age not stated)	· pleasant odour (perfumes/colognes): subjects had higher self-set goals, higher self-efficacy (males only), and were more efficient in a simple clerical task compared to subjects in the neutral odour group
	2 Air fresheners (Renuzit Fresh n Dry Powder Soft; Glade Rainshower Fresh) (concentration not stated, but was judged as being in the range of normal home use)	time not stated (ambient room odour; BR)		· pleasant odour: subjects reported higher monetary goals, showed better performance in negotiation tasks, and reported lower tendencies to resolve conflict with avoidance or competition (but not for collaboration/compromise) · pleasant odour: subjects reported high mood ratings · the authors concluded that pleasant scents may improve the attitudes and performance of people in working environments
1990 Knasko et al.	No odours used; subjects were merely told they were being exposed to a pleasant, unpleasant, or neutral odour	15 min (non-sniffing; BR)	90 healthy adults (18-35 y)	· subjects in the pleasant group were in a more pleasant mood and rated the room as smelling more pleasant than subjects in the neutral/unpleasant groups · no difference in arousal, dominance, or performance tasks between groups
1989 Cann and Ross	Ammonium sulphide, Cologne (Island Gardenia)	10-15 min (ambient room odour; BR)	63 male university students (age not stated)	· pleasant or unpleasant odour had no effect on social judgments (ratings of physical attractiveness of female photos)

BR: birhinal; H_2S: hydrogen sulphide; min: minutes; MR-L: monorhinal left side; MR-R: monorhinal right side; ms: milliseconds; PEA: phenylethyl alcohol; ppb: parts per billion; ppm: parts per million; ppt: parts per trillion; s: seconds; SZ: schizophrenia; v/v: volume per volume; wt/wt: weight per weight; y: years

Appendix E: Summary of changes in mood and task performance (continued)

Reference	**Odour Type and Concentration**	**Exposure** (sniff/non-sniffing) (BR/MR-L/MR-R)	**Population** (age)	**Study Findings**
1989 Ludvigson and Rottman	Cloves (0.0057–0.0167 g/m^3), Lavender (0.0131–0.0314 g/m^3)	50 min (ambient room odour; BR)	72 university students (age not stated)	· inconsistent results of odour on cognitive functioning and affect (e.g., lavender ↓ arithmetic reasoning in first session, but not the second session) · odour had no effect on mood score
1988 Lorig and Schwartz	Eucalyptus (60% v/v), Lavender (60% v/v), Spiced apple (concentration not stated)	1 min (non-sniffing; BR)	9 healthy adults (18-24 y)	· spiced apple and eucalyptus ↓ anxiety and tension compared to lavender; mood changes may be related to odour-induced EEG theta activity changes · no differences in 13 other mood outcomes (e.g., relaxed, tense, happy, bored)
1983 Rotton	Ethyl mercaptan (1.6 ppm)	duration based on task completion (ambient room odour; BR)	48 healthy university students (age not stated)	· malodour ↓ emotional scores for pleasure, arousal, and feelings of dominance · malodour ↓ judgments of photographs of individuals (well-being, energy, positive evaluations) and paintings (worth and professionalism, but not tastefulness)
		15 or 30 min (ambient room odour; BR)	80 healthy university students (age not stated)	· malodour: ↓ performance of complex tasks but not simple tasks · malodour exposure time correlated with ↓ feelings of pleasure · 30 min exposure: negative behavioral effects were observed (↓ tolerance to frustration, ↓ arousal, and ↓ feelings of dominance)
1981 Baron	Perfume (Jungle Gardenia)	time not stated (non-sniffing; BR)	94 male university students (age not stated)	· pleasant odour ↑ attraction towards a female dressed informally (jeans/ sweatshirt), but ↓ attraction towards a female dressed formally (skirt/blouse) · the authors concluded that pleasant odour can influence social behavior, but other factors (such as mode of dress) are likely involved

BR: birhinal; H_2S: hydrogen sulphide; min: minutes; MR-L: monorhinal left side; MR-R: monorhinal right side; ms: milliseconds; PEA: phenylethyl alcohol; ppb: parts per billion; ppm: parts per million; ppt: parts per trillion; s: seconds; SZ: schizophrenia; v/v: volume per volume; wt/wt: weight per weight; y: years

Appendix F: Summary of hemodynamic imaging studies (fMRI, PET)

Reference	Odour Type and Concentration	Exposure (sniff/non-sniffing) (BR/MR-L/MR-R)	Population (age)	Study Findings
2013 Karunanayaka et al.	Lavender (0.032%, 0.10%, 0.32%, and 100%)	6 s (non-sniffing; BR)	20 healthy adults (mean: 26 y)	· functional connectivity analysis demonstrated several parallel olfaction-related neural networks; these included: I) bilateral parietal-occipital association cortices, II) bilateral striatum, III) bilateral primary olfactory cortex, IV) bilateral dorsolateral prefrontal cortex, V) bilateral polar and rostral prefrontal cortex · the authors hypothesized that these networks represented the underlying brain sub-networks of olfaction during the procedure
2013 Nigri et al.	*n*-Butanol, 1-Octen-3-ol (concentration not stated)	30 s (non-sniffing; BR)	17 healthy adults (24-64 y; mean: 36 y)	· unpleasant odours ↑ activity bilaterally in the piriform cortex, amygdala, OFC, and hippocampus, as well as unilaterally in the left cerebellar crus II · piriform cortex and amygdala demonstrated high bilateral efferent connectivity while the medial OFC had high afferent connectivity · the authors concluded that olfactory information is scattered by the amygdala and piriform cortex and then gathered and integrated in the medial OFC
2012a Bensafi et al.	Chocolate, Linden blossom, Peach, Rose (all 1% v/v) (labeled according to source (food/flower) or practice (body lotion))	30 s (non-sniffing; BR)	21 female adults (mean: 24 y)	· both types of labels led to ↑ activity in OFC · odours labeled according to source: ↑ activity in the cingulate cortex and insula · neural olfactory representation varied with verbal label categories
2012b Bensafi et al.	Carbon dioxide (40% v/v), Orange (20% v/v), PEA (20% v/v), CO_2+Orange, CO_2+PEA	30 s (non-sniffing; BR)	21 healthy adults (mean: 23 y)	· both mixtures: ↑ activity in the superior temporal gyrus and caudate nucleus · mixture indicated as pleasant by each subject: ↑ activity in the anterior cingulate gyrus, ventral tegmental area, and right insula · mixture indicated as unpleasant by each subject: ↑ activity in left insula · cingulate cortex, midbrain involved in crossmodal integration of pleasantness
2012 Hummel et al.	Androstadienone, Hydrogen sulphide, 2-Methyl-3-sulfanylbutan-1-ol (2M3M)	1 s (non-sniffing; MR-R)	10 children (9-12 y); 10 young adults (17-20 y)	· children: surplus activity in the piriform cortex and amygdala (primary olfactory areas) · young adults: surplus activity in the insula and frontal gyri (related to cognitive or affective processing)
2012 Kjelvik et al.	Anise, Banana, Chocolate, Lemon, Musk, Peppermint, Smoke, Toffee, Vanillin (concentration not stated)	10.4 s (non-sniffing; BR)	17 female adults (20-35 y; mean: 25 y)	· identified odours: ↑ activity in left entorhinal cortex, right hippocampus, posterior parahippocampal gyrus, OFC, frontal gyrus, and temporal gyrus · non-identified odours: ↑ activity in OFC and piriform cortex, ↓ activity in the entorhinal cortex and hippocampus · the authors concluded that the entorhinal cortex and hippocampus are involved in odour identification, while the piriform cortex and OFC are involved in both smelling and odour identification

BA: Brodmann Area; BR: birhinal; conc: concentration; min: minute; MR-L: monorhinal left side; MR-R: monorhinal right side; ms: milliseconds; NIRS: near-infrared spectroscopy; OFC: orbitofrontal cortex; PEA: phenylethyl alcohol; s: seconds; UPSIT: University of Pennsylvania Smell Identification Test; v/v: volume per volume; y: years

Appendix F: Summary of hemodynamic imaging studies (fMRI, PET) (continued)

Reference	**Odour Type and Concentration**	**Exposure** (sniff/non-sniffing) (BR/MR-L/MR-R)	**Population** (age)	**Study Findings**
2012 Krusemark and Li	Acetophenone (0.00015-5%), Anisole (0.0005-5%), Eugenol (0.001-5%), Guaiacol (0.0005-5%), Trimethylamine (0.00005-0.00025%), Valeric acid (0.0005%), Mixtures of above odorants	2 s (sniff; BR)	14 healthy adults (18-28 y; mean: 21 y)	· odours ↑ activity in the right posterior piriform cortex · unpleasant mixtures compared to neutral mixtures: activity in the posterior piriform cortex correlated with subjects' anxiety ratings after the task · unpleasant compared to neutral: ↑ connectivity between the right posterior piriform cortex and the right amygdala and hippocampus · unpleasant compared to neutral: subjects' anxiety ratings after the task correlated with connectivity between the left posterior piriform cortex and the bilateral amygdala (i.e., the connectivity between the left olfactory sensory cortex and the emotion system was dependent on subject anxiety)
2012 Villemure et al.; 2009 Villemure and Bushnell	China rain floral scent, Creamsicle, Lemon meringue, Violet (all 0.3% and 3% v/v); Mint (0.5% and 5% v/v); Pyridine (0.1% and 1% v/v) (most pleasant/unpleasant odour chosen by subject)	5 s (non-sniffing; BR)	14 healthy adults (18-28 y; mean: 23 y)	· pleasant odour: ↓ pain-related activity within the anterior cingulate cortex, medial thalamus, and primary and secondary somatosensory cortices · activity in the lateral inferior frontal cortex correlated with the mood-related modulation of pain
				· pleasant odour: activity in the left and right ventral striatum correlated with the amount of pain reduction · pleasant odour: ventral striatum activity negatively covaried with activity in the medial thalamus and dorsal anterior cingulate cortex, two areas thought to be involved in perception of pain unpleasantness · effect of pleasant odours on pain were mediated by the ventral striatum
2011 Billot et al.	Isoamyl acetate, PEA	1, 3, or 6 inhalations (non-sniffing; BR)	25 university students (20-24 y)	· bimodal (isoamyl acetate): using pure olfactory (PEA) as a reference, short-duration stimulus ↑ activity in the caudate nucleus and OFC, while long-duration stimulus ↑ activity in the posterior insular cortex and post-central gyrus · different regions of the brain are activated with varying durations of exposure to bimodal odorant
2011 Garcia-Gonzalez et al.	Heptanal, Hexanoic acid, Virgin olive oil (6 different varieties)	9 s (non-sniffing; BR)	14 healthy adults (28-47 y; mean: 34 y)	· all odours: ↑ activity in the middle, inferior, and superior frontal gyri, insular cortex, inferior temporal gyrus · pleasant odours: max response in the inferior frontal gyrus · unpleasant odours: max response in the inferior parietal lobule, superior temporal gyrus, and anterior cingulate gyrus · premotor cortex (BA 6) involved in odour intensity · middle frontal gyrus, inferior parietal lobule, and inferior frontal gyrus (BA 9, 40,47) involved in odour familiarity

BA: Brodmann Area; BR: birhinal; conc: concentration; min: minute; MR-L: monorhinal left side; MR-R: monorhinal right side; ms: milliseconds; NIRS: near-infrared spectroscopy; OFC: orbitofrontal cortex; PEA: phenylethyl alcohol; s: seconds; UPSIT: University of Pennsylvania Smell Identification Test; v/v: volume per volume; y: years

Appendix F: Summary of hemodynamic imaging studies (fMRI, PET) (continued)

