The Link between Odors and Illness

How Health Cognitions affect Odor Perception

Patricia Bulsing

Cover Design: Maurice Bulsing

Printed by: GVO drukkers & vormgevers B.V. | Ponsen & Looijen

ISBN: 978-90-393-5113-0

The Link between Odors and Illness

How Health Cognitions affect Odor Perception

Het verband tussen geur en ziekte:
Hoe ideeën over gezondheid de waarneming van geur beïnvloeden

(met een samenvatting in het Nederlands)

Proefschrift

ter verkrijging van de graad van doctor aan de Universiteit Utrecht
op gezag van de rector magnificus, prof. dr. J. C. Stoof,
ingevolge het besluit van het college van promoties in het openbaar te verdedigen
op vrijdag 11 september 2009 des middags te 12.45 uur

door

Patricia Johanna Bulsing

geboren op 11 april 1980, te ‘s Gravenhage

Promotor
Prof. dr. M.A van den Hout

Co-promotor
Dr. M.A.M. Smeets

All research in this thesis was funded by the Dutch Organization for Scientific Research (NWO; grant 452-03-334).

Table of contents

Chapter 1

General introduction

Perception of odor is influenced by cognitive and experiential factors. These top-down influences on odor perception can be profound: While it is extremely unlikely that when people look at a cucumber they will mistake it for mildew, it is not uncommon for an odor to be identified as either a cucumber or mildew (Herz & Von Clef, 2001). The implication of this is that one and the same odor may evoke different interpretations and behavioral responses.

This thesis deals with top-down influences of health-related cognitions on odor perception in situations where the odor may signal potential health effects. The problem that triggered our interest in this topic is the phenomenon that some people attribute health effects to exposures to environmental odors even at low concentrations that are well-tolerated by the majority of the population.

I will start this introduction by addressing this phenomenon. Then, I will explain why a top-down approach was chosen for the studies reported in this thesis, and I will clarify why we focused on perception. Finally, I will go over the research objectives, followed by an overview of the studies reported in Chapters 2 – 6.

Background

The problem: odors and health effects

This thesis deals with adverse health effects attributed to odors. The reader will realize that, clearly, chemical exposures *can* in fact cause health effects via toxicological mechanisms, in which case the odor accompanying the exposure functions as a signal, warning the individual of the presence of the obnoxious chemical, and an avoidance reaction is only appropriate. In a mild form, exposure to volatile chemicals such as ammonia can cause sensory irritation via stimulation of the trigeminal nerve that innervates the nose, eyes, and throat. Trigeminal irritation leads to sensations of burning or stinging that can be slightly painful. Often these effects are reversible, in the sense that when the chemical is removed, the symptoms will subside. In the example of ammonia, the odor that serves as a signal of possible sensory irritation can be perceived at concentrations below those that will produce sensory irritation, although some individuals experience irritation at the same (threshold) concentrations at which they start to perceive the odor (Smeets et al., 2007). While sensory irritation is considered a mild health effect of chemical exposure, at higher concentrations many chemical compounds will provoke more serious effects that may not be reversible (somatic irritation, chronic toxicity, acute toxicity, Schiffman et al., 2000). In those cases, odors may be perceived as accompanying the exposure and they may function as effective warning signals leading to avoidance behavior, but associated health effects can be well explained by toxicological models irrespective of the odor of the chemical.

Sometimes however, odors induce health effects while the nature of the exposure precludes any somatic responses. Toxicological models are insufficient to explain such cases and psychological models appear to be more appropriate. A condition in which health complaints are attributed to, essentially harmless odors, and where somatic responses are not expected, is known as *Multiple Chemical Sensitivities (MCS)*, also referred to as Idiopathic *Environmental Intolerance* (Labarge &

McCaffrey, 2000). Individuals with MCS often report symptoms such as fatigue, headaches, dizziness, depression, shortness of breath and sensory irritation to chemical exposures in the environment, often characterized by odors. These symptoms are reported to concentrations of various types of chemicals, such as perfumes, diesel fuel, cleaning agents and solvents, often at low levels that are well–tolerated by most people (Labarge & McCaffrey, 2000). Das-Munshi, Rubin, and Wessely (2006) reviewed 37 provocation studies conducted in laboratories involving masked and unmasked exposures to chemicals in sensitive and control populations. They concluded that although chemically sensitive individuals did react to chemical exposures, the most likely underlying mechanism was not related to the chemical, but rather to psychological mechanisms, involving the top-down influence of beliefs and learning (e.g. via classical conditioning) on the expression of the somatic response. Based on a summary of a small number of studies, Johansson, Millqvist, Nordin and Bende (2006) estimate the prevalence of chemical sensitivities in the population to be between 16 and 33%. The prevalence in the Netherlands is difficult to estimate, since MCS is not an accepted health condition here (Gezondheidsraad, 1999).

Aside from MCS, health reports have been attributed to odor exposures in relation to industry (e.g. sugar manufacturing, oil refineries, wastewater facilities), agriculture (animal operations involving cows, pigs and poultry; composting), traffic, office buildings (*so-called sick buildings*) and individual households (Smeets, 2009). In these cases the impact from odor exposures on the individual may not be as profound or long-lasting as is the case for MCS patients, but the impact on wellbeing and health can nonetheless be substantial. Again, the number of people suffering from odor-related effects under those conditions is hard to estimate, since the effects - and those impacted - are often confined to a small area and may not be registered. Overall, the number of Dutch people who reported being (sometimes) bothered by stench from traffic, industry, agriculture, or open fires was greater than 30% as established by the Centraal Bureau voor de Statistiek (CBS) in 2008.

Theoretical models

So far, the theoretical model most often referred to when explaining how health effects arise from environmental odor exposures is the biopsychosocial model. In contrast to the traditional biomedical model, in which illness is explained from biological abnormalities following fixed cause-and-effect relationships, psychosocial factors are allocated a central role in addition to biological factors, leaving room for belief systems about causal relations between odors and health (Taylor, 2003: see also Spurgeon, 2002).

The concept of stress – referring to a negative emotional experience, which is accompanied by predictable biochemical, physiological, cognitive and behavioral changes, aimed at changing the stressful event or adjustment to its effects (Baum, 1990) – plays an important role in models on health and environmental factors (for noise, stress and health: Van Kamp, 1990; for odor, see Fraser & Day, 1972). Stressors in the environment may lead to activation of the sympathetic nervous system, preparing the individual for a "fight-or-flight" reaction. As a result, the individual experiences e.g. increased blood pressure, increased heart rate, sweating. When stressed, the hypothalamic-pituitary-

adrenal axis (HPA-axis) is activated, leading to the production of cortisol which helps the individual return to physiological baseline. The individual who experiences stress or stress-related physiological effects may attribute these effects to the odor, in the sense that these effects are interpreted as health effects directly resulting from the chemical exposure. Thus, someone who feels short of breath after smelling a bad odor emanating from a plant nearby may experience this effect as directly caused by inhalation of the bad smell.

In the experimental work by Van den Bergh and colleagues (1995, 1997, 1998) towards understanding somatic responses in reaction to odors, learning through classical conditioning of odors plays an important role. During an acquisition phase, participants inhaled CO_2 enriched air (i.e. an Unconditioned Stimulus; US), which led to physiological reactions mimicking the fear response: increased breathing, dizziness, breathlessness, increased heart rate etc (i.e. an Unconditioned Response; UR). At the same time, an odor was presented along with the CO_2, such that participants smelled an odor while experiencing the effect of CO_2. After the acquisition phase, the odor by itself triggered the fear response (i.e. the odor became a Conditioned Stimulus; CS). Although the primary interest of Van den Bergh et al. was not so much in MCS, but rather the human fear response, these experiments demonstrate that by classical conditioning, somatic responses and symptom reports also encountered in MCS can be evoked after exposure to an odor which first did not elicit any health symptoms (see also Shusterman, 2001).

Finally, in the cognitive-perceptual model of chemosensory perception by Dalton and Hummel (2000) and Smeets and Dalton (2005) the emphasis is on the top-down influence of previously stored knowledge or beliefs about odors and health, as well as of pre-existing states and traits of the individual (e.g. neuroticism) on the perception of and reaction to chemosensory stimuli in the environment. In this model, learning plays an important role in the explanation of how odor perceptions themselves can change, and how such changes can modulate physiological health effects. Here, learning can refer either to instructional learning – i.e. when people are told how to interpret their environment – leading to beliefs about how odors may lead to illness not necessarily related to own experience, or to classical conditioning – in which odors become signals of approaching harm related to own experience. Until recently, implicit influences via affectively colored attitudes did not receive much attention, but they clearly need to be also acknowledged in this model.

Why a top-down approach?

In this thesis, a top-down approach of olfaction was adopted for two reasons. The first reason is that a bottom-up explanation of health effects after exposure to low and non-toxic concentrations of chemicals by toxicological models has proven to be insufficient. Toxicological models can be considered bottom-up in that they try to explain adverse health effects as a consequence of exposure to chemicals from the characteristics of those chemicals, with the emphasis on the dose or amount of exposure. They can also be considered as biomedical models in that they do not strongly acknowledge psychosocial effects.

There have been some attempts to explain health effects after non-toxic exposures in terms of bottom-up processes. It has been suggested e.g. that immunological abnormalities are involved but consistent laboratory findings supporting this premise are lacking (Labarge & McCaffrey, 2000). Yet others have proposed time-dependent sensitization processes, whereby repeated sub-threshold stimulation of e.g. the olfactory bulb and the amygdala ultimately amplify reactivity to chemical exposures (Bell et al., 1997). Although this has been demonstrated in animals (but only in response to high doses), experimental data in humans sustaining this latter explanation do not exist (Labarge & McCaffrey, 2000).

Top-down explanations for understanding odor-related illnesses have been offered with more success: there is direct evidence for the role of psychological factors in the initiation of health complaints as a consequence of odor exposure. For instance, Shusterman, Lipscomb, Neutra, and Satin (1991) demonstrated that individuals who lived near hazardous waste sites and who were worried about the odor source reported significantly more health symptoms compared to people who were less worried.

Dalton and her group explored top-down cognitive influences on health symptoms reports in a laboratory setting. In a series of studies, it was demonstrated that expecting an odorant to be harmful, as opposed to expecting that same odorant to be healthful or neutral, increased health symptoms reports, such as nose, throat, and eye irritation and light-headedness (Dalton, Wysocki, Brody, & Lawley, 1997; Dalton, 1999). A proposed mechanism to account for this is that expecting negative health effects may trigger feelings of anxiety and stress, automatically resulting in closer monitoring of internal, bodily signals that may indicate potentially harmful effects (Shusterman, 2001; see also *theoretical models*). The previously mentioned studies on classical conditioning by the group of Van den Bergh also fall under the rubric of top-down effects.

In conclusion, whereas health effects as in MCS are insufficiently explained by basic toxicological principles, explanations incorporating the influence of cognitive factors, like beliefs, expectations, or the effects of learning, offer a better account for reported odor-associated health effects.

A second reason for adopting a top-down approach is related to recent developments in the field of olfactory perception in general. In their book, *Learning to Smell*, Wilson and Stevenson (2006) give an overview of both bottom-up, as well as top-down theories aimed at understanding odor quality perception. Searching for systematic relationships between physical properties of odorants, receptor structures, and the final odor percept seemed a logical first approach, especially in the light of successful stimulus-response models in other sensory modalities, such as color perception, which is based on interactions between frequency of light and photoreceptors. Based on the idea that the sense of smell would follow a similar organization, researchers put much effort in the search for "primary" odors (as an equivalent of primary colors), specific anosmias (as an equivalent of specific color blindness), or cross-adaptation of similarly structured or smelling odorants, all of which were expected to unravel the neuronal organisation of the sense of smell. However, none of these bottom-up attempts yielded satisfying explanations for how olfaction works, which led Wilson and Stevenson (2006) to conclude that the sense of smell is not an analytical, stimulus-response system as previously

believed, but functions more like an object recognition system, largely influenced by learning and association processes.

In conclusion, a top-down perspective was adopted in this thesis, based on the fact that both research on odor-associated health effects and olfactory perception in general suggest that traditional, analytical accounts of olfaction cannot explain behavioral and sensory responses in reaction to exposure, whereas models which allow the influence of other, contextual factors can.

Why focus on perception?

In the same series of studies that showed that expecting negative health consequences from odor exposure affected health symptom reports to those exposures, changed perception was reported (Dalton et al., 1997; Dalton, 1999). That is, participants whose interpretations were manipulated in a negative direction gave higher intensity and irritancy ratings to the odor compared to participants whose interpretations were manipulated in positive or neutral directions (Dalton et al., 1997; Dalton, 1999). This led Dalton to propose that the effects of bias manipulation on health responses to odors were modulated by changes in perception of the odor (Dalton, 2002, 2003).

Recent studies applying fMRI techniques demonstrate that perception of chemical stimuli can indeed be modulated by cognitive factors. For example, Nitschke et al. (2006) induced various expectations about the taste of bitter substances. It was shown that if participants expected that a highly aversive bitter substance would taste only slightly bitter, the substance was perceived according to induced expectancies, and thus as less bitter. Additionally, it was demonstrated that expecting a less intense stimulus decreased brain activity related to the processing of these stimuli: neurons in the primary taste cortex were less activated, even though this region was initially believed to be completely stimulus-driven, and thus only activated by sensory input from taste receptors and somatosensory neurons.

De Araujo, Rolls, Velazco, Margot, and Cayeux (2005) modulated perception and brain responses by providing two different verbal labels, "cheddar cheese" or "body odor", during the presentation of one and the same odor (isovaleric acid). Neurons in the medial orbitofrontal cortex, which region is known to become more activated in response to pleasant odors (Gottfried, O'Doherty, & Dolan, 2002) were significantly more activated by the odor when it was labelled "cheddar cheese" than when it was labelled "body odor". This showed that expectations about the degree of pleasantness influence how and where in the brain the stimulus is processed.

Even more profound evidence of top-down modulated sensory responses comes from the study conducted by Li, Howard, Parrish and Gottfried (2008). They showed that two indistinguishable odour enantiomers (i.e. mirror-image molecules that smell identical) became distinguishable after one of the two was conditioned to an electric shock. In other words, people can acquire the ability to differentiate between odours that initially smell exactly the same, meaning perceptual sensitivity was enhanced.

In conclusion, top-down influences of cognition on odor perception do not seem to be limited to the context of health, but have also been demonstrated in broader contexts. Cognitions have been

reported to penetrate phases of information processing that were initially believed to be entirely stimulus-driven, and thus inaccessible to any top-down modulation.

Finally, similar ideas are encountered in the field of clinical and health psychology, where recent models on, for example, psychopathology also acknowledge the possibility and influence of changes in perceptual processing (e.g. the model of medically unexplained symptoms; Brown, 2004; the model of cognitive mechanisms underlying threat processing; Bar-Heim et al., 2007; the model of selective processing in anxiety; Mathews & Mackintosh, 1998).

We are witnessing a shift in scientific focus from top-down influences on health responses to top-down influences on perception as potentially modulating such health responses. This is an exciting development and promises a better understanding of the etiology and maintenance of maladaptive health and behavioral responses to an individual's environment and opens up new avenues for treatment and prevention.

Objectives and scope

Thesis outline

The general theme of the thesis deals with the top-down influence of cognitions about odors and health on perceptions of odors. From this general theme two objectives have been derived: Objective 1 involves the determination of the *content* of cognitions related to odors and health that are supposed to exert a top-down influence. What kinds of cognitions do people hold when it comes to odors and health? Objective 2, then, is to determine the nature and magnitude of the effects of top-down influences on olfactory perception.

Objective 1: The content of cognitions associated with odors

We addressed the content of cognitions by studying *automatically activated* associations between odors and health that are not necessary accessible to introspection but may nevertheless affect behavior. We included this line of research in our project for several reasons. First of all, we found that people have a hard time verbalizing their ideas about odors and health (Smeets, Bulsing & Boeije, in preparation)[1], and about the sense of smell in general (Engen, 1987). This probably relates to the fact that olfactory information processing often acts on an implicit level, without any conscious awareness (Köster, 2002): people rarely sit down to contemplate their own olfactory experiences. Because of the

[1] We also studied *explicit* representations of odors and relations between odor and health, as in cognitions or previously stored knowledge, accessible to introspection: This line of research is still ongoing and has not been included in this thesis (but will be reported elsewhere). It involves the construction of a questionnaire which measures beliefs about the possible effects odors can have on health (Odor Beliefs Questionnaire; OBQ).

implicit nature of olfaction, it seems unlikely that explicit beliefs and controlled cognitive processes related to olfaction guide very quick, initial approach or avoidance evaluations. It would be more fitting with this implicit nature to presume a pathway that relies on quick, pre-attentive associations between odors and health effects, as opposed to rich networks of knowledge structures. Therefore we chose a method which enables us to study olfactory cognitions that act on a more implicit or automatic level: Two odor-variants of the Implicit Association Test were constructed, described in Chapter 2 and 3, respectively (IAT; Greenwald, McGhee, & Schwartz, 1998).

Chapter 2 describes a study in which the experienced valence of the concept odor was explored (not yet taking into account the association with the concept health). Three experiments were conducted to investigate whether people's primary, automatic association with the concept odor had either a more positive or a more negative connotation. During the administration of the odor-IAT participants had to classify words that appeared one by one on a computer screen into categories. During a first part of the test, participants had to use one and the same key for classifying odor-related words (e.g. scent, aroma) and positive words (e.g. love, success). During a second part of the IAT, participants had to use one and the same key for classifying odor-related words and negative words (e.g. war, failure). Half of the participants started in the reversed order. Participants who demonstrated shorter reaction times while classifying odor word and positive words using the same key, as opposed to odor words and negative words, were assumed to have a positive implicit attitude toward the concept odor, whereas participants who showed shorter reaction times while classifying odor and negative words compared with odor and positive words were believed to have a negative attitude toward the concept odor. The underlying assumption of the IAT is that pre-existing attitudes interfere with the assignment: if someone already has a negative attitude toward a certain concept of interest, it will be easier to associate that concept with another negative concept instead of with a positive concept.

For the main experiment in Chapter 2, two groups of participants with distinct "odor behavior" were invited and subjected to the odor-IAT. It was tested whether "approaching behavior" was reflected by positive automatic odor associations. This could in turn give an indication of the impact of automatic associations on odor avoidance behavior.

The study reported in *Chapter 3* was conducted to investigate automatic *health associations* with the concept odor. We tested whether there was evidence for an automatic odor-illness association or for an automatic odor-healthiness association. To this end, the positive vs. negative categories of the odor-IAT used in Chapter 2, was replaced by a healthy vs. unhealthy dimension.

Objective 2: Top –down influence of cognitions on perception

The research presented in the second part of this thesis focused on the determination of the nature and magnitude of the effects of cognitions on odor perception. To test the hypothesis that top-down effects affect basic stimulus encoding phases (i.e. intensity encoding), rather than, or in addition to, more interpretational stages of information processing (i.e. interpretation of salience), the effects of cognitive manipulations on temporal processing of olfactory information were tested, based on the

reasoning that early "perceptual" effects of cognitive manipulation should show up earlier rather than later during olfactory information processing. To this end we employed olfactory Event-Related Potentials (OERPs), which technique is the gold standard for the investigation of temporal processing of information. In addition to assessment of temporal processing of the odor stimulus, we studied the influence of cognitions on sniffing behavior. The choice for this endpoint was based to the fact that it has been compared to eye-movements, and thus would provide us with a measure of olfactory sampling behavior or olfactory attention. Top-down effects related to biasing information about the adversity of an odor on smelling of the odor would be reflected in differences in attention to, and thus sniffing of, the odor stimulus.

Chapter 4 presents a study in which we investigated to what extent the sensory response in reaction to an odor was modulated by cognitive information using the OERP approach. Cognition was manipulated using instructional learning, i.e. providing the participant with information about how the odor should be interpreted. It was investigated whether expecting negative health consequences while smelling an odor affected the later, more interpretational phases of olfactory information processing (the P2 peak in the ERP), or already the early, basic perceptual phases of information processing (the N1 peak). The early N1 peak of the ERP reflects stimulus characteristics like intensity and quality, whereas the late positivity (here referred to as the "P2 peak") is associated with more cognitive aspects of perception, like stimulus salience or novelty (Pause & Krauel, 2000; Nordin et al., 2005; Lundsröm, Seven, Olsson, Schaal, & Hummel, 2006). Changes in peak amplitudes are associated with processing intensity (a higher peak amplitude indicates more activated or synchronized neurons), changes in latencies with processing speed (shortened latencies relate to faster processing; Hummel & Kobal, 2002). If cognitions about what should be expected when smelling an odor affect perception of basic stimulus characteristics of that odor, this should be reflected by effects on the early N1 peak, and not only by effects on the later P2 peak.

Chapter 5 presents two OERP studies in which the influence of cognitions about health effects from odor exposure on the perception on those odors was investigated. Now expectancies regarding health effects were induced by means of classical conditioning, whereby the odor signaled approaching harm: An unpleasant and a pleasant odor (in two separate experiments) were conditioned to sensory irritation induced by the presentation of CO_2 in the nose. Two odors with contrasting valence were employed to test whether there were effects of *belongingness* on odor perception. Belongingness refers to the phenomenon that classical conditioning seems to be more effective if an CS is used that is congruent in valence to the US than when it the CS is incongruent in valence. Consequently, individuals would be less likely to associate the pleasant CS odor with the unpleasant US irritant. We tested whether effects of belongingness were reflected in the OERP signal associated with the perception of the CS odor. This part of the study was largely explorative, as it was not entirely evident how such differences would reflect in the OERP signal.

In *Chapter 6*, a study is described in which we examined whether expectations about health effects attributed to a particular odor exposure affect olfactory sampling or sniffing of that odor. Sniffing can be considered the olfactory equivalent of eye movements, and can be used to monitor

attention shifting for olfactory information. Three groups of participants had to smell and identify four different odors, including a "target", by matching them to previously provided odor descriptions. All odors and descriptions were the same for each group, except for the description of the target odor. In the negative bias group, the target was described as a chemical rest product, in the positive bias group as an aromatherapy scent, and in the neutral group as a standard odor for olfactory research. It was anticipated that individuals who expected an odor to be aversive to their health would sniff less vigorously in order to reduce exposure to the presumed harmful substance.

Chapter 7 is a General discussion in which I summarize and combine the main findings presented in the empirical chapters 2 to 6. Subsequently, new hypotheses for future research are presented.

References

Bar-Heim, Y., Lamy, D., Pergamin, L., Bakermans-Kranenburg, M., & IJzendoorn, M. H. (2007). Threat-related attentional bias in anxious and nonanxious individuals: A meta-analytic study. *Psychological Bulletin*, 133, 1-24.

Baum, A. (1990). Stress, intrusive imagery, and chronic distress. *Health Psychology*, 9, 653-675.

Bell, I. R., Rossi, J, Gilbert, M. E., Kobal, G., Morrow, L. A., Newlin, D. B., Sorg, B. A., & Wood, R. W. (1997). Testing the neural sensitization and kindling hypothesis for illness from low levels of environmental chemicals. *Environmental Health Perspectives*, 105 (suppl. 2), 457-466.

Brown, R. J. (2004). Psychological mechanisms of medically unexplained symptoms: An integrative conceptual model. *Psychological Bulletin*, 130, 793-812.

Centraal Bureau voor de Statistiek (2008). De Nederlandse samenleving 2008. Den Haag/Heerlen: Centraal Bureau voor de Statistiek.

Dalton, P. (1999). Cognitive influences on health symptoms from acute chemical exposure. *Health Psychology*, 18, 1-12.

Dalton, P. (2002). Odor, irritation, and perception of health risk. *International Archives of Occupational and Environmental Health*, 75, 283-290.

Dalton, P. (2003). Upper airway irritation, odor perception and health risk due to airborne chemicals. *Toxicology Letters*, 140-141, 239-248.

Dalton, P., & Hummel, T. (2000). Chemosensory function and response in idiopathic environmental intolerance. *Occupational Medicine*, 15, 539-556.

Dalton, P., Wysocki, C. J., Brody, M. J., & Lawley, H. J. (1997). The influence of cognitive bias on the perceived odor, irritation and health symptoms from chemical exposure. *International Archives of Occupational and Environmental Health*, 69, 407-417.

Das-Munshi, J., Rubin, G. J., & Wessely, S. (2006). Multiple chemical sensitivities: A systematic review of provocation studies. *The Journal of Allergy and Clinical Immunology*, 18, 1257 – 1264.

De Araujo, I. E., Rolls, E. T., Velazco, M. I., Margot, C., & Cayeux, I. (2005). Cognitive modulation of olfactory processing. *Neuron*, 46, 671-679.

Engen, T. (1987). Remembering Odors and their Names. *American Scientist*, 75, 497-503.

Fraser, J. A. & Day, J. C. (1972). Receptor reaction to odor and stress: a paradigm and methodological exploration. *Athmospheric Environment*, 10, 151-157.

Gezondheidsraad (1999). Meervoudig Chemisch Overgevoeligheid. Den Haag: Gezondheidsraad. Publicatie nr. 1999/01.

Gottfried, J. A., O'Doherty, J., & Dolan, R. J. (2002). Appetitive and aversive olfactory learning in humans studied using event-related functional magnetic resonance imaging. *Journal of Neuroscience*, 22, 10829-10837.

Greenwald, A. G., McGhee, D. E., & Schwartz, J. L. K. (1998). Measuring individual differences in implicit cognition: The implicit association test. *Journal of Personality and Social Psychology*, 74, 1464-1480.

Herz, R. S., & Von Clef, J.. (2001). The influence of verbal labelling on the perception of odors: evidence for olfactory illusions? *Perception*, 30, 381 – 391.

Hummel, T., Kobal, G., 2002. Olfactory event related potentials. In: Simon, S., Nicolelis, M. (Eds.), *Methods in Chemosensory Research*. Boca Raton: CRC press.

Johansson, A., Millqvist, E., Nordin, S., & Bende, M. (2006). Relationship between self-reported odor intolerance and sensitivity to inhaled capsaicin. *Chest*, 129, 1623-1628.

Köster, E. P. (2002). The specific characteristics of the sense of smell. In: Rouby, C., Schaal, B., Dubois, D., Gervais, R., Holley, A. (Eds), *Olfaction, taste, and cognition* (pp 27-43). Cambridge: University Press.

Labarge, A. S., & McCaffrey, R. J. (2000). Multiple Chemical Sensitivity: A review of the theoretical and research literature. *Neuropsychology Review*, 10, 183-211.

Li, W., Howard, J. D., Parrish, T. B., & Gottfried, J. A. (2008). Aversive learning enhances perceptual and cortical discrimination of indiscriminable odor cues. *Science*, 319, 1842-1845.

Lundsröm, J. N., Seven, S., Olsson, M. J., Schaal, B., & Hummel, T. (2006). Olfactory Event-Related Potentials reflect individual differences in odor valence perception. *Chemical Senses*, 31, 705-711.