Reference	Odour Type and Concentration	Exposure (sniff/non-sniffing) (BR/MR-L/MR-R)	Population (age)	Study Findings
2011 Grabenhorst et al.	Indole (6%), Jasmin (mixture of 8 chemicals), Mixture of Indole and Jasmin (subjects were required to perceive Indole as an unpleasant odour)	4 s (sniff; BR)	14 healthy adults (mean: 26 y)	·↑ activity in the superior frontal gyrus when paying attention to the pleasant odour jasmine ·↑ activity in the superior frontal gyrus also with mixture of jasmine and indole (non-attend condition) · odour mixtures with pleasant and unpleasant components recruit the same neural processing in the brain that is involved with selective attention; this may explain how unpleasant odorants in such mixtures may be masked and the overall mixture perceived as pleasant
2011 Iannilli et al.	Menthol (50% or 66% v/v)	250 ms (non-sniffing; MR-R)	17 healthy adults (mean: 48 y); 17 anosmic adults (mean: 41 y)	· normosmic: right anterior lobe of cerebellum activated more strongly by high concentration and the anterior cingulate cortex and medial frontal gyrus activated more strongly by the lower concentration · anosmic: no differences in activations between low and high concentrations
2011 Kokan et al.	Citral (95%), PEA (pure)	30 s (non-sniffing; BR)	14 female university students (18-23 y; mean: 20 y)	· using NIRS, odours showed ↑ activity in the left OFC · ↑ activity in the right OFC in subjects who correctly identified the odour · the authors concluded that the left OFC is involved in olfaction, and the right OFC is involved in odour familiarity judgments
2010 Albrecht et al.	Carbon dioxide (concentrationrange: 25-70%) (meta-analysis of 9 studies (3 unpublished))	250 ms - 1 s (non-sniffing; BR, MR-R, or MR-L)	170 healthy adults (from 9 studies) (21-61 y)	·↑ activity consistently observed in the brainstem, ventrolateral posterior thalamic nucleus, anterior cingulate cortex, insula, precentral gyrus, and primary and secondary somatosensory cortices; these areas are involved with the processing of intranasal nociceptive stimuli ·↑ activity also consistently seen in olfactory areas - piriform cortex, insula, OFC · significant overlap seen in brain activations between trigeminal and olfactory stimuli, indicating an interconnectivity between these processes
2010 Aoyama et al.	Breast milk, Formula milk (concentration not stated)	30 s (non-sniffing; BR)	26 healthy newborns (2-9 days)	· using NIRS, maternal breast milk induced an ↑ in OFC activity relative to formula milk · OFC activity did not vary with odour intensity · the authors concluded that neonates can distinguish between odours of maternal breast milk and formula
2010 Reske et al.	Rotten yeast (0.1 g/mL), Vanilla (0.05 g/mL)	2 s (non-sniffing; MR-R)	15 healthy women (21-47 y; mean: 37 y)	· unpleasant odour (yeast): ↑ activity in the superior temporal gyrus, precentral gyrus, OFC, anterior cingulate gyrus, insula, and motor areas · neutral odour (vanilla): ↑ activity in the right/left anterior superior frontal gyrus and right parietal cortex relative to air · stronger brain responses observed with unpleasant odour than neutral odour

BA: Brodmann Area; BR: birhinal; conc: concentration; min: minute; MR-L: monorhinal left side; MR-R: monorhinal right side; ms: milliseconds; NIRS: near-infrared spectroscopy; OFC: orbitofrontal cortex; PEA: phenylethyl alcohol; s: seconds; UPSIT: University of Pennsylvania Smell Identification Test; v/v: volume per volume; y: years

Appendix F: Summary of hemodynamic imaging studies (fMRI, PET) (continued)

Reference	Odour Type and Concentration	Exposure (sniff/non-sniffing) (BR/MR-L/MR-R)	Population (age)	Study Findings
2010 Rolls et al.	Citral (1 M), Hexanoic acid (10% v/v), Isovaleric acid (15% v/v), Vanillin (4 M)	2 s (non-sniffing; BR)	12 healthy adults (mean: 27 y)	· dorsal part of medial prefrontal cortex and agranular insula activated during odour pleasantness judgment · dorsolateral prefrontal cortex, ventral premotor cortex, and anterior insula activated during odour intensity judgment · mid-OFC activated when rating pleasantness on a continuous scale
2009 Albrecht et al.	*S*-(–)-nicotine (concentration just above each subjects olfactory detection threshold)	500 ms (non-sniffing; MR-L)	19 healthy adult smokers (22-45 y; mean: 29)	· olfactory and trigeminal systems both activated by nicotine, even at low concentrations that were not perceived as painful · olfactory activations: piriform cortex, frontal cortices, cingulate cortices, insulae, and supramarginal cortices · trigeminal activations: thalamus, subcentral gyrus (secondary somato-sensory)
2009 Boyle et al.	Citral (13.7% v/v), Pyridine (1.8% v/v), Mixtures of citral and pyridine (proportions varying from 10/90 to 90/10)	2 s (non-sniffing; BR)	12 healthy adults (mean: 23 y)	· activity in lateral OFC ↑ with odorant impurity; activity in anterior OFC was ↑ with binary mixtures and deactivated with single odours · relative to single odours, odour mixtures also ↑ unilateral activity in the left cingulate, right parietal cortex, and superior frontal cortex · binary mixtures are found to be processed differently than single odours
2009 Grabenhorst and Rolls	Citral (1 mol/L), Hexanoic acid (10% v/v), Isovaleric acid (15% v/v), Vanillin (4 mol/L)	2 s (sniff; BR)	12 healthy adults (mean: 27 y)	·↑ activity in anterolateral OFC and anterior insula during judgments of relative pleasantness and unpleasantness, respectively (i.e., compared to previous odour) ·↑ activity in medial and mid-OFC during judgments of absolute pleasantness
2009 Howard et al.	Amyl acetate, *R*-(–)-Carvone, Citronellol, PEA (concentration not stated, but odours were of similar intensities)	10 s (sniff; BR)	6 adults (22-35 y)	· spatial pattern of activity in the posterior piriform cortex and OFC could be used to discriminate between different odorants (mean fMRI data showed no significant differences)
	3 odour groups: Minty (*R*-(–)-carvone, *L*-menthol, methyl salicylate), Woody (cedrol, methyl cedryl ketone, vetiver acetate), Citrus (citral, citronellol, *R*-(+)-limonene)	6 s (sniff; BR)	4 adults (22-35 y)	· odours of similar quality (e.g., minty) showed similar patterns of spatial activity in the posterior piriform cortex, suggesting that the distributed activity in this area provides information about odour quality; this effect was not seen in the anterior piriform cortex, amygdala or OFC
2009 Hummel et al.	Carbon dioxide (60% v/v)	1 s (non-sniffing; MR-L)	12 healthy men (30-58; mean: 36 y)	·↑ activity in the postcentral gyrus (primary and secondary somatosensory cortices); activity was stronger in the right hemisphere (contralateral) ·↑ activity also piriform cortex (primary olfactory cortex) · the authors concluded that trigeminal stimulation activates both the trigeminal and olfactory systems
2009 Katata et al.	PEA, Undecalactone (concentration not stated)	30 s (non-sniffing; BR)	30 healthy adults (18-35 y; mean: 21 y)	·↑ activity in the bilateral middle OFC, left lateral OFC, right insula, and bilateral anterior/middle cingulate gyri · in subjects perceiving an odour as unpleasant, the left middle OFC and right lateral OFC were more often activated; in subjects perceiving an odour as pleasant, the right anterior cingulate gyrus was more often activated ·↑ activity in left middle OFC in those who did not correctly identify the odour

BA: Brodmann Area; BR: birhinal; conc: concentration; min: minute; MR-L: monorhinal left side; MR-R: monorhinal right side; ms: milliseconds; NIRS: near-infrared spectroscopy; OFC: orbitofrontal cortex; PEA: phenylethyl alcohol; s: seconds; UPSIT: University of Pennsylvania Smell Identification Test; v/v: volume per volume; y: years

Appendix F: Summary of hemodynamic imaging studies (fMRI, PET) (continued)

Reference	Odour Type and Concentration	Exposure (sniff/non-sniffing) (BR/MR-L/MR-R)	Population (age)	Study Findings
2009, 2007 Kobayashi et al.	Isovaleric acid (concentration not stated, but intensity was considered to be strong)	5 s (non-sniffing; BR)	13 healthy adults (5 with dysosmia) (17-69 y)	·↑ bilateral activity in lower areas of the frontal cortex, especially the right side, in normal subjects; no changes found in dysosmia subjects · no significant change in activity in upper areas of frontal cortex
2008 Bensafi et al.	Carbon dioxide (37% and 49%), Hydrogen sulphide (9% and 27%)	1 s (non-sniffing; MR-R)	8 healthy women (mean: 27 y)	· olfactory (H_2S): ↑ activity in the right medial frontal gyrus, right insular gyrus, right hippocampus, and right putamen · the contrast of high vs low H_2S showed ↑ activity in the right cerebellum, left medial frontal gyrus, right superior frontal gyrus and entorhinal cortex, right angular gyrus, left precuneus, and primary visual cortex · trigeminal (CO_2): ↑ activity in the anterior cingulate gyrus, left/right superior temporal gyrus, right cerebellum, left/right supramarginal gyrus, and right post-central gyrus · the contrast of high vs low CO_2 showed ↑ activity in 3 regions of the cingulate cortex (anterior medial, posterior medial, ventral posterior) · different neural systems are involved in the processing of intensity/ unpleasantness in the trigeminal and olfactory systems
2008 Ciumas et al.	Butanol (1% v/v), Camphor, Cedar oil, Coffee, Eugenol, Grapefruit, Lavender oil, Linen oil (all pure)	15 s (non-sniffing; BR)	21 healthy adults (20-28 y)	· ↑ bilateral activity in the amygdala, piriform, anterior insular, and cingulate cortices; familiar odours also caused ↑ activity in the right parahippocampus and left Brodmann areas 44, 45 and 47
2008 Iannilli et al.	Carbon dioxide (65%)	250 ms (non-sniffing; MR-R)	18 healthy adults (mean: 31 y)	·↑ activity in the frontal lobe, right insula, thalamus, putamen, temporal lobe, and cingulate gyrus
2008 Lombion et al.	Isoamyl acetate, PEA (concentrations not stated, but odorant levels were judged to be of equal intensity and pleasantness)	9 s (non-sniffing; BR)	15 healthy women (2-23 y)	· both olfactory (PEA) and bimodal (isoamyl acetate) odours ↑ activity in the amygdala, entorhinal cortex, piriform cortex, insula, anterior insula, anterior/ posterior orbital gyrus, and middle/inferior/superior frontal gyrus ·↑ activity in left cerebellum linked to olfactory component of odour ·↑ activity in right insular cortex and ↓ activity in right inferior occipital left post-central gyrus linked to trigeminal component of odour
2008 Plailly et al.	Butanol, *a*-Ionone, 2-Phenylpropionaldehyde, Rose oxide (pure)	3 s (sniff; BR)	12 healthy adults (22-37 y; mean: 28 y)	·↑ bilateral activity in the anterior/posterior piriform cortices and OFC · attend condition: relative to the non-attend condition, ↑ functional coupling was observed from the posterior piriform cortex to the mediodorsal thalamus and from the mediodorsal thalamus to the OFC · attend condition: forward indirect pathway (anterior piriform cortex–posterior piriform cortex–mediodorsal thalamus–OFC) showed greater activity than the forward direct pathway (anterior piriform cortex–OFC) · indirect transthalamic pathway found to be involved in odour processing and is modulated by attention

BA: Brodmann Area; BR: birhinal; conc: concentration; min: minute; MR-L: monorhinal left side; MR-R: monorhinal right side; ms: milliseconds; NIRS: near-infrared spectroscopy; OFC: orbitofrontal cortex; PEA: phenylethyl alcohol; s: seconds; UPSIT: University of Pennsylvania Smell Identification Test; v/v: volume per volume; y: years

Appendix F: Summary of hemodynamic imaging studies (fMRI, PET) (continued)

Reference	**Odour Type and Concentration**	**Exposure** (sniff/non-sniffing) (BR/MR-L/MR-R)	**Population** (age)	**Study Findings**
2008 Rolls et al.	Indole (6%), Jasmin (mixture of 8 chemicals), Mixture of Indole and Jasmin	4 s (non-sniffing; BR)	13 healthy adults (mean: 26 y)	·↑ activity in inferior frontal gyrus when focusing on intensity and ↑ activity in hypothalamus and medial OFC when focusing on pleasantness · brain systems involved in odour pleasantness differ from those involved with odour intensity
2008 Tanida et al.	Fragrance (floral green)	Continuous exposure for 4 weeks	31 female college students (mean: 22 y)	· after 4 weeks exposure, NIRS demonstrated that odour altered the dominant side of stress-induced prefrontal cortex activity (from right side to left side) · this change in prefrontal cortex activity was associated with a ↓ in facial sebum secretion (in subjects who showed right-dominant prefrontal cortex activity and hypersecretion of sebum prior to odour exposure); this effect was thought to be mediated by a ↓ in activity of the hypothalamic–pituitary–adrenal axis
2007 Bensafi et al.	Actual odours: Ammonium sulphide (4×10^{-4} v/v), Strawberry oil (10^{-2} v/v) Imagined odours: Rotten eggs, Strawberry	1.67 s (sniffing; BR)	16 healthy adults (mean: 27 y)	· imagined odours produced similar activity in the primary olfactory cortex and the insular cortex to real odours · the frontal piriform cortex showed different responses between real and imagined odours (increased activity following real odours) · unpleasant odour (real or imagined) induced greater activity in the frontal piriform cortex and left insula than pleasant odour (real or imagined)
2007a Boyle et al.	Carbon dioxide (60% v/v), PEA (20% v/v)	1 s (non-sniffing; MR-R or MR-L)	15 healthy men (23-59 y; mean: 35 y) (same as study below)	· olfactory odour (PEA) to right nostril: ↑ unilateral activity in the right medial OFC, right amygdala, and left rostral insula · trigeminal (CO_2) to either nostril: ↑ activity in trigeminal and olfactory areas (superior temporal gyrus, pre-central gyrus, post-central gyrus, cerebellum, ventrolateral thalamus, insula, contralateral piriform cortex, and OFC) · CO_2 mainly ↑ contralateral activity, while PEA mainly ↑ ipsilateral activity · the authors concluded that trigeminal processing involves similar cortical regions to olfactory system, yet remains separate from the olfactory system
2007b Boyle et al.	Carbon dioxide (60% v/v), PEA (20% v/v), Mixture of CO_2 and PEA	1 s (non-sniffing; MR-R)	15 healthy men (23-59 y; mean: 35 y) (same as study above)	· when contrasted with the sum of its parts, the CO_2/PEA mixture ↑ activity in olfactory-related areas (left medial cortex, lateral OFC) and areas of cross-modal processing (rostral insula, superior temporal gyrus, right intraparietal sulcus), as well as in the right posterior cingulate and left precentral gyrus · an artificial olfactory/trigeminal mixture appears to produce greater cortical activity than the sum of its components
2007 Duan et al.	Lavender (concentration not stated)	40 min (non-sniffing; BR)	10 healthy women (20-27 y; mean: 23)	·↑ activity in the OFC, posterior cingulate cortex, brainstem (pons), thalamus, and cerebellum (PET) ·↓ activity in the pre/post-central gyrus and frontal eye field