Mathews, A., & Mackintosh, B. (1998). A cognitive model of selective processing in anxiety. *Cognitive Therapy and Research*, 22, 539-560.

Nitschke, J. B., Dixon, G. E., Sarinopoulos, I., Short, S. J., Cohen, J. D., Smith, E. E., Kosslyn, S. M., Rose, R. M., & Davidson, R. J. (2006). Altering expectancy dampens neural response to aversive taste in primary taste cortex. *Nature Neuroscience*, 9, 435-442.

Nordin, S., Martinkauppi, M., Olofsson, J., Hummel, T., Millqvist, E., & Bende, M. (2005). Chemosensory perception and event-related potentials in self-reported chemical hypersensitivity. *International Journal of Psychophysiology*, 55, 243-255.

Pause, B. M., & Krauel, K. (2000). Chemosensory event-related potentials (CSERP) as a key to the psychology of odors. *International Journal of Psychophysiology*, 36, 105 – 122.

Schiffman, S. S., Walker, J. M., Dalton, P., Lorig, T. S., Raymer, J. H., Shusterman, D., & Williams, C. M. (2000). Potential health effects of odor from animal operations, wastewater treatment, and recycling of byproducts. *Journal of Agromedicine*, 7, 7-81.

Shusterman, D. (2001). Odor-associated health complaints: competing explanatory models. *Chemical Senses*, 26, 339-343.

Shusterman, D., Lipscomb, J., Neutra, R., & Satin, K. (1991). Symptom Prevalence and Odor-Worry Interaction near Hazardous Waste Sites. *Environmental Health Perspectives*, 94, 25-30.

Smeets, M.A.M. (in press). Air Quality. In: Goldstein, B (Ed)., *Encyclopedia of Perception*. Sage.

Smeets, M. A. M., Bulsing, P. J., Van Rooden, S., Steinmann, R., de Ru, J. A., Ogink, N. W. M., Van Thriel, C., & Dalton, P. H. (2007). Odor and Irritation Thresholds for Ammonia: A Comparison between Static and Dynamic Olfactometry. *Chemical Senses*, 32, 11-20.

Smeets, M. A. M., & Dalton, P. H. (2005). Evaluating the human response to chemicals: Odor, irritation and non-sensory factors. *Environmental Toxicology and Pharmacology*, 19, 581-588.

Spurgeon, A. (2002). Models of unexplained symptoms associated with occupational and environmental exposures. *Environmental Health Perspectives*, 110, Suppl 4, 601-605.

Taylor, S.E. (2003). *Health Psychology* (5th ed.). New York: McGraw-Hill.

Van den Bergh, O., Kempynck, P. J., Van de Woestijne, K. P., Baeyens, F., & Eelen, P. (1995). Respiratory learning and somatic complaints: A conditioning approach using CO_2-enriched air inhalation. *Behaviour Research and Therapy*, 33, 517-527.

Van den Bergh, O., Stegen, K., & Van de Woestijne, K. P. (1997). Learning to have psychosoamtic complaints: Conditioning of respiratory behavior and complaints in psychosomatic patients. *Psychosomatic Medicine*, 59, 13-23.

Van den Bergh, O., Stegen, K., & Van de Woestijne, K. P. (1998). Memory effects of symptom reporting in a respiratory

learning paradigm. *Health Psychology*, 17, 241-248.

Van Kamp, I. (1990). Coping with noise and its health consquences. Proefschrift. STYX: Groningen.

Wilson, D. A., & Stevenson, R. J. 2006. *Learning to Smell*. Baltimore: The John Hopkins University Press.

Chapter 2

Positive implicit attitudes toward odor words

This chapter is based on:

Bulsing, P.J., Smeets, M.A.M., & van den Hout, M.A. (2007). Positive Implicit Attitudes toward Odor Words. *Chemical Senses*, 32, 525-534.

Abstract

Associations between certain odors and for instance health effects may lead to positive or negative attitudes toward these odors. However, in experiments we conducted using the Implicit Association Test (IAT) we encountered attitudes even to odor "words". The IAT is based on the principle that reaction times measuring the association between words from a target dimension (in this case, odor vs. a neutral reference category) and an attribute dimension (i.e., positive or negative words) reflect the attitude to the target, where attitude-congruent associations between target and attribute are reflected by shorter reaction times. In a first experiment, we found distinctly positive attitudes to the concept odor in a student sample, which was replicated in a second experiment. In the main experiment, participants in the Aromatherapy group, who prefer using scented consumer products for relaxation purposes, showed a significantly more positive attitude toward odor words in the IAT than a control group, who did not have such a preference. The fact that results from the implicit test were not always associated with explicitly stated attitudes toward the odor words attests to the fact that the IAT measures the attitude of interest in a different way. As such, the IAT has added value in circumstances where explicit tests can be biased.

Introduction

Perceptions of, and reactions to, odors are significantly affected by beliefs about the possible health consequences of environmental exposure to odorous compounds. In an experimental setting Dalton (1999) demonstrated that the induction of beliefs about the harmful consequences of exposure to a certain odorant led to an increase in perceived intensity and irritancy of that particular odorant. In addition, the frequency and intensity of symptom perceptions were also increased. Dalton concluded that people's reactions to ambient odors are mediated by cognitive processes.

These findings correspond to real-world situations. For instance, people who are more worried about exposure effects because they believe that environmental odors have a negative effect on health report significantly more health effects compared with others who do not adhere to that belief (Schiffman, 1998). One of the supposed mechanisms to account for this is that the belief that certain odors are hazardous for one's health may trigger feelings of anxiety or stress, which results in closer monitoring of internal signals that may indicate potentially harmful effects (Williams & Lees-Haley, 1993; Shusterman, 2001).

Likewise, beliefs about alleged healthful effects of odors on health can influence people's perceptions in a positive fashion. Many people buy scented products for relaxation or healing purposes, causing a boost in the sales of aromatherapeutic products. Consumers apparently subscribe to the premise of natural essences having holistic, medicinal effects that contribute, if not just to psychological wellbeing, to enhanced physical health. This is in line with another part of Dalton's (1999) study in which it was demonstrated that beliefs about the "healing" consequences of exposure to a certain odorant resulted in lower levels of symptom reports. Thus, expectations about the effects of odors on health can bias perceptions of odors in either a negative or also a positive direction.

There is benefit in a quick categorization of odors as either healthful or harmful. Without this top-down influence on information processing (processing that is initiated by knowledge, expectation, or belief; Kosslyn & Rosenberg, 2001) every odor would be evaluated as a novel stimulus. Rapid categorization of odors probably reflects previously learned associations. In newborns the olfactory system seems to be a "tabula rasa"; they show equal responses to, according to adults, pleasant and unpleasant stimuli (Engen, 1988). Hedonic categorization starts to develop once the child learns that certain odors are associated with pleasant or safe contexts and other odors with unpleasant or dangerous contexts. For instance, certain odors that are perceived during pleasant moments (e.g. the body odor of the mother while feeding the child) will consequently acquire a safe connotation.

Epple and Herz (1999) and Herz et al. (2004) demonstrated in an experimental setting that previously learned odor associations can affect subsequent behavior. They exposed participants to an odor while inducing a frustrating mood. The same odor negatively influenced performance (less task persistence) on a cognitive task during another part of the experiment, indicating that participants had associated the odor with the prior experience.

In sum, beliefs about health effects of odors can be either negative (odors might be harmful or dangerous) or positive (odors can be healthful or safe), based on previously learned associations between certain odors and either negative or positive contexts. In turn these odor beliefs can influence behavior later on. This positive versus negative categorization of, in this case, odors is akin to the definition of "attitudes", which are described as "evaluations of virtually any aspect of the social world" (Eagle & Chaiken, 1993, in Baron et al., 1998) or "the association between a concept and an evaluation" (Fazio et al., 1982). It can be argued that as people evaluate odors that are part of their social world as either positive or negative, they develop positive or negative "odor attitudes".

Odor attitudes can be assessed using self-report questionnaires (e.g. the Illness Perception Questionnaire; Moss-Morris, et al., 2002, or the Chemical Sensitivity Scale for Sensory Hyperreactivity; Nordin et al., 2004). However, self-report questionnaires carry some limitations. One is their susceptibility to effects of social desirability. In terms of odor perception, participants may feel embarrassed to report using aromatherapy products, or they may feel uncomfortable revealing their concerns about environmental odor exposures. Furthermore, people may have never thought about the topic under investigation, or are simply not consciously aware of their attitudes (Fazio & Towles-Schwen, 1999). In general, people do not have a clear notion about how their attitudes influence their behavior. For instance, if someone is not aware of associating certain odors with health risks, a questionnaire will not be able to uncover this negative attitude and will consequently not be predictive of behavior.

To test attitudes in an implicit way, tests like the Implicit Association Test (IAT; Greenwald et al., 1998) have been developed. The term "implicit test" in this context refers to the fact that participants (a) are not necessarily aware of the fact that the attitude is being measured (b) do not need conscious access to the attitude, and (c) have no control over the measurement outcome (De Houwer, 2005).

During administration of the IAT words appear one by one on a computer screen. Participants are requested to categorize these words as quickly as possible into categories of interest, by pressing the corresponding keys on a computer keyboard. An example of a typical IAT is presented in Table 1. During a first block, participants learn to differentiate as quickly as possible between two categories of a target dimension (e.g. male versus female names; when a name belonging to the female category appears on the computer screen, participants have to press key A; when a male name appears, they have to press key B). During the next block, participants are trained to differentiate between two other word categories of an *attribute* dimension (e.g. positive and negative words; when a word belonging to the positive category is presented, they have to press key A; when a negative word appears, they have to press key B). Then, during a next block, words from both the target and the attribute dimension are randomly presented. One category of the target dimension and one category of the attribute dimension share the same response key during this stage (e.g. response key A for positive words and female names and key B for negative words and male names). During the final block, response keys for the target dimension are switched, while the

response keys for the attribute dimension remain the same (e.g. response key A for positive words and male names and key B for negative words and female names). Intrinsic association strengths between the target concepts and the attributions will influence performance speed and accuracy during the two combined blocks. Switching the required response type from attitude-incongruent to attitude-congruent will have less of an interfering effect than switching from congruent to incongruent. In the abovementioned example, reaction times and error rates will decrease during the final block if someone has a (implicit) negative attitude towards females (first positive words and female names share the same key; then negative words and female names share the same key). In case of a negative attitude towards males, the principle works the other way around; reaction times and error rates will increase during the final block, because the required response changes from attitude incongruent to attitude congruent.

Table 1
An example of a typical Implicit Association Test design

Block	**Key A**	**Key B**
1	Female name	Male name
2	Positive word	Negative word
3	Female name or Positive word	Male name or Negative word
4	Male name	Female name
5	Male name or Positive word	Female name or Positive word

The IAT is a promising method to indirectly measure strengths of associations in a variety of research fields. De Jong et al. (2001), for example, measured implicit dysfunctional beliefs related to social anxiety. Associations were measured between neutral and social situation words ("sitting room" versus "presentation") and positive and negative outcomes ("succeed" versus "rejection"). Compared to low anxious participants, high anxious participants showed the expected decrease in task performance when required responses to the stimuli switched from belief-congruent to belief-incongruent, that is, when the switch was made from social situation words and negative outcome words sharing the same key to social situation words and positive outcome words sharing the same key. Others have used the IAT to measure implicit attitudes towards nature (Schultz et al., 2004), alcohol (Wiers et al., 2002), smoking (Huijding et al., 2005), and high-fat foods (Roefs & Janssen, 2002).

In conclusion, since the influences of odor attitudes on perception and on behavior may be implicit, and because of methodological limitations of explicit questionnaires, it is important that implicit methods be developed in this area. Here, an odor version of the IAT is introduced.

The present study is part of a larger project which aims to uncover attitudes towards odors and health in an implicit manner, and how these attitudes influence perception of, and reactions to, environmental odors. We started out with an IAT that, simply, measured positive and negative associations with the concept Odor, to explore whether people display distinct attitudes (either

positive or negative) towards that concept by itself, not yet taking into account the relation with the concept of Health. We tested this Odor-IAT within a sub-sample suspected to exhibit distinctly positive odor attitudes: Participants who preferred using scented consumer products as a means of relaxation. This group was compared with participants who did not have such a preference. It was hypothesized that participants who use scented products have less difficulty with associating the concept Odor with positive words, compared to the non-product-users, indicating an (implicit) positive attitude towards the concept Odor in the product-users group.

However, the results of the construction phase of the Odor-IAT turned out to be noteworthy as well. When the test was conducted in a general sample of participants in which no distinct attitudes were necessarily expected the results unexpectedly demonstrated definite positive attitudes toward the concept Odor. This effect was replicated in a second experiment. Since these results were unexpected and robust, it was decided to also briefly report these two first experiments. The main experiment is subsequently reported as Experiment 3.

EXPERIMENTS 1 AND 2

Method

Participants

For Experiment 1 sixty Psychology students from Utrecht University (52 female and 8 male) were tested. Mean age was 21.9 years (*SD* = 2.4). Sixty-seven students (57 female and 10 male) were tested for Experiment 2. Mean age in this group was 21.2 years (*SD* = 2.5). The sample size for the second experiment was determined by a power analysis based on a medium effect size found in Experiment 1. For an ANOVA analysis with reaction time as dependent variable a sample of 66 participants would suffice to achieve 80% power with two-tailed testing at an alpha level of .05 (Cohen, 1988). Participants received either course credit or financial remuneration for their participation.

Stimulus words

The target dimension of the Odor-IAT consisted of two word categories: the House category (porch, basement, room, hallway, attic), and the Odor category (whiff, aroma, smell, nose, scent). The attribution dimension also consisted of two word categories: the Good category, consisting of positive words (pleasure, love, success, peace, talent), and the Bad category, consisting of negative words (fail, waste, naughty, war, abuse). Following De Jong et al. (2001), the House category was chosen because it may be assumed that this category is a neutral one and thus that neither the concept House nor the exemplars of this concept are intrinsically associated with the concepts Good or Bad. We checked all words for their frequency and length (in Dutch) in order to have two comparable word categories on

both dimensions. In addition, an independent student sample ($N = 44$) was asked to rate the valence of the five House exemplar words and the five Odor exemplar words as positive, neutral or negative. The same was done for the Good and Bad exemplar words. Negative ratings were recoded to -1, neutral ratings to 0 and positive ratings to 1. Sum scores of the scored valence of the 5 exemplars per concept (with possible scores between -5 and 5) were compared. The House exemplar words and the Odor exemplar words were rated as equally neutral, $t(43) = 1.31$, $p = .20$ ($M_{odor} = .98$, $SD = 1.65$ and $M_{house} = .66$, $SD = 1.18$). The Good exemplar words were rated as positive ($M_{good} = 4.77$, $SD = .60$) and the Bad exemplar words were rated as negative ($M_{bad} = -4.25$, $SD = 1.10$).

Procedure

Following Greenwald et al. (1998) the Odor-IAT consisted of five blocks, and two practice blocks. Figure 1 demonstrates the counterbalanced design of the test. During Block 1 participants were trained on how to differentiate between the Odor words and the House words of the target dimension. There were five House words and five Odor words which were presented twice, resulting in 20 trials. Subsequently, participants had to use the same response keys for classification of the five Good words and the five Bad words, which were presented twice, resulting in 20 trials. During Practice Block 3a the two former tasks were combined. Half of the participants started the combined task with pressing the same key for Odor words and Good words (Order 1). The other half started this block with pressing the same key for Odor words and Bad words (Order 2; see also Figure 1). Because Block 3a was a practice block, words from all concepts were presented once (20 trials), and reaction times and error rates were not registered. Block 3b was the same as Block 3a (and depicted as one block in Figure 1), except that now registration took place and words from all concepts were presented twice (40 trials). During Block 4, the target categories changed positions on the computer screen, resulting in a required switched response for the target words. Again the five Odor words and the five House words were presented twice (20 trials). No exemplar words from the Good and Bad categories were presented during this block. Practice Block 5a was a new combined task, due to the target dimension switch. Words from all concepts were presented once (20 trials). Block 5b was the same as Block 5a (again depicted as one block in Figure 1), except that registration took place and all words were presented twice (40 trials).

Participants were instructed to categorize as quickly and accurately as possible the words into the four categories (Odor, House, Good, Bad) by pressing the corresponding response keys on a computer keyboard. The words which had to be classified appeared one by one in the centre of the screen. During each IAT Block the category concepts remained visible in the left and right upper corners of the screen (see Figure 1). Order 1 and Order 2 had both two versions where the target-attribute pairs were allocated to different sides of the screen. Participants had to respond by pressing the "q" (index finger left hand) for words that belonged to a category in the left corner and the "p" (index finger right hand) for words that belonged to a category in the right corner. In case of a wrong answer, a red cross appeared. Participants had to correct the mistake by quickly pressing the alternate key. As soon as the correct key was pressed, the next word appeared.

Participants in Experiment 2 were asked to score the explicit valence of the Odor, House, Good and Bad exemplars after completing the test, such that the implicit test outcome could be compared to explicit evaluations.

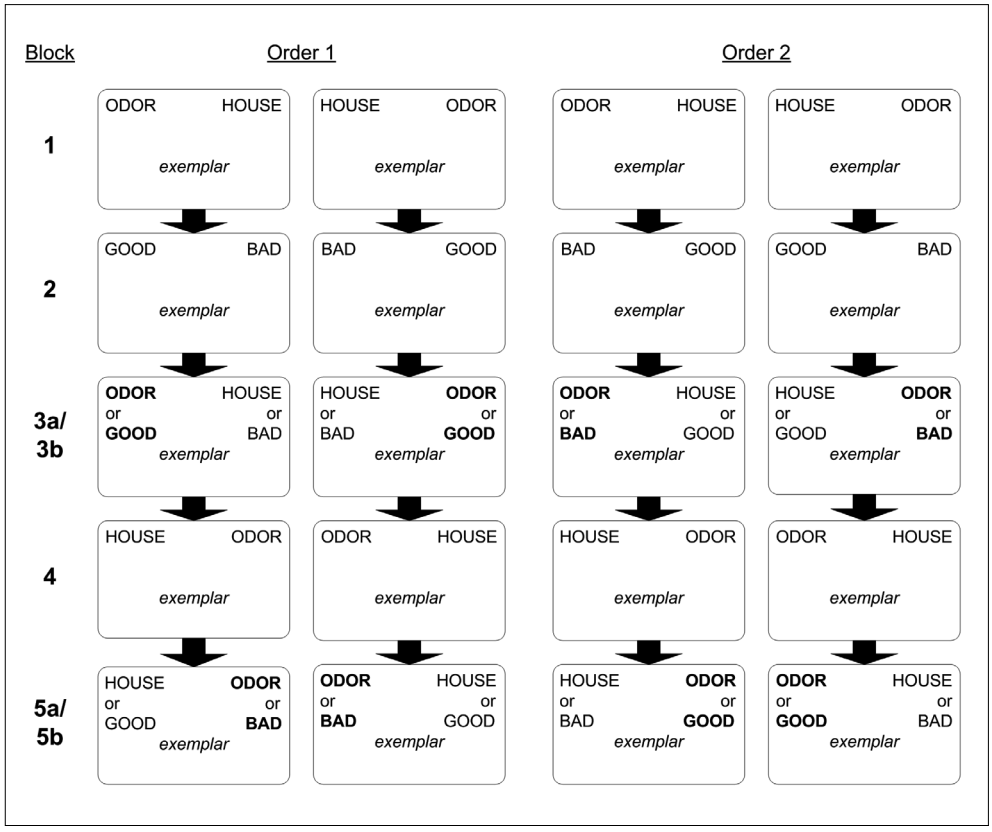

Figure 1. Counter-balanced design of the Odor-IAT: Participants in Order 1 start the combined task with the Odor and Good Block (in either the left or the right upper corner of the computer screen) and then complete the Odor and Bad Block (again in either the left or the right upper corner of the screen). Participants in Order 2 start the combined task with the Odor and Bad Block and then complete the Odor and Good Block. Word exemplars appear in the centre of the screen. If a word belongs to a concept at the left side, participants have to press a left key, if a word belongs to a concept at the right side, participants have to press a right key.

Results

Data reduction

Following Greenwald et al. (1998) reaction times below 300 ms were recoded to 300 ms (3, 0.02% [Experiment 2]), and reaction times above 3000 ms were recoded to 3000 ms (45, 0.42%

[Experiment 1]; 35, 0.29% [Experiment 2]). Reaction times for trials answered incorrectly were excluded for further reaction time analyses (677, 6.27% [Experiment 1]; 751, 6.23% [Experiment 2]). An alpha level of .05 was used for all statistical tests.

Reaction times

For the two critical combined Blocks (3b and 5b) of the Odor-IAT, mean reaction times are shown separately for Order 1 and Order 2 in Table 2 and Figure 2 (solid lines [Experiment 1], and dashed lines [Experiment 2]). A 2 (Association: Odor and Good versus Odor and Bad) X 2 (Order: Order 1 versus Order 2) ANOVA with reaction time as dependent variable was conducted for both experiments. This revealed a main effect of Association, $F(1,58) = 7.36$, $p < .01$ in Experiment 1, indicating that reaction times were shorter during Odor and Good Blocks. Additionally, a significant Association X Order interaction effect was found in both experiments, ($F(1,58) = 14.89$, $p < .01$ [Experiment 1], and $F(1,65) = 12.42$, $p < .01$ [Experiment 2]). Post-hoc testing showed that participants had significantly more difficulty with the Odor and Bad Block when they had first completed the Odor and Good Block, ($t(29) = -5.08$, $p < .01$, [Order 1; Experiment 1], and $t(32) = -3.68$, $p < .01$ [Order 1; Experiment 2]). Participants who had first completed the Odor and Bad Block and then the Odor and Good Block did not show significantly more difficulty with the new combined task, ($t(29) = -.75$, $p = .46$ [Order 2; Experiment 1], and $t(33) = 1.72$, $p = .10$ [Order 2; Experiment 2]). This implies that it was easier to unlearn the Odor and Bad association, than to unlearn the Odor and Good association (see Figure 2).

Table 2

Mean reaction times in milliseconds and error rates (SDs between parentheses) for Order 1 and Order 2 during phases of the test where the concept Odor had to be associated with the concepts Good and Bad, shown separately for Experiment 1 and Experiment 2

Order	Blocks	Reaction times	Error rates
Experiment 1 (N = 60)			
Order 1[a] (*n* = 30)	Odor and Good	730.59 (105.47)	.05 (.05)
	Odor and Bad	875.81 (178.52)	.07 (.06)
Order 2[b] (*n* = 30)	Odor and Bad	783.73 (171.77)	.09 (.06)
	Odor and Good	809.03 (160.98)	.07 (.04)
Experiment 2 (N = 67)			
Order 1[a] (*n* = 33)	Odor and Good	723.74 (104.48)	.05 (.05)
	Odor and Bad	811.36 (146.49)	.08 (.07)
Order 2[b] (*n* = 34)	Odor and Bad	756.46 (138.60)	.09 (.07)
	Odor and Good	813.54 (171.26)	.07 (.05)

[a] Participants in Order 1 first had to complete the Odor and Good Block and then the Odor and Bad Block.

[b] Participants in Order 2 first had to complete the Odor and Bad Block and then the Odor and Good Block.

Figure 2. Mean reaction times in milliseconds for Order 1 and Order 2 during the phases of Experiment 1 and Experiment 2 where the concept Odor had to be associated with the concepts Good or Bad

Error rates

A 2 (Association: Odor and Good versus Odor and Bad) X 2 (Order: Order 1 versus Order 2) ANOVA with error rate as dependent variable was conducted for both experiments. This revealed a main effect of Association, (F(1,58) = 9.08, p < .01 [Experiment 1], and F(1,65) = 5.16, p = .03 [Experiment 2]), showing that fewer errors were made during Odor and Good Blocks, compared to Odor and Bad Blocks (see Table 2).

Explicit ratings Experiment 2

Scores of explicit ratings differed for the House and Odor exemplar words, t(66) = 3.44, p < .01; Odor exemplar words were rated significantly more positive compared to House exemplar words (M_{odor} = 1.67, SD = 1.84 and M_{house} = .90, SD = 1.20), indicating an explicit positive attitude toward the Odor words. As expected, the Good exemplar words were rated as positive compared to the neutral words (M_{good} = 4.99, SD = .12); Bad exemplar words were rated as negative compared to the neutral words (M_{bad} = -4.66, SD = .62).

Discussion

Participants showed faster reaction times during blocks where the concept Odor had to be associated with the concept Good compared to blocks where the concepts Odor and Bad had to be associated. Additionally, fewer errors were made during Odor and Good Blocks. Unexpectedly, the Odor-

IAT demonstrated a distinctly positive attitude towards the concept Odor in two independent participant samples, reflecting a robust effect. Interestingly, these first results suggest that people have affective attitudinal tendencies to a wider range of concepts commonly regarded as neutral.

Prior to conducting Experiment 1, and as stated earlier, an independent sample had rated the target exemplar words from the Odor and House categories as equally neutral. However, when assessed in the same sample (Experiment 2), both explicit and implicit attitudes to odor words were now found to be positive. Explicit evaluation of odor words might have been influenced by implicit odor attitudes activated during the Odor-IAT.

In the main experiment, Experiment 3, we investigated whether the Odor-IAT is capable of distinguishing between individuals, whose odor attitudes may be expected to be different. We tested this cross-sectionally by comparing IAT results of two samples of participants selected on self-reported preference of use of scented consumer products.

EXPERIMENT 3

To test whether the Odor-IAT was able to distinguish individuals who prefer using scented consumer products as a means of relaxation from individuals who do not have such a preference, participants were selected based on their score on a questionnaire developed for the purpose of this experiment. Participants were told that the questionnaire aimed to examine students' relaxation habits, in order to minimize the chance that they were aware of our specific interest in utilization of scented consumer products. The short questionnaire consisted of two parts. The first part contained six irrelevant items (e.g. "Do you go to the cinema from time to time to clear your mind?", or "Do you sometimes drink alcohol to become more relaxed?"). Two odor items were interspersed with these 6 items, to measure whether participants used fragranced products or odorized candles for relaxation purposes: "Do you sometimes use odorized products like scented shower gel to relax yourself?", and "Do you light odorized candles now and then to relax yourself or to feel healthier?" Participants had to answer these questions with "yes" or "no". A yes answer to the odor items was recoded to 2; a no answer to 0. The second part of the questionnaire is demonstrated in Table 3. Participants were instructed to rank the alternatives according to preference from 1 to 4. Numbers in front of the odor-related answers (see Table 3) were recoded (the first choice was recoded to 4, the second choice to 3, the third choice to 2, and the fourth choice to 1). In this manner, participants could have scores varying from 1 to 20 (0 – 4 from the first part of the questionnaire; 1 – 16 from the second part).