BA: Brodmann Area; BR: birhinal; conc: concentration; min: minute; MR-L: monorhinal left side; MR-R: monorhinal right side; ms: milliseconds; NIRS: near-infrared spectroscopy; OFC: orbitofrontal cortex; PEA: phenylethyl alcohol; s: seconds; UPSIT: University of Pennsylvania Smell Identification Test; v/v: volume per volume; y: years

Appendix F: Summary of hemodynamic imaging studies (fMRI, PET) (continued)

Reference	**Odour Type and Concentration**	**Exposure** (sniff/non-sniffing) (BR/MR-L/MR-R)	**Population** (age)	**Study Findings**
2007 Grabenhorst et al.	Indole (4-6%), Jasmin (mixture of 8 chemicals), Mixture of Indole and Jasmin (subjects were required to consider Indole as an unpleasant odour)	4 s (sniff; BR)	14 healthy adults (mean: 26 y)	· activity in the primary olfactory areas correlated with intensity rating, but not odour pleasantness · activity in the medial, anterior, and lateral OFC ↑ with pleasantness rating · activity in the posterior mid-OFC, dorsal anterior cingulate cortex, and agranular insular cortex ↑ with unpleasantness rating · in areas of the brain associated with pleasant odours, the odour mixture produced similar activations to jasmine; in areas of the brain associated with unpleasant odours, the odour mixture produced similar activations to indole · thus, the positive and negative hedonic aspects of an odour mixture can be simultaneously and independently represented by different areas of the brain
2007 Habel et al.	Rotten yeast	3 s (non-sniffing; MR-R)	21 healthy males (mean: 31 y)	· subjects with odour-induced impairment of working memory: higher activation in areas related to emotion (mainly the temporal and medial frontal cortex) as well as compensatory activations in prefrontal regions (known to be involved in cognitive down-regulation of emotions) · subjects not affected by odour in working memory task: higher activation in the fronto-parieto-cerebellar working memory network including the precuneus · the authors concluded that subjects not affected by the odour during the working memory task may have been better able to counteract the detrimental influence of negative stimulation and to effectively sustain/increase activation in areas associated with the task-relevant working memory network
2007 Miyanari et al.	Alinamin, Alinamin F (compounds have the same medicinal properties, but Alinamin is a stronger odorant. Following intravenous injection, subjects will smell a garlic-odour in their expired breath)	~53 s (average time of garlic odour in expired breath after iv infusion) (non-sniffing; BR)	12 healthy men (27-42 y; mean: 31 y)	· both odours: ↑ activity in the left orbitofrontal gyrus and right superior frontal gyrus, and secondary olfactory cortex · strong odour: ↑ activity in the left subthalamic nucleus, right precentral gyrus, and right insula · weak odour: ↑ activity in the right superior frontal gyrus and cerebellum · cortical processing appears to differ for strong and weak odours
2007 Murata et al.	Isovaleric acid (13.5%)	8 s (non-sniffing; BR)	17 healthy adults (16-28 y; mean: 24 y)	· subjects given odour warning: ↑ activity in the putamen extending to the insula, amygdala, and inferior frontal gyrus; odour recognition was quick · no odour warning: ↑ activity in the anterior cingulate cortex, entorhinal cortex, putamen and inferior frontal gyrus; odour recognition was difficult · brain activity impacted by odour expectation or focus of attention

BA: Brodmann Area; BR: birhinal; conc: concentration; min: minute; MR-L: monorhinal left side; MR-R: monorhinal right side; ms: milliseconds; NIRS: near-infrared spectroscopy; OFC: orbitofrontal cortex; PEA: phenylethyl alcohol; s: seconds; UPSIT: University of Pennsylvania Smell Identification Test; v/v: volume per volume; y: years

Appendix F: Summary of hemodynamic imaging studies (fMRI, PET) (continued)

Reference	**Odour Type and Concentration**	**Exposure** (sniff/non-sniffing) (BR/MR-L/MR-R)	**Population** (age)	**Study Findings**
2007 Plailly et al.	Clove (10% v/v), Coconut (10% v/v), Douglas fir (10% v/v), Grass (1% v/v), Lemon (10% v/v), Lily (10% v/v), PEA (pure), Strawberry (10% v/v)	2 s (sniff; BR)	16 healthy adults (mean: 25 y)	· odour detection task (using 2 different odours): ↑ activity in the left lateral orbital gyrus and right/left inferior frontal gyrus · odour detection task (using 2 identical odours): ↑ activity in the right/left lateral orbital gyrus, and left inferior frontal gyrus · discrimination task: relative to sensory detection of same odour, ↑ activity in the left anterior insula and frontopolar gyrus; compared to no odour, further activity ↑ in left lateral orbital/inferior frontal and middle frontal gyri · the authors concluded that the left insula may be involved with evaluation of odour properties
2007 Vaidya et al.	Vanillin, Methylvaleric acid (concentration not stated)	not clear (possibly 40 s) (non-sniffing; BR)	12 healthy adults (19-48 y; mean: 30 y)	· unpleasant (methylvaleric acid): self-reported ratings of extraversion correlated with ↑ activity in the occipital cortex and inferior temporal gyrus, and ↓ activity in the cerebellum · pleasant (vanillin): self-reported ratings of extraversion correlated with ↑ activity in the amygdala and occipital cortex · the authors concluded that there are systematic individual differences in the patterns of odour-induced brain activation
2007 Zelano et al.	Citral, Eucalyptol, Hydrogen sulphide, Mercapto-ethanol, Peach, Priopionic acid, Strawberry, Valeric acid (concentrations were varied per subject to generate equal intensity ratings for all odorants)	1.7 s (sniff; BR)	14 healthy subjects (20-39 y)	· activity in right frontal piriform cortex varied with valence (unpleasant odours induced greater activity than pleasant odours) · activity in right olfactory tubercle and right dorsomedial thalamus varied with modality (pure olfactory odours induced greater activity than bimodal odours) · activity in left frontal piriform cortex, left tubercle, right/left entorhinal cortex, right/left amygdala, and right/left OFC varied with both valence and modality · negative valence and irritation, though closely related, appear to be represented by different neural processes
2006 Gottfried et al.	Lemon-like odours (Citronellol, Geraniol, Nonanal, Undecanal); Vegetable-like odours (1-octen-3-ol, 3-octanol, *trans*-2-octenal, *trans*,*trans*-2,4-octadienal) (concentration not stated)	1 s (sniff; BR)	16 healthy adults (mean: 25 y)	· the piriform cortex is involved with odour dissociation: posterior regions encode perceived odour quality (i.e., lemon-like vs vegetable-like) while anterior regions encode molecular structure
	4 Alcohols (C-4, C-6, C-8, C-10); 4 aldehydes (C-4, C-6, C-8, C-10) (concentration not stated)	1 s (sniff; BR)	18 healthy adults (mean: 25 y)	· confirmed above findings that posterior piriform cortex encodes odorant quality while the anterior piriform context encodes molecular structure
2006 Harada et al.	Scatol, Strawberry, Vanilla (concentration not stated)	60 s (sniff; BR)	13 healthy adults (23-31 y)	· using NIRS, all odours showed ↑ bilateral activity in orbitofrontal region but not other areas (parietal, temporal, occipital regions)

BA: Brodmann Area; BR: birhinal; conc: concentration; min: minute; MR-L: monorhinal left side; MR-R: monorhinal right side; ms: milliseconds; NIRS: near-infrared spectroscopy; OFC: orbitofrontal cortex; PEA: phenylethyl alcohol; s: seconds; UPSIT: University of Pennsylvania Smell Identification Test; v/v: volume per volume; y: years

Appendix F: Summary of hemodynamic imaging studies (fMRI, PET) (continued)

Reference	**Odour Type and Concentration**	**Exposure** (sniff/non-sniffing) (BR/MR-L/MR-R)	**Population** (age)	**Study Findings**
2006 Li et al.	Acetophenone (0.1% v/v), *L*-Carvone (5% v/v), *DL*-Menthol (10% v/v), PEA (5% v/v)	2 s (sniff; BR)	16 healthy adults (20-38 y; mean: 24 y)	· prolonged exposure to one odorant led to improved ability to differentiate between related (in quality or molecular structure) and novel odorants · learning-induced improvement in odour perception correlated with ↑ activity in the piriform cortex and OFC · the authors concluded that neural codes of odour quality rely on experience, learning, and odour structure
2005 Djordjevic et al.	Lemon, PEA, Pine, Strawberry (10% v/v)	2 s (non-sniffing; BR)	67 healthy adults (18-32 y; mean: 21 y)	·↑ bilateral activity in the primary olfactory, insular, and parietal cortices ·↑ unilateral activity in the right posterior OFC, right frontal cortex, right cingulate gyrus, right thalamus, left occipital cortex, left cerebellum, left substantia nigra, and left hypothalamus
2005 Hummel et al.	Carbon dioxide, Hydrogen sulphide, PEA (concentration not stated)	1 s (non-sniffing; BR)	19 healthy adults (mean 36 y)	· all odours: ↑ activity in the ventral insula, middle frontal gyrus, and supplemental motor area (stronger right-sided activation); these regions represent the areas of overlap between trigeminal and olfactory processing · olfactory odours only (H_2S, PEA): ↑ activity in the cerebellum (left anterior lobe, right posterior lobe) and the parahippocampal gyrus · trigeminal odour (CO_2): ↑ activity in midbrain, frontal operculum, superior temporal gyrus, dorsolateral OFC, medial frontal gyrus, anterior caudate nucleus · trigeminal odour (CO_2) induced more overall activity, but weaker cerebellar activity, compared to olfactory odours (H_2S, PEA)
2005 Osterbauer et al.	Caramel, Lemon, Spearmint, Strawberry (concentration not stated)	6 s (non-sniffing; BR)	10 healthy adults (22-35 y)	·↑ bilateral activity in the piriform cortex, amygdala, and putamen ·↑ unilateral activity in the right orbitofrontal gyrus and left insular cortex
2005 Porter et al.	Amyl acetate, Eugenol, PEA, Propionic acid	1 inhalation (sniff; MR-R or MR-L)	16 healthy adults (22-30 y)	·↑ bilateral activity in the temporal piriform, frontal piriform, tubercle, cuneus, precuneus, red nucleus/superior colliculus, inferior frontal gyrus, cingulate, precentral gyrus, superior temporal gyrus ·↑ unilateral activity in the left superior marginal gyrus, left frontal cortex, and right inferior temporal gyrus · the left temporal piriform cortex and the superior temporal gyrus showed ↑ activity during olfactory localization; these are the same areas thought to be involved in auditory and visual localization
2005 Sabri et al.	Grass oil (1% v/v), Leather oil (100% v/v)	5 s (non-sniffing; BR)	9 healthy adults (mean: 25 y)	· non-attend condition (attention diverted elsewhere): change in odour ↑ activity in subgenual cingulate cortex and central posterior OFC · attend condition (count odour changes): cluster of ↑ activity in right OFC

BA: Brodmann Area; BR: birhinal; conc: concentration; min: minute; MR-L: monorhinal left side; MR-R: monorhinal right side; ms: milliseconds; NIRS: near-infrared spectroscopy; OFC: orbitofrontal cortex; PEA: phenylethyl alcohol; s: seconds; UPSIT: University of Pennsylvania Smell Identification Test; v/v: volume per volume; y: years

Appendix F: Summary of hemodynamic imaging studies (fMRI, PET) (continued)

Reference	**Odour Type and Concentration**	**Exposure** (sniff/non-sniffing) (BR/MR-L/MR-R)	**Population** (age)	**Study Findings**
2005 Small et al.	Butanol, Chocolate, Farnesol, Lavender (concentration not stated)	1 s (non-sniffing; orthonasal BR or retronasal)	11 healthy adults (age not stated)	· neural response differed between orthonasal and retronasal exposures, primarily with food odours · for example, chocolate retronasally ↑ activity in the perigenual cingulate, medial OFC, posterior cingulate, and superior temporal gyrus, while chocolate orthonasally ↑ activity in hippocampus, caudolateral OFC, thalamus, amygdala, and several regions of the insula and overlying temporal, parietal, and frontal opercula · for all odours, Rolandic operculum activity ↑ more with retronasal exposure than orthonasal exposure
2005 Wang et al.	Lavender (10% v/v), Spearmint (10% v/v)	5 s (non-sniffing; BR)	19 healthy adults (21-74 y)	·↑ activity in primary olfactory cortex, entorhinal cortex, hippocampus, parahippocampal gyrus, thalamus, hypothalamus, OFC, and insular cortex
2005 Winston et al.	Anisole, Citral, 2-Heptanol, Valeric acid (concentration not stated, but low and high intensity ratings were matched across individuals)	~2 s (sniff; BR)	17 healthy adults (20-29 y; mean: 24 y)	· activity in the posterior piriform cortex and medial OFC impacted by odour intensity but not valence; activity in the right anterior OFC varied with odour intensity and odour type · all odours at both concentrations ↑ activity in amygdala; the amygdala response varied with odour intensity for pleasant and unpleasant smells, but not for neutral smells · the authors concluded that activity in the amygdala responds preferentially to emotionally significant odours (pleasant or unpleasant)
2005 Zelano et al.	Citral, Eugenol, Limonene, PEA, Propionic acid (all odorants at suprathreshold concentrations)	5 s (sniff; BR)	12 healthy adults (mean: 30 y)	· attended condition (making odour judgment): ↑ activity in the frontal piriform cortex and olfactory tubercle compared to unattended condition (making tone judgment); activity in the attention-dependent region also ↑ in anticipation of the odour task · attended and unattended conditions: ↑ activity in temporal piriform cortex
2004 Herz et al.	Perfume with a positive emotional valence for each subject (e.g., Body shop white musk, Opium for women), Neutral perfume (generic)	30 s (non-sniffing; BR)	5 healthy women (mean: 22 y)	·↑ activity in the amygdala and hippocampal regions during recall to personally significant odour perfume
2004 Ishimaru et al.	Isovaleric acid, PEA, Undecalactone (concentration not stated, but intensity was varied over 8 levels)	10 s (non-sniffing; BR)	5 healthy adults (mean: 26 y)	·↑ bilateral activity in OFC (right more than left) · right OFC responded more changes in intensity than the left side

BA: Brodmann Area; BR: birhinal; conc: concentration; min: minute; MR-L: monorhinal left side; MR-R: monorhinal right side; ms: milliseconds; NIRS: near-infrared spectroscopy; OFC: orbitofrontal cortex; PEA: phenylethyl alcohol; s: seconds; UPSIT: University of Pennsylvania Smell Identification Test; v/v: volume per volume; y: years

Appendix F: Summary of hemodynamic imaging studies (fMRI, PET) (continued)

Reference	Odour Type and Concentration	Exposure (sniff/non-sniffing) (BR/MR-L/MR-R)	Population (age)	Study Findings
2004 Kareken et al.	Amyl acetate (10% v/v), Clove (10% v/v), Coconut (10% v/v), Lime (10% v/v), Peach (10% v/v), Pine (5% v/v), Orange (10% v/v)	2 s (sniff or non-sniffing; BR)	15 healthy adults (mean: 26 y)	·↑ bilateral activity in piriform cortex, which was present during both sniffing and non-sniffing ·↑ unilateral activity in the right amygdala/uncus and left medial orbital gyrus during sniffing; ↑ unilateral activity in the right posterior insula and left amygdala/uncus during non-sniffing · activity in OFC present during odorant sniffing, but not non-sniffing; sniffing may play a role in higher-order analysis of odours
2004 Popp et al.	Butyric acid (10% v/v), Vanillin (10% v/v)	10 s (non-sniffing; BR)	4 healthy adults (32-39 y)	· pleasant odour (vanillin): ↑ activity in the left middle frontal gyrus and left superior temporal gyrus relative to unpleasant odour · unpleasant odour (butyric acid): ↑ activity in the left inferior frontal gyrus, left lingual gyrus, right putamen, anterior cingulate cortex, right transverse temporal gyrus and right precentral gyrus relative to pleasant odour
2004 Savic and Berglund	Butanol (1% v/v), Camphor (10% v/v), Cedar oil, Coffee, Eugenol, Grapefruit, Lavender oil, Linseed oil (no dilution for these six odorants)	15 s (non-sniffing; BR)	14 healthy men (23-32 y)	· familiar and unfamiliar odours ↑ activity in amygdala, piriform cortex, and parts of anterior cingulate cortex and ↓ activity in parts of the parietal cortex · familiar odours: ↑ activity in the left frontal cortex, right parahippocampus , and left parietal cortex incorporating precuneus; familiarity ratings correlated with left frontal cortex and right parahippocampus activity · familiar and unfamiliar odours are processed partly by different cerebral circuits; familiar odours may induce covert activation of non-olfactory circuits (memory, stress, etc)
2003 Anderson et al.	Citral, Valeric acid (one low intensity, one high intensity exposure for each odour; concentration not stated)	1.66 s (sniff; BR)	16 healthy adults (mean: 22 y)	· amygdala/piriform cortex activity associated with odour intensity, but not odour valence · OFC activity associated with odour valence but not odour intensity
2003 Ferdon and Murphy	Amyl acetate (2% v/v)	12 s (non-sniffing; BR)	20 healthy adults (20-84 y)	·↑ bilateral activity in the posterior quadrangular lobule (VI), superior semilunar lobule (Crus I), and inferior semilunar lobule (Crus II); higher activation in the left hemisphere
2003 Gottfried and Dolan	Ammonium sulphide (0.2% v/v), Blue cheese liquid extract (1% v/v), Mackerel brine (99.9% v/v), Paraffin oil (pure), Pine needle essential oil (50% v/v), Rose maroc essential oil (5% v/v), Sweet orange essential oil (pure), Vanillin (10% v/v)	850 ms (sniff; BR)	15 healthy adults (22-34 y)	·↑ bilateral activity in the piriform cortex, insula, and centroposterior OFC ·↑ unilateral activity left amygdala and left anterior cingulate cortex ·↑ activity in left anterior piriform cortex during unpleasant odours and ↑ activity in right medial OFC during pleasant odours
2003 Heining et al.	Acrid rubbish, Animal feces, Banana, Cat urine, IBQ musty odour, Vanilla (concentration not stated)	15 s (unclear) (non-sniffing; BR)	16 healthy men (age not stated)	· all odours: ↑ activity in left anterior insula · disgusting odours only (acrid rubbish, animal feces): ↑ activity in the right anterior insula and right ventral striatum

BA: Brodmann Area; BR: birhinal; conc: concentration; min: minute; MR-L: monorhinal left side; MR-R: monorhinal right side; ms: milliseconds; NIRS: near-infrared spectroscopy; OFC: orbitofrontal cortex; PEA: phenylethyl alcohol; s: seconds; UPSIT: University of Pennsylvania Smell Identification Test; v/v: volume per volume; y: years

Appendix F: Summary of hemodynamic imaging studies (fMRI, PET) (continued)

Reference	**Odour Type and Concentration**	**Exposure** (sniff/non-sniffing) (BR/MR-L/MR-R)	**Population** (age)	**Study Findings**
2003 Kareken et al.	Thirty UPSIT odorants (no further details given)	1 inhalation (sniff; BR)	11 healthy adults (mean: ~51 y)	· odour sensation: ↑ bilateral activity in the medial temporal areas (piriform and uncus/ anterior entorhinal); ↑ unilateral activity in right orbital cortex and left anterior insula · odour discrimination: ↑ activity in the left hippocampus, left inferior temporal gyrus, and Broca's area · odour identification: ↑ activity in Broca's area, left inferior frontal gyrus, posterior insula, and left anterior insula
2003 Rolls et al.	*a*-Ionone, Geranyl acetate, Hexanoic acid, Isovaleric acid, Linalyl acetate, Octanol (all odours at 5% v/v)	8 s (non-sniffing; BR)	11 healthy adults (age not stated)	· pleasant odours: ↑ activity in medial-rostral OFC; activity in this area correlated with subjective pleasantness ratings · unpleasant odours: ↑ activity in lateral OFC; activity in this area negatively correlated with subjective pleasantness ratings · pleasant, unpleasant: ↑ activity in anterior cingulate cortex and anterior insula · piriform and entorhinal areas deal with odour intensity, while orbitofrontal areas are involved with odour pleasantness
2003 Royet et al.	126 odorants with varying hedonicity (e.g., Butyric acid, Cinnamon, Lavender, Lemon, Lilac, Mint, Onion, Pepper, Raspberry, Pine, Rose, Tobacco) (1-10% v/v)	3-5 s (non-sniffing; BR)	28 healthy adults (20-30 y)	· odour exposure: ↑ activity in the insula, OFC, superior temporal gyrus and precentral gyrus · hedonicity task: ↑ activity in the insula, OFC, hypothalamus, amygdala, lateral sulcus, and piriform cortex · unpleasant odours induced more activation than pleasant odours · ↑ activity during hedonicity judgment compared to passive exposure
2003 Wicker et al.	20 odorants (e.g., Apricot, Banana, Butyric acid, Isovaleric acid, Hexane, Mint, Onion) (1-10% v/v)	12 s (non-sniffing; BR)	14 healthy men (20-27 y)	· pleasant and unpleasant odours both ↑ activity in amygdala (large overlap) · unpleasant odours ↑ bilateral activity in the anterior insula, while pleasant odours ↑ unilateral activity in a posterior site of the right insula (no overlap)
2002 Gottfried et al.	4-Methylpentanoic acid (5% v/v), PEA (0.1% v/v), Vanillin (8% w/v)	~750 ms (1 sniff) (sniff; BR)	15 healthy subjects (18-31y; mean: 23y)	· all odours: prolonged ↑ bilateral activity in the piriform cortex along the posterior aspect, amygdala, and posterior OFC · unpleasant (4-methylpentanoic acid): ↑ activity in left posterior OFC, right dorsal amygdale, left lateral hypothalamus, right insula/frontal operculum · pleasant (vanillin): ↑ activity in medial anterior frontal piriform cortex and medial OFC · neutral (PEA): ↑ activity in the left posterior piriform cortex

BA: Brodmann Area; BR: birhinal; conc: concentration; min: minute; MR-L: monorhinal left side; MR-R: monorhinal right side; ms: milliseconds; NIRS: near-infrared spectroscopy; OFC: orbitofrontal cortex; PEA: phenylethyl alcohol; s: seconds; UPSIT: University of Pennsylvania Smell Identification Test; v/v: volume per volume; y: years

Appendix F: Summary of hemodynamic imaging studies (fMRI, PET) (continued)

Reference	Odour Type and Concentration	Exposure (sniff/non-sniffing) (BR/MR-L/MR-R)	Population (age)	Study Findings
2002 Savic et al.	Acetone (99.9%), Vanillin (99%)	15 s (non-sniffing; BR)	12 healthy women (20-28 y)	· vanillin: ↑ bilateral activity in amygdala and piriform cortex; no deactivations · acetone: ↑ activity in the anterior and central insula and claustrum, posterior anterior cingulate, a left somatosensory area, cerebellum, ventral and dorsal medial thalamus, lateral hypothalamus, and pons/medulla · acetone: ↓ activity in primary and secondary visual cortex, right secondary auditory cortex, right sensorymotor cortex, supplementary motor cortex, and parahippocampal gyri
2001 Bartocci et al.	Neomidil (a detergent), Remove® (adhesive remover)	10 s (non-sniffing; BR)	20 pre-term newborns (0-35 days)	· using NIRS, both odours induced ↓ blood oxygenation in the orbitofrontal gyrus; the ↓ was significantly greater in the right side than the left
2001 Bengtsson et al.	Butanol (1% v/v), Cedar oil (10% v/v), Eugenol (10% v/v), Lavender oil (10% v/v), Vanillin (pure)	15 s (non-sniffing; BR)	23 healthy adults (20-28 y)	·↑ bilateral activity in amygdala, piriform cortex, putamen, and insular cortex ·↓ activity in the parietal cortex
2001 Henkin and Levy	Actual odours: Amyl acetate, Menthone, Pyridine (concentration not stated) Imagined odours: Banana, Peppermint	60 s (non-sniffing; BR)	24 healthy adults (22-44 y; mean: 28 y)	· in general, pleasant odours led to more activations in the left hemisphere than the right (amyl acetate: L>R ($p<.005$); menthone: L>R (non-significant)) · imagined odours showed a similar pattern · no hemisphere differences observed for the unpleasant odour (pyridine)
2001 Kareken et al.	Sixteen UPSIT odorants (no further details given)	1 inhalation (sniff; BR)	15 elderly subjects (healthy or Alzheimers) (mean: 72 y)	·↑ bilateral activity in piriform (frontotemporal junction) and ↑ unilateral activity in right anterior ventral temporal cortex; subjects with Alzheimers showed lower activity in right piriform and right anterior ventral cortex ·↑ activity also seen in culmen and right dentate nucleus of cerebellum
2001 Poellinger et al.	PEA (pure)	9 s or 60 s (non-sniffing; BR)	10 healthy adults (24-44 y; mean: 30 y)	· 9s stimulus: ↑ activity in primary olfactory cortex · 60s stimulus: short, phasic activity ↑ in the piriform, entorhinal cortex, amygdala, hippocampus and parts of the anterior insula, which was followed by a prolonged ↓ below baseline; sustained activity ↑ in the OFC; short activity ↑ in the mediodorsal nucleus of the thalamus and the caudate nucleus
2001 Royet et al.	156 odorants with varying hedonicity (e.g., Butyric acid, Cinnamon, Lavender, Lemon, Lilac, Mint, Onion, Pepper, Raspberry, Pine, Rose, Tobacco) (1-10% v/v)	3-5 s (1 inhalation) (non-sniffing; BR)	12 healthy men (20-30 y)	· detection and intensity tasks: ↑ activity in middle frontal gyrus · hedonicity task: ↑ activity in superior frontal gyrus, OFC, subcallosal area, anterior cingulate, inferior/middle temporal gyrus, cuneus/lingual gyrus, and primary visual areas · familiarity task: ↑ activity in anterior cingulate, superior frontal gyrus, middle frontal gyrus, and orbitofrontal area · for all tasks: ↓ activity in right and left temporo-occipital areas, posterior cingulate gyrus, and right superior frontal gyrus