Table 3

The second part of the selection questionnaire for Experiment 3

What do you consider as a "special treatment"?	A breakfast in bed A massage with essential oils * Someone who takes care of my shopping An invitation to my favourite restaurant
What will boost your energy after an exhausting day?	My favourite music A nice fragrance * Cold wind A refreshing walk
You have the entire Saturday for yourself. What are your plans?	To invite friends to come to your place To read an exciting book To go shopping To take a warm and scented bath *
What store do you prefer to go to?	A cloth store A big department store A music store A perfume store *

Note. Participants were asked to rank the alternatives according to preference from 1 to 4, by placing corresponding numbers in front of the answers (odor-related items are here indicated by a *).

285 Psychology students from Utrecht University were asked to complete the questionnaire. Mean score was 9.73 (*SD* = 3.71). Individuals with extreme scores (approximately 1.5 standard deviation above the mean and 1.5 standard deviation below the mean) were approached to participate. Participants with high scores (≥ 14), reflecting frequent use of or preference for scented products, were invited and included in the what we will refer to as the Aromatherapy group (*N* = 32, *M* = 15.28, *SD* = 1.30). Participants with low scores (≤ 5) served as controls (*N* = 31, *M* = 4.03, *SD* = 1.45).

Method

Stimulus materials and procedures were the same as in Experiment 1 and 2. Explicit attitudes were again collected after the experiment. Halfway during the experiment we realized that attitudes towards the concept as a whole (so towards the words "odor" and "house"), would be equally relevant as attitudes towards the individual exemplar words belonging to those categories (de Houwer, 2002). Thus 52 percent of the participants scored both exemplars as well as concepts.

Participants

There were 29 participants in the Aromatherapy group (27 female and 2 male), and 26 (18 female and 8 male) in the Control group. Mean age of the Aromatherapy group was 21.3 years (*SD* = 5.0),

and of the Control participants 20.4 years (*SD* = 2.8). Participants received either course credits or financial remuneration for their participation. Participants were not informed about the purpose of the test prior to participation.

Results

Data reduction

Reaction times above 3000 ms (25; 0.25%) were recoded to 3000 ms. Reaction times for trials answered incorrectly (588; 5.94%) were excluded for further reaction time analyses.

Reaction times

For the two critical combined Blocks (3b and 5b) of the Odor-IAT, mean reaction times are shown separately for Order 1 and Order 2 and for the Aromatherapy and Control group in Table 4 and Figure 3. A 2 (Association: Odor and Good versus Odor and Bad) X 2 (Order: Order 1 versus Order 2) X 2 (Group: Aromatherapy versus Control) ANOVA with reaction time as dependent variable revealed a main effect of Association, $F(1,51) = 17.99$, $p < .01$, indicating reaction times were lower during Odor and Good Blocks, compared to Odor and Bad Blocks. In addition, a significant Group X Association interaction was found, $F(1,51) = 8.30$, $p < .01$. Post-hoc testing showed that the Control participants did not have more or less difficulty with either the Odor and Good Block or the Odor and Bad Block, $t(25) = -1.15$, $p = .26$. The Aromatherapy group, however, showed significantly shorter reaction times during Odor and Good Blocks, compared to Odor and Bad Blocks, $t(28) = -4.53$, $p < .01$.

Table 4

Mean reaction times in milliseconds and error rates (SDs between parentheses) for Order 1 and Order 2 during phases of Experiment 3 where the concept Odor had to be associated with the concepts Good and Bad, shown separately for the Aromatherapy and the Control group

Order	Blocks	Reaction times	Error rates
Aromatherapy group (*n* = 29)			
Order 1[a] (*n* = 16)	Odor and Good	794.70 (136.21)	.07 (.07)
	Odor and Bad	976.33 (160.26)	.09 (.07)
Order 2[b] (*n* = 13)	Odor and Bad	998.73 (392.67)	.11 (.11)
	Odor and Good	752.63 (103.16)	.05 (.04)
Control group (*n* = 26)			
Order 1[a] (*n* = 13)	Odor and Good	728.86 (153.95)	.04 (.03)
	Odor and Bad	811.82 (129.05)	.07 (.07)
Order 2[b] (*n* = 13)	Odor and Bad	928.71 (241.47)	.09 (.11)
	Odor and Good	929.95 (261.37)	.06 (.06)

[a] Participants in Order 1 first had to complete the Odor and Good Block and then the Odor and Bad Block.

[b] Participants in Order 2 first had to complete the Odor and Bad Block and then the Odor and Good Block.

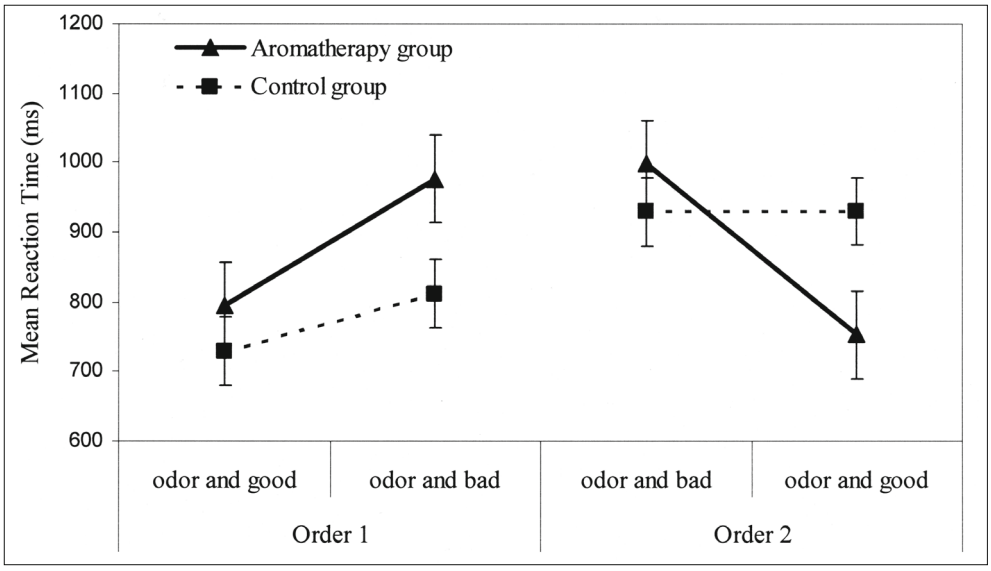

Figure 3. Mean reaction times in milliseconds for Order 1 and Order 2 during phases of Experiment 3 where the concept odor had to be either associated with the concepts Good or Bad, shown separately for the Aromatherapy and Control group

Error rates

A 2 (Association: Odor and Good versus Odor and Bad) X 2 (Order: Order 1 versus Order 2) X 2 (Group: Aromatherapy versus Control) ANOVA with error rate as dependent variable revealed a main effect of Association, $F(1,51) = 13.66$, $p < .01$, showing that fewer errors were made during Odor and Good Blocks, compared to Odor and Bad Blocks (see Table 4).

Explicit ratings

Explicit ratings differed for the House and Odor exemplars, $t(54) = 6.31$, $p < .01$: Odor exemplars were rated significantly more positive compared to House exemplars ($M_{odor} = 2.27$, $SD = 1.59$ and $M_{house} = .29$, $SD = 1.29$), indicating an explicit positive attitude toward the Odor words. However, Aromatherapy participants did not differ from the Control participants in explicit rating of the Odor exemplars, $F(1,53) = .04$, $p = .84$ ($M_{aroma} = 2.32$, $SD = 1.63$ and $M_{control} = 2.23$, $SD = 1.59$), and the House exemplars, $F(1,53) = .07$, $p = .79$ ($M_{aroma} = .24$, $SD = 1.48$ and M_{contro}l $= .33$, $SD = 1.12$).

For the concept words "House" and "Odor" on the other hand, no significant difference in explicit rating was found, $t(27) = .83$, $p = .42$, indicating that the concepts Odor and House did not differ in explicit valence (respectively $M_{odor} = .39$, $SD = .50$ and $M_{house} = .29$, $SD = .46$). Again, no group difference was found between Aromatherapy participants and Control participants on the explicit ratings of the concept Odor, $F(1, 26) = 1.78$, $p = .19$ ($M_{aroma} = .25$, $SD = .45$ and $M_{control} = .50$, $SD = .13$) and of the concept House, $F(1, 26) = .22$, $p = .64$ ($M_{aroma} = .33$, $SD = .14$ and $M_{control} = .25$, $SD = .45$).

As expected, the Good words were rated by both groups as positive compared to the neutral words (M = 4.91, SD = .32); Bad words were rated as negative compared to the neutral words (M = -4.36, SD = .87).

Discussion

Again, participants had significantly less difficulty with the Odor and Good association, compared to the Odor and Bad association. This result replicated an intrinsic positive attitude towards odors already found in Experiment 1 and 2. In this third experiment, this effect was mainly caused by the Aromatherapy participants: they showed significantly shorter reaction times when they had to associate the concept Odor with positive words, then when they had to associate Odor with negative words. For the Controls performance speed during Odor and Good Blocks and Odor and Bad Blocks was not significantly different. The Odor-IAT was able to distinguish between the two participant groups, selected on degree of preference for odorized products as a means of relaxation.

As in Experiment 2, explicit attitudes towards Odor exemplar words were found to be more positive as compared to House exemplar words. However, the between-group distinction in implicit odor attitude was not reflected by a between-group difference in explicit odor attitude. Likewise, even though the explicit attitude towards odor words was positive on average, this was not the case for the concept-word "Odor". These results suggest that the Odor-IAT measures an implicit attitude that is distinctly different from explicit odor attitudes.

General Discussion

Three experiments were conducted to explore attitudes towards the concept Odor in an implicit manner, using an odor version of the IAT. The results of main Experiment 3 can be summarized as follows: while participants who preferred using scented consumer products as a means of relaxation showed a definite positive attitude to the concept Odor, participants who did not have such a preference, showed neither a positive nor a negative attitude towards that concept. Apparently, the distinction between the groups based on self-reported preference for scented products was reflected by a distinction in attitudes to the concept of odor measured implicitly by the Odor-IAT. Additionally, from the experiments conducted in a general sample of students of Psychology, in which no definite attitudes towards the concept of odor were expected, overall results revealed positive attitudes to the concept Odor, which was reflected by shorter reaction times and lower error rates during the Odor and Good Blocks in Experiments 1 and then replicated in Experiment 2.

The Odor-IAT measured odor attitudes in an implicit way: Firstly, because participants were not required to think about odors or state any opinions, but were instructed to press a key upon seeing an odor word. Secondly, during debriefing, most participants indicated not being aware of the purpose of the test. Thirdly, results obtained with the Odor-IAT were not always paralleled by the results obtained with the explicit test. It may thus be concluded that the Odor-IAT may serve as

a useful tool to predict behaviors to odor exposures when those behaviors are believed to be driven priory by unconscious motives. However, before being able to fully appreciate the advantages versus limitations of using implicit measures in the odor realm, the following issues need to be addressed.

For instance, the Control participants in Experiment 3 showed different reactions on the Odor-IAT compared to participants tested in Experiment 1 and 2. The Control group was selected based on their limited use of, or preference for, scented consumer products, while participants in Experiment 1 and 2 were not screened on any particular odor-related behavior. It would appear that within the population tested in all the experiments, subpopulations with a more or less positive attitude can be distinguished, leading to a predominantly positive average attitude. The overall positive attitude found in the first two experiments is probably best explained by the fact that they were conducted using Psychology students as participants, most of whom were female (approximately 82 %). Because the low number of male participants in either experiment did not allow a comparison between the sexes, it was decided to conduct an exploratory meta-analysis on a combination of samples (154 females versus 28 males). The analysis indeed provided support for the explanation that the main finding of positive attitudes towards the Odor concept was carried by the female sub-sample rather than the male sub-sample, as the male sub-sample responded significantly slower during Odor and Good Blocks than the female sub-sample. The hypothesis of sex differences in odor attitudes should however be tested independently using equal samples of both sexes. For now, we conclude that definite positive attitudes to the concept of Odor were assessed using an implicit test in Experiments 1 and 2, and that individual differences in attitudes were associated in a meaningful manner to odor-related preferences using an explicit test in Experiment 3.

Besides investigating the effect of sex on the Odor-IAT, the test should be further validated based on scores of other, well-defined groups, to investigate whether the odor attitudes assessed with the Odor-IAT reveal distinct attitudes that show a meaningful relation to relevant behaviors of these groups. Examples of such populations are individuals with Multiple Chemical Sensitivity or residents who are involuntarily exposed to obnoxious fumes from nearby industry. Logically, the Odor-IAT should show distinct negative attitudes in those populations.

Additionally, it should be further investigated how implicit and explicit methods relate to one another and which of the two methods is most suitable for behavior prediction. By looking at the explicit ratings made by the independent participant sample (but from the same population) prior to Experiment 1 it could be concluded that both the Odor exemplar words and the House exemplar words are equally neutral. The explicit ratings of the participants in Experiment 2, who had just completed the Odor-IAT, revealed a positive evaluation of the Odor exemplar words. Here implicit and explicit ratings both showed positive attitudes towards odors. However, participants had already completed the Odor-IAT, which might have influenced explicit attitudes. Participants in Experiment 3 again evaluated the Odor words as more positive than the House words, but no group difference was found between the Aromatherapy participants and the controls, which showed that the Odor-IAT was capable of assessing individual differences that could not be assessed on the basis of explicit attitudes. In our experiments, the valence of odor attitudes as measured by the explicit test seemed to

depend on whether or not the test was administered together with the Odor-IAT. For future testing, it is advised to administer the explicit test independently from, and well in advance of, the Odor-IAT in the same population.

In other domains, implicit and explicit methods sometimes do and sometimes do not correlate (Nosek, 2005), which raises the question whether, and in what cases, people's conscious and unconscious attitudes are different and which attitude most likely drives behavior. Fazio and Olson (2003) concluded that implicit measures are useful in predicting behavior that is difficult to control or behavior in situations where people do not have the opportunity to control the impact of automatically activated attitudes on behavior. This implicit method seems therefore most suitable for odor behavior prediction. However, before claiming this with certainty, the Odor-IAT should again be compared with explicit self-report measurements and in turn with relevant behavior.

Another issue has to do with the role of a neutral reference category (De Houwer, 2002). In other IAT studies, two complementary concepts are often selected for the target dimension. In the example described in the introduction for instance, male and female names are used as target concepts, where a negative attitude towards male names, could also be interpreted as a positive attitude towards female names. In this example both interpretations are informative, because the conclusion remains the same (e.g. a more positive attitude towards females compared to men is equivalent to a more negative attitude towards males compared to females). In the present study the observed attitudes towards the concept Odor are in fact all relative to attitudes towards the concept House, which latter concept was used in our experiments as the neutral reference category. It was assumed, in advance, that people would not have a negative or positive attitude towards the House concept (see also De Jong et al., 2001).

Therefore, the results have been interpreted as positive attitudes towards odors, not as negative attitudes towards the concept House, although, in theory, this interpretation is also possible. Still, we feel that the results of Experiment 3 strengthen the interpretation of the results in terms of positive odor attitudes, since there is no reason to assume that participant in the Aromatherapy group had a more negative attitude towards the House concept than controls. In general, implicit attitude tests have been conducted with concepts about which people tend to have outspoken attitudes, such as racial (e.g. Smith-McLallen et al., 2006), gender (e.g. Geer & Robertson, 2005) or body weight issues (e.g. Chambliss et al., 2004). In the case of a sensory modality being the concept, such as olfaction in this case, we would not expect outspoken attitudes towards the concept itself, unless it was related to health or tested in special populations. The fact that our results clearly demonstrate distinctly positive attitudes, suggests that people have affective attitudinal tendencies to a wider range of concepts commonly regarded as neutral. This is an interesting topic for future research.

Acknowledgments

We would like to thank Martin Laverman for his technical contribution to this research and Marisol Krosendijk for her assistance in data acquisition. This work was funded by NWO grant 452-03-334 to the second author.

References

Cohen, J. (1992). A Power Primer. *Psychological Bulletin*, 112, 155-159.

Chambliss, H. O., Finley, C. E., & Blair, S. N. (2004). Attitudes toward Obese Individuals among Exercise Science Students. *Medicine and Science in Sports and Exercise*, 36, 468-474.

Dalton, P. (1999). Cognitive influences on health symptoms from acute chemical exposure. *Health Psychology*, 18, 1-12.

De Houwer, J. (2002). The Implicit Association Test as a tool for studying dysfunctional associations in psychopathology: strengths and limitations. *Journal of Behavior Therapy and Experimental Psychiatry*, 33, 115-133.

De Houwer, J. (2005). What are implicit measures and why are we using them? In R. W. Wiers & A. W. Stacy (Eds.), *The handbook of implicit cognition and addiction*. Thousand Oaks, CA: Sage Publishers.

De Jong, P., Pasman, W., Kindt, M., & van den Hout, M. A. (2001). A reaction time paradigm to assess (implicit) complaint-specific dysfunctional beliefs. *Behaviour Research and Therapy*, 39, 101-113.

Eagle, A. H., & Chaiken, S. (1993). The psychology of attitudes. In R. A. Baron, D. Byrne, and B. T. Johnson (Eds.), *Exploring Social Psychology* (pp. 100). Needham Heights, MA: Allyn and Bacon.

Engen, T. (1988). The acquisition of odour hedonics. In S. van Toller, & G.H. Dodd (Eds.), Perfumery – *The psychology and biology of fragrance* (pp.79-90). London: Chapman and Hall Publishers.

Epple, G., & Herz, R. S. (1999). Ambient odors associated to failure influence cognitive performance in children. *Developmental Psychobiology*, 35(2), 103-107.

Fazio, R. H., Chen, J., McDonal, E. C., & Sherman, S. J. (1982). Attitudes accessibility, attitude-behavior consistency, and strength of the object-evaluation association. In Nosek, B. A. (2005). Moderators of the relationship between implicit and explicit evaluation. *Journal of Experimental Psychology*, 134, 565-584.

Fazio, R. H., & Olson, M. A. (2003). Implicit Measures in Social Cognition Research: Their Meaning and Use. *Annual Review of Psychology*, 54, 297-327.

Fazio, R. H., & Towles-Schwen, T. (1999). The MODE model of attitude-behavior processes. In S. Chaiken & Y. Trope (Eds.), *Dual Process Theories in Social Psychology* (pp. 97-116). New York: Guilford.

Geer, J. H., & Robertson, G. G. (2005). Implicit Attitudes in sexuality: Gender differences. *Archives of Sexual Behavior*, 34, 671-677.

Greenwald, A. G., McGhee, D. E., & Schwartz, J. L. K. (1998). Measuring individual differences in implicit cognition: The implicit association test. *Journal of Personality and Social Psychology*, 74, 1464-1480.

Herz, R. S., Schankler, C., & Beland, S. (2004). Olfaction, Emotion and Associative Learning: Effects on Motivated Behavior. *Motivation and Emotion*, 28, 363-383.

Huijding, J., de Jong, P. J., Wiers, R. W., & Verkooijen, K. (2005). Implicit and explicit attitudes toward smoking in a smoking and a nonsmoking setting. *Addictive Behaviors*, 30, 949-961.

Kosslyn, S., & Rosenberg, R. (2001). *Psychology: the Brain, the Person, the World*. Allyn and Bacon, Needham Heights, MA.

Moss-Morris, R., Weinman, J., Petrie, K. J., Horne, R., Cameron, L. D., & Buick, D. (2002). The revised illness perception questionnaire (IPQ-R). *Psychology & Health*, 17, 1-16.

Nordin, S., Millqvist, E., Löwhagen, O., & Bende, M. (2004). A short Chemical Sensitivity Scale for assessment of airway sensory hyperreactivity. *International Archives of Occupational and Environmental Health*, 77, 249-254.

Nosek, B. A. (2005). Moderators of the relationship between implicit and explicit evaluation. *Journal of Experimental Psychology*, 134, 565-584.

Roefs, A., & Janssen, A. (2002). Implicit and explicit attitudes toward high-fat foods in obesity. *Journal of Abnormal Psychology*, 111, 517-521.

Schiffman, S. S. (1998). Livestock odors: implications for human health and well-being. *Journal of Animal Science*, 76, 1343-1355.

Schultz, P.W., Shriver, C., Tabanico, J.J., & Khazian, A.M. (2004). Implicit connections with nature. *Journal of Environmental Psychology*, 24(1), 31-42.

Shusterman, D. (2001). Odor-associated Health Complaints: Competing Explanatory Models. *Chemical Senses*, 26, 339-343.

Smith-McLallen, A., Johnson, B. T., Dovidio, J. F., & Pearson, A. R. (2006). Black and white: The role of color bias in implicit race bias. *Social Cognition*, 24, 46-73.

Wiers R. W., Van Woerden, N., Smulders, F. T. Y., & De Jong, P. J. (2002). Implicit and explicit alcohol-related cognitions in heavy and light drinkers. *Journal of Abnormal Psychology*, 111, 648-658.

Williams, C. W., & Lees-Haley, P. R. (1993). Perceived Toxic Exposure: A Review of Four Cognitive Influences on Perception of Illness. *Journal of Social Behavior and Personality*, 8 (3), 489-506.

Chapter 3

The implicit association between odors and illness

This chapter is based on:

Bulsing, P.J., Smeets, M.A.M., & van den Hout, M.A. (2009). The Implicit Association between Odors and Illness. *Chemical Senses*, 34, 111-119.

Abstract

Some individuals ascribe health symptoms to odor exposures, even when none would be expected based on toxicological dose-effect relationships. In these situations, symptoms are believed to have been mediated by beliefs regarding the potential health effects from odorants, which implies a controlled type of information processing. From an evolutionary perspective, such a form of processing may hardly be the only route. The aim of the present study was to explore the viability of a fast and implicit route, by investigating automatic odor-related associations in the context of health. An Implicit Association Test assessing association strengths between the concept odor and the concepts healthy and sick was conducted. Three experiments (N = 66, N = 64, and N = 64) showed a significantly stronger association between the concepts odor and sick than between odor and healthy. These results did not match explicit associations, and provide evidence for a fast and automatic route of processing that may complement consciously controlled processes. A dual-processing theory of olfactory information is proposed leading to new hypotheses regarding the development and maintenance of odor-induced health symptoms.

Introduction

Odors signal the presence of airborne chemicals, some of which, at certain concentrations, cause adverse health effects. Examples of such direct health effects are irritation of the nasal mucosa, increased nasal secretion, respiratory changes, and central nervous system effects (Schiffman et al., 2000). Alternatively, some odorants are the byproducts of bacterial activity associated with decomposition, or bad hygiene (e.g. sulfides, organic acids and amines). In such instances, contact with the odor *source* should be avoided, but the odorant itself is no direct trigger of health effects and can be considered "only" an exposure marker (Schiffman & Williams, 2005). However, some people report health symptoms not as a consequence of inhaling highly toxic chemicals or ingesting rotten food, but in response to perception of associated, essentially harmless odors. The most extreme variant of odor-related illness is Idiopathic Environmental Intolerance (IEI) or Multiple Chemical Sensitivity (MCS; Ross et al., 1999; Das-Munshi et al., 2007). Individuals suffering from IEI or MCS report symptoms in response to (intense) odors in general. Such odor-induced health symptoms are hard to understand from a toxicological perspective - concentrations do not exceed levels where bodily effects are expected - and in these instances, psychological explanations can be helpful (e.g. Dalton et al., 1997; Devriese et al., 2000; Shusterman, 2001).

Dalton and Hummel (2000) proposed an information-processing model of chemosensory perception to explain individual differences in interpretations of and reactions to odors in the context of health (see also: Smeets & Dalton, 2005). Besides "bottom-up" processing of olfactory information (initiated by the stimulus itself; e.g. concentration, quality), effects of "top-down" processing play a central role in this model, referring to influences of beliefs and expectations on the perception and interpretation of the olfactory stimulus. Knowledge and beliefs and sometimes clear misconceptions regarding potential health effects from exposure to odorous chemicals can be considered "mental models", that facilitate the access to relevant information and application of that information to further processing (Reiser et al., 1985). Is has been repeatedly demonstrated that such top-down processes indeed influence individual perception and reactions to odors (e.g., the influence of various coping styles; Cavalini et al., 1991; personality; Smeets & Dalton, 2005; being environmentally worried; Shusterman, 2001; and psychological stress; Dayal et al., 1994).

Although top-down influences of mental models on odor perception and the production of health effects are no doubt important, some caution as to their precise role is warranted. First of all, the use of the term "mental models" suggests a rich network of connected propositions (Reiser et al., 1985) that is both comprehensive and consistent. However, preliminary data from our laboratory on the content of such mental representations through focus groups and interviews (unpublished data) have revealed that there are substantial individual differences in degree of sophistication of these knowledge structures. In most people, the mental model is not exhaustive – that is to say, it may hold beliefs regarding what symptoms may follow from exposure to odorants, but shows gaps concerning the mechanism by which odorants would provoke these symptoms, or concerning the general workings of the sense of smell. Thus, the notion that smelling an odor activates an advanced mental network of interrelated cognitions concerning olfaction and health

is probably an overstatement of the mental process that takes place in most people. Secondly, the mental model may hold incompatible beliefs, or misconceptions, and is often difficult to access via introspection. As noted earlier by Leventhal et al. (1980), the cognitive structure comprising illness representations may be nonverbal (but rather perceptual), and thus difficult to represent verbally. And finally, the mental model approach suggests extensive information processing of olfactory input. However, this idea does not correspond with our general conception of the sense of smell as the gatekeeper of the senses, whose function it is to quickly decide whether to approach or avoid. The function of olfaction would actually be better served by a capacity-free, unconscious and automatic form of information processing, than by a capacity-dependent, conscious, and controlled manner of processing (Bargh, 1989).

Although we do not question the influence of mental models, it is unlikely that they guide quick, initial approach or avoidance evaluation by extensive and controlled cognitive processes. This reasoning suggests the presence of another pathway which assists people's perceptions of and reactions to environmental odors. Such a pathway would predominantly rely on quick associations between odors and health effects, as opposed to rich networks of knowledge structures, and on pre-attentive, perceptual associations. The notion of olfactory cognitive processing as a dual-route system, with one automatic, involuntary route enabling rapid approach or avoidant responses, as well as a higher-level, conscious and deliberate route to making consciously and deliberate evaluations, is in line with recent models of information processing (e.g. the model of medically unexplained symptoms; Brown, 2004; the model of cognitive mechanisms underlying threat processing; Bar-Heim et al., 2007; the model of selective processing in anxiety; Mathews & Mackintosh, 1998).

The aim of the present study was to explore the viability of this first route, by investigating automatic odor-related associations in the context of health. To this end, the Implicit Association Test was conducted (IAT; Greenwald et al., 1998), whereby association strengths between the concept odor and the concepts healthy and sick were assessed. The term "implicit test" (or "indirect measure") in the context of the IAT refers to the fact that participants 1) are not necessarily aware of the fact that the association is being measured, 2) do not need conscious access to the association, and 3) have less control over the measurement outcome compared to questionnaires (De Houwer, 2006). Others take a slightly different viewpoint, and prefer to classify the IAT as a measurement tool which measures activated associations which have not been participant to validation processes, whereby "validation" refers to deliberate consideration about the truthfulness of one's automatic associations (Gawronski et al., 2007). In other words, the IAT is considered to capture ideas which have not been consciously "checked". During the IAT, items belonging to one of four concepts (in the present case: odor, house, healthy, sick) are categorized as quickly as possible in two categories by pressing one of two response keys. In a first part of the test, items representing the concepts odor and healthy are categorized by pressing one and the same key, while items representing the neutral house category and the concept sick are categorized by an alternative key. In the second part of the IAT, now items representing the concepts odor and sick share the first one

key, while items belonging to the concepts neutral and healthy share the other key. The comparison between response times of the two conditions is an indication of association strengths between the concepts. For instance, participants who categorize items more quickly when odor is paired with healthy, compared to the condition when odor is paired with sick, are presumed to have an implicit dominant association between the concepts odor and healthy.

The present paper describes the results of three IAT experiments. From an adaptive tendency, we expected that the concept of odor would be more closely associated with the concept of illness than with the concept of health, since the role of odors to signal the presence of chemicals or foods of which the inhalation or ingestion may promote illness is probably more important than the role of odors to signal chemicals or foods that promote health. The results of Experiment 1 indeed provided support for the prediction of an implicit odor-illness association.

After Experiment 1 we decided to conduct two additional experiments for two reasons: 1) to test whether the odor-illness association was a general and a stable one, and 2) to test whether the use of neutral target category house influenced the results. The latter refers to the fact that the IAT always measures associations with a certain concept of interest (in this case odor) relative to the associations with the other concept (in this case house). For example, most IATs use opposite concepts (De Houwer, 2002), like male versus female, or black versus white, whereby a strong positive association with the concept male, automatically implies a more negative association with the concept female (which is more negative in this example). Since the concept odor does not have its own contrary counterpart, we used a matching or reference category on the assumption that neither the concept nor the exemplars of the concept were intrinsically associated with healthy or sick, and thus that an odor-sick association or an odor-health association did not necessarily imply an house-healthy association or a house-sick association, respectively (see also De Jong et al., 2001). However, to be certain that the results of Experiment 1 were really based on an intrinsic association between odors and illness, the neutral reference category was replaced by two different ones in two additional experiments. If the dominant association between odor and illness found in Experiment 1 was caused by the choice of a relatively positive reference category, it would disappear after substitution with a truly neutral category.

Experiment 2A describes an IAT with an Odor versus Clothes target dimension. Experiment 2B describes an IAT with an Odor versus Sound target dimension. The concept clothes again represents objects, like house, that we presume to be of neutral value. On the other hand, participants might coincidentally have implicit positive associations with all kinds of objects, and thus the concept sound was chosen in Experiment 2B. Because sound refers to the sense of audition, and odor to the sense of olfaction, sound as reference category may be a better match than any object category.

Method

Participants

In Experiment 1, 67 students from Utrecht University (57 females, 10 males) were tested. Mean age was 20.77 (*SD* = 2.25). In Experiment 2A, 65 students were tested (46 females and 19 males). Mean age was 21.45 years (*SD* = 3.41). In Experiment 2B, 64 students were tested (46 females and 18 males). Mean age of this group was 22 years (*SD* = 2.34). Participants received either course credits or financial remuneration for their contribution. They were not informed about the test purpose prior to their participation.

Stimulus words

One of the dimensions of the IAT used in Experiment 1 consisted of the two word categories: house (porch, basement, room, hallway, attic), and odor (whiff, aroma, smell, nose, scent). The other dimension also consisted of two word categories: the healthy category, containing words related to positive health (vital, fit, strong, well, and happy), and the sick category, containing words related to negative health (weak, fever, flu, headache, and virus). All words were checked for their frequency and length (in Dutch) in order to have two comparable word categories on both dimensions. The concept house had been chosen as a neutral category previously, because it was assumed that neither this concept nor the exemplars of the concept were intrinsically associated with the concepts good or bad (Bulsing et al., 2007; see also De Jong et al., 2001). Likewise, we assumed that the concept house would be neutral in terms of "healthiness", and thus that neither the concept itself nor the exemplar words would be intrinsically associated with the concepts healthy or sick. To explore whether this was the case, we had an independent student sample (*N* = 47) rate the "healthiness" of the concept words house and odor, and the associated five exemplar words for all four concepts on a 5-points-scale (ranging from 1 to 5) with unhealthy (low scores) versus healthy (high scores) as extreme categories. Mean ratings of the concept words house and odor were 3.21 (*SD* = .66) and 3.49 (*SD* = .78), respectively. Mean ratings of the five exemplar words were 3.01 (*SD* = .28) for the house words, 3.27 (*SD* = .43) for the odor words, 1.52 (*SD* = .41) for the sick words, and 4.61 (*SD* = .40) for the healthy words. In conclusion, the odor and house concept words and exemplar words were rated as neutral, the healthy and sick exemplar words were rated as healthy and unhealthy, respectively.

For Experiment 2A the house category of Experiment 1was replaced with the clothes category (coat, pants, socks, shoes, shirt), and for Experiment 2B the house category was replaced with the category sound (listen, tones, vibration, ear, hearing). The odor category was identical to that in Experiment 1. The other dimension again consisted of the two word categories healthy and sick. An independent student sample (*N* = 37) rated the healthiness of the concept words clothes, sound, and odor, and the five exemplar words of all five categories (clothes, sound, odor, healthy, sick) on a 5-points-scale (ranging from 1 – 5) with unhealthy (low scores) versus healthy (high scores) as extreme categories. Mean ratings of the concept words clothes, sound, and odor were 3.27 (*SD* = .45), 3.22 (*SD* = .48), and 3.46 (*SD* = .73), respectively. Mean ratings of the five exemplar

words were 3.07 (*SD* = .32) for the clothes words, 3.18 (*SD* = .40) for the sound words, 3.17 (*SD* = .39) for the odor words, 1.45 (*SD* = .34) for the sick words, and 4.36 (*SD* = .36) for the healthy words. In conclusion, the odor, clothes, and sound concept words and exemplar words were rated as neutral in terms of healthiness, the healthy and sick exemplar words were rated as healthy and unhealthy, respectively.

Procedure

The IAT was programmed in E-prime, version 1.2. Following Greenwald et al. (1998) the test consisted of five blocks, and two practice blocks. During Block 1 participants were trained on how to differentiate between the odor words and the house words. The five house words and five odor words were presented twice (Block 1: 20 trials). Subsequently, participants had to use the same response keys for classification of the five healthy words and the five sick words, which were also presented twice (Block 2: 20 trials). During practice Block 3a the two former tasks were combined. Half of the participants started the combined task with pressing the same key for odor words and healthy words (Order 1). The other half started this block with pressing the same key for odor words and sick words (Order 2). Because Block 3a was a practice block, words from all concepts were presented once (Block 3a: 20 trials), and reaction times were not registered. Block 3b was the same as Block 3a, except that now registration took place and words from all concepts were presented twice (Block 3b: 40 trials). During Block 4, the categories house and odor changed positions on the computer screen, resulting in a required switched response for the associated words. Again the five odor words and the five house words were presented twice (Block 4: 20 trials). No exemplar words from the healthy and sick categories were presented during this block. Practice Block 5a was again a block where the two tasks were combined, but now with the switched odor/house dimension. Words from all concepts were presented once (Block 5a: 20 trials). Block 5b was the same as Block 5a, except that registration took place and all words were presented twice (Block 5b: 40 trials).

Participants were instructed to categorize as quickly and accurately as possible the words into the four categories by pressing the corresponding response keys on a computer keyboard. The words which had to be classified appeared one by one in the centre of the screen. During each IAT block the category concepts remained visible in the left and right upper corners of the screen. Order 1 and Order 2 had both two versions where the target-attribute pairs were allocated to different sides of the screen. Participants had to respond by pressing the "q" (index finger left hand) for words that belonged to a category in the left corner and the "p" (index finger right hand) for words that belonged to a category in the right corner. In case of a wrong answer, a red cross appeared. Participants had to correct the mistake by quickly pressing the alternate (correct) key. As soon as the correct key was pressed, the next word appeared.

After completion of the test, participants were asked to rate the explicit "healthiness valence" of the concept and exemplar words on a 5-points-scale with unhealthy (low scores) versus healthy (high scores) as extreme categories. In this manner, differences between participants' implicit and

explicit associations were assessed. They were debriefed about the study aim before leaving.

Procedures of Experiment 2A and 2B were the same as in Experiment 1.

Analyses

A repeated measures ANOVA with within-subject factor Association (odor and healthy versus odor and sick) and between-subjects factor Order (order 1 versus order 2) was conducted on the dependent variable reaction times of the two critical blocks (3b and 5b). A significant main effect of Association would indicate that either the odor and healthy block or the odor and sick block was completed faster. It was expected that this would be the case for the odor and sick blocks. IAT effects were reported along with main effects of Association. IAT effects are defined as the differences in mean latency between compatible blocks and incompatible blocks (Greenwald et al., 1998). Since we expected to find a dominant odor-illness association, the odor and sick block was considered a compatible block, whereas the odor and healthy block was considered an incompatible block. Consequently, we expected that the mean latency of the compatible block would be shorter compared to the mean latency of the incompatible block, as reflected by positive IAT effect scores (incompatible block minus compatible block). A main effect of Order would indicate that one order (first odor and healthy and then odor and sick versus first odor and sick and then odor and healthy) would be easier to complete compared to the other order. It was expected that both orders would be equal in terms of their difficulty. A significant interaction effect between Order and Association would demonstrate that switching from one block to the other block would be easier for one order as compared to the other. Here, it was expected that switching from an incompatible block to a compatible block (Order 1) would be easier compared to switching from a compatible block to an incompatible block (Order 2).

IAT effects were additionally calculated with the improved D600 scoring algorithm as proposed by Greenwald et al. (2003; e.g. better resistance to artefacts associated with the speed of responding and to procedural influences). Following their formula, practice blocks were now included in the analyses, error penalties (600 ms) were given, and results were standardized at the level of the participant. The D600 measure was calculated such that higher scores indicated faster performance during odor and sick blocks as opposed to odor and healthy blocks.

The alpha level was set at 0.05. Post-hoc tests were conducted after significant interactions of Order x Association. Bonferroni corrections were applied and alpha levels were set at 0.025. As an indication of effect size, the partial eta squared (η_p^2) is reported along with all significant main and interaction effects.

Results Experiment 1

Data reduction

Following Greenwald et al. (1998) reaction times below 300 ms were recoded to 300 ms (n = 1; 0.01%), and reaction times above 3000 ms were recoded to 3000 ms (n = 36; 0.30%). Reaction

times of incorrect trials were excluded for further reaction time analysis (n = 715; 5.93%). This did not apply for the calculation of the D600 measure, where reaction times and incorrect trials were not recoded or excluded. Box plots depicting the distribution of individual mean latencies on the odor and sick block and on the odor and healthy block showed that one participant was a significant outlier on both blocks. Data of this participant (Order 1) were excluded from all analyses.

Reaction times

For the two combined blocks (3b and 5b), mean reaction times are shown separately for order 1 and order 2 in Table 1. A main effect of Association was found, $F(1,64) = 25.51$, $p < .01$, $\eta_p^2 = .29$, showing that reaction times were shorter during odor and sick blocks, compared to odor and healthy blocks ($M_{Healthy}$ = 836 ms, SD = 175 ms, M_{Sick}= 766 ms, SD = 150 ms, IAT effect = 70). Additionally, a significant Association X Order interaction effect was found: $F(1,64) = 45.91$, $p < .01$, $\eta_p^2 = .42$. Post-hoc testing demonstrated that participants in order 1, who first completed the odor and healthy block, did not show more difficulty after switching to the new combined task where they had to associate odor and sick: $t(33) = -1.13$, $p = .27$ (order 1: $M_{Healthy}$ = 798 ms, SD = 162 ms, M_{Sick} = 823 ms, SD = 151 ms). However, participants in order 2 who first completed the odor and sick block, and then the odor and healthy block, demonstrated more difficulty with the new task, $t(31) = 9.31$, $p < .025$ (order 2: $M_{Healthy}$: 876 ms, SD = 182 ms, M_{Sick}: 705 ms, SD = 124 ms). There was no main effect of Order, $F < 1.0$.

A positive D600 IAT effect was calculated (0.20), demonstrating that participants associated the concept odor significantly more with the concept sick than with the concept healthy, $t(65) = 3.11$, $p < .01$.

Explicit ratings

Explicit ratings of the participants who completed the experiment differed from the ratings made by the independent student sample preceding the construction of the IAT with regard to the exemplar categories house and odor, $t(65) = -6.01$, $p < .01$, showing that odor words were rated as healthier than house words (M_{Odor} = 3.34, SD = .42, M_{House} = 3.10, SD = .30). The concept words were rated as equal in terms of healthiness, $t(65) = 1.23$, $p = .22$, indicating that both concept names were rated as equally neutral in terms of healthiness (M_{Odor} = 3.42, SD = .68, M_{House} = 3.33, SD = .51).

Table 1

Mean reaction times in milliseconds (SDs between parentheses) for order 1 and order 2 during phases of Experiment 1 where the concept odor had to be associated with the concepts healthy and sick

Order	Blocks	Reaction times
Order 1[a] (*n* = 34)	Odor and Healthy	797.99 (162.27)
	Odor and Sick	822.94 (150.98)
Order 2[b] (*n* = 34)	Odor and Sick	704.83 (124.27)
	Odor and Healthy	875.92 (181.53)

[a] Participants in Order 1 first had to complete the Odor and Healthy Block and then the Odor and Sick Block.

[b] Participants in Order 2 first had to complete the Odor and Sick Block and then the Odor and Healthy Block.

Conclusion

Participants showed shorter reaction times during blocks where they had to associate the concept odor with the concept sick, compared to blocks where they had to associate the concept odor with healthy, reflected by a positive (and significant D600) IAT effect score. Additionally, they demonstrated more difficulty when switching to the odor and healthy block, than when switching to the odor and sick block. Thus, participants were quicker to associate odor with illness than odor with health, which implies a stronger association for the former pairing than the latter.

Although the concept word odor was rated equally neutral as house in terms of its healthiness, the odor exemplar words were rated as healthier compared to the house exemplars. Explicit odor and health associations are apparently different from implicit odor and health associations.

Results Experiment 2A and 2B

Data reduction

Reaction times below 300 ms were recoded to 300 ms (n = 1; 0.01% [Experiment 2A]; n = 0 [Experiment 2B]), and reaction times above 3000 ms were recoded to 3000 ms (n = 6; 0.05% [Experiment 2A]; 73;.63% [Experiment 2B]) Incorrect trials were excluded for further reaction time analysis (n = 740; 6.32% [Experiment 2A]; n = 838; 7.19% [Experiment 2B]). Box plots depicting the distribution of individual mean latencies on the odor and sick block and on the odor and healthy block showed that one participant was a significant outlier on both blocks. Data of this participant (Order 1, Experiment 2A) were excluded from all analyses.

Reaction times

For the two combined blocks (3b and 5b) mean reaction times are shown separately for order 1 and order 2, and Experiment 2A and 2B in Table 2. For Experiment 2A, a main effect of Association was found, $F(1,62) = 9.85$, $p < .01$, $\eta_p^2 = .14$, showing that reaction times were shorter during odor and sick blocks, compared to odor and healthy blocks ($M_{Healthy}$ = 868 ms, SD = 168 ms, M_{Sick}= 809

ms, *SD* = 183 ms, IAT effect = 59, [Experiment 2A]). During Experiment 2B, reaction times were also lower for the odor and sick combination (M_{Sick}= 946 ms, *SD* = 263 ms) than for the odor and healthy combination ($M_{Healthy}$ = 962 ms, *SD* = 212 ms, IAT-effect = 16). However, this main effect did not reach significance, $F < 1.0$ (Experiment 2B). A significant Association X Order interaction effect was found for both experiments, $F(1,62) = 9.89$, $p < .01$, $\eta_p^2 = .14$ (Experiment 2A), and $F(1,62) = 6.47$, $p = .01$, $\eta_p^2 = .09$ (Experiment 2B). Post hoc testing demonstrated that participants in order 1 who first completed the odor and healthy block did not show more difficulty after switching to the new combined task where they had to associate odor and sick, Experiment 2A: $t(32) = -.01$, $p = 1.00$ (order 1: $M_{Healthy}$ = 822 ms, *SD* = 137 ms, M_{Sick} = 822 ms, *SD* = 163 ms), and Experiment 2B: $t(32) = -1.22$, $p = .23$ (order 1: $M_{Healthy}$ = 943 ms, *SD* = 214 ms, M_{Sick} = 988 ms, *SD* = 265 ms). However, participants in order 2 who first completed the odor and sick block and then the odor and healthy block demonstrated more difficulty with the new task, Experiment 2A: $t(30) = 4.03$, $p < .025$ (order 2: $M_{Healthy}$: 918 ms, *SD* =185 ms, M_{Sick}: 794 ms, *SD* = 204 ms), Experiment 2B; $t(30) = 2.48$, $p < .025$ (order 2: $M_{Healthy}$: 983 ms, *SD* = 212 ms, M_{Sick}: 901 ms, *SD* = 258 ms). There was no main effect of Order, $F < 1.0$ (Experiment 2A and 2B).

A positive D600 IAT effect was calculated (.24 [Experiment 2A]; .10 [Experiment 2B]), demonstrating that participants associated odor significantly more with the concept sick than with the concept healthy, Experiment 2A: $t(63) = 4.50$, $p < .01$, Experiment 2B: $t(63) = 2.07$, $p = .04$.

Explicit ratings

For Experiment 2A, explicit healthiness ratings of the word exemplars did not differ between the odor words and the clothes words, $t(63) = .03$, $p = .97$, (M_{Odor} = 3.19, *SD* = .40, $M_{Clothes}$ = 3.19, *SD* = .43) . The same was true for Experiment 2B, $t(63) = -.66$, $p = .51$, (M_{Odor} = 3.14, *SD* = .46, M_{Sound} = 3.18, *SD* = .41). Mean ratings for the concept words did not differ either, $t(63) = .80$, $p = .43$. (M_{Odor} = 3.27, *SD* = .63, $M_{Clothes}$ = 3.19, *SD* = .65 [Experiment 2A]), and $t(63) = .59$, $p = .56$ (M_{Odor} = 3.39, *SD* = .70, M_{Sound} = 3.33, *SD* = .67 [Experiment 2B]).

Table 2

Mean reaction times in milliseconds (SDs between parentheses) for order 1 and order 2 during phases where the concept odor had to be associated with the concepts healthy and sick, shown separately for Experiment 2A and 2B

Order	**Blocks**	**Reaction times**
Experiment 2A (N = 64)		
Order 1[a] (*n* = 33)	Odor and Healthy	821.90 (136.53)
	Odor and Sick	822.03 (162.92)
Order 2[b] (*n* = 31)	Odor and Sick	794.47 (203.71)
	Odor and Healthy	917.59 (184.81)

Experiment 2B (N = 64)		
Order 1[a] (*n* = 33)	Odor and Healthy Odor and Sick	942.50 (213.78) 988.40 (265.10)
Order 2[b] (*n* = 31)	Odor and Sick Odor and Healthy	901.05 (258.19) 983.31 (212.00)

[a] Participants in Order 1 first had to complete the Odor and Healthy Block and then the Odor and Sick Block.

[b] Participants in Order 2 first had to complete the Odor and Sick Block and then the Odor and Healthy Block.

Conclusion

In both experiments, participants showed shorter reaction times during blocks in which they had to associate the concept odor with sick, compared to blocks where they had to associate odor with healthy, which was also reflected by positive (and significant D600) IAT effect scores. This main effect reached significance during Experiment 2A, but not during Experiment 2B. However, both during Experiment 2A and 2B, participants demonstrated significantly more difficulty with switching from the odor and sick block to the odor and healthy block than the other way around. These results again suggest an implicit association between the concepts odor and sick: The odor-illness association turns out to be a robust one.

Explicit evaluation of the exemplar and concept words revealed no differences between the categories. These results demonstrate that explicit, intentional evaluations do not reflect implicit ones.

Remarkably, we observed a difference in reaction times between the IAT using the concept sound as a neutral contrast category (Experiment 2B) and the other two experiments which used house and clothes as contrast categories (Experiments 1 and 2A). Reaction times in general were approximately 100 ms higher during Experiment 2B compared to the other two experiments. This is surprising, since experimental hardware and procedures were exactly identical in all experiments. It could be argued that Experiment 2B was harder to complete, because the two concepts which had to be associated with the health dimension related both to sensory modalities, whereas in the other two experiments the control concepts (house and clothes) were not sensory modalities. This would imply the sensory modality exemplar words are conceptually closer, leading to higher decision times during the categorization process of the exemplar words. Despite this complicating factor, a significant D600 IAT effect was observed for Experiment 2B, indicating a stronger odor-sick association than an odor-healthy association.

Extra analyses to rule out effects of exemplar word selection

The aim of the three experiments was to investigate intrinsic odor and health associations. We conducted additional analyses in order to rule out any alternative explanations, related to selection of the exemplar words that could have accounted for the observed odor-illness association. For example, De Houwer (2001) argues that the IAT primarily measures associations at the level

of the categories (in this case: odor, house, clothes, sound, healthy, sick) and that category labels determine IAT effects more strongly than the exemplar words that happen to be selected (i.e., the "label effect"). However, others have argued that exemplar words do in fact influence association strengths (Bluemke & Friese, 2006). With this latter argument in mind, we reexamined our exemplar words and found two possible confounding factors which could have contributed to the present results. First of all, the sick and healthy exemplar words seemed to differ in terms of their semantic proximity to the concept odor. That is, the sick category consisted of words like fever, flu, and virus, words that seem to have a stronger a-priori link to the concept odor than the exemplar words belonging to the healthy category, like fit, well and vital, which do not have a a-priori link to odor. If that is the case, it would explain why we found an implicit odor-illness association rather than an implicit odor-health association. Secondly, the sick and healthy exemplar words differed in terms of their abstractness: the sick category mostly consisted of concrete words (e.g. flu, headache, virus), whereas the healthy category mostly consisted of abstract words (e.g. well, happy, vital). To account for such influences, reaction time analyses were conducted again, but instead of calculating mean reaction times of all 5 exemplar words per category, only the words "strong" (representing the healthy category) and "weak" (representing the sick category) were included in the analyses, since these two words are both equal in terms of their semantic proximity to the concept odor (in relation to the first argument), as well as in terms of their abstractness (in relation to the second argument). The same pattern of results appeared. Associations between the concepts odor and weak were stronger compared to associations between odor and strong (Experiment 1: $t(65) = -3.31$, $p < .01$; $M_{weak} = 832.02$, $SD = 270.76$, $M_{strong} = 1008.95$, $SD = 427.27$; Experiment 2A: $t(63) = 2.36$, $p < .05$; $M_{weak} = 864.34$, $SD = 389.87$, $M_{strong} = 1366.03$, $SD = 1610.67$; Experiment 2B: $t(63) = 1.76$, $p = .08$; $M_{weak} = 1045{,}20$, $SD = 1193.51$, $M_{strong} = 1609.30$, $SD = 2210.85$). In conclusion, after controlling for possible confounding factors, we still found a robust odor-sick association.

Discussion

A robust implicit odor-illness association

Three experiments demonstrated that participants were quicker to associate odor with sick than odor with healthy, and that participants had more difficulty switching from odor and sick associations to odor and healthy associations than the other way around. Additionally, all three experiments showed positive D600 IAT effects, implying a stronger implicit association between the concepts odor and sick than between odor and healthy. This odor-illness association remained visible after controlling for possible confounding factors. It can be concluded therefore that the association between odor and illness is a robust one.

Implicit associations were assessed independently of, and did not match, explicit associations between the concepts. Although the distinction between implicit versus explicit information processing has received attention previously in the odor literature (e.g. Nordin et al., 1995; Degel & Köster, 1999; Köster et al., 2002; Dematte et al., 2006), it has not been applied in the context of

odors as signals of illness or health (but see: Witthöft et al., 2006).

The finding that people intrinsically associate the concept odor with illness, regardless of self-reported attitudes, raises the question as to the purpose served by such fast and automatic associations between odors and illness, rather than between odors and health.

Better safe than sorry

The implicit odor-illness association probably has its roots in a predisposition for organisms to primarily attend to negative inputs coming from the environment (Pratto & John, 1991). This general propensity for negative information can even be found at pre-attentive levels (Ogawa & Suzuki, 2004). From an evolutionary perspective, survival is obviously better served by automatically scanning the environment for possible danger, so as to always be prepared for a "flight" reaction. This same reasoning could be applied to the perception of odors. It is a safer strategy to quickly signal an odorant coming from a potentially poisonous food source or a predator, and thus prevent death, than to signal an odorant coming from a wholesome and nutritious source or a potential mate and thus extend life. From the point of view of signal detection theory (Swets, 1964) the criterion for detecting danger should be lower than that for detecting safety, so as to increase one´s chances of survival. The present results may reflect such a perceptual strategy.

Besides the tendency to (implicitly) focus attention on negative information in general, certain stimuli or objects seem to have, even in the absence of actual danger, a strong innate association with possible harmful consequences. This biological "preparedness" indicates that certain stimuli which once posed serious threat to our early ancestors, are still easily classified as harmful today (Öhman & Mineka, 2001). This is reflected by the fact that fears and phobias for spiders, snakes and water are far more common compared to fears for cars or even guns (Seligman, 1971). Since one of the ancient functions of olfaction is to signal possible danger, odors can also be considered such "prepared stimuli", having an innate association with danger and illness, as was demonstrated in the present study[2]. As a result of this innate odor-illness connection, *newly* learned associations between odors and adverse health effects are in turn more easily established (based on Garcia & Koelling, 1966).

Miasma theory: "All smell is disease"

The implicit odor-illness association shown here may have been strengthened by the belief that odors themselves can influence health in a negative way. A theory that has presumably contributed to the spreading and persistence of these beliefs is the Miasma theory. This theory is based

[2] Although it is difficult to determine whether certian odor-illness associations are truly innate or actually based on learned associations: Embryo's are already exposed to various chemicals in the womb through food ingestion by the mother, and might "learn" in this stage which chemicals should be approached later on (Mennella et al., 1995).

on beliefs of Hippocrates (460 – 377 BC) who suspected a relation between illness and places "where the air is dank and foul". The malodors he referred to were called "miasma". The notion of miasma triggered the theory that diseases may originate due to the inhalation of vapors emitted by rotting animal and vegetable materials (Bloom, 1965; Miller, 1962; Franco & Williams, 2000). Hundreds of years later, in the 19th century, the miasmatists helped to improve health care and living conditions by stating that "all smell is disease", consequently motivating people (including governments) to tackle malodor sources and thereby unintentionally improving sanitation (Collins, 2006). Although the miasma theory has been abandoned by scientists for quite some time - it has been accepted that bacteria were directly responsible for causing disease with odors being produced as by-products-, the belief that odors negatively influence health still seems to resonate today (Dalton, 2007).