BA: Brodmann Area; BR: birhinal; conc: concentration; min: minute; MR-L: monorhinal left side; MR-R: monorhinal right side; ms: milliseconds; NIRS: near-infrared spectroscopy; OFC: orbitofrontal cortex; PEA: phenylethyl alcohol; s: seconds; UPSIT: University of Pennsylvania Smell Identification Test; v/v: volume per volume; y: years

Appendix F: Summary of hemodynamic imaging studies (fMRI, PET) (continued)

Reference	Odour Type and Concentration	Exposure (sniff/non-sniffing) (BR/MR-L/MR-R)	Population (age)	Study Findings
2000 Bartocci et al.	Colostrum, Vanilla (concentration not stated)	30 s (non-sniffing; BR)	23 healthy newborns (6-192 hrs)	· using NIRS, vanilla was found to ↑ activity in left OFC · colostrum: results were variable (increases, decreases, or no change) for activity in left OFC
2000 Kobal and Kettenmann	Vanillin (2.1 ppm)	1 s (non-sniffing; MR-R or MR-L)	6 healthy adults (25-36 y; mean: 30 y)	·↑ bilateral activity in the orbitofrontal gyrus, gyrus rectus, temporal lobe (right>left), lateral frontal region (right>left) and medial frontal region · neither the orbitofrontal nor the temporal areas showed activity after clean air exposure
2000 Qureshy et al.	Cinnamon, F & D, Famica bouquet, Grandmate, Mulberry, PEA, Quest, Rainfresh, Sandalwood, Summer-flower, Undecanoic acid, Vanilla, Woodland mist (concentration not stated)	6 s (non-sniffing; BR)	8 healthy Japanese men (18-26 y)	·↑ unilateral activity in the left orbitofrontal region, right piriform cortex, left middle frontal lobe, and left cuneus
2000 Royet et al.	120 odorants with varying hedonicity (e.g., Butyric acid, Cinnamon, Lavender, Lemon, Lilac, Mint, Onion, Pepper, Raspberry, Pine, Rose, Tobacco) (1-10% v/v)	3-5 s (1 inhalation) (non-sniffing; BR)	12 healthy men (20-30 y)	Emotional condition task (pleasantness judgment): · strong ↑ in activity in left OFC, temporal pole, and right superior frontal gyrus · weaker ↑ in activity in the right OFC and hypothalamus ·↑ bilateral activity in the amygdala, cerebellum, and hippocampus; ↑ unilateral activity in left piriform cortex and right superior temporal gyrus and claustrum Neutral condition task (no judgment): ·↑ bilateral activity in inferior parietal lobules
2000 Savic et al.	Butanol (1% v/v), Cedar oil (10% v/v), Eugenol (10% v/v), Lavender oil (10% v/v)	15 s (non-sniffing; MR-R or MR-L)	18 healthy women (22-27 y)	·↑ unilateral activity in right amygdala and piriform cortex (confluent cluster), right OFC, left insula, right thalamus, and anterior cingulate
2000 Savic and Gulyas	Butanol, Butylacetate, Cedar oil, Eugenol, Guaia, Lavender oil, Methylsalicylate (conc: 1-10% v/v)	10-15 s (non-sniffing; MR-R or MR-L)	18 healthy women (22-27 y)	·↑ bilateral activity in orbitofrontal-inferior frontal cortex, primary olfactory cortex, insula-claustrum, and anterior cingulate · odour intensity detection task: ↑ activity in left insula and right cerebellum · odour discrimination task: ↑ activity in left insula, right cerebellum, right subiculum-hippocampus and caudate nucleus, brainstem and dorsal thalamus, anterior cingulate, and the orbitofrontal, opercular, and prefrontal cortices
2000 Sobel et al.	Decanoic acid, Propionic acid, Valeric acid, Vanillin (concentrationwas subject dependent: lowest concentration that enabled >90% detection accuracy)	800 ms (sniff; BR)	8 healthy adults (20-39 y; mean: 25 y)	·↑ bilateral activity in orbitofrontal gyrus, cingulate gyrus, olfactory tubercle, area of claustrum, superior temporal gyrus, peri-insular region, frontal gyrus, anterior medial dorsal thalamus, amygdala, hippocampus, and caudate nucleus
2000 Zatorre et al.	Acetophenone (85 mmol/L), Cyclodecanone (50 mmol/L), Isoamyl acetate (67 mmol/L), Pyridine (2.0 mmol/L), Thymol (100 mmol/L), 1,8 Cineole (60 mmol/L)	1 inhalation (sniff; BR)	12 healthy adults (mean: 23 y)	·↑ activity in the right OFC, occipital cortex, and cerebellum during both pleasantness and intensity judgments ·↑ activity in the right parietal cortex and hypothalamus during the pleasantness but not the intensity judgment · no activity change in the piriform region

BA: Brodmann Area; BR: birhinal; conc: concentration; min: minute; MR-L: monorhinal left side; MR-R: monorhinal right side; ms: milliseconds; NIRS: near-infrared spectroscopy; OFC: orbitofrontal cortex; PEA: phenylethyl alcohol; s: seconds; UPSIT: University of Pennsylvania Smell Identification Test; v/v: volume per volume; y: years

Appendix F: Summary of hemodynamic imaging studies (fMRI, PET) (continued)

Reference	Odour Type and Concentration	Exposure (sniff/non-sniffing) (BR/MR-L/MR-R)	Population (age)	Study Findings
1999 Levy et al.	Actual odours: Amyl acetate, Menthone (concentration not stated) Imagined odours: Banana, Peppermint	60 s (non-sniffing; BR)	21 healthy adults (22-48 y; mean: 30 y)	·↑ bilateral activity in frontal cortex, (right more than left) including entorhinal cortex, and the temporal cortex and tips (left more than right), and near the cingulate cortex and hippocampus ·↑ activity in the cingulate cortex and regions near the hippocampus · some differences were noted between anterior, middle, and posterior sections · imagined odours activated the brain in the same general regions as actual odours, but to a much lesser extent
1999 Royet et al.	126 odorants with varying hedonicity (e.g., Butyric acid, Cinnamon, Lavender, Lemon, Lilac, Mint, Onion, Pepper, Raspberry, Pine, Rose, Tobacco) (1-10% v/v)	4-5 s (non-sniffing; BR)	9 healthy men (20-40 y)	· familiarity task: ↑ activity in the right medial frontal gyrus (BA 11), subcallosus gyrus (BA 25), left inferior and superior frontal gyri (BA 9, 47), and anterior cingulate gyrus (BA 32) · edibility judgment: ↑ activity in the right superior occipital gyrus (BA 19) and the inferior occipital gyrus (BA 17, 18)
1999 Schneider et al.	Rotten yeast (0.2 g/mL)	3 s (non-sniffing; MR-R)	24 males (12 with social phobia) (18-45 y)	·↑ activity in the amygdala, thalamus, cerebellum, occipital cortex, dorsolateral prefrontal cortex, cingulate gyrus posterior, medial temporal cortex, and superior temporal cortex
1999a Yousem et al.	Eugenol, PEA, PEA alternating with Hydrogen sulphide (concentration not stated)	1 s (non-sniffing; BR)	10 healthy adults (18-80 y)	·↑ activity in right perisylvian region, right and left superior frontal, and right inferior frontal regions · adults: additional ↑ activity in left perisylvian and both cingulate regions
1999b Yousem et al.	Eugenol, PEA, PEA alternating with Hydrogen sulphide (concentration not stated)	1 s (non-sniffing; BR)	16 healthy adults (18-44 y; mean:~28 y)	·↑ bilateral activity in frontal lobes with higher activation of right superior frontal compared to the left ·↑ bilateral activity in temporal lobes, with higher activation in right perisylvian region compared to the left
1998 Birbaumer et al.	Fermented yeast (concentration not stated)	3 s (non-sniffing; BR)	12 adults (healthy or with social phobia) (mean: 26 y)	· ↑ bilateral activity in the amygdala but not the thalamus in both groups
1998 Fulbright et al.	Clementine, Isovaleric acid (concentration not stated)	40 s (non-sniffing; BR)	13 healthy adults (mean: 30 y)	· clementine: ↑ bilateral activity in frontal regions BA 8, BA 46/9, and insula;↑ unilateral activity of BA 32 (left) and BA 6 (right) · isovaleric acid: ↑ bilateral activity in frontal regions BA 6, BA 32, BA 46/9, and the insula; no activation of BA 8
1998 Sobel et al.	Decanoic acid, Vanillin (concentration not stated)	1.5 s (sniff or non-sniffing; BR)	13 healthy adults; 1 anosmic adult (mean: 28 y)	·↑ activity in the anterior and lateral OFC, piriform, peri-insular region, superior temporal region, and parts of the limbic system · sniffing (with or without odorant) ↑ activity in the piriform cortex and the medial and posterior orbitofrontal gyri, while odorants (with or without sniffing) ↑ activity mainly in the lateral and anterior orbitofrontal gyri

BA: Brodmann Area; BR: birhinal; conc: concentration; min: minute; MR-L: monorhinal left side; MR-R: monorhinal right side; ms: milliseconds; NIRS: near-infrared spectroscopy; OFC: orbitofrontal cortex; PEA: phenylethyl alcohol; s: seconds; UPSIT: University of Pennsylvania Smell Identification Test; v/v: volume per volume; y: years

Appendix F: Summary of hemodynamic imaging studies (fMRI, PET) (continued)

Reference	Odour Type and Concentration	Exposure (sniff/non-sniffing) (BR/MR-L/MR-R)	Population (age)	Study Findings
1998 Zald et al.; 1997 Zald and Pardo	Mixture of Dimethyl sulphide, Ethanethiol, and Methanethiol (25 ppm each)	60 s (non-sniffing; BR)	17 healthy women (19-49 y)	·↑ bilateral activity in the amygdala with sulphide mixture but not mildly aversive odorants; changes in activity in the left amygdala correlated with subjective unpleasantness ratings ·↑ unilateral activity in the left OFC with both odorant groups · right OFC and left OFC appear to be functionally coupled at rest and when smelling no odour, but uncouple when smelling unpleasant odour · right amygdala and left amygdala appear to be functionally coupled at rest, but uncouple when smelling no odour or unpleasant odour · for unpleasant odours, activity in the left OFC and left amygdala increased proportionally
	Four mildly aversive UPSIT odorants (no further details given)	8 s (non-sniffing; BR)		
1997 Levy et al.	Amyl acetate, Menthone, Pyridine (concentration not stated)	7 s (non-sniffing; BR)	17 healthy adults (22-41 y; mean: 27 y)	·↑ activity in the OFC, entorhinal cortex, and cingulate gyrus · activated brain regions did not differ between pleasant and unpleasant odours
1997 Yousem et al.	Eugenol, Geraniol, Methyl salicylate, Patchouli, Rosemary, Ylang-ylang (concentration not stated)	30 s (sniff; BR)	5 healthy men (29-43 y)	· olfactory odours (eugenol, geraniol, methyl salicylate): ↑ activity in the OFC (right greater than left) and cerebellum · bimodal odours (patchouli, rosemary, ylang-ylang): ↑ activity in the right OFC and cerebellum, as well as the visual, precuneate, temporal, and cingulate areas · for repeated exposures: ↓ activation (habituation) was found with olfactory odours and ↑ activation with bimodal odours
1994 Koizuka et al.	PEA (concentration not stated)	1 inhalation (unclear) (sniff; BR)	5 healthy adults (24-28 y)	·↑ bilateral activity in the OFC, piriform cortex, and inferior frontal lobe
1992 Zatorre et al.	Butter extract, Citronella, Hawes lemon oil, Kirsch, Lavender, Maple extract, Patchouli, Shalimar (concentration not stated)	1 inhalation (unclear) (sniff; BR)	11 healthy adults (mean: 23 y)	·↑ bilateral activity at junction of the inferior frontal and temporal lobes (piriform cortex) ·↑ unilateral activity in right OFC

BA: Brodmann Area; BR: birhinal; conc: concentration; min: minute; MR-L: monorhinal left side; MR-R: monorhinal right side; ms: milliseconds; NIRS: near-infrared spectroscopy; OFC: orbitofrontal cortex; PEA: phenylethyl alcohol; s: seconds; UPSIT: University of Pennsylvania Smell Identification Test; v/v: volume per volume; y: years

Appendix G: Summary of electromagnetic studies (EEG, MEG)

Reference	Odour Type and Concentration	Exposure (sniff/non-sniffing) (BR/MR-L/MR-R)	Population (age)	Study Findings
2013 Croy et al.	Hydrogen sulphide (4 ppm), PEA (40% v/v), Peach (40% v/v)	200 ms (non-sniffing; MR-R or MR-L)	42 healthy adults (20-38; mean: 25 y)	· unpleasant (H_2S): ↓ N1 and P2 latencies and ↑ P2 amplitude compared to pleasant odour; ↓ P2 amplitude with repeated exposure (which may be related to a decrease in attention towards the odour) · pleasant (PEA, Peach): EEG responses did not change with repeated exposure
2013 Iannilli et al.	Carbon dioxide (45% v/v), Hydrogen sulphide (8 ppm)	250 ms (non-sniffing; MR-R)	15 healthy women (20-35; mean: 26 y)	· trigeminal neural response differed from the olfactory response up to 300 ms after stimulus onset · trigeminal (CO_2): contrasted with H_2S, ↑ activity in noxious/somatosensory specific brain areas (posterior cingulate, posterior lobe of cerebellum) · olfactory (H_2S): contrasted with CO_2, ↑ activity in olfactory-related areas (ventromedial prefrontal cortex (entorhinal cortex–gyrus rectus–olfactory tract))
2013 Sayorwan et al.	Rosemary oil (10% v/v)	7 min (non-sniffing; BR)	20 healthy adults (18-28 y; mean: 21 y)	·↓ alpha 1 and alpha 2 activity; ↑ beta activity · topographic map demonstrated decreased scattering of alpha 1 waves in the frontal area and the right posterior brain region, and decreased scattering of alpha 2 waves in all brain regions
2012 Huart et al.	Carbon dioxide (55% v/v), PEA (50% v/v)	200 ms (non-sniffing; MR-R)	11 healthy adults (24-30 y)	· trigeminal (CO_2): ↑ N1 and P2 amplitudes · trigeminal (CO_2): ↑ EEG responses in the time-frequency domain · olfactory (PEA): N1, P2 amplitudes did not differ from air (in most subjects) · olfactory (PEA): ↑ EEG responses in the time-frequency domain; the magnitude of this response correlated with olfactory performance scores
2012 Sayorwan et al.	Lavender oil (10% v/v)	7 min (non-sniffing; BR)	20 healthy adults (18-35 y; mean: 23 y)	·↑ alpha and theta activity in all brain areas; no change to beta activity · topographic map demonstrated increased scattering power in alpha brain, particularly in bilateral temporal and central area
2010 Bulsing et al.	Hydrogen sulphide (10 ppm), PEA (40% v/v)	250 ms (non-sniffing; BR)	61 female university students (mean: 23 y)	· H_2S: ↓ N1 latencies and ↑ N1 and P3 amplitudes in the painful expectancy condition (subjects expected chemosensory irritation) compared to the non-painful expectancy condition · PEA: ↓ N1 latencies and ↑ N1 amplitude in the painful expectancy condition · the authors concluded that expectation that an odour is irritable may change perception of that odour
2010 Lascano et al.	Hydrogen sulphide (4 ppm)	200 ms (non-sniffing; MR-R or MR-L)	12 healthy adults (22-46 y)	· 4 steps of odour processing at 200-1000 ms: ·~250-350 ms: ipsilateral activation of mesial and lateral temporal cortex (amygdala, parahippo-campal gyrus, superior temporal gyrus, insula) · additional contralateral activation of mesial areas (~350-550 ms), lateral temporal areas (~550-600 ms) and middle and inferior frontal gyrus (~600-850 ms)

BR: birhinal; CNV: contingent negative variation; EEG: electroencephalography; ERP: event-related potential; MEG: magnetoencephalography; min: minutes; MR-L: monorhinal left side; MR-R: monorhinal right side; ms: milliseconds; N1: first negative polarity peak of ERP; N400: negative peak at 400 ms of ERP; OFC: orbitofrontal cortex; P2: second positive polarity peak of ERP; P3: third positive polarity peak of ERP; P200: positive peak at 200 ms of ERP; P300: positive peak at 300 ms of ERP; PEA: phenylethyl alcohol; ppb: parts per billion; ppm: parts per million; s: seconds; y: years

Appendix G: Summary of electromagnetic studies (EEG, MEG) (continued)

Reference	Odour Type and Concentration	Exposure (sniff/non-sniffing) (BR/MR-L/MR-R)	Population (age)	Study Findings
2010 Poncelet et al.	Mint (10% and 40% v/v; experienced earlier in life for Algerian-French subjects); PEA (10% and 40% v/v; experienced equally across cultures)	250 ms (non-sniffing; BR)	37 healthy adults (mean: 24 y)	· both odours: higher concentrations ↓ ERP latencies (N1, P2) · Algerian-French subjects showed longer P2 latencies than European-French subjects in response to mint; no differences between groups were found for PEA
2010 Walla and Deecke	Hydrogen sulphide (3 ppm and 0.03 ppm), PEA (100% and 5%)	1 s (non-sniffing; MR-R)	10 adults (mean: 24 y)	· all odours: ↑ MEG activity at 300 ms for all picture categories; this was thought to reflect early subconscious processing of interacting olfactory and visual data · MEG activity at ~700 ms was altered by odour primarily for pictures representing flower, fear, and disgust; this later-window activity was thought to reflect conscious processing; the authors concluded that odours have different effects on different visually-induced emotions
2009 Boesveldt et al.	PEA (40% v/v)	1 s (non-sniffing; MR-R)	21 healthy adults (50-73 y; mean: 59 y)	· ↑ theta and ↓ beta MEG activity (central right and temporal regions) · ↓ local beta band functional connectivity (left central, frontal regions) and ↑ inter-hemispheric delta band functional connectivity (bilateral temporal regions) · no differences in intra-hemispheric functional connectivity
2009 Iijima et al.	Incense (agarwood), Rose oil	3 min (non-sniffing; BR)	15 healthy adults (23-39 y; mean: 30 y)	· incense: ↑ alpha 2 activity in bilateral posterior regions · incense: ↑ P3 amplitude during the 'wait' instruction of a push/wait motor task · the authors concluded that incense enhanced cortical activity and improved the inhibition process of motor response
2009 Scheibe et al.	Carbon dioxide (44% v/v), PEA (25% v/v)	200 ms (non-sniffing; MR-R or MR-L)	17 healthy adults (mean: 22 y)	· trigeminal (CO_2) produced larger N1 and P2 amplitudes and shorter N1 and P2 latencies than olfactory odour (PEA)
2008 Laudien et al.	Isobornyl acetate (9.3% v/v)	300 ms (non-sniffing; BR)	45 healthy women (18-46 y; mean: 23 y)	· N1, P2, and P3-2 latencies differed between three bias groups: subjects told the odour was a healthy extract had ↓ latencies, while those told the odour was hazardous had ↑ latencies · ERP amplitudes did not differ between bias groups · harmful bias group showed ↑ activity in the fronto-central and occipital regions; healthy bias group showed ↑ activity in left temporal region
2007 Bulsing et al.	Carbon dioxide (60% v/v), Hydrogen sulphide (10 ppm)	200 or 500 ms (non-sniffing; BR)	30 female university students (mean: 22 y)	· N1 latencies were ↓ in the painful expectancy condition (subjects expected chemosensory pain) compared to the non-painful expectancy condition · N1,P2 amplitudes or P2 latency did not differ based on expectancy condition · expectancies of chemosensory pain alter early aspects of olfactory processing
2006 Frasnelli et al.	Hydrogen sulphide (2 ppm and 8 ppm), PEA (10% and 40% of saturated air)	100 to 300 ms (non-sniffing; BR)	20 healthy adults (20-30 y)	· higher conc: odour duration associated with ↑ ERP amplitudes; no effect on ERP latencies · lower conc: no effect of odour duration on ERP amplitudes or latencies

BR: birhinal; CNV: contingent negative variation; EEG: electroencephalography; ERP: event-related potential; MEG: magnetoencephalography; min: minutes; MR-L: monorhinal left side; MR-R: monorhinal right side; ms: milliseconds; N1: first negative polarity peak of ERP; N400: negative peak at 400 ms of ERP; OFC: orbitofrontal cortex; P2: second positive polarity peak of ERP; P3: third positive polarity peak of ERP; P200: positive peak at 200 ms of ERP; P300: positive peak at 300 ms of ERP; PEA: phenylethyl alcohol; ppb: parts per billion; ppm: parts per million; s: seconds; y: years

Appendix G: Summary of electromagnetic studies (EEG, MEG) (continued)

Reference	Odour Type and Concentration	Exposure (sniff/non-sniffing) (BR/MR-L/MR-R)	Population (age)	Study Findings
2006 Laudien et al.	Menthol, PEA (20% v/v)	500 ms (non-sniffing; BR)	20 healthy women (mean: 23 y)	· in subjects with induced feelings of helplessness, P2 and P3-1 amplitudes were ↓, and N1, P2, and P3-1 latencies were ↑ · ERP latencies/amplitudes may be influenced by emotional status of subjects
2006 Lorig et al.	Citral (10% v/v), PEA (20% v/v), Vanillin (13% w/v)	600 ms: 4 odour components at 150 ms each (non-sniffing; BR)	10 university students (18-22 y)	· time sequence of exposure altered pattern of brain electrical activity · fast transition (3 odour changes per 600 ms): ↑ left temporal lobe activity · slow transition (1 odour change per 600 ms): ↑ cortex activity bilaterally
2006 Lundström et al.	Androstenone (20% v/v)	250 ms (non-sniffing; BR)	22 healthy adults (17-55; mean: 27 y)	· subjects describing the odour as a 'body odour' had larger P3 amplitude than subjects describing the odour as a 'non-body odour'; valence was negatively correlated with P3 amplitude · no differences in P1, N1 amplitudes or any peak latencies · thus, the P3 component appears to reflect the processing of odour valence
2006 Miyanari et al.	Alinamin, Alinamin F (compounds have the same medicinal properties, but Alinamin is a stronger odorant. Following intravenous injection, subjects will smell a garlic-odour in their expired breath)	~149 s (average length of time of garlic odour in expired breath after iv infusion) (non-sniffing; BR)	9 healthy adults (25-53 y; mean: 34 y)	· both odours: ↑ MEG activity in the right and left superior and middle frontal gyri and the right precentral gyrus · strong odour: ↑ activity in the left temporal, parietal, and occipital lobes · weak odour: ↑ activity in the right temporal, parietal, and occipital lobes · strong and weak odours may be processed in different areas (left and right hemispheres, respectively)
2006 Stuck et al.	Carbon dioxide (40% and 60% v/v), Hydrogen sulphide (2 and 4 ppm)	200 ms (non-sniffing; MR-R or MR-L)	95 healthy adults (18-80 y; mean: 46 y)	· CO_2: lower concentration associated with ↓ N1 and P2 amplitudes and ↑ N1 and P2 latencies · H_2S: lower concentration associated with ↓ P2 amplitude; no difference in N1 amplitude or N1-P2 latencies · H_2S: higher P2 amplitude associated with lower odour thresholds; shorter P2 latency associated with higher odour identification score
2005 Field et al.	Lavender (fragrance in cleansing gel)	2 min (non-sniffing; BR)	11 healthy adults (age not stated)	· ↑ relative left frontal EEG activity (post-exposure) · ↑ frontal theta and beta power, but not alpha or delta power (post-exposure) · greater relative left frontal EEG activity has been found to be an indicator of positive mood
2005 Masaoka et al.	Isovaleric acid, PEA (individual odour detection and recognition thresholds used)	One inhalation (non-sniffing; BR)	17 healthy men (mean: 32 y)	· odour detection: ↑ alpha activity in the limbic area and cortex (entorhinal cortex, hippocampus, amygdala, premotor area and centroposterior OFC) · odour recognition: ↑ alpha activity in rostro-medial OFC · alpha activity was phase-locked to inspiration

BR: birhinal; CNV: contingent negative variation; EEG: electroencephalography; ERP: event-related potential; MEG: magnetoencephalography; min: minutes; MR-L: monorhinal left side; MR-R: monorhinal right side; ms: milliseconds; N1: first negative polarity peak of ERP; N400: negative peak at 400 ms of ERP; OFC: orbitofrontal cortex; P2: second positive polarity peak of ERP; P3: third positive polarity peak of ERP; P200: positive peak at 200 ms of ERP; P300: positive peak at 300 ms of ERP; PEA: phenylethyl alcohol; ppb: parts per billion; ppm: parts per million; s: seconds; y: years

Appendix G: Summary of electromagnetic studies (EEG, MEG) (continued)