A dual-processing perspective

As already stated in the introduction of this paper, the distinction between an automatic, effortless, and unconscious information processing system on the one hand, and a more controlling, voluntary, and conscious system on the other hand, plays a central role in recent models of cognitive information processing in psychopathology (e.g. Brown, 2004; Bar-Heim et al., 2007; Mathews & Mackintosh, 1998). With respect to olfaction, automatically activated odor-illness associations could facilitate olfactory information processing by giving it a "jump start". Still, bottom-up processing of odor characteristics and contextual influences can suppress or rectify reactions based on such initial associations. This distinction seems useful as an extension of the information-processing model of chemosensory perception mentioned earlier (Dalton & Hummel, 2000; Smeets & Dalton, 2005). From such a dual-processing perspective, it could be hypothesized that the foundation for the development and maintenance of odor-induced health symptoms – referring to the symptoms that cannot be clarified by toxicological models - should be searched in an imbalance between the two information processing systems. Based on the analog with signal detection theory introduced earlier, classifying harmless odors as dangerous could be equated with the false alarms that unavoidably accompany low criteria. Alternatively, it is possible that controlled cognitive processes are insufficiently capable of suppressing automatic avoidance associations, or reinforce them. This perspective may foster interesting new hypotheses for future research to improve our understanding of unexplained illness from exposure to environmental odors, as in people suffering from MCS or IEI. For example, it could be hypothesized that individuals who suffer from IEI have stronger implicit associations between odors and sick than healthy individuals, or that individuals with strong odor-illness associations interpret ambiguous/unknown odors as more threatening compared to individuals with less strong associations, or that those who have stronger odor-illness associations produce or report more adverse health effects than controls.

Other odor associations

In closing, we of course acknowledge that the function of the sense of smell goes beyond warning

for possible danger, and that associations between the concept odor and concepts other than illness may well be of an approach kind. With respect to food or eating, odors signal nutritious and appealing food products, and IATs will probably also reveal positive associations with the concept odor in such contexts. In animals odors play a significant role in demarcation of territory or drive mating behavior, which predict avoidance and approach, respectively. Unfortunately it is still very hard to conduct IATs among animals (but for exciting new IAT possibilities, see: Bones & Johnson, 2007).

Acknowledgements

The authors would like to thank Martin Laverman for his technical contribution to this research, and Jantine Slotboom, Rik Vos, and Margreet Worm for their contribution to the data acquisition phase of Experiment 1. This work was funded by NWO grant 452-03-334 to the second author.

References

Bargh, J.A. (1989). Conditional automaticity: varieties of automatic influence in social perception and cognition (pp. 3-51). In J. S. Uleman & J. A. Bargh (Eds.), *Unintended thought.* New York: Guildford Press.

Bar-Heim, Y., Lamy, D., Pergamin, L., Bakermans-Kranenburg, M., & IJzendoorn, M. H. (2007). Threat-related attentional bias in anxious and nonanxious individuals: A meta-analytic study. *Psychological Bulletin, 133*, 1-24.

Bloom, B. L. (1965). The "Medical Model", Miasma theory, and community mental health. *Community Mental Health Journal, 1*, 333-338.

Bluemke, M., & Friese, M. (2006). Do features of stimuli influence IAT effects? *Journal of Experimental and Social Psychology, 42*, 163-176.

Bones, A. K., & Johnson, N. R. (2007). Measuring the immeasurable: Or "Could Abraham Lincoln take the Implicit Association Test? *Perspectives on Psychological Science*, *2*, 406-411.

Brown, R. J. (2004). Psychological mechanisms of medically unexplained symptoms: An integrative conceptual model. *Psychological Bulletin, 130*, 793-812.

Bulsing, P. J., Smeets, M. A. M., & van den Hout, M. A. (2007). Positive implicit attitudes towards Odor Words. *Chemical Senses, 32*, 525-534.

Cavalini, P. M., Koeter-Kemmerling, L. G., & Pulles, M. P. (1991). Coping with odour annoyance and odour concentrations: Three field studies. *Journal of Environmental Psychology, 11*, 123-142.

Collins, C. (2006, June). Causes of fevers: miasma versus contagion. *The Biomedical Scientist.* Retrieved September, 13, 2007, from www.ibms.org/index.cfm?method=science.history_zone&subpage=history_fevers

Dalton, P. (2007, April). What is the "Mal" in Malodor? In K. Rankin & C. Christensen (Chair), *Human Axillae: Why?* Symposium conducted at the XXIXth Annual Meeting of the Association for Chemoreception Sciences, Sarasota, USA.

Dalton, P., & Hummel, T. (2000). Chemosensory function and response in idiopathic environmental intolerance. *Occupational Medicine, 15*, 539-556.

Dalton, P., Wysocki, C. J., Brody, M. J., & Lawley, H. J. (1997). The influence of cognitive bias on the perceived odor, irritation and health symptoms from chemical exposure. *International Archives of Occupational and Environmental Health, 69*, 407-417.

Das-Munshi, J., Rubin, G., & Wessely, S. (2007). Multiple chemical sensitivities: A systematic review of provocation studies. *Journal of Allergy and Clinical Immunology, 188*, 1257-1264.

Dayal, H. H, Baranowski, T., Li, Y., & Morris, R. (1994). Hazardous chemicals: Psychological dimensions of the health sequelae of a community exposure in Texas. *Journal of Epidemiology and Community Health, 48*, 560-568.

Degel, J., & Köster, E. P. (1999). Odors: Implicit memory and performance effects. *Chemical Senses, 24*, 317-325.

De Houwer, J. (2001). A structural and process analysis of the implicit association test. *Journal of Experimental and Social Psychology*, 37, 443–451.

De Houwer, J. (2002). The Implicit Association Test as a tool for studying dysfunctional associations in psychopathology: Strengths and limitations. *Journal of Behavior Therapy and Experimental Psychiatry, 33*, 115-133.

De Houwer, J. (2006). What are implicit measures and why are we using them? In R. W. Wiers & A. W. Stacy (Eds.), *The handbook of implicit cognition and addiction* (pp. 11-28). Thousand Oaks, CA: Sage Publishers.

De Jong, P., Pasman, W., Kindt, M., & van den Hout, M. A. (2001). A reaction time paradigm to assess (implicit)

complaint-specific dysfunctional beliefs. *Behavior Research and Therapy*, *39*, 101-113.

Dematte, L. M., Sanabria, D., & Spence, C. (2006). Olfactory-tactile compatibility effects demonstrated using a variation of the Implicit Association Test. *Acta Psychologica, 124*, 332-343.

Devriese, S., Winters, W., Stegen, K., Van Diest, I., Veulemans, H., Nemery, B., Eelen, P., Van de Woestijne, K., & Van den Bergh, O. (2000). Generalization of acquired somatic symptoms in response to odors: a pavlovian perspective on multiple chemical sensitivity. *Psychosomatic Medicine, 62*, 751-759.

Franco, D. A., & Williams, C. E. (2000). "Airs, waters, Places" and other Hippocratic writings: Inferences for control of foodborne and waterborne disease. *Journal of Environmental Health, 62*, 9-14.

Garcia, J., & Koelling, R. A. (1966). Relation of cue to consequence in avoidance learning. In M. Domjan & B. Burjhard (Eds.), *The Principles of Learning & Behavior* (pp.76-78), California: Brooks/Cole Publishing Company.

Gawronski, B., LeBel, E. P., & Peters, K. R. (2007). What do implicit measures tell us? Scrutinizing the validity of three common assumptions. *Perspectives on Psychological Science, 2*, 181-193.

Greenwald, A. G., McGhee, D. E., & Schwartz, J. L. K. (1998). Measuring individual differences in implicit cognition: The implicit association test. *Journal of Personality and Social Psychology, 74*, 1464-1480.

Greenwald, A. G., Nosek, B. A., & Banaji, M. R. (2003). Understanding and using the implicit association test: I. An improved scoring algorithm. *Journal of Personality and Social Psychology, 85*, 197-216.

Köster, E. P., Degel, J., & Piper, D. (2002). Proactive and retroactive interference in implicit odor memory. *Chemical Senses, 27*, 191-206.

Leventhal, H., Meyer, D., & Nerenz, D. (1980). The common sense representation of illness danger. In S. Rachman (Ed.), *Med Psychol* (pp. 7-30). New York: Pergamon Press.

Mathews, A., & Mackintosh, B. (1998). A cognitive model of selective processing in anxiety. *Cognitive Therapy and Research, 22*, 539-560.

Mennella, J. A., Johnson, A., & Beauchamp, G. K. (1995). Garlic ingestion by pregnant women alters the odor of amniotic fluid. *Chemical Senses, 20*, 207-209.

Miller, G. (1962). "Airs, Waters and Places" in history. *Journal of the History of Medicine and Allied Sciences, 17*, 129-140.

Nordin, S., Monsch, A. U., & Murphy, C. (1995). Unawareness of smell loss in normal aging and Alzheimer's disease: Discrepancy between self-reported and diagnosed smell sensitivity. *Journals of Gerontology. Series B, Psychological Sciences and Social Sciences, 50*, 187-192.

Ogawa, T., & Suzuki, N. (2004). On the saliency of negative stimuli: Evidence from attentional blink. *Japanese Psychological Research, 46*, 20–30.

Öhman, A., & Mineka, S. (2001). Fears, phobias, and preparedness: Toward an evolved module of fear and fear learning. *Psychological Review, 108*, 483-522.

Pratto, F., & John, O. P. (1991). Automatic vigilance: The attention-grabbing power of negative social information. *Journal of Personality and Social Psychology, 61*, 380-391.

Reiser, B. J., Black, J. B., & Abelson, R. P. (1985). Knowledge structures in the organization and retrieval of autobiographical memories. *Cognitive Psychology, 17*, 89-137.

Ross, P. M., Whysner, J., Covello, V. T., Kuschner, M., Rifkind, A. B., Sedler, M. J., Trichopoulos, D., & Williams, G. M. (1999). Olfaction and symptoms in the multiple chemical sensitivities syndrome. *Preventive Medicine, 28*,

467-480.

Schiffman, S. S., Walker, J. M., Dalton, P., Lorig, T. S., Raymer, J. H., Shusterman, D., & Williams, C. M. (2000). Potential health effects of odor from animal operations, wastewater treatment, and recycling of byproducts. *Journal of Agromedicine, 7*, 7-81.

Schiffman, S. S., & Williams, C. M. (2005). Science of odor as a potential health issue. *Journal of Environmental Quality, 34*, 129-138.

Seligman, M. E. P. (1971). Phobias and preparedness. *Behavior Therapy, 2*, 307-320.

Shusterman, D. (2001). Odor-associated health complaints: Competing explanatory models. *Chemical Senses, 26*, 339-343.

Smeets, M. A. M., & Dalton, P. H. (2005). Evaluating the human response to chemicals: Odor, irritation and non-sensory factors. *Environmental Toxicology and Pharmacology, 19*, 581-588.

Swets, J. A. (1964). *Signal detection and recognition by human observers*. New York: Wiley.

Witthöft, M., Gerlach, A. L., & Bailer, J. (2006). Selective attention, memory bias, and symptom perception in idiopathic environmental intolerance and somatoform disorders. *Journal of Abnormal Psychology, 115*, 397-407.

Chapter 4

Influence of chemosensory pain-expectancy on olfactory event related potentials

This chapter is based on:

Bulsing, P.J., Smeets, M.A.M., Hummel, T., & van den Hout, M.A. (2007). Influence of Chemosensory Pain-Expectancy on Olfactory Event Related Potentials. *NeuroImage*, 38, 164-170.

Abstract

Health symptoms attributed to environmental odor exposure are not well understood. Cognitive factors seem to play a significant role in odor-related illness. In the present study, we investigated whether such influences are predominantly interpretational (i.e. best understood as interpretations of perceived odors), or also perceptual (i.e. affect perceptions of the characteristics of the odor). To investigate the neuronal activation behind such processes olfactory ERPs were recorded. The experiment consisted of two conditions: one where participants expected just several administrations of one odor (labelled as the "non-painful" condition), and one where they also expected, in between the odor administrations, to feel irritation in the nose (labelled as the "painful" condition). Participants received painless H_2S stimuli during both conditions. To reinforce pain expectancy, a CO_2 pulse was given occasionally during the "painful" condition. Crucial comparisons were made between reactions to H_2S, under the two expectancy conditions. Detection sensitivity (reflected by amplitudes and latencies of the early N1 peak) and stimulus salience (reflected by amplitudes and latencies of the late "cognitive" positivity) were examined. Peak amplitudes were unaffected by expectancy condition. However, a significant main effect of expectancy on the N1 latency was found, which suggests that expecting a painful stimulus reduces the time to detect a harmless odor. In conclusion, expectancies seem to alter early aspects of odor perception.

Introduction

Exposure to ambient odors may lead to health effects if this occurs at levels that cause irritation or other toxicological effects. Conversely, health symptoms may also be reported in reaction to odors that are far below irritation levels, for instance odors related to repetitive or incidental emissions from agriculture (Schiffman, 1998), industry (Dayal et al., 1994), traffic (Lercher et al., 1995) or as part of illnesses such as Multiple Chemical Sensitivity (Ross et al., 1999). The reported symptoms include eye, nose and throat irritation, headache, nausea, cough, "stress", drowsiness, and alterations in mood (Schiffman et al., 2000; Bell et al., 1996).

The mechanism by which health symptoms are induced in these situations are still not well understood, but beliefs about the safety of an odor seem to play an important role. This was demonstrated in an elegant series of experiments by Dalton (1999), in which an overall effect of induced belief was found on the perceived intensity and irritation of the odor to which volunteers where exposed in an exposure chamber. Not only did the participants report higher levels of health symptoms after they had been exposed to what they believed to be industrial solvents, they also perceived the intensity of odor and irritancy (e.g. burning, stinging) to be higher than when they believed they were exposed to natural extracts or neutral compounds. As noted by Dalton (1999), the fact that the manipulation of belief significantly affected odor and irritation intensities, which can be considered as the primary sensory signals of a chemical substance, suggests that the top-down influence on interpretation of odors is considerable.

The notion that conceptual knowledge can influence perception in itself may be fairly uncontroversial, but the questions that remain are *how*, or in what sense and to what extent? For a long time, theoretical accounts of how such influences might occur have been lacking. For example, Bruner and Goodman (1947) met with a lot of scepticism when they argued for recognizing value and need as organizing factors in perception. Their theory was based on their finding that the greater the value of a coin, the greater the deviation of estimated size from actual size (especially by poor children). The scepticism was probably due to the long-time dominance of linear information processing models of perception, in which the flow of information was unidirectional and top-down influences therefore impossible (e.g. Gardner, 1987), or of the computational approach (e.g. Marr, 1982) in which high-level information was only assumed to play a role in the last phase of perceptual processing, in which object shapes are already fully analyzed.

However, more recent findings typically employing cognitive neuroscience methods have shown that high-level and low-level processing can be very much interlinked (e.g. Lee et al., 1998; Ganis et al., 2003; Kosslyn & Thompson, 2003), allowing exchange of information between stages of perceptual and cognitive processing previously believed to be exclusively "low" or "high"-level or only feed-forward.[3]

Several of these studies were aimed at elucidating how expectations about upcoming events or

[3] Interestingly, Sterzer and Rees' finding (2006) that neural activity in human primary visual cortex (V1) corresponds to perceived size rather than actual object size could retrospectively strengthen Bruner and Goodman's claim that value and need can affect perception of the size of a coin!

stimuli alter the perception of those events or stimuli. For example, using fMRI, Nitschke et al. (2006) showed that participants, who expected a highly aversive bitter substance to taste only mildly aversive, reported the stimulus to be less bitter than when they were correctly informed. Analogously, neurons in the primary taste cortex (which responds only to sensory input from taste receptors and somatosensory neurons) were less activated during these misleading taste trials. This demonstrated that expecting a less intense stimulus decreased brain responsiveness to these stimuli in areas believed to directly respond to taste.

In a similar vein, De Araujo et al. (2005) showed that semantic information modulates olfactory representations in the brain. In line with previous work (Herz et al., 2001), they provided a visual word descriptor, "cheddar cheese" or "body odor", during delivery of a test odor and clean air. Neural responses in the medial orbitofrontal cortex were examined, which region typically becomes more activated in response to pleasant odors (Gottfried et al., 2002). Neurons in this region were significantly more activated by both the test odor and clean air when labelled "cheddar cheese" than when labelled "body odor". In other words, the test odor and clean air were both encoded as more pleasant after manipulating expectations about the stimulus in a positive direction, compared to a more negative direction. This demonstrates that expectations about the degree of pleasantness modulate how and where in the brain stimulus information is processed.

Thus, expectations about an upcoming event may alter perceptual processing of that event even at a "deep" level. Starting from an interest in health effects from exposure to odorous volatiles in the in- and outdoor environment, we investigated how expectancies about the harmfulness of an environmental chemosensory stimulus affect the perception of chemosensory stimuli in general. Expectations of harmfulness were based on having the participant experience a stimulus that activated the trigeminal nerve in the nose, which provoked sensations that can be slightly painful (tingling or burning). This stimulus was labelled as the painful stimulus. In addition, participants received an experience with a sulphur-like compound that only activated the olfactory nerve. This was labelled as the non-painful stimulus. By informing participants what to expect during the various parts of the experiment ("no chance of receiving painful stimuli" versus "a distinct chance of receiving a painful stimulus"), two cognitive sets were created: one where they expected to feel pain, and one in which they expected to just smell an odor. Irrespective of cognitive set participants would mainly receive the non-painful odor. It was investigated how the expectation of the painful chemosensory stimulus affected the perception of the non-painful odor using an olfactory event related potential (OERP) method. Crucial comparisons were made between reactions to the odor, under the different expectancy conditions.

The OERP method was chosen because OERPs allow the investigation of the sequential, early processing of olfactory information (Hummel & Kobal, 2002). The early N1 peak of the ERP reflects stimulus characteristics like intensity and quality, whereas the late positivity (here referred to as the "P2 peak") is associated with more cognitive aspects of perception, like stimulus salience or novelty (Pause & Krauel, 2000; Nordin et al., 2005; Lundsrom et al., 2006). Changes

in peak amplitudes are associated with processing intensity (a higher peak amplitude indicates more activated or synchronized neurons), changes in latencies with processing speed (shortened latencies relate to faster processing; Hummel & Kobal, 2002). Besides examining peak amplitudes and latencies, ratings of intensity and pleasantness were obtained, to investigate the role of expecting chemosensory induced pain on subjective odor perception.

The present study set out to answer the following question: Does expectancy of pain change the early and/or late peak of the OERP? More in general: Does expectancy only affects the later, more interpretational phases of information processing, or can its influence be traced to the early, basic perceptual phases of information processing? We predicted that the P2 peak of the perceived olfactory stimulus associated with pain expectancy would increase in amplitude, and decrease in latency after the induced pain expectancy, as an indication of a higher degree of salience of the stimulus. Or in other words, we predicted that salience of the olfactory stimulus would increase in the pain condition, because participants had to "check" during each trial whether they were exposed to the "painful" or the "non-painful" stimulus. In addition we predicted that, if a salient chemosensory stimulus is expected, this would reflect in an increased amplitude and shortened latency of the early N1 peak as indicative of a perceptual event.

Method

Participants

Thirty volunteers participated in this study. They were all students at the University of Dresden and recruited by advertisement spread throughout the university campus. Only women were tested, to exclude as much variability as possible (Lundström & Hummel, 2006; Stuck et al., 2006). Mean age was 22.1 years (*SD* = 2.7). Only participants who did not smoke, did not have asthma, were not pregnant, and had a normal sense of smell (tested by the identification test of the "Sniffin' Sticks" test; Kobal et al., 2000) were invited to participate. The study was conducted in accordance with the Declaration of Helsinki. All participants gave their informed consent, and received moderate financial remuneration for their participation.

Stimuli and presentation

H_2S (10 ppm) was used as the "non-painful" odor stimulus, and CO_2 (60 % v/v) as the "painful" irritating stimulus. H_2S stimuli had a 200 ms duration; CO_2 stimuli had a 500 ms duration. A semi-random inter stimulus interval of 55 - 65 seconds was used. These stimulus concentrations and durations were determined during pilot testing, such that the non-painful stimulus would be a clearly perceptible, but non-irritating odor, while the painful stimulus had to elicit clear and relatively strong irritation that was moderately painful. A panel of 5 experienced observers participated in pilot studies to identify the required stimulus conditions.

Stimuli were presented by a dynamic air-dilution olfactometer (Burghart Instruments, Wedel, Germany) that does not alter the mechanical or thermal conditions of the mucosa (Kobal, 1981).

The stimuli were presented in a constantly flowing air stream of 6 L/min, with controlled temperature and humidity (36 °C, 80% relative humidity). During the entire experiment participants had to carry out a simple computer game (tracking task) to stabilize both vigilance and eye movements; using a joystick, they had to keep a small square inside a larger one, which moved unpredictably. Participants received white noise through headphones to mask switching clicks of the olfactometer. They used the velopharyngeal closure breathing technique (Kobal, 1981), to prevent air flow through the nose.

Procedure

Participants were randomly assigned to one of four sequences. All sequences consisted of two "Non-Pain-Expectancy" blocks and two "Pain-Expectancy" blocks in a pseudo-counterbalanced order (see Table 1). We chose not to use the block orders "Pain / Pain / Non-Pain / Non-Pain" and "Non-Pain / Non-Pain / Pain / Pain", in order to keep the experiment sufficiently diverse (and to avoid sleepiness). Participants received the following information before onset:

The following experiment consists of 4 different blocks. Before each block you will get information about the stimuli you will receive during that particular block. Some blocks contain only *non-painful* stimuli; you will only smell an odor from time to time. Other blocks contain, besides non-painful odors, also some stimuli that can be *painful*. They will feel like burning in the nose. Within a "non-painful" block, you will only receive non-painful odor stimuli. Within a "painful" block you will receive most of the time the non-painful odors, *but also two to five painful stimuli*. Each block will take approximately 10 to 15 minutes.

Table 1

Experimental design: Participants were assigned to one of four sequences. All sequences consisted of two Non-Pain-Expectancy Blocks and two Pain-Expectancy

Sequence	Block 1	Block 2	Block 3	Block 4
A	Non-Pain	Pain	Non-Pain	Pain
B	Non-Pain	Pain	Pain	Non-Pain
C	Pain	Non-Pain	Pain	Non-Pain
D	Pain	Non-Pain	Non-Pain	Pain

Participants were given the possibility to practice with the technique of velopharyngeal closure and with the tracking task, while getting used to sit as still as possible with electrodes on the head, and while listening to the white noise through headphones. Additionally, one H_2S and one CO_2 stimulus were presented before onset of the experiment, in order to demonstrate what was meant by "non-painful" and "painful" stimuli, respectively.

During the actual experiment, expectancies were induced before each stimulus block. Before Non-Pain-Expectancy blocks participants were given the following information: "There is no chance that you will receive painful stimuli; you will only get non-painful odors". Before Pain-Expectancy blocks participants were told: "There is a chance that you will receive painful stimuli".

Non-Pain-Expectancy blocks consisted of 10 trials where participants only received the non-painful H_2S stimulus. Pain-Expectancy blocks also consisted of 10 H_2S trials. Additionally, 3 - 4 CO_2 stimuli were presented randomly during these blocks, only to induce and reinforce expectancies of pain. The CO_2 pulses were distributed evenly within blocks and no more than two CO_2 pulses were presented in succession, without a H_2S stimulus in-between. To ensure enough observations/registrations to average an ERP, reactions to H_2S during the two Non-Pain-Expectancy blocks, and reactions during the two Pain-Expectancy blocks were taken together (and from now referred to as the "non-painful condition" and the "painful condition", respectively). After the experiment, it was checked whether participants were aware of the specific test purpose (none of them were). In turn, they were debriefed about our hypotheses.

Ratings

After each stimulus block participants were asked to rate experienced arousal, stimulus intensity and pleasantness on a visual analogue scale (VAS; Aitken, 1969). Questions asked were "How did you feel during the former block?" ("very relaxed" versus "very tense"; measuring arousal), "How strong did you think the non-painful/painful stimuli were during the former block?" ("not strong at all" versus "very strong"; measuring intensity), and "How much did you like the non-painful/painful stimuli during the former block?" ("I didn't like them at all" versus "I liked them very much"; measuring pleasantness). Lines between extreme categories were 9.5 cm. Each line was measured from left to right.

Mean VAS scores (intensity and pleasantness) of all H_2S stimuli (presented during the non-painful and painful condition) were compared to the VAS scores of the CO_2 stimuli, to check whether participants rated CO_2 as more intense and more unpleasant. Furthermore, it was checked whether the cognitive manipulation had succeeded; mean arousal scores during the non-painful condition were compared to scores during the painful condition. Finally, mean intensity and pleasantness ratings of H_2S during the non-painful condition were compared with intensity and pleasantness ratings of H_2S during the painful condition, to investigate whether expectancies had any influence on subjective stimulus perception.

Event Related Potentials

EEG records of 2048 ms including a 500 ms pre-stimulus period were obtained from the midline sites Fz (frontal), Cz (central), and Pz (parietal) of the international 10-20 system, referenced to linked earlobes (A1+A2) and grounded on the forehead. Eye-blink artefacts were monitored from Fp2/A1+A2, and single recordings with artefacts larger than 50 μV during the critical recording period were discarded. The records were amplified, filtered (bandpass 0.02-15 Hz), digitized (250

Hz sampling frequency), stored on disk, and averaged off-line separately for electrode sites and the two expectancy conditions (non-painful versus painful). Base-to-peak amplitudes and latencies of N1 and P2 were evaluated.

Results

Ratings

Participants rated CO_2 as less pleasant, compared to H_2S, $t(29) = -2.19$, $p = .04$ ($M_{CO2} = 1.50$, $SD = 1.69$, $M_{H2S} = 2.42$, $SD = 1.79$), and as more intense, $t(29) = 6.56$, $p < .01$ ($M_{CO2} = 6.35$, $SD = 2.20$, $M_{H2S} = 3.20$, $SD = 1.55$). For the non-painful and painful condition subjective arousal, stimulus intensity and pleasantness mean VAS scores are shown in Table 2. Participants indicated to feel more tense during the painful condition, compared to the non-painful condition, $t(29) = 7.19$, $p < .01$, indicating that the CO_2 trials during the painful condition had indeed led to more arousal, because of the possible occurrence of the painful stimulus. Experienced intensity and pleasantness of H_2S did not differ significantly between the two conditions.

Table 2

Mean arousal, intensity and pleasantness ratings (SDs between parentheses) for the non-painful and painful condition

	Non-Painful	**Painful**
Arousal	2.73 (1.61)	4.82 (1.64)
Intensity H_2S	3.41 (1.74)	2.98 (1.60)
Pleasantness H_2S	2.35 (1.94)	2.49 (1.86)

Event Related Potentials

Individual and averaged EEG traces of both the non-painful and painful condition are depicted in Figure 1.

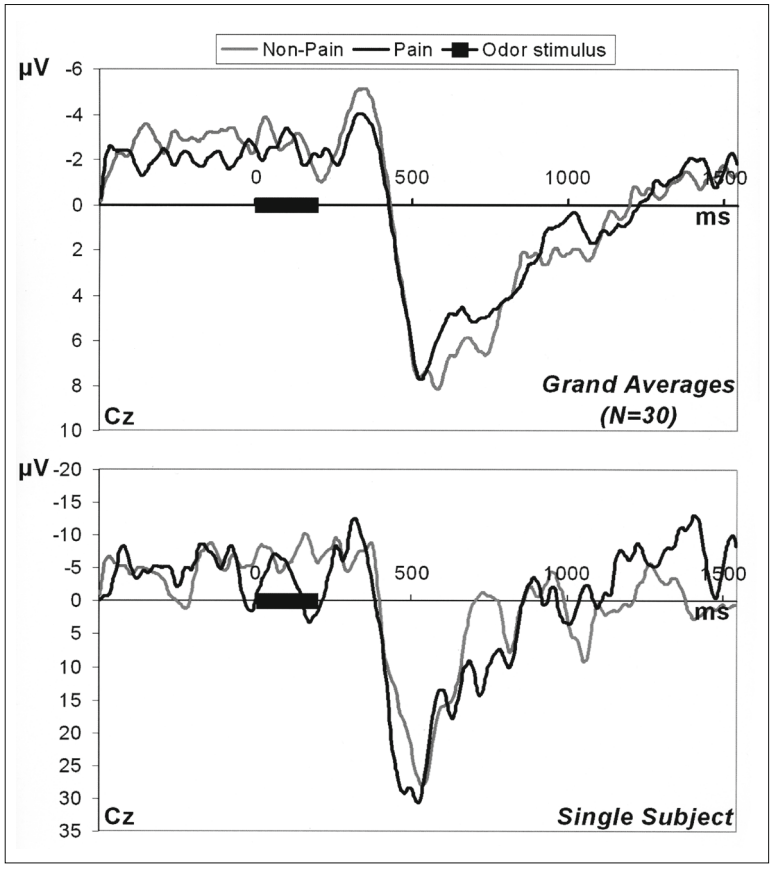

Figure 1. Grand average olfactory ERP (upper panel) and single subject olfactory ERP (lower panel) in response to the odor stimulus, compared between the non-painful and painful condition. The electrode site depicted is Cz.

Amplitudes

Mean amplitudes and standard deviations of N1 and P2, recorded at Fz, Cz, and Pz are presented in Table 3. Two repeated measures ANOVAs with within-subject factors "Electrode Site" (Fz, Cz, Pz) and "Expectancy Condition" (Painful versus Non-Painful), conducted separately for the dependent variables N1 and P2 amplitudes revealed no significant main effects of Expectancy Condition, $F(1,24) = 1.52$, $p = .23$ (for N1), $F(1,24) = .24$, $p = .63$ (for P2). For the P2 peak, there was a significant main effect of the factor Electrode Site, $F(2,23) = 18.02$, $p < .01$. Post-hoc testing

with Bonferroni corrections demonstrated that P2 amplitude was in general highest at Pz, and lowest at Fz, as it is expected for OERP (Hummel & Kobal, 2002). No significant interactions between the factors Electrode Site and Expectancy Condition were found on amplitudes, $F(2,23) = 2.33$, $p = .12$ (for N1), $F(2,23) = 1.38$, $p = .27$ (for P2).

Table 3

Mean amplitudes in μV and latencies in ms (SDs in parentheses) for N1 and P2, recorded at electrode sites Fz, Cz and Pz, separately shown for the non-painful and painful condition

Peak – Condition	Fz	Cz	Pz
Amplitudes			
N1 – Non-Pain	-3.07 (3.74)	-4.73 (6.89)	-5.10 (5.67)
N1 – Pain	-3.50 (3.00)	-4.50 (3.77)	-4.62 (4.24)
P2 – Non-Pain	10.54 (7.52)	16.02 (8.02)	17.27 (8.52)
P2 – Pain	10.51 (8.81)	14.70 (8.10)	16.17 (8.44)
Latencies			
N1 – Non-pain	352 (67)	338 (57)	345 (47)
N1 – Pain	327 (55)	336 (63)	338 (48)
P2 – Non-pain	561 (95)	572 (94)	575 (103)
P2 – Pain	554 (87)	558 (85)	557 (86)

Latencies

Mean latencies and standard deviations of N1 and P2, recorded at Fz, Cz, and Pz are presented in Table 3 and Figure 2. Two repeated measures ANOVAs with within-subject factors "Electrode Site" (Fz, Cz, Pz) and "Expectancy Condition" (Painful vs. Non-Painful), conducted separately for the dependent variables N1 and P2 latencies showed a significant main effect of Expectancy Condition at the N1 latency, $F(1,24) = 4.94$, $p = .04$, indicating that N1 latencies were shorter during the painful condition, compared to the non-painful condition ($M_{pain} = 334$, $SD = 48$; $M_{non\text{-}pain} = 345$, $SD = 55$). The main effect of Expectancy Condition on P2 latencies failed to reach significance, $F(1,24) = .67$, $p = .42$. However, on average, P2 latencies exhibited the same changes as they had been observed for the latencies of N1 (see Figure 2, panel B). No significant interactions between the factors Electrode Site and Expectancy Condition were found on latencies, $F(2,23) = .80$, $p = .46$ (for N1), $F(2,23) = .62$, $p = .55$ (for P2).

Discussion

The present study set out to investigate whether expectancy of chemosensory irritation/pain influences early perceptual processing of an, otherwise safe but unpleasant, olfactory stimulus. We investigated OERP signals in response to the non-painful odor H_2S under two different expectancy conditions: One where participants expected chemosensory pain and one where they did not

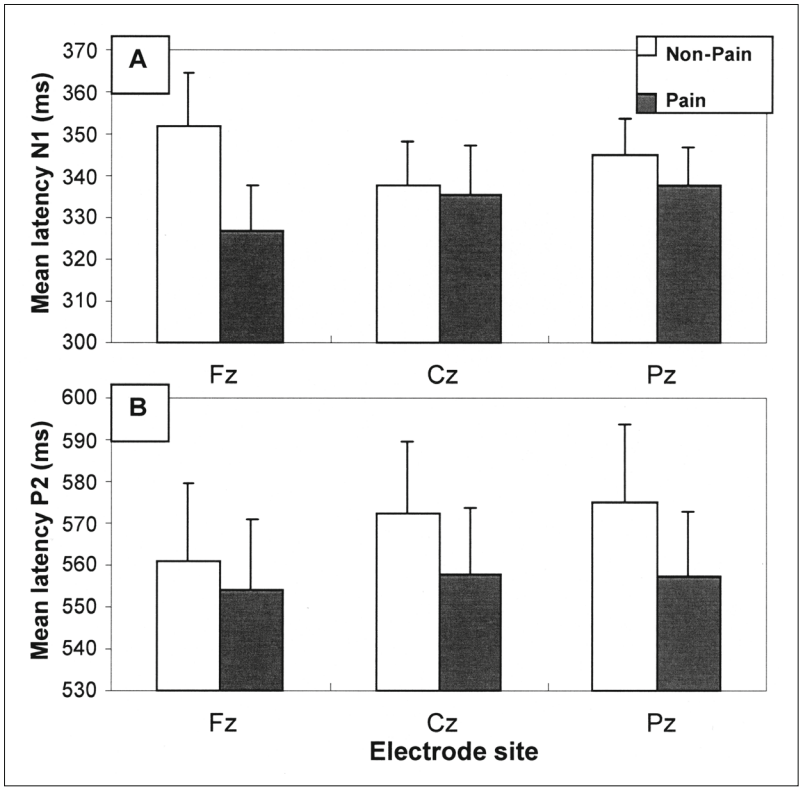

Figure 2. Latencies of the N1 and P2 peak in ms, compared between the non-painful and painful condition, separately shown for electrode sites Fz, Cz, and Pz.

expect any pain. It was concluded that 1) both early and late peaks did not increase in amplitude during the painful condition as expected, but that 2) pain-expectancy influenced processing speed: N1 latencies were significantly shorter within the painful condition, compared to the non-painful condition. Thus, expectancies of chemosensory pain increased processing speed at the early olfactory N1 peak, which is related to the encoding of exogenous stimulus characteristics such as stimulus intensity and quality. This suggests that expectancies have an influence on information processing of chemosensory stimuli at a very basic and early perceptual level. Two questions need to be addressed: First, what exactly does the finding of a shortened latency of the N1 peak imply, and secondly, why were no effects found on the late peak of the signal?

Relevant findings reported in the literature with respect to our results relate to the effects of selective attention on the N1 peak. Pause (2002) reviewed three studies on the influence of selective attention. In these studies, attention was manipulated by having participants attend to the stimuli in one condition and ignore them in the other. Aside from effects on the amplitude of the late cognitive peak, shorter latencies of the N1 in the attend condition were reported. Although it was not our intention to manipulate attention in the present research, the specific manipulation

of expectancy would naturally lead the participants to "get ready" and attend selectively to the stimulus, or essential features thereof, resulting in increased speed of processing of the stimulus. On the other hand, it is important to note that for selective attention to be assessable, (at least) two stimuli or tasks need to be presented simultaneously, such that the participant can attend to either one or the other. In that sense, our task gives no indication of selective attention, as participants were presented with only a single stimulus at the time[4].

Related to this, Krauel et al. (1998) noted that attentional effects on the early sensory components have not been reported in visuo-spatial attention tasks and are therefore interesting in the context of olfaction, because "it implies a high share of temporal coding within olfactory processing" (Krauel et al., 1998, p. 429; see also Fabiani et al., 2000). Citing Näätänen (1992), they go on to state that attentional modulation of the more exogenous components such as the N1 suggests that neuronal transmission is already influenced before the "initial stimulus representation". This notion sounds like an equivalent of what is known in visual perception research as the "perceptual anticipation theory" (Kosslyn & Thompson, 2003). This theory posits that the strong anticipation of perceiving an object or scene can actually lead to the creation of a depictive representation (in the early visual cortex) resulting in a mental image. Furthermore, the act of looking for a characteristic in an imaged object or scene can lead to the generation of an image of that characteristic. Returning to chemosensory perception and the results reported here, perceptual anticipation would imply that anticipation of trigeminal pain could lead to the activation of a somatosensory representation of this type of pain which facilitates the subsequent discrimination between pain and olfaction, resulting in reduced N1 latencies.

The fact that no P2 changes were observed implies that there were no major differences in salience of the H_2S stimulus between the "non-pain" and "pain" expectation condition. We had predicted that the expectation of a noxious chemosensory stimulus will alter early processing and interpretation of a safe chemosensory stimulus. There are, however, various explanations for the absence of this effect. First of all, the stimuli we used were fairly easy to discriminate. CO_2, which was used as the trigeminal stimulus to induce pain, has little or no odor (Frölich, 1851). H_2S, on the other hand, has a very typical odor, but does not cause any trigeminal sensation at the concentration that was used (Kobal & Hummel, 1998). Consequently, in order for participants to quickly decide whether or not the stimulus they were presented with was the painful one, they only had to attend to the odor. In other words, as soon as they perceived the odor, they knew they were receiving a safe trial and any additional effects of salience or interpretation related to the

[4] As one reviewer pointed out, the tracking task also requires attention. As a result of pain versus non-pain expectancy conditions, there could be associated variations in attention allocated to the odor versus the tracking task. In order to evaluate this post-hoc explanation, a new study would have to be conducted. However, such variations in attention do not affect our main conclusion, which hold that expecting pain decreased N1 peak latency.

expectation failed to carry over to the late ERP peak. The discrimination between olfactory and trigeminal stimuli may have been facilitated by the fact that olfactory information seems to be processed faster than trigeminally mediated information (Geisler & Murphy, 2000). The overall implication is that when stimuli associated with possible danger are sufficiently discriminable, expectations have only limited effect on how the information is processed.

Another explanation for the absence of marked effects on the P2 lies in the frequency with which the CO_2 stimulus was actually presented during the painful condition. In a block-design, only 3-4 CO_2 trials were presented for every 10 H_2S trials in a "pain" block, which was done to reduce any discomfort on part of the participant as much as possible. Since most stimuli were not painful after all, and participants knew the majority of trials would be safe, effects of salience might have been minor.

The fact that no effects of expectation of pain were found on the later cognitive components is interesting in itself. It suggests that adding a special feature to an ambiguous stimulus could serve to disambiguate that stimulus and affect information processing. In other words, if some kind of safety signal is added to a stimulus that might otherwise be interpreted as harmful, potential interpretations of that stimulus as dangerous or harmful does not take place.

Apart from clarifying the effect of pain expectancy on the N1 peak and the absence of effects on the P2 peak, there are other issues which need to be addressed. It has been demonstrated that prior exposure to a trigeminal stimulus can influence odor perception later on (Jacquot et al., 2004). Our intention was to increase feelings of arousal by warning participants for painful stimuli. The CO_2 stimuli during these parts of the experiment served only to reinforce expectancy and to demonstrate that the warning was a reliable one. However, due to this experimental design, the pain condition and the non-pain condition differed in two ways. Besides various verbal manipulations, the number of CO_2 presentations differed per condition (3-4 trials per Pain Expectancy Blocks versus none per Non-Pain Expectancy Blocks). One may thus ask whether higher ratings of arousal in the pain expectancy condition exhibited a reaction to our verbal expectancy induction or to the actual experience of pain due to the CO_2. Similarly, effects found on the N1 latency could be mediated by expectations, but also by pain experiences. However, due to our experimental design we are fairly sure that higher arousal ratings and shorter N1 latencies can be subscribed to our cognitive manipulation, not actual effects of CO_2. Participants received only 3 to 4 trials of 500 ms of CO_2 per Pain-Expectancy Block. In sum, participants were exposed to CO_2 for 3.5 seconds during the entire experiment. Additionally, there was always at least a one-minute break between a CO_2 trial and the next odor presentation to assure enough time for receptor cells to stabilize again before the next stimulus delivery (Hummel & Kobal, 2002).

Finally, one may ask why participants did not rate the odor as more intense during the painful condition, compared to the non-painful condition, as an expectation of possible harm was believed to increase intensity ratings (Dalton, 1999). However, by taking our ERP results into account, the absence of expectancy effects on subjective ratings correspond to the absence of effects on the late cognitive P2 peak. In other words, no effect of our expectancy induction was seen on two variables

measuring more interpretational-related aspects of perception. As already stated, it is highly likely that this results from the distinctness of the two stimuli that were used. As soon as participants smelled the odor, they knew that the stimulus was the safe one, and effects of salience had no influence on "late" subjective intensity or pleasantness ratings.

In conclusion, the results from this study reflect effects of expectation on early perceptual processing in the sense that expecting a painful chemosensory stimulus leads to faster encoding of exogenous physical characteristics of other incoming stimuli. As soon as the incoming stimulus is determined not to match, interpretation in terms of the alternative (in this case "safe") stimulus is made. Further encoding and interpretation of the stimulus are no longer affected by the expectation that the stimulus will be painful. In this study, perception of a "safe" chemosensory stimulus was not affected by expectations of a painful chemosensory stimulus. Thus, perceivers were not "fooled" by advance warnings. An explanation in terms of the discriminability of the employed stimuli was offered. In future experiments, it might be worthwhile to use less discriminative stimuli. It may be expected that the expectation of a painful stimulus accompanied by an odor is more likely to affect the perception of a similar, but non-painful, odor accompanied by changes in both the N1 and P2 peaks.

Acknowledgments

The authors would like to thank Joke Baas, Jan Kroeze, Nisan Mol, Franziska Krone, Simona Negoias, and Marga Veldhuizen for their contribution to this research. This work was funded by NWO grant 452-03-334 to the second author.

References

Aitken, R. C. (1969). Measurements of feelings using visual analogue scale. *Proceedings of the Royal Society of Medicine, 62*, 989-996.

Bell, I. R., Miller, C. S., Schwartz, G. E., Peterson, J. M., & Amend, D. (1996). Neuropsychiatric and somatic characteristics of young adults with and without self-reported chemical odor intolerance and chemical sensitivity. *Archives of Environmental Health, 51*, 9-21.

Bruner, J. S., & Goodman, C. C. (1947). Value and need as organizing factors in perception. *Journal of Abnormal Social Psychology, 42*, 33-44.

Dalton, P. (1999). Cognitive influences on health symptoms from acute chemical exposure. *Health Psychology, 18*, 579-590.

Dayal, H. H., Baranowski, T., Li, Y. H., & Morris, R. (1994). Hazardous chemicals: psychological dimensions of the health sequelae of a community exposure in Texas. *Journal of Epidemiology and Community Health, 48*, 560-568.

De Araujo, I. E., Rolls, E. T., Velazco, M. I., Margot, C., & Cayeux, I. (2005). Cognitive modulation of olfactory processing. *Neuron, 46*, 671 – 679.

Fabiani, M., Gratton, G., & Coles, M. G. H. (2000). Event-related brain potentials. In: Cacioppo, J.T., Tassinary, L.G., Berntson, G.G. (Eds.), *Handbook of Psychophysiology* (pp. 53-84), 2nd edn., New York: Cambridge University Press.

Fröhlich, R. (1851). Ueber einige Modificationen des Geruchsinnes. Akad. Wiss. Wien, math.-nat. CL, 6, 322-328.

Ganis, G., Thompson, W. L., Mast, F. W., & Kosslyn, S M. (2003). Visual imagery in cerebral visual dysfunction. *Neurologic Clinics, 21*, 631-646.

Gardner, H. (1987). *The mind's new science: A history of the cognitive revolution*. New York: Basic Books.

Geisler, M. W. & Murphy, C. (2000). Event-related brain potentials to attended and ignored olfactory and trigeminal stimuli. *International Journal of Psychophysiology, 37*, 309 – 315.

Gottfried, J. A., O'Doherty, J., & Dolan, R. J. (2002). Appetitive and aversive olfactory learning in humans studied using event-related functional magnetic resonance imaging. *Journal of Neuroscience, 22*, 10829-10837.

Herz, R. S., & Von Clef, J. (2001). The influence of verbal labelling on the perception of odors: evidence for olfactory illusions? *Perception, 30,* 381 – 391.

Hummel, T., & Kobal, G. (2002). Olfactory event related potentials. In: Simon, S., Nicolelis, M. (Eds.), *Methods in Chemosensory Research*, CRC press, Boca Raton.

Jacquot, L., Monnin, J., & Brand, G. (2004). Influence of nasal trigeminal stimuli on olfactory sensitivity. *Comptes Rendus Biologies, 327*, 305-311.

Kobal, G., Klimek, L., Wolfensberger, M., Gudziol, H., Temmel, A., Owen, C. M., Seeber, H., Pauli, E., & Hummel, T. (2000). Multicenter investigation of 1036 subjects using a standardized method for the assessment of olfactory function combining tests of odor identification, odor discrimination, and olfactory thresholds. *European Archives of Otorhinolaryngology, 257*, 205-211.

Kobal, G. (1981). Elektrophysiologische Untersuchungen des Menschlichen Geruchssinns. Thieme Verlag, Stuttgart.

Kobal, G., & Hummel, T. (1998). Olfactory and intranasal trigeminal event-related potentials in anosmic patients. *Laryngoscope, 108*, 1033-1035.

Kosslyn, S. M., & Thompson, W. L. (2003). When is early visual cortex activated during visual mental imagery? *Psychological Bulletin, 129*, 723-746.

Krauel, K., Pause, B. M., Sojka, B., Schott, P., & Ferstl, R. (1998). Attentional modulation of central odor processing. *Chemical Senses, 23*, 423-432.

Lee, T. S., Mumford, D., Romero, R., & Lamme, V. A. (1998). The role of the primary visual cortex in higher level vision. *Vision Research, 38*, 2429-2454.

Lercher, P., Schmitzberger, R., & Kofler, W. (1995). Perceived traffic air pollution, associated behavior and health in an alpine area. *The Science of the Total Environment, 169*, 71-74.

Lundström, J. N, & Hummel, T. (2006). Sex-specific hemispheric differences in cortical activation to a bimodal odor. *Behavioural Brain Research, 166*, 197-203.

Lundsröm, J. N., Seven, S., Olsson, M. J., Schaal, B., & Hummel, T. (2006). Olfactory Event-Related Potentials reflect individual differences in odor valence perception. *Chemical Senses, 31*, 705-711.

Marr, D. (1982). *Vision: A Computational Investigation in the Human Representation and Processing of Visual Information*, W.H. Freeman, San Francisco.

Nitschke, J. B., Dixon, G. E., Sarinopoulos, I., Short, S. J., Cohen, J. D., Smith, E. E., Kosslyn, S. M., Rose, R. M., & Davidson, R. J. (2006). Altering Expectancy dampens neural response to aversive taste in primary taste cortex. *Nature Neuroscience, 9*, 435-442.

Nordin, S., Martinkauppi, M., Olofsson, J., Hummel, T., Millqvist, E., & Bende, M. (2005). Chemosensory perception and event-related potentials in self-reported chemical hypersensitivity. *International Journal of Psychophysiology, 55*, 243-255.

Pause, B. M., & Krauel, K. (2000). Chemosensory event-related potentials (CSERP) as a key to the psychology of odors. *International Journal of Psychophysiology, 36*, 105 – 122

Pause, B. M. (2002). Human brain activity during the first second after odor presentation (pp. 309-324). In: Rouby, C., Schaal, B., Dubois, D., Gervais, R., Holley, A. (Eds.), *Olfaction, taste, and cognition*. Cambridge: Cambridge University Press.

Ross, P. M., Whysner, J., Covello, V. T., Kuschner, M., Rifkind, A. B., Sedler, M. J., Trichopoulos, D., & Williams, G. M. (1999). Olfaction and symptoms in the multiple chemical sensitivities syndrome. *Preventive Medicine, 28*, 467-480.

Schiffman, S. S. (1998). Livestock odors: implications for human health and well-being. *Journal of Animal Science, 76*, 1343-1355.

Schiffman, S. S., Walker, J. M., Dalton, P., Lorig, T. S., Raymer, J. H., Shusterman, D., & Williams, C. M. (2000). Potential health effects of odor from animal operations, wastewater treatment, and recycling of by products. *Journal of Agromedicine, 7*, 7-81.

Sterzer, P., & Rees, G. (2006). Perceived size matters. *Nature Neuroscience, 9*, 302-304.

Stuck, B. A., Frey, S., Freiburg, C., Hörmann, K., Zahnert, T., & Hummel, T. (2006). Chemosensory event-related potentials in relation to side of stimulation, age, sex, and stimulus concentration. *Clinical Neurophysiology, 117*, 1367-1375.

Chapter 5

Conditioning odor to trigeminal irritation alters odor perception: Evidence from olfactory event Related Potential Research

This chapter is based on:
Bulsing, P.J., Smeets, M.A.M., Gemeinhardt, C., Laverman, M., Schuster, B., van den Hout, M.A., & Hummel, T. Conditioning Odor to Trigeminal Irritation alters Odor Perception: Evidence from Olfactory Event Related Potential Research (submitted for publication).

Abstract

The influence of experiential factors on the final olfactory percept turns out to be much more substantial than previously thought. The aim of the present research was to investigate such influences in an ecologically valid, health-relevant context: We studied whether learning that an odor can cause adverse health effects alters perception of that odor. An odor (Study 1: H_2S; Study 2: PEA) was classically conditioned to trigeminal irritation (caused by CO_2 presentation). Olfactory Event Related Potentials (OERPs) were measured, which enabled us to determine effects of learning on the temporal course of olfactory processing. When the conditioned odor was H_2S, latencies and amplitudes of both the N1 and P2 peak of the ERP were shortened and increased, respectively, suggesting faster and more intense processing of early encoding as well as stimulus salience information. When the conditioned odor was PEA, only the N1 amplitude was increased. These results, obtained with OERP, provide converging evidence for earlier and comparable conclusions regarding the profound top-down influence of cognition on odor perception reached with fMRI. Furthermore, the results suggest that a-priori hedonic valence of an odor affects how susceptible the olfactory percept is to modulation via top-down learning.

Introduction

Evidence has accumulated supporting a profound top-down influence of experiential factors on olfactory perception (for an overview see Wilson and Stevenson, 2006). A number of recent studies have demonstrated these effects employing fMRI, e.g. showing that aversive conditioning induces plasticity in the primary olfactory (piriform) cortex resulting in enhanced discriminability of previously indistinguishable odors (Li et al., 2008), and that providing the visual word descriptor "body odor" versus "cheddar cheese" along with an identical test odor resulted not only in evaluation of that odor as significantly more unpleasant, but also in significant and meaningful differences in activation of medial orbitofrontal/anterior cingulate cortex and amygdala (De Araujo et al., 2005). The combined findings from these studies reinforce the conclusions from earlier psychophysical studies (such as by Herz and Von Clef, 2001) that information processing modulates odor perception in a top-down fashion.

Aside from the obvious relevance for our general understanding of odor perception, the notion that experience, cognition and cortical plasticity all combine to mould our sense of smell may have profound applied implications. For example, it can facilitate our understanding of why some individuals perceive otherwise innocuous odors in the environment as hazardous and attribute health symptoms to these exposures (Schiffman et al., 2000). Various experiments by Dalton and her group (Dalton et al.,1997; Dalton, 1999) demonstrated that inducing beliefs about harmful consequences of exposure to certain odorants resulted in both increased intensity and irritancy perception of those odorants as well as enhanced frequency and intensity of symptom reports. These findings led Dalton to propose that changes in health effects and symptom reporting are modulated by changes in odor perception (Dalton, 2002, 2003). Dalton's perspective is supported by a recent, systematic review of 37 laboratory provocation studies in individuals with multiple chemical sensitivities (MCS) involving both a "real" as well as a placebo provocation or control resting state (Das-Munshi et al., 2006). The authors found that individuals with MCS were less likely to respond to active provocation under conditions of strict blinding or when the experimental stimulus was masked. They concluded that, most likely, behavioral conditioning is the mechanism of action leading MCS sufferers to respond to the provocation, and they recommend that future work focus on such approaches. In sum, top-down influences in the form of behavioral or (cognitive) instructional learning regarding experienced or presumed health effects from environmental exposure to odors may modulate odor perception, which changes, in turn, modulate health effects that are experienced in the context of the odor.

The aim of the present research was to test the first premise, i.e. that influences of learning that an odor has adverse health consequences can alter the perceptual processing of that odor in a health-relevant context using an Olfactory Event Related Potentials (OERP) paradigm. The studies mentioned earlier employed fMRI, which has high spatial resolution, thus allowing to pinpoint where in the brain experimental manipulations take effect. In contrast, Electroencephalography (EEG) has high temporal resolution: If cognition and learning exert top- down influences on perception, correlated activities should not only be encountered in areas of the brain associated with

perceptual processing, but they should also occur early during information processing, when odor characteristics are encoded. A demonstration of early effects may be considered as converging evidence for earlier findings employing fMRI, thus strengthening the same conclusion.