Reference	Odour Type and Concentration	Exposure (sniff/non-sniffing) (BR/MR-L/MR-R)	Population (age)	Study Findings
2005, 2003a Walla et al.	Carbon dioxide, Hydrogen sulphide, PEA (concentration not stated)	300 ms (non-sniffing; MR-R)	20 healthy adults (mean: 26 y)	· olfactory odours (H_2S, PEA): ↓ MEG activity at ~260 ms during face encoding (reflects subconscious odour processing and competition with face encoding for cortical resources) · trigeminal odour (CO_2) or subjects with awareness of PEA odour: ↑ MEG activity at ~700 ms during face encoding (reflects conscious odour perception)
2004 Livermore and Hummel	Carbon dioxide (40% v/v), Hydrogen sulphide (4.0 ppm), Linalool (20% v/v), Linalool plus Carbon dioxide, Linalool plus Hydrogen sulphide	200 ms (non-sniffing; MR-R)	35 healthy adults (18-44 y; mean: 24 y)	· odour mixtures generally produced larger amplitudes than single odours; latencies differed between the five odour exposures · trigeminal (linalool, CO_2): larger N1 amplitudes at central site than parietal site · olfactory (H_2S): higher amplitudes at parietal site or no clear difference between amplitudes at central and parietal sites
2003 Frasnelli et al.	Carbon dioxide (45-65% v/v)	100 to 300 ms (non-sniffing; MR-R)	20 healthy adults (18-38 y; mean: 25 y)	· CO_2 concentration correlated with ERP N1 and P3 amplitudes; no effect on ERP latencies · CO_2 duration correlated with P3 amplitude, but not N1 amplitude; no effect on ERP latencies
2003 Harada et al.	Methyl-cyclopentenolone (concentration not stated)	500 ms (non-sniffing; BR)	10 healthy adults; 40 subjects with dysosmia (13-81 y)	· in healthy subjects, positive peaks were observed at 350 ms (P1) and 700 ms (P2); activity was highest in the centro-occipital region · subjects with smell disorders: P1 was seen in only 7 subjects (possibly representing trigeminal nerve activation); P2 peak was not observed (possibly representing olfactory nerve response)
2003 Kim et al.	PCK (components from Japanese cypress; 150× and 500× dilution), 2-mercaptoethanol (150× and 300× dilution)	12 min (unclear) (non-sniffing; BR)	12 male university students (22-26 y)	· pleasant (PCK): ↓ alpha and beta activity in the post-exposure resting state · pleasant (PCK): 150×, but not 500× dilution, ↑ activity in left frontal area · unpleasant (2-mercaptoethanol): 150×, but not 500× dilution, ↓ alpha activity in the exposure resting state
2003 Min et al.	Basil oil, Jasmine oil, Lavender oil, Lemon oil, Skatole, Ylang-ylang oil	90s (unclear) (non-sniffing; BR)	10 general workers, 10 perfume researchers, 10 perfume salespersons (mean: 28 y)	· general workers/salespersons: ↑ functional connectivity in posterior, temporal, parietal, and frontal regions · researchers: ↑ functional connectivity in frontal region; the focused activity in the frontal region possibly reflects the ↑ function of the OFC · activity varied inversely with odour preference in researchers and salespersons, but not general workers, suggesting that functional coupling in occupationally exposed subjects may be related to odour preference
2003b, 2002 Walla et al.	PEA (concentration not stated)	300 ms (non-sniffing; MR-R)	20 healthy adults (19-35 y)	· ↓ MEG activity at ~300-500 ms during word encoding, regardless of odour perception (reflects subconscious odour processing and competition with word processing for cortical resources) · prolonged ↑ in MEG activity at ~650-900 ms during word encoding in subjects who perceived the odour (reflects conscious odour perception)

BR: birhinal; CNV: contingent negative variation; EEG: electroencephalography; ERP: event-related potential; MEG: magnetoencephalography; min: minutes; MR-L: monorhinal left side; MR-R: monorhinal right side; ms: milliseconds; N1: first negative polarity peak of ERP; N400: negative peak at 400 ms of ERP; OFC: orbitofrontal cortex; P2: second positive polarity peak of ERP; P3: third positive polarity peak of ERP; P200: positive peak at 200 ms of ERP; P300: positive peak at 300 ms of ERP; PEA: phenylethyl alcohol; ppb: parts per billion; ppm: parts per million; s: seconds; y: years

Appendix G: Summary of electromagnetic studies (EEG, MEG) (continued)

Reference	Odour Type and Concentration	Exposure (sniff/non-sniffing) (BR/MR-L/MR-R)	Population (age)	Study Findings
2003 Welge-Lüssen et al.	Carbon dioxide (60% v/v), Hydrogen sulphide (4 ppm), PEA (40% v/v)	200 ms (non-sniffing; MR-R or MR-L)	20 health adults (21-39 y; mean: 27 y)	· ERPs showed fair to good reliability over 3 test sessions, with most correlations ranging between 0.4 and 0.75 · correlations were better for ERP latencies than ERP amplitudes · ERPs considered a reliable assessment measure for odour research
2002 Bensafi et al.	Floral mixture (1/1000 dilution)	5 s (non-sniffing; BR)	15 female university students (mean: 20 y)	· in subjects exposed to odour, the late positive complex (P3 at ~550 ms) was more positive for unpleasant faces than pleasant faces (i.e., frontal activity induced during an emotional judgment was modulated by pleasant (incongruous) odour) · odour had no effect on the N400 wave
2002 Hiruma et al.	Hiba (*Thujopsis dolabrata*; a conifer)	38-50 min (ambient room odour; BR)	16 female adults (19-22 y)	· odour ↑ amplitude of early CNV (an index of arousal level) and late CNV (associated with motor preparation) during a reaction time task · this effect was observed at the frontal and central positions, but not the parietal position
2002 Sanders et al.	Lavender (10%), Rosemary (10%)	3 min (non-sniffing; BR)	40 adults (mean: 31 y)	· lavender, but not rosemary, induced ↑ relative left frontal EEG activity · greater relative left frontal EEG activity has been found to be an indicator of positive mood; thus, this study supports the idea that lavender odour may have antidepressant properties
2002 Sano et al.	Components of green odour (*n*-hexanol, *n*-hexanal, 3*Z*-hexenol, 3*Z*-hexenal, 2*E*-hexenol, 2*E*-hexenal, 3*E*-hexenol, 3*E*-hexenal) (all solutions 0.03% v/v)	time not stated (non-sniffing; BR)	128 healthy women (18-22 y)	· despite the high similarity in chemical structure and odour, the varying compounds induced either an ↑, no change, or a ↓ in P300; no sign of synergism in the 2-component mixtures
	3*Z*-hexenol (the dominant odorant of green odour) (0.1% w/w, 10% w/w)		31 healthy women (18-22 y)	· 3*Z*-hexenol ↓ P300 relative to control · amplitude-decreasing effect was larger with the 0.1% than the 10% concentration; the 0.1% odour was also considered to be more pleasant · authors found that odour pleasantness, rather than concentration, led to the P300 amplitude ↓
2002 Thesen et al.	Amyl acetate (1493 ppm)	200 ms (non-sniffing; MR-R)	20 healthy adults (mean: 51 y)	· olfactory ERPs stayed relatively consistent over a 4-week interval; therefore, a reliable assessment measure for odour research
2002 Wang et al.	Amyl acetate (2193 ppm)	35 to 200 ms (non-sniffing; BR)	12 university students (18-25 y)	· odour exposure time correlated with ERP N1-P2 amplitude; both factors also correlated with odour detection score · no effect of exposure time on N1 latency
2001 Hamada et al.	Lavender, Lemon, Soy sauce (concentration not stated)	500 ms (sniff; BR)	2 subjects (age not stated)	· olfactory-evoked responses were observed over the right cortex (peak latency ~350 ms) · oscillatory peaks were observed over the right frontal cortex with longer latency (~1090 ms), but only in 9 of 26 trials

BR: birhinal; CNV: contingent negative variation; EEG: electroencephalography; ERP: event-related potential; MEG: magnetoencephalography; min: minutes; MR-L: monorhinal left side; MR-R: monorhinal right side; ms: milliseconds; N1: first negative polarity peak of ERP; N400: negative peak at 400 ms of ERP; OFC: orbitofrontal cortex; P2: second positive polarity peak of ERP; P3: third positive polarity peak of ERP; P200: positive peak at 200 ms of ERP; P300: positive peak at 300 ms of ERP; PEA: phenylethyl alcohol; ppb: parts per billion; ppm: parts per million; s: seconds; y: years

Appendix G: Summary of electromagnetic studies (EEG, MEG) (continued)

Reference	Odour Type and Concentration	Exposure (sniff/non-sniffing) (BR/MR-L/MR-R)	Population (age)	Study Findings
2001 Kemp et al.	Eucalyptus, Methylated spirits, Whiskey (concentration not stated)	60 s (non-sniffing; BR)	33 healthy adults (mean: 52 y)	· alpha, beta1, beta2, or theta activity were not altered during odour presentation
2001 Masago et al.	Eugenol (95%), Limonene (85%)	200 ms (non-sniffing; MR-L)	7 male university students (21-23 y)	· ERP latencies did not differ between eugenol and limonene · limonene produced a significantly larger late positive complex (P3) amplitude than eugenol · ERP latencies ↓ and P3 amplitude ↑ when subjects paid attention to the odour relative to performing an auditory distracter task
2000 Geisler and Murphy	Ammonia (366 ppm), Amyl acetate (1493 ppm)	200 ms (non-sniffing; MR-R)	26 healthy adults (mean: 26 y)	· olfactory odour (amyl acetate) produced shorter N1, P2, and P3 ERP latencies than the trigeminal odour (ammonia); latencies were shorter when subjects were rating odour intensity relative to not rating intensity · trigeminal (ammonia): produced larger N1-P2 peak amplitudes than the olfactory (amyl acetate); P3 amplitude was greater when rating odour intensity
2000 Kline et al.	Valerian, Vanilla (concentration not stated, but odours were of similar intensities)	30 s (sniff; BR)	49 older women (58-70 y)	· pleasant odour (vanilla) ↑ relative left frontal EEG activity compared to unpleasant (valerian) or no odour
2000 Kobal and Kettenmann 1997 Kettenmann et al.	Hydrogen sulphide (0.78 ppm), Vanillin (2.1 ppm)	200 ms (non-sniffing; MR-R or MR-L)	10 healthy adults (20-40 y; mean: 32 y)	·↑ bilateral MEG activity in superior temporal plane and parainsular cortex (at 226-380 ms), parts of the insular cortex (at 306-486 ms), and the superior temporal sulcus (at 518-730 ms); no activation of OFC · H_2S: no stimulation of left insular cortex at 306-486 ms, suggesting a role for odour hedonic in this region
1999 Covington et al.	Isoamyl acetate (100%, 50%, 10% v/v or 960 ppm, 793 ppm, 152 ppm at the nose piece)	1 s (unclear) (non-sniffing; BR)	28 healthy adults (mean: 46 y)	· medium and high odour concentrationinduced shorter ERP P2 and N2 latencies than the low conc; no effect of intensity on N1 or P3 latencies · no effect of odour intensity on ERP amplitudes
1998 Diego	Lavender (10%), Rosemary (10%)	3 min (non-sniffing; BR)	40 adults (mean: 31 y)	· lavender: ↑ frontal alpha power and beta 2 power (suggesting ↑ drowsiness) · rosemary: ↓ frontal alpha power (suggesting ↑ alertness)
1998, 1996 Harada et al.	Methyl-cyclopentenolone, Scatol (concentration not stated)	50 s (non-sniffing; BR)	10 healthy adults (22-27 y)	· methyl-cyclopentenolone (pleasant): delta band coherence ↓ in the frontal region, and alpha 1 and alpha 2 bands ↑ in the bilateral temporal regions · scatol (unpleasant): delta band coherence ↓ in the frontal region, and alpha 1 and alpha 2 bands ↑ in the fronto-occipital regions
1998 Hummel et al.	Carbon dioxide (52%), Hydrogen sulphide (2.1 ppm), Vanillin (0.8 ppm)	200 ms (non-sniffing; MR-L)	48 healthy adults (15-74 y)	· trigeminal (CO_2) produced the largest N1, N1-P2, and P2 amplitudes and shortest N1 and P2 latencies, relative to the olfactory odours · trigeminal (CO_2) induced max amplitudes at the vertex · olfactory (vanillin, H_2S) induced max amplitudes at the parietal sites

BR: birhinal; CNV: contingent negative variation; EEG: electroencephalography; ERP: event-related potential; MEG: magnetoencephalography; min: minutes; MR-L: monorhinal left side; MR-R: monorhinal right side; ms: milliseconds; N1: first negative polarity peak of ERP; N400: negative peak at 400 ms of ERP; OFC: orbitofrontal cortex; P2: second positive polarity peak of ERP; P3: third positive polarity peak of ERP; P200: positive peak at 200 ms of ERP; P300: positive peak at 300 ms of ERP; PEA: phenylethyl alcohol; ppb: parts per billion; ppm: parts per million; s: seconds; y: years

Appendix G: Summary of electromagnetic studies (EEG, MEG) (continued)