In the two studies described here, we used classical conditioning to induce the expectation of adverse health effects from smelling an odor as recommended by Das-Munshi et al. (2006). An odor was conditioned to stimulation of the trigeminal nerve in the nose, a combination of stimulation that may occur when encountering high concentrations of e.g. volatile solvents (Shusterman, 2001). Olfactory Event Related Potentials (ERPs) were measured, which enabled us to determine effects of learning on the temporal course of olfactory processing. A distinction is typically made between the "early" N1 peak, which has been associated with stimulus properties, such as intensity and quality, and the "late" P2 peak (in other sensory modalities often referred to as P300 or P3), which has been associated with cognitive aspects of perception, like stimulus salience or novelty (e.g. Bensafi et al., 2007; Geisler and Murphy, 2000; Krauel et al., 1998; Lundström et al., 2006; Nordin et al., 2005).

In a previous OERP-study we investigated how the expectation of pain affected odor perception (Bulsing et al., 2007) by providing participants with the information that in the following block of stimuli they would receive no painful stimuli versus some painful stimuli. The painful stimulus was the trigeminal irritant CO_2, the non-painful stimulus was the odorant H_2S, both of which were delivered to the nose using an olfactometer. Throughout a "no-pain" block, only H2S stimuli were presented, while throughout a "pain" block, the presentation of H2S trials was interspersed with 3-4 trials of CO_2 presentations to reinforce the expectation of pain. ERP registration to the odor (H_2S) presentations alone (so without interference of CO_2) were compared across the "pain" and "no pain" expectancy conditions. Results showed shortened N1 latencies during the "pain" compared to the "no-pain" condition, with no effects on N1 amplitude or P2 latency or amplitude. While these results underscore the hypothesis of early perceptual effects of expectation, it is surprising that no effects of e.g. salience were encountered on the P2. The explanation for this absence may lie in the fact that during "pain" blocks participants knew that, although they should prepare for a painful stimulus, it might as well just be the non-painful odor. The trick then became to quickly detect which of the two it is as soon as possible after trial onset. Since H_2S and CO_2 are very discriminable – the former being an odor stimulating the olfactory nerve, the latter being an irritant stimulating the trigeminal nerve- effects of expectation of pain may not have outlived the early detection phase N1 to affect the P2, as the odor was no longer salient after it had been detected as the safe chemosensory stimulus. Thus, we came up with a design where the stimulus is (the same) odorant under both the "pain" and "no-pain" condition. We used classical conditioning, as this type of learning is considered the core mechanism for inducing expectations (Domjan, 1993). Although the design of the later studies is more complicated than that of the previous study (Bulsing et al., 2007), it was more effective, as will become evident later.

For reasons outlined above, we expected successful conditioning of the odor to irritation to reflect in changes in the N1 peak, due to early top-down perceptual effects, as well as affect the "cognitive" P2 peak of the ERP, due to salience effects. Classical conditioning is often conducted using neutral stimuli

as conditioned stimuli. For adults, most naturally occurring odors already have acquired meanings, and "neutral" odors are hard to find. To investigate the influence of pre-existing hedonic value on the effect of learning on perception, we conducted two similar experiments using both an odor generally considered as unpleasant (rotten egg: Study 1) and an odor generally considered as pleasant (rose: Study 2).

Materials and Method

Participants

All participants (only females) came to the lab for screening purposes. To examine general olfactory functioning, the identification part of the Sniffin' Sticks test battery was administered (Kobal et al., 2000). If participants were unable to identify at least 9 out of 12 odors, they were excluded from further participation. Next, sensitivity to the odorant that would be used during the experiment was tested. Participants who were unable to detect at least 12 out of 15 odorant presentations, which were administered at unpredictable moments by means of an olfactometer, were excluded. Additionally, eye blink behavior in response to these presentations was checked. Participants who blinked in response to more than 50% of these presentations were also excluded, since too many blinks would distort ERP recordings during the actual experiment. CO_2 sensitivity in response to 3 CO_2 presentations, again administered at unpredictable moments, was assessed, in order to check whether participants demonstrated a genuinely adverse reaction a startle or blinking reflex, which was necessary for the cognitive manipulation (inducing CO_2 expectancy) to succeed. If a participant met all inclusion criteria, she was invited to the actual experiment performed on a separate day.

For Study 1, in which the unpleasant odor of H_2S was used, 60 participants were screened. Reasons for exclusion were low sensitivity to the stimuli (H_2S: 14 participants, CO_2: 6 participants), and blinking in response to the majority of the odor stimuli (4 participants). Five participants did not show up for the actual experiment for unknown reasons. The final H_2S group consisted of 31 participants. Mean age was 22.6 years (*SD* = 2.6). For Study 2, in which the pleasant odor of PEA was used, 55 other participants were screened. Participants were excluded because they were not sensitive enough to PEA (5 participants), or blinked too often in response to the odor presentations (12 participants). Eight participants did not show up for the actual experiment. The final group consisted of 30 participants. Mean age was 24.1 years (*SD* = 2.8). All participants signed informed consent, and received financial remuneration for their participation. Both studies were conducted in accordance with the Declaration of Helsinki on biomedical research in human participants; the protocol was reviewed by the Ethics Committee of the University of Dresden Medical School.

Stimuli

In Study 1, H_2S (10 ppm) was used as the Conditioned Stimulus (CS). In Study 2, PEA (40% v/v) was used as the CS. All CS presentations had a duration of 250 ms. CO_2 (60% v/v) was used as the aversive Unconditioned Stimulus (US). In a number of pilot studies habituation to CO_2 was ob-

served in repeated presentations, as reflected by a reduced startle reflex in response to stimulus presentation. Therefore, CO_2 pulses had a duration of 500 ms, but increased with 50 ms every 10 presentations (from 500 to 550 ms, from 550 to 600 ms, etc.), such that experienced intensity or annoyance would remain relatively high, regardless of habituation. These stimulus concentrations and durations were determined during previous experiments, with similar requirements as were posed for the present research, i.e. the odor had to be a clearly perceptible, but non-irritating stimulus, while the CO_2 pulses had to elicit clear and relatively strong irritation that was moderately painful (Bulsing et al., 2007).

Stimuli were presented by a dynamic air-dilution olfactometer (Burghart Instrument, Wedel, Germany) that allows odorant presentation without altering the mechanical or thermal conditions of the mucosa (Kobal, 1981). The stimuli were presented in a constantly flowing air stream of 7.2 L/min, with controlled temperature and humidity (36˚C, 80% relative humidity). Participants used the velopharyngeal closure breathing technique (Kobal, 1981): They were trained to use the levator veli palatini muscle to elevate the soft-palate in order to isolate the pharyngeal cavity from the nasal cavity. This technique prevents intranasal respiratory airflow, ensuring the absence of interference from respiration on stimulus presentation (Kobal, 1981), and thus stimuli could be presented non-synchronously to inhalation. They received white noise through headphones to mask the sound of clicking accompanying the presentation of stimuli.

Procedure

Upon arrival at the lab, participants received information about the experimental procedure before onset. They were asked to repeat the procedure orally, in order to check whether it was fully comprehended. If not, the procedure was explained again. Participants sat down in front of the computer screen, and electrodes and olfactometer tubes were positioned. They were thereupon reminded of the breathing technique which they had already practiced during the screening session.

The participants started with a training phase, which involved a repetition of the instructions on the computer screen. Additionally, rating of various stimulus characteristics on visual analogue scales (VAS) was practiced: 1) Pain expectancy (i.e. the degree to which participants expected to receive an exposure to CO_2, which feeling is best described as a sting: "*Do you think you will feel a painful sting in your nose after you have smelled the odor?*"; Extreme categories of the VAS: "*I don't think so*" at the left side vs. "*I think so*" at the right side of the scale), 2) Odor intensity ("*Intensity (odor)?*"; Extreme categories VAS: "*No odor/Not intense*" at the left side vs. "*Very intense*" at the right side of the scale), 3) Odor annoyance ("*Annoyance (odor)?*"; Extreme categories: "*No odor/not annoying*" vs. "*Very annoying*"), and 4) CO_2 Annoyance ("*Annoyance (sting)?*"; Extreme categories: "*No sting/not annoying*" vs. "*Very annoying*"). The experiment was programmed in E-prime (version 1.2, Psychology Software Tools). After the training, the experiment proceeded with an acquisition (conditioning) phase and a test phase. Participants were unaware of the distinction between these phases as there was no intermission between them.

Acquisition phase

In the ERP paradigm, within-subjects comparisons across conditions are preferred, due to the substantial variations between individuals in the signal (Luck, 2005). Comparing two expectancy levels *within* participants required a design in which participants were led to believe that one and the same odor could be both irritating as well as not irritating. The induction of these expectations was the aim of the Acquisition phase, and was accomplished by introducing a *discriminative* or *contextual* stimulus in the form of a visual cue that was presented prior to the CS as a predictor of whether the CS that would follow would signal the US or not. The discriminative stimuli used were a "98%" sign and the "0%" sign shown on a computer screen, with the former indicating a high chance that the odor would be paired with the painful sting of CO_2, and the latter indicating that the odor would not be paired with CO_2. Consequently, the same odor was both reinforced by the US when preceded by the 98% cue, as well as un-reinforced when preceded by the 0% cue (see the upper part of part A of Figure 1). We will further refer to these trials as 98%-odor-CO_2 trails and 0%-odor-no CO_2 trials.

A potential problem with this type of trials was that the expectation of adverse effects was determined exclusively by the discriminative stimuli 98% and 0%, and would have fully formed before actual odor onset, whereas it was our intention for the expectation to be activated no sooner than when the odor was perceived. To realize this, two control trials were devised. These constituted of combinations of the discriminative stimuli 98% and 0%, respectively, and clean air (CA) presentations (instead of odor), which were never followed by the US (to be referred to as 98%-CA-no CO_2 and 0%-CA-no CO_2 trials). Thus, by including CA presentations, participants learned that the presence of the odor was an essential factor for the presentation of trigeminal irritation, in other words: only when they perceived the 98% in combination with the odor, they should expect the irritating sting to follow, not just when seeing the 98% cue. Thus, the expectation would only fully form following onset of odor presentation, and we would be able to capture it when inspecting the associated OERP signal.

The left part of Table 1 shows the number of expectation cues and related presentations during the Acquisition phase. In agreement with the 98% cue (instead of "100%") 1 out of 10 odor presentations following the 98% cue remained un-reinforced by CO_2 during the Acquisition phase. That is, no CO_2 pulse was given here, even though the odor was present. In both expectancy conditions only 8 CA trials were presented, as opposed to 10 odor trials which would have matched the trials that involved odors as stimuli, in order to slightly shorten the experiment.

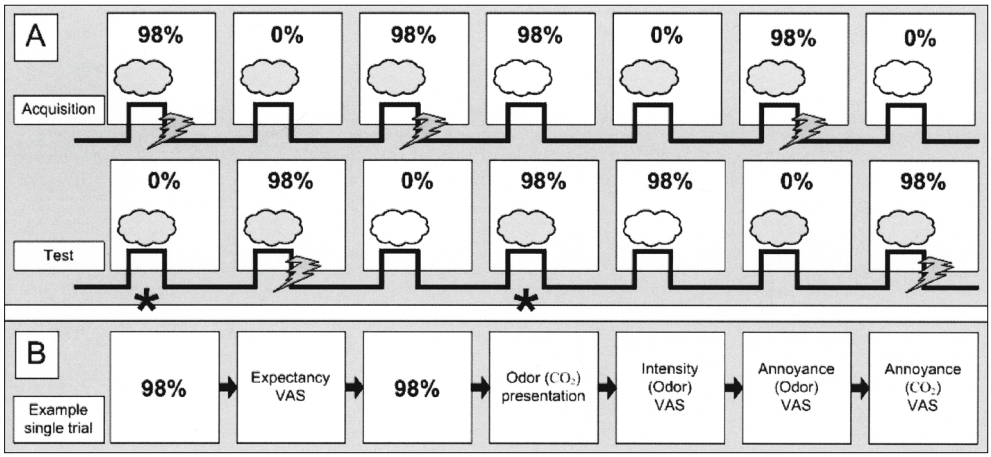

Figure 1. A) Upper part of A: Example of trials during the Acquisition phase. In this phase, participants learn that the combination of the 98% cue and the odor (dark-colored cloud) is predictive for pain (trigeminal irritation as a result of CO_2 presentation; indicated by a flash of lightning). They also learn that the 98% cue is not sufficient for pain, but that the odor is an essential factor: If the 98% cue is followed by clean air (white cloud) no pain will follow. The 0% cue always indicates safety: either the odor or clean air without CO_2 will be presented. Lower part of A: example of trials during the Test phase. This phase resembles the Acquisition phase, except that approximately 1/3 of the 98% trials where an odor is presented, remains un-reinforced, that is, no CO_2 is presented. Olfactory ERPs (not contaminated with CO_2) during these un-reinforced trials, but where pain was expected ("Pain Expectancy condition") were compared with olfactory ERPs during 0% trials where an odor was presented, but where no pain was expected ("No pain Expectancy"; both conditions indicated by *). B) Example of a single trial. Each trial starts with the presentation of the visual cue (either "98%" or "0%"), followed by the Expectancy VAS ("Do you think you will feel a painful sting in your nose after you have smelled the odor?"). In turn, the visual cue is repeated. Then, the odor (either reinforced or not by CO_2) or clean air is presented, followed by the 3 questions regarding odor intensity, odor annoyance, and CO_2 annoyance.

Table 1

Frequency of visual cues and chemosensory presentations, separately shown for the Acquisition and Test phase

Cue and related presentation(s)	Acquisition	Test
98%-odor-CO_2	9	23
98%-odor-no CO_2	1	16*
98%-CA	8	16
0%-odor-no CO_2	10	16*
0%-CA	8	16

Note. Statistical comparisons were made between the 16 reactions (ERPs and subjective ratings) to the odor during the Pain Expectancy condition (visual cue: "98%") and the 16 reactions to the odor during the No pain Expectancy condition (visual cue: "0%"; un-reinforced) of the test phase. These trials are indicated by *.

Each separate trial in the Acquisition phase took approximately 40 seconds, and consisted of the following events (see Table 2 and part B of Figure 1): 1) *Expectation cueing*, involving the presentation of the expectation cue (either "0%" or "98%") for 4 s. Following the offset of this cue participants were given maximally 6 s to rate the extent to which they expected to experience pain if an odor was presented next as a manipulation check. The expectation cue was then repeated for 6 s. This was deemed necessary after participants had reported forgetting the cue in a pilot study. There was a variable period lasting between 3 to 23 s between the offset of the Expectation cue and the onset of the odor or CA presentation. This period served to increase uncertainty about stimulus onset such that expectations could build. The exact duration depended on the speed of completing the sensory ratings on a previous trial, as will be explained below. 2) *Odor Presentation*, consisting of the presentation of the odor or CA, followed by a CO_2 pulse in specific cases, after a delay of 1500 ms. The entire odor presentation phase always had a duration of 3 s, even if no CO_2 pulse was presented. 3) *Sensory rating*, where participants rated odor intensity, odor annoyance, and CO_2 annoyance. Participants were allowed up to 6 s to complete each of the ratings. If they answered faster than these 6 s, the program automatically moved on to the next rating question, and ultimately, to the next trial. In this manner, variations in duration of the expectation build-up could occur as they depended on individual speed of completing the ratings, with the duration of each trial remaining constant. The purpose of the variation was to maximize uncertainty with respect to the exact time of the next stimulus-onset after the second expectation cue. Trials were semi-randomly presented using two different prepared orders.

Table 2
Composition of a single trial

Phase	Events	Duration
Expectation cueing	Cue presentation ("0%" or "98%")	4 s
	Rating of expectancy (VAS)	6 s (max)
	Cue repetition	6 s
	Expectancy build-up	3 – 23 s
Odor presentation	CS / Clean air presentation	250 ms
	(Clean air)	1500 ms
	(US presentation)	500 – 700 ms
Sensory rating	Rating of intensity odor (VAS)	6 s (max)
	Rating of annoyance odor (VAS)	6 s (max)
	Rating of annoyance CO_2 (VAS)	6 s (max)

Test phase

In the Test phase, the effects of conditioning an odor to sensory irritation (which was established in the acquisition phase) on the perception of the odor were assessed. The procedure during the test phase was almost identical to the Acquisition phase, with the only difference being the num-

ber of trials per stimulus combination. In the right part of Table 1 the number of expectation cues and subsequent presentations during the test phase are displayed. Since the intention was to conduct a within-participant comparison of the OERP signal associated with perception of the odor across the two expectancy conditions without contamination of the signal by CO_2 presentation, 16[5] of each of the crucial type of trials (i.e. 98%-odor-no CO_2 or Pain Expectancy condition and 0%-odor-no CO_2 or No pain Expectancy condition) were included. In order to maintain high expectations of pain following the combination of the 98% cue and the odor, and thus prevent extinction, 24 reinforced 98%-odor trials followed by CO_2 were presented (and thus almost 2/3 of the 98%-odor trials were reinforced).

After the experiment, it was checked whether participants were aware of the purpose of the experiment.

Rating analyses

Mean VAS ratings of pain expectancy during the Pain Expectancy condition versus the No pain Expectancy condition were compared, in order to check whether conditioning had succeeded. Furthermore, it was checked whether the US (CO_2) remained sufficiently annoying during the entire experiment. Mean VAS ratings of CO_2 annoyance during the first half of the experiment were compared to mean VAS ratings during the second half of the experiment. Mean VAS scores of experienced intensity and annoyance of the 16 98%-odor-no CO_2 (Pain Expectancy condition) and the 16 0%-odor-no CO_2 (No pain Expectancy condition) were compared, to investigate whether the perception of the odor had changed as a result of conditioning.

OERP Recordings and Analysis

EEG signals were recorded for 2048 ms per trial, covering a 500 ms pre-stimulus period (baseline), 250 ms of CS (odor or clean air) presentation, followed by s 1334 post-stimulus period which was sufficient to capture all EEG responses to the stimulus. Recordings were obtained from the midline sites Fz (frontal), Cz (central), and Pz (parietal) of the international 10-20 system, referenced to linked earlobes (A1+A2). This duration has proven to be sufficient to capture all EEG potentials related to an olfactory event. Eye-blink artefacts were monitored from Fp2/A1+A2, and single recordings with artefacts larger than 50 μV during the critical recording period were discarded. The records were amplified, filtered (bandpass 0.02-15 Hz), digitized (250 Hz sampling frequency), stored on disk, and averaged off-line separately for the three electrode sites and the two expectancy conditions (Pain versus No pain Expectancy). Base-to-peak amplitudes and latencies (the amount of neuronal activation allocated to processing and processing speed, respectively; Hummel and Kobal, 2002) of N1 and P2 were examined.

[5] At least 8 trials should be averaged to obtain a reliable olfactory ERP (Hummel & Kobal, 2002).We chose to average 16 identical trials to improve the signal.

For both Studies 1 and 2 Repeated Measures ANOVAs with within-subject factors "Electrode Site" (Fz, Cz, Pz), and "Expectancy Condition" (Pain versus No pain) were conducted for the dependent variables N1 and P2 amplitudes and latencies. The alpha level was set at 0.05. All tests were conducted one-tailed unless indicated, based on our expectation that classical conditioning might lead to shorter latencies and higher amplitudes.

Results

STUDY 1

Ratings H_2S

Manipulation checks: Pain expectancy ratings were significantly higher in the Pain Expectancy condition as opposed to the No pain Expectancy condition (M_{pain} = 81, SD = 18, $M_{no\ pain}$ = 5, SD = 6; $t(30) = 23.59$, $p < .01$), indicating that the context manipulation had succeeded. In other words, if participants saw the "98%" cue, they indeed expected the US, whereas the "0%" cue induced (almost) no US expectancy. In order to check whether US annoyance remained sufficiently high during the experiment, as the US had to remain an unpleasant experience throughout the experiment, annoyance ratings from the first half of the experiment were compared to ratings from the second half of the experiment. US habituation during the experiment did not occur: US annoyance ratings did not change significantly over the course of the experiment ($M_{first\ half}$ = 64, SD = 20, $M_{second\ half}$ = 69, SD = 23; $t(30) = 1.84$, $p = .08$, two-tailed).

Effects of manipulation: Odor intensity ratings were not significantly higher in the Pain Expectancy condition compared to the No pain Expectancy condition (M_{pain} = 27, SD = 17, $M_{no\ pain}$ = 25, SD = 16; $t(30) = 1.29$, $p = .10$). Odor annoyance ratings, on the other hand, did differ significantly between conditions, where the odor was rated as more annoying in the Pain condition compared to the No pain condition (M_{pain} = 25, SD = 19, $M_{no\ pain}$ = 22, SD = 18; $t(30) = -2.19$, $p = .02$). This demonstrates that learned associations between an odor and an aversive consequence altered the perceived hedonics of the odor.

Event-related potential results H_2S

N1 peak

Mean amplitudes and latencies of the N1 peak, recorded at Fz, Cz, and Pz are presented in Table 3. Figure 2 (left panel) shows the grand average olfactory ERPs per electrode site. On N1 amplitude, a significant main effect of Expectancy Condition was found ($F(1,30) = 5.80$, $p = .01$), indicating that conditioning the odor to the US increased the early N1 amplitude (M_{pain} = -4.47, SD = 4.08; $M_{no\ pain}$ = -3.01, SD = 2.90). There was no main effect of Electrode ($F < 1.0$), but an interaction effect between Expectancy Condition and Electrode ($F(2,29) = 3.92$, $p = .02$). Post-hoc tests with Bonferroni corrections demonstrated that the difference between the Pain and No pain Expectancy

condition was significant at electrodes Cz ($p < .01$) and Pz ($p = .01$), but not at Fz. This indicates that different brain areas were activated to different degrees under the two conditions (see also Kettenmann et al., 1996).

On N1 latency, a significant main effect of Expectancy Condition was found ($F(1,30) = 23.48$, $p < .01$), revealing that latencies were shorter during the Pain Expectancy condition compared to the No pain Expectancy condition ($M_{pain} = 327$, $SD = 63$; $M_{no\ pain} = 394$, $SD = 76$). There was also a main effect of Electrode ($F(2,29) = 2.53$, $p = .05$). Post-hoc test with Bonferroni corrections demonstrated that latencies were shortest, although not significantly so, at Cz and longest at Fz ($M_{Fz} = 365$, $SD = 59$, $M_{Cz} = 357$, $SD = 59$, $M_{Pz} = 359$, $SD = 59$; two-tailed). There was no interaction effect between Expectancy Condition and Electrode ($F(2,29) = 1.12$, $p = .17$).

Table 3

Study 1 (H_2S): Mean amplitudes in μV and latencies in ms (SDs in parentheses) for the N1 and P2 peak, recorded at electrode sites Fz, Cz, and Pz, separately shown for the Pain and the No pain Expectancy condition

	Electrode Site		
Condition	**Fz**	**Cz**	**Pz**
Amplitudes N1			
Pain	-4.11 (3.66)	-4.72 (4.44)	-4.59 (4.99)
No pain	-3.86 (3.48)	-2.78 (3.38)	-2.39 (3.14)
Latencies N1			
Pain	333 (65)	322 (65)	327 (63)
No pain	398 (76)	392 (76)	391 (78)
Amplitudes P2			
Pain	8.69 (4.45)	11.67 (6.03)	12.72 (6.14)
No pain	6.95 (4.49)	10.00 (5.26)	11.54 (5.57)
Latencies P2			
Pain	499 (68)	493 (72)	497 (73)
No pain	533 (81)	525 (76)	526 (75)

P2 peak

Mean amplitudes and latencies of the P2 peak, recorded at Fz, Cz, and Pz are presented in Table 3 (see again the left panel of Figure 2 for the grand average ERPs per electrode site). On P2 amplitude, a significant main effect of Expectancy Condition was found ($F(1,30) = 12.73$, $p < .01$), showing that conditioning the odor to the US increased the P2 amplitude ($M_{pain} = 11.03$, $SD = 5.27$; $M_{no\ pain} = 9.50$, $SD = 4.61$). Additionally, a significant main effect of Electrode was found ($F(2,29) = 22.35$, $p < .01$). Post-hoc testing with Bonferroni corrections demonstrated that P2 amplitude was general highest at Pz, and lowest at Fz, as is expected for olfactory ERPs (Hummel and Kobal, 2002; $M_{Fz} = 7.82$, $SD = 4.24$, $M_{Cz} = 10.84$, $SD = 5.47$, $M_{Pz} = 12.13$, $SD = 5.50$; all p's $< .01$, two-tailed). No

interaction effect between Electrode and Expectancy Condition was found ($F < 1.0$).

The same analysis was conducted for the dependent variable P2 latency. A significant main effect of Expectancy Condition was found ($F(1,30) = 3.52$, $p = .04$), showing that P2 latencies were shorter in the Pain Expectancy condition ($M_{pain} = 496$, $SD = 67$; $M_{no\ pain} = 528$, $SD = 76$). There was no main effect of Electrode ($F(2,29) = 1.29$, $p = .15$), and no interaction between Expectancy Condition and Electrode ($F < 1.0$).

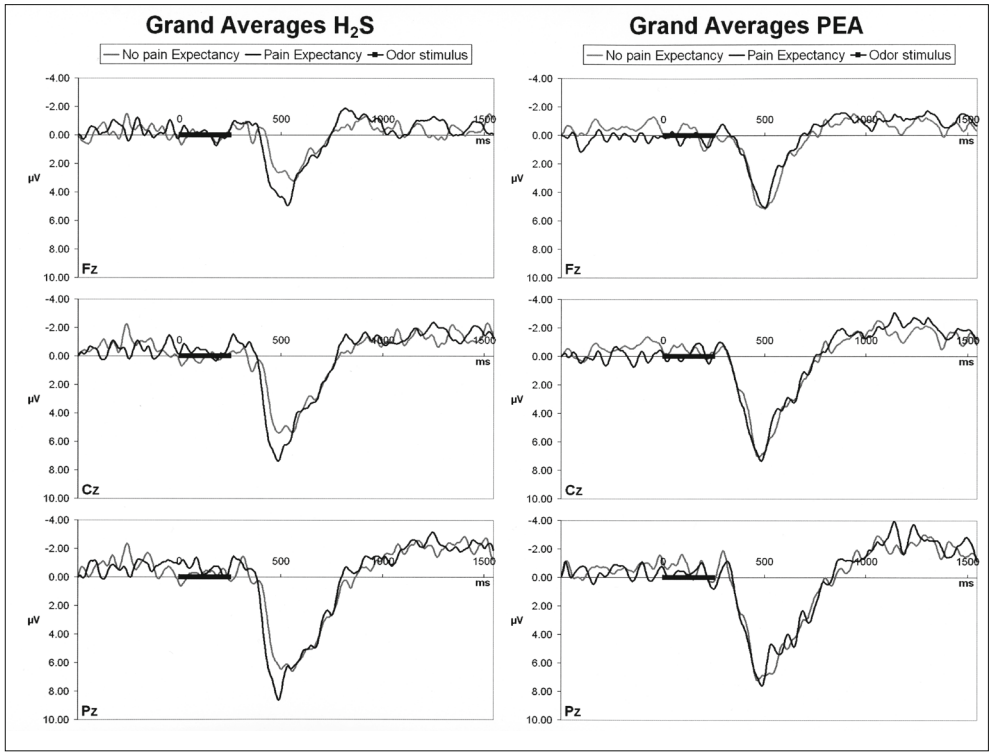

Figure 2. Grand average olfactory ERPs for H_2S (left part of the Figure) and PEA (right part of the Figure), compared between the Pain and No pain Expectancy condition, and separately depicted for the electrode sites Fz, Cz, and Pz.