Reference	Odour Type and Concentration	Exposure (sniff/non-sniffing) (BR/MR-L/MR-R)	Population (age)	Study Findings
1998 Krauel et al.	Linalool (2% v/v), Eugenol (2% v/v)	200 ms (non-sniffing; MR-L)	6 healthy men (20-25 y)	· attend condition: P3-1, P3-2 amplitudes were increased relative to the non-attend condition; earlier peaks (N1, P2) were not affected · attend condition: all peak latencies (N1, P2, N2, P3) were shorter relative to non-attend condition
	Body odour of same sex donor	600 ms (non-sniffing; MR-R)	5 healthy adults (20-27 y)	· attend condition: P3-1, P3-2 amplitudes were increased relative to the non-attend condition; earlier peaks (N1, P2) were not affected · attend condition: early peak latencies (N1, P2, N2) were shorter relative to non-attend condition; no effect on P3 peak latencies
1998 Martin et al.	Liquid concentrates of Almond (10% v/v), Chocolate essence (100%), Cumin seed oil (100%), Garlic/Onion (100%), Spearmint (10% v/v), Strawberry (10% v/v), Vegetable (100%)	38 s (non-sniffing; BR)	21 university students (17-37 y)	· chocolate and spearmint ↓ EEG theta activity in the right frontal region · odours had no significant effect on other EEG frequency bands (delta, alpha, beta1, or beta2)
	Real food odours: Baked beans (30 g), Chocolate essence (2 µl), Coffee dissolved in hot water (110 mL), Hot water (110 mL), Rotting pork (1 inch^2)	76 s (non-sniffing; BR)	15 healthy adults (age not stated)	·↓ theta activity in response to chocolate (central areas) and rotting pork (left temporal region) · chocolate induced greater alpha and beta1 activity compared to rotting pork · changes in theta activity may reflect shifts in attention or cognitive load during odour perception
1998 Tateyama et al.	Vanillin (84, 56, 28, and 7 % v/v)	200 ms (non-sniffing; MR-R)	16 healthy adults (17-34 y; mean: 26 y)	· odour concentration positively correlated with ERP amplitudes (P1-N1, N1-P2, N1-P3, P3) and negatively correlated with latencies (P1, N1, P2, P3) · subjects with lower odour thresholds (for butanol) had shorter latencies · no association between odour thresholds and amplitudes
1998 Tonoike et al.	Amyl acetate (1%), Geraniol (1%)	300 ms (non-sniffing; MR-R or MR-L)	6 healthy males (age not stated)	·↑ bilateral MEG activity (asymmetrical) in the orbitofrontal sulcus (at 350-450 ms)
1997 Pause et al.	Linalool (0.16-1.45 ppm), Menthol (0.10-4.15 ppm)	200 ms (non-sniffing; MR-R or MR-L)	11 healthy adults (mean: 26 y)	· increasing olfactory odour (linalool) led to ↓ N1 latencies, but did not affect ERP amplitudes · increasing trigeminal odour (menthol) led to ↑ N1 and P2 amplitudes, but did not affect of N1 or P2 latencies · late positive complex (P3) amplitude generally ↑ when subjects paid attention to odour; P3 varies with subjective odour significance rather than exogenous odour features · amount of attention to odour had no effect on peak latencies
1997 Sakuma et al.	Amyl acetate, PEA (concentration not stated)	100 ms (non-sniffing; MR-L)	14 healthy adults (25-42 y; mean: 32 y)	· odours induced two magnetic field peaks: one at ~300 ms and another at ~600 ms; this activity occurred in the bilateral Sylvian fissure regions · the magnetic field peaks corresponded to the EEG P1 (~300 ms) and N1 (~600 ms) components

BR: birhinal; CNV: contingent negative variation; EEG: electroencephalography; ERP: event-related potential; MEG: magnetoencephalography; min: minutes; MR-L: monorhinal left side; MR-R: monorhinal right side; ms: milliseconds; N1: first negative polarity peak of ERP; N400: negative peak at 400 ms of ERP; OFC: orbitofrontal cortex; P2: second positive polarity peak of ERP; P3: third positive polarity peak of ERP; P200: positive peak at 200 ms of ERP; P300: positive peak at 300 ms of ERP; PEA: phenylethyl alcohol; ppb: parts per billion; ppm: parts per million; s: seconds; y: years

Appendix G: Summary of electromagnetic studies (EEG, MEG) (continued)

Reference	Odour Type and Concentration	Exposure (sniff/non-sniffing) (BR/MR-L/MR-R)	Population (age)	Study Findings
1996 Kettenmann et al.	Hydrogen sulphide (2.5 ppm), PEA (500 ppm), Vanillin (2.1 ppm)	200 ms (non-sniffing; MR-R or MR-L)	6 healthy adults (25-51 y; mean: 31 y)	·↑ bilateral MEG activity around the superior temporal sulcus; response peaked ~700 ms after stimulus · brain activity did not differ between odours
1996 Lorig et al.	Butanol (4% and 2%) (2 conditions: mouth-breathing with odour delivered asynchronous with breathing (passive condition), and nasal inhalation (active condition))	250 ms (sniff and non-sniffing; MR-R or MR-L)	12 university students (18-22 y; mean 19 y)	· concentration correlated with P2 amplitude · P2 amplitude also varied as a function of exposure condition and spatial distribution; P2 ↑ in non-sniffing condition relative to sniff condition · scalp distribution of N1 peak differed with concentration and condition; N1 amplitude did not vary significantly with concentration or condition
1996 Pause et al.	Citral (10 ppb and 844 ppb)	200 ms (non-sniffing; MR-R or MR-L)	5 healthy women (20-35 y; mean: 27 y)	· early ERP components (N1, P2) are modulated by odour concentration (larger amplitude and shorter latency with higher concentration) · late positive components (P3-1, P3-2) are modulated by subjective odour significance (higher amplitudes when subjects detected rare and meaningful stimuli)
1995 Brauchli et al.	PEA (76 ppb), Valeric acid (23 ppb)	30 s (non-sniffing; BR)	4 healthy men (mean: 24 y)	· unpleasant (valeric acid) significantly ↑ EEG alpha2 power in the frontal and parietal locations · odours had no significant effect on other EEG frequency bands (theta, beta1, or alpha1)
1995 Evans et al.	Amyl acetate (50% v/v)	40 ms (non-sniffing; MR-R)	33 healthy adults (18-83 y)	· P2 latency correlated with odour identification score, suggesting that P2 is involved in olfactory processing · ERP amplitudes not associated with odour identification scores · ERP amplitudes or latencies not associated with odour threshold scores
1994 Murphy et al.	Amyl acetate (1100 ppm)	230 ms (non-sniffing; MR-R)	14 healthy adults (20-84 y)	· odour detection threshold significantly correlated with N1 and P2 amplitudes
1993 Lorig et al.	Butanol (4%, 1.33%, 0.444% v/v or 1647, 550, 183 ppm at the subject's nose)	1 s (non-sniffing; BR)	15 healthy adults (17-54 y; mean: 29 y)	· conc-dependent ↑ in amplitude of a P300-like component (320-520 ms) [P2] · subjects with higher odour sensitivity tended to have higher amplitudes in frontal locations and lower amplitudes (most negative) in right temporal region
1993 Van Toller et al.	Bangalol, Eucalyptus oil/ammonia mixture, Indole, Linalyl acetate, White sapphire (concentration not stated, but odours were of similar intensities)	10 s (non-sniffing; BR)	15 adults (19-48 y)	· odours induced a generalized pattern of EEG electrical responses · EEG alpha activity correlated with increasing intensity of psychometric responses (strength, familiarity, pleasantness) at electrodes located in a precentral gyrus area across both hemispheres
1992 Kendal-Reed et al.	4 different baby foods (25 g each of chicken dinner, chocolate pudding, beef dinner, and fish in tomato sauce)	25 s (non-sniffing; BR)	8 infants (3 months)	· infants showed a change in the pattern of cortical activity when presented with odour · cortical response did not differ between odours

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Appendix G: Summary of electromagnetic studies (EEG, MEG) (continued)

Reference	**Odour Type and Concentration**	**Exposure** (sniff/non-sniffing) (BR/MR-L/MR-R)	**Population** (age)	**Study Findings**
1992 Klemm et al.	Birch tar (10% v/v), Galbanum (10% v/v), Heliotropine (25% v/v), Jasmine (100%), Lavender (100%), Lemon (100%), Peppermint (10% v/v)	2 mins (non-sniffing; BR)	16 female university students (age not stated)	· wide variation in EEG responses to odours · the most consistent responses were found in the theta frequency band in the left anterior region and the right hemisphere regions (mainly with birch tar, jasmine, lavender and lemon odours)
1992 Kobal et al.	Carbon dioxide (52% v/v), Hydrogen sulphide (0.78 ppm), Menthol (21.07 ppm), Vanillin (2.06 ppm)	200 ms (non-sniffing; BR)	11 healthy adults (25-46 y)	· trigeminal odours induced much larger ERP amplitudes than olfactory odours · trigeminal (menthol, CO_2) induced max amplitudes at the vertex · olfactory (vanillin, H_2S) induced max amplitudes at parietal and central sites · suggests that olfactory ERPs involve at least 2 neuronal populations
1992 Livermore et al.	Carbon dioxide, Carvone, Hydrogen sulphide (concentration not stated, but odours were of similar intensities), Binary mixtures of these odours	200 ms (non-sniffing; MR-L)	30 healthy adults (18-37 y; mean: 27 y)	· trigeminal odour (CO_2) induced max amplitude at the vertex · olfactory (H_2S) and bimodal (carvone) odours induced max amplitude at parietal and central sites · stimulation with binary mixtures produced smaller P2 amplitudes than the single odours combined · in binary mixtures of CO_2 and carvone, suppression of CO_2 intensity by carvone was paralleled by a ↓ in ERP amplitudes · ERP latencies ↓ in binary mixtures of CO_2 and either olfactory odour; this suggests that both systems are involved in the time-domain of ERPs
1992 Prah and Benignus	Toluene (1600, 8000, and 16000 ppm)	500 ms (non-sniffing; MR-L)	8 healthy men (18-30 y)	· odour intensity correlated with ↑ P1 amplitude · odour intensity was not associated with P1 latency, although a trend between increasing odour concentration and shorter latency was observed
1991 Lorig et al.	Galaxolide fragrance (80%, 20%, and 5% v/v)	10 s (non-sniffing; BR)	12 university students (18-21 y)	· odour intensity ↑ P200 and P300 amplitude during auditory odd-ball task (counting infrequent tones) · amplitude of P200, but not P300, was ↑ in the undetectable odour condition (5% v/v) relative to no odour
1990 Lorig and Roberts	Galbanum, Jasmine, Lavender, Mixture of the three odours (concentration not stated, but odours were of similar intensities)	4 s (non-sniffing; BR)	18 university students (18-22 y)	· greatest CNV responses observed in frontal regions, especially left frontal area · for the mixture, CNV responses varied depending on their expectations; this suggests a cognitive component to EEG CNV responses
1988 Kobal and Hummel	Anethol (0.53 mg/L), Benzaldehyde (3.5 mg/L), Carbon dioxide (66% v/v), Limonene (6.0 mg/L), Menthol (0.065 mg/L), PEA (0.51 mg/L), Vanillin (0.034 mg/L), mixture of Vanillin/CO_2	200 ms (non-sniffing; MR-R or MR-L)	13 adults (22-35 y)	· all odours induced event-related potentials · intensity ratings of odours positively correlated with peak amplitudes and negatively correlated with peak latencies
1988 Lorig and Schwartz	Eucalyptus (60% v/v), Lavender (60% v/v), Spiced apple (concentration not stated)	1 min (non-sniffing; BR)	9 healthy adults (18-24 y)	· odours induced ↓ EEG theta activity; the EEG alterations were related to self-reports of mood (↓ anxiety and tension)

BR: birhinal; CNV: contingent negative variation; EEG: electroencephalography; ERP: event-related potential; MEG: magnetoencephalography; min: minutes; MR-L: monorhinal left side; MR-R: monorhinal right side; ms: milliseconds; N1: first negative polarity peak of ERP; N400: negative peak at 400 ms of ERP; OFC: orbitofrontal cortex; P2: second positive polarity peak of ERP; P3: third positive polarity peak of ERP; P200: positive peak at 200 ms of ERP; P300: positive peak at 300 ms of ERP; PEA: phenylethyl alcohol; ppb: parts per billion; ppm: parts per million; s: seconds; y: years

Appendix G: Summary of electromagnetic studies (EEG, MEG) (continued)

Reference	**Odour Type and Concentration**	**Exposure** (sniff/non-sniffing) (BR/MR-L/MR-R)	**Population** (age)	**Study Findings**
	5 floral note perfumes (5% v/v)		10 healthy adults (18-56 y)	· the five odours produced varying levels of EEG alpha and theta activity over the left and right hemispheres · similar odours can lead to very different patterns of neurophysiological activity

BR: birhinal; CNV: contingent negative variation; EEG: electroencephalography; ERP: event-related potential; MEG: magnetoencephalography; min: minutes; MR-L: monorhinal left side; MR-R: monorhinal right side; ms: milliseconds; N1: first negative polarity peak of ERP; N400: negative peak at 400 ms of ERP; OFC: orbitofrontal cortex; P2: second positive polarity peak of ERP; P3: third positive polarity peak of ERP; P200: positive peak at 200 ms of ERP; P300: positive peak at 300 ms of ERP; PEA: phenylethyl alcohol; ppb: parts per billion; ppm: parts per million; s: seconds; y: years