Conclusion Study 1

Conditioning the unpleasant odor of H_2S to trigeminal irritation resulted in a more negative evaluation of the odor. Additionally, the N1 and P2 peak appeared earlier, and had larger amplitudes, indicating faster and more intensive processing of the conditioned odor stimulus. This suggests that learned associations between an unpleasant odor and an aversive health consequence alter the way odor characteristics are encoded (as reflected by effects on the N1 peak), and interpreted (as reflected by a changed P2 peak and evaluations). To test whether these effects are limited to aversive CSs or also occur for pleasant odors was tested in Study 2.

STUDY 2

Ratings PEA

Manipulation checks: Pain expectancy ratings were significantly higher in the Pain Expectancy condition as opposed to the No pain Expectancy condition (M_{pain} = 85, SD = 20, $M_{no\ pain}$ = 7, SD = 9; $t(29)$ = -18.79, p < .01), again indicating that the context manipulation had succeeded. In order to check whether US annoyance remained significantly high during the experiment, annoyance ratings of the first half of the experiment were compared to the second half of the experiment. Again, annoyance did not decrease due to habituation ($M_{first\ half}$ = 62, SD = 18, $M_{second\ half}$ = 66, SD = 19; $t(29)$ = -1.92, p = .06, two-tailed).

Effects of manipulation: PEA intensity ratings did not differ between conditions (M_{pain} = 19, SD = 11, $M_{no\ pain}$ = 19, SD = 13; $t(29)$ = .44, p = .33). However, annoyance ratings did, with the odor rated as significantly more annoying in the Pain Expectancy condition (M_{pain} = 6.95, SD = 7.18; $M_{no\ pain}$ = 5.61, SD = 5.82; $t(29)$ = -2.37, p = .01) even though, on a scale of 1 to 100 overall annoyance was low. Still, this demonstrates that the learned association between the odor and a negative consequence altered the way the odor was evaluated later on.

Event-related potential results PEA

N1 peak

Mean amplitudes and latencies of the N1 peak, recorded at Fz, Cz, and Pz are presented in Table 4. Figure 2 (right panel) shows the grand average olfactory ERPs per electrode site. On N1 amplitude a significant main effect of Expectancy Condition was found ($F(1,29)$ = 5.59, p = .02), indicating that conditioning PEA to the US increased the early N1 amplitude (M_{pain} = -3.97, SD = 3.15; $M_{no\ pain}$ = -2.59, SD = 2.51). There was no main effect of Electrode (F < 1.0), and no interaction effect between Expectancy Condition and Electrode ($F(2,28)$ = 2.08, p = .07).

On N1 latency no significant main effect of Expectancy Condition was found (F < 1.0). There was a main effect of Electrode ($F(2,28)$ = 2.84, p = .04). Post hoc testing with Bonferroni corrections demonstrated shortest latencies at Pz, and longest latencies at Fz, although not significantly so (M_{Fz} = 355, SD = 92, M_{Cz} = 350, SD = 95, M_{Pz} = 346, SD = 94; two-tailed). There was no interaction effect between Expectancy and Electrode (F < 1.0).

P2 peak

Mean amplitudes and latencies of the P2 peak, recorded at Fz, Cz, and Pz are presented in Table 4 (see the right panel of Figure 2 for the grand average ERPs per electrode site). On P2 amplitude, no significant main effect of Expectancy Condition was found (F < 1.0). However, a significant main effect of Electrode was found ($F(2,28)$ = 25.95, p < .01). Post-hoc testing with Bonferroni corrections demonstrated that P2 amplitude was general highest at Pz, and lowest at Fz (M_{Fz} = 8.89, SD = 4.46, M_{Cz} = 11.68, SD = 4.56, M_{Pz} = 12.13, SD = 4.20; all p's < .01, two-tailed). Again, this confirms

previous work on olfactory ERPs (Hummel and Kobal, 2002). Additionally, a significant interaction effect between Electrode and Expectancy Condition was found ($F(2,28) = 3.55$, $p = .02$). Post hoc tests showed that for both the Pain and the No pain Expectancy condition, amplitudes differed between Pz and Fz (Pz largest, Fz smallest, all p's < .01, two-tailed), whereas differences between Cz and Pz did not reach statistical significance. Once more, this indicates that the two different conditions produced differential activation of cortical generators of the P2 component.

On P2 latency, no significant main effect of Expectancy Condition was found ($F < 1.0$). However, there was a significant main effect of Electrode ($F(2,28) = 4.93$, $p = .01$). Post-hoc testing demonstrated that latencies measured at Cz were shortest, and latencies measured at Fz were longest ($M_{Fz} = 509$, $SD = 70$, $M_{Cz} = 493$, $SD = 71$, $M_{Pz} = 497$, $SD = 70$; only significant between Cz and Fz, $p = .01$, two-tailed). No interaction between Expectancy Condition and Electrode was found ($F < 1.0$).

Conclusion Study 2

Conditioning the pleasant odor of PEA to trigeminal irritation resulted in a more negative evaluation of the odor. Additionally, the N1 peak had a larger amplitude, indicating more neuronal resources allocated to the early encoding phase of processing. This demonstrates that learned associations between a pleasant odor and an aversive consequence alter the way odor characteristics are encoded (effects on the N1 peak), and interpreted (changed evaluations), although to a lesser degree compared to the situation in which an unpleasant odor was conditioned to irritation.

Table 4

Study 2 (PEA): Mean amplitudes in μV and latencies in ms (SDs in parentheses) for the N1 and P2 peak, recorded at electrode sites Fz, Cz, and Pz, separately shown for the Pain and the No pain Expectancy condition

	Electrode Site		
Condition	**Fz**	**Cz**	**Pz**
Amplitudes N1			
Pain	-4.45 (3.70)	-3.95 (3.14)	-3.50 (3.82)
No pain	-2.40 (2.88)	-2.63 (2.97)	-2.73 (3.61)
Latencies N1			
Pain	357 (104)	348 (107)	345 (106)
No pain	353 (94)	351 (94)	347 (94)
Amplitudes P2			
Pain	8.32 (5.24)	11.74 (5.87)	12.22 (4.66)
No pain	9.45 (4.20)	11.62 (4.22)	12.05 (4.37)
Latencies P2			
Pain	505 (85)	489 (88)	494 (87)
No pain	512 (70)	498 (68)	500 (69)

Comparison Study 1 and 2

OERPs in response to H_2S can not be directly compared to OERPs in response to PEA (OERPs differ between odorants in relation to the hedonic characteristic of the odor, Lundström et al., 2006; and ERPs can be best compared within instead of between participants; Luck, 2005). However, we can clearly observe that the effect of expecting pain while inhaling an unpleasant odor alters perception to a much greater extent than when pain is expected while smelling a pleasant odor. Whereas all peak latencies and amplitudes were affected by the cognitive manipulation when the odorant was H_2S, only N1 peak amplitude was directly affected when the odorant was PEA. In the discussion, we will further elaborate on the role of hedonics in the present findings.

It should be noted that differences between olfactory ERPs measured in Study 1 and 2 could not be explained by differences in intensity of the two odorants used in Study 1 and 2. Intensity ratings of H_2S did not differ significantly from PEA intensity ratings ($F(1,59) = 3.14$, $p = .08$; two-tailed; $M_{H2S} = 25.63$, $SD = 16.13$, $M_{PEA} = 19.18$, $SD = 11.85$). Annoyance ratings on the other hand, did differ between studies. Not surprisingly, the odor of H_2S was rated as more annoying than PEA ($F(1,59) = 24.0$, $p < .01$, two-tailed, $M_{H2S} = 23.04$, $SD = 17.66$, $M_{PEA} = 6.28$, $SD = 6.35$).

Discussion

We demonstrated that the expectation of adverse health effects, induced by learning, while smelling the odor of H_2S altered both the early and late peak of the associated OERP. This result is different from that obtained in an earlier study (Bulsing et al., 2007), in which we also investigated the influence of expectation of trigeminal pain on the perception of H_2S, and found effects only on N1 latency. As outlined earlier, this is probably explained by the conditional nature of the earlier experiment: if the participant perceived the odor instead of the irritant, she would know immediately at the beginning of a trial the trial was "safe" and pain was no longer expected. Thus, the effect of expectancy might not run its full course to affect perceptual processing at a later phase in the OERP signal, the P2 peak, which has been associated with cognitive processing of odor stimuli (Kobal, 2003), reflecting stimulus significance (Pause and Krauel, 2000), valence (Lundström et al., 2006), and novelty (Hummel and Heilmann, 2008). The present study demonstrates that when CO_2 presentation does not occur instead of H_2S, but at unexpected moments during presentation of CO_2, effects of expectation prevail beyond the N1 to affect the P2.

The early N1 peak has been associated with exogenous stimulus characteristics (Kobal, 2003), and is presumed to be independent of a participant's mental state or arousal (Näätänen et al., 1993, but see e.g. Krauel et al., 1998). The N1 is in general determined by physical stimulus features, such as intensity or quality (Pause & Krauel, 2000; Hummel & Kobal, 2002). The findings from both studies reported here have in common an effect on the early N1 peak amplitude, show that the effects of expectation of adverse health effects from odor inhalation do not - if they occur at all- remain confined to the processing of meaning and salience of the perceived stimulus, but also - or rather - affect perception of the basic characteristics of the stimulus itself.

The process of (selective) attention has been proposed to explain shortened N1 latencies (Krauel et al., 1998; Pause & Krauel, 2000; Pause, 2002). Indeed, expecting an odor to be harmful would cause an individual to be more attentive to that odor resulting in enhanced or faster perception of the stimulus (see also Bulsing et al., 2007). For the N1 amplitude on the other hand, the role of attentional or cognitive factors seems to be small or even absent (Pause & Krauel, 2000). However, we did find effects of our cognitive manipulation on N1 amplitudes. If participants expected trigeminal irritation, but were only presented with an odor, N1 amplitudes increased. Pause et al. (1997) showed enlarged N1 peaks with increasing concentrations of chemosensory stimuli that simultaneously activate both the olfactory and trigeminal nerve. The fact that we found enlarged N1 amplitudes suggests that the odor *acquired* a trigeminal component after conditioning the odor to trigeminal irritation. In other words, expecting the odor to be painful seems to give the odor trigeminal properties. A comparison of Study 1 with Study 2 illustrated that the magnitude of the expectancy effect on brain potentials was smaller for the pleasant odor of roses - PEA – relative to the unpleasant odor of rotten eggs - H_2S. When the exact same procedures that were applied with H_2S as the conditioned stimulus were repeated with PEA as the conditioned stimulus, only the amplitude of the N1 peak was affected. In both studies, the odorant was evaluated as more annoying when pain was expected - but not more intense - than when no pain was expected.

Our findings resemble the ones by Van den Bergh et al. (1995, 1997, 1998), who demonstrated successful conditioning of unpleasant, but not pleasant odors to CO_2-enriched air, resulting in increased respiratory frequency in response to the unpleasant odor. The difference in brain activity cannot be explained by differences in perceived intensity of these odorants, as no significant difference in perceived intensity associated with these odors across Studies 1 and 2 was found. Van den Bergh et al. attributed this selective conditioning to "belongingness", or in other words, to the affective similarity between the CS and US (see also Hamm et al., 1989). Previously learned associations between H_2S and spoilt food on the one hand, and PEA and beautiful flowers on the other, may be more difficult to overcome than when the hedonic valence of the CS and US are of opposite valence. That is, the olfactory percept may be less susceptible to modulation via top-down learning.

Another explanation holds that H_2S, considered by most to be a foul odor, has a so-called "preparedness" which renders it easier to associate with the unpleasant irritancy experienced from CO_2, than PEA. The notion of preparedness implies that *in the course of evolution* particular stimuli acquired the ability to easily become predictors of particular USs (see also Garcia and Koelling, 1966; Seligman, 1971). Although the present findings may reflect an innate tendency to associate unpleasant odors with unpleasant outcomes, it is impossible to tell nature and nurture apart.

The finding, obtained in the studies reported here, of profound effects on early brain processing of olfactory stimuli associated with adverse health effects, goes against traditional perspectives on perception (as described by Gardner, 1987) that followed linear and unidirectional information processing approaches in which there was no room for feedback from expectation on earlier stages of perception. Although such strict bottom-up approaches have been largely abandoned, they

seem to still govern much of our thinking, as effects of expectation on early brain processing seem counterintuitive to many. Yet, these findings are in line with a long string of recent findings demonstrating "deep penetration" mainly using brain imaging of top-down cognition on perception of a stimulus, pertaining to olfaction (Li et al., 2008; de Araujo et al., 2005; Gottfried, 2008), taste (Nitschke, 2006; Grabenhorst et al., 2008), and visual perception (Kosslyn and Thompson, 2003). By employing an ERP-paradigm, which has a superior temporal resolution compared to imaging techniques, we are here providing converging evidence with regard to the magnitude and depth of top-down effects. Furthermore, so-called "objective" changes at the level of the brain in association with top-down learning, support changes in subjective evaluations of perceptual characteristics of odors associated with harmful versus healthful effects as reported by Dalton et al. (1997, 1999) and others (Herz and Von Clef, 2001; Distel and Hudson, 2001). In addition, they rule out other explanations such as that altered reports of intensity, hedonics and health symptoms reflect response biases (Köster, 2002), as response biases by definition should not affect early perceptual processing or be reflected in neural correlates associated with such processing.

The findings from this study confirm the notion that the expectation that an odor is painful may change perception of that odor. Consequently, health symptoms attributed to odor exposures could be modulated by these changes as posited by Dalton (1999), although this hypothesis still remains to be fully tested by including endpoints related to health effects (e.g. ocular hyperemia, nasal secretion; Smeets et al., 2002) in studies such as the present one.

Health effects from environmental odor exposure are conventionally construed as reflecting individual differences in interpretation of otherwise stable percepts arising from verifiable exposures. This perspective can no longer be held, in view of the finding that the neurophysiological basis of perception may be subject to change as much as interpretations are.

Acknowledgements

This research was funded by NWO 452-03-334 to M.A.M.S.

References

Bensafi, M., Frasnelli, J., Reden, J., & Hummel, T. (2007). The neural representation of odor is modulated by the presence of a trigeminal stimulus during odor encoding. *Clinical Neurophysiology, 118*, 696-701.

Bulsing, P. J., Smeets, M. A. M., Hummel, T., & Van den Hout, M. A. (2007). Influence of chemosensory pain-expectancy on olfactory event-related potentials. *Neuroimage, 38*, 164-170.

Dalton, P. (1999). Cognitive influences on health symptoms from acute chemical exposure. *Health Psychology, 18*, 579-590.

Dalton, P. (2002). Odor, irritation, and perception of health risk. *International Archives of Occupational and Environmental Health, 75*, 283-290.

Dalton, P. (2003). Upper airway irritation, odor perception and health risk due to airborne chemicals. *Toxicology Letters, 140-141*, 239-248.

Dalton, P., Wysocki, C. J., Brody, M. J., & Lawley, H. J. (1997). The influence of cognitive bias on the perceived odor, irritation and health symptoms from chemical exposure. *International Archives of Occupational and Environmental Health, 69*, 407-417.

Das-Munshi, J., Rubin, G. J., & Wessely, S. (2006). Multiple chemical sensitivities: A systematic review of provocation studies. *Journal of Allergy and Clinical Immunology, 18*, 1257 – 1264.

De Araujo, I. E., Rolls, E. T., Velazco, M. I., Margot, C., & Cayeux, I. (2005). Cognitive modulation of olfactory processing. *Neuron, 46*, 671 – 679.

Distel, H., & Hudson, R. (2001). Judgment of odor intensity is influenced by subjects' knowledge of the odor source. *Chemical Senses, 26*, 247-251.

Domjan, M. (1993). *The principles of learning and behavior*. Wadsworth, Belmont.

Garcia, J., & Koelling, R. A. (1966). Relation of cue to consequence in avoidance learning. In: Domjan, M., Burjhard, B. (Eds), *The Principles of Learning & Behavior*, (pp. 76-78). Brooks/Cole Publishing Company, CA.

Gardner, H. (1987). *The mind's new science: A history of the cognitive revolution.* New York: Basic Books.

Geisler, M. W., & Murphy, C. (2000). Event-related brain potentials to attended and ignored olfactory and trigeminal stimuli. *International Journal of Psychophysiology, 37*, 309–315.

Gottfried, J. A. (2008). Perceptual and neural plasticity of odor quality coding in the human brain. *Chemosensory Perception, 1*, 127-135.

Grabenhorst, F., Rolls, E. T., & Bilderbeck, A. (2008). How cognition modulates affective responses to taste and flavor: Top-down influences on the orbitofrontal and pregenual cingulate cortices. *Cerebral Cortex, 18*, 1549-1559.

Hamm, A. O., Vaitl, D., & Lang, P. J. (1989). Fear conditioning, meaning, and belongingness: a selective association analysis. *Journal of Abnormal Psychology, 98*, 395-406.

Herz, R. S., & Von Clef, J. (2001). The influence of verbal labeling on the perception of odors: evidence for olfactory illusions? *Perception, 30*, 381-391.

Hummel, T., & Heilmann, S. (2008). Olfactory event-related potentials in response to ortho- and retronasal stimulation with odors related or unrelated to foods. *International Dairy Journal, 18*, 874-878.

Hummel, T., & Kobal, G. (2002). Olfactory event related potentials. In: Simon, S., Nicolelis, M., (Eds.), *Methods in Chemosensory Research*. CRC press, Boca Raton.

Kettenmann, B., Hummel, C., Stefan, H., & Kobal, G. (1996). Magnetoencephalographical recordings: separation of

cortical responses to different chemical stimulation in man. *Functional Neuroscience (EEG Suppl), 46*, 287-290.

Kobal, G. (1981). Elektrophysiologische Untersuchungen des Menschlichen Geruchssinns. Thieme Verlag, Stuttgart.

Kobal, G. (2003). Electrophysiological measurement of olfactory function. In: Doty R.L., (Ed.), *Handbook of Olfaction and Gustation* (p*p* 229-249), New York: Marcel Dekker Inc.

Kobal, G., Klimek, L., Wolfensberger, M., Gudziol, H., Temmel, A., Owen, C. M., Seeber, H., Pauli, E., & Hummel, T. (2000). Multicenter investigation of 1036 participants using a standardized method for the assessment of olfactory function combining tests of odor identification, odor discrimination, and olfactory thresholds. *European Archives of Otorhinolaryngology, 257*, 205-211.

Kosslyn, S. M., & Thompson, W. L. (2003). When is early visual cortex activated during visual mental imagery? *Psychological Bulletin, 129*, 723-746.

Köster, E. P. (2002). The specific characteristics of the sense of smell. In: Rouby, C., Schaal, B., Dubois, D., Gervais, R., Holley, A. (Eds), *Olfaction, taste, and cognition*. University Press, Cambridge, p*p* 27-43.

Krauel, K., Pause, B. M., Sojka, B., Schott, P., & Ferstl, R. (1998). Attentional modulation of central odor processing. *Chemical Senses, 23*, 423-432.

Li, W., Howard, J. D., Parrish, T. B., & Gottfried, J. A. (2008). Aversive learning enhances perceptual and cortical discrimination of indiscriminable odor cues. *Science, 319*, 1842-1845.

Luck, S. J. (2005). *An introduction to the event-related potential technique.* Cambridge: The MIT Press.

Lundström, J. N., Seven, S., Olsson, M. J., Schaal, B., & Hummel, T. (2006). Olfactory Event-Related Potentials reflect individual differences in odor valence perception. *Chemical Senses, 31*, 705-711.

Näätänen, R., Paavilainen, P., Tiitinen, H., Jiang, D., & Alho, K. (1993). Attention and mismatch negativity. *Psychophysiology, 30*, 436-450.

Nitschke, J. B., Dixon, G. E., Sarinopoulos, I., Short, S. J., Cohen, J. D., Smith, E. E., Kosslyn, S. M., Rose, R. M., Davidson, R. J. (2006). Altering expectancy dampens neural response to aversive taste in primary taste cortex. *Nature Neuroscience, 9*, 435-442.

Nordin, S., Martinkauppi, M., Olofsson, J., Hummel, T., Millqvist, E., & Bende, M. (2005). Chemosensory perception and event-related potentials in self-reported chemical hypersensitivity. *International Journal of Psychophysiology, 55*, 243-255.

Pause, B. M. (2002). Human brain activity during the first second after odor presentation. In: Rouby, C., Schaal, B., Dubois, D., Gervais, R., Holley, A. (Eds), *Olfaction, taste, and cognition*. University Press, Cambridge, pp. 309-323

Pause, B. M., & Krauel, K. (2000). Chemosensory event-related potentials (CSERP) as a key to the psychology of odors. *International Journal of Psychophysiology, 36*, 105-122.

Pause, B. M., Sojka, B., & Ferstl, R. (1997). Central processing of odor concentration is a temporal phenomenon as revealed by chemosensory event-related potentials (CSERP). *Chemical Senses, 22*, 9-26.

Schiffman, S. S., Walker, J. M., Dalton, P., Lorig, T. S., Raymer, J. H., Shusterman, D., & Williams, C. M. (2000). Potential health effects of odor from animal operations, wastewater treatment, and recycling of by products. *Journal of Agromedicine, 7*, 7-81.

Seligman, M. E. P. (1971). Phobias and preparedness. *Behavior Therapy, 2*, 307-320.

Shusterman, D. (2001). Odor-associated health complaints: competing explanatory models. *Chemical Senses, 26*, 339-343.

Smeets, M., Maute, C., & Dalton, P. (2002). Acute sensory irritation from exposure to isopropanol (2-propanol) at TLV in workers and controls: objective versus subjective effects. *The Annuals of Occupational Hygiene, 46*, 359–373.

Van den Bergh, O., Kempynck, P. J., Van de Woestijne, K. P., Baeyens, F., & Eelen, P. (1995). Respiratory learning and somatic complaints: A conditioning approach using CO2-enriched air inhalation. *Behaviour Research and Therapy, 33*, 517-527.

Van den Bergh, O., Stegen, K., & Van de Woestijne, K. P. (1997). Learning to have psychosoamtic complaints: Conditioning of respiratory behavior and complaints in psychosomatic patients. *Psychosomatic Medicine, 59*, 13-23.

Van den Bergh, O., Stegen, K., & Van de Woestijne, K. P. (1998). Memory effects of symptom reporting in a respiratory learning paradigm. *Health Psychology, 17*, 241-248.

Wilson, D. A., & Stevenson, R. J. (2006). *Learning to Smell*. Baltinmore: The John Hopkins University Press.

Chapter 6

Hold that sniff: Effects of health-related cognitions on sniffing of an environmental odor

This chapter is based on:

Bulsing, P.J., Smeets, M.A.M., Lorig, T., & van den Hout, M.A. Hold that Sniff: Effects of Health-Related Cognitions on Sniffing of an Environmental Odor (submitted for publication).

Abstract

We investigated whether a cover story about health effects from odor exposure altered sniffing of that odor. Participants smelled and identified four odors, including a "target". There were three groups based on target cover story: negative bias (n = 22, "chemical rest product"), positive bias (n = 20, " aromatherapy product"), and neutral (n = 21, "standard odor"). Odors were rated on attributes such as intensity, and dangerousness. Sniffing was measured via a nasal air pressure transducer. Because the manipulation was only partially successful – the neutral group rated the odor relatively negatively - statistical comparisons were conducted between high versus low danger raters of the target. This revealed a smaller area under the curve and a shorter sniff duration among high danger raters. Thus, sniffing is not affected by a story about possible health effects, only by whether people actually believe an odor to be dangerous.

Introduction

Recently, there has been an upsurge of interest in top-down influences of cognition on the perception of odor. Several studies demonstrated changes in odor perception and brain activity (e.g. in primary olfactory cortex) when smelling an odorant after manipulations of meaning via learning (Li et al., 2008), and labeling (de Araujo et al., 2005). These findings suggest that the perception of odor can vary depending on context, or, in other words, that one and the same odorant is not always perceived in the same manner. Based on an extensive review of the neurobiological and psychological literature on olfaction, Wilson and Stevenson (2006) arrived at a similar conclusion in their book *Learning to Smell*. The authors stated that the traditional computational view which aims to explain odor perception analytically, starting from molecular properties, poses problems for understanding individual differences in hedonic, quality and intensity perceptions of odor stimuli. Instead, they propose a synthetic account of odor perception, which holds that olfactory percepts are stored as *odor objects*, in the sense that learning which volatile chemical features occur together leads to the storage of a holistic representation of that feature combination (e.g. "coffee"). Following this notion, top-down influences of semantic or other-modality information are crucially important in formation of the odor object.

The aim of the present study is to apply this theory in the area of odors and health, more specifically to health effects attributed to odor exposure. We investigated how expectations regarding health effects from an odor affect attention to that odor, by using sniffing as an index of attention. Attention refers to the selection that is inherent in the processing of information (Kosslyn, 1994), for example because of capacity limitations or organizational purposes, or of interest or importance of a particular type of information on part of the perceiver. Attention can be shifted to the object of interest, causing an increase in energy and effort allocated to processing of information inside what is often called the "attention window" (Kosslyn, 1994) with the object of interest at its focus, and a decrease in energy and effort allocated to the processing of information outside of the attention window.

In visual perception, eye-tracking has been used to monitor oculomotor shifts in attention across the visual field, based on the underlying notion that the more frequent or the longer people look at specific regions of, or objects in, the visual field, the more attention they devote to these regions or objects, and the more information is processed related to them. Eye movements have demonstrated a top-down regulated attentional process; expectations can modulate where in the visual field the eyes will fixate and return (Krauzlis & Adler, 2001). In odor perception, sniffing is considered the olfactory equivalent of oculomotor movement: just as visual attention is regulated by changes in stimulus properties in a bottom-up fashion by triggering movements in the ocular muscles (e.g. by quickly turning the eyes towards an unsuspected object entering into the periphery of the visual field), changes in the olfactory stimulus influence sampling of that stimulus by altering depth and duration of the sniff (e.g. when an odor suddenly becomes much weaker or stronger; Laing 1982, Mainland and Sobel, 2006; Frank, Dulay & Gesteland, 2003).

As still little is known about top-down influences of cognition on smell, we set out to investi-

gate how expectations about health effects attributed to a particular odor exposure affect sniffing of that odor. Experiences of health effects from odorous emission such as headaches, fatigue, shortness of breath, and dizziness have for example been reported by individuals with Multiple Chemical Sensitivity (MCS: Labarge & MacCaffrey, 2000), and have been attributed to chemicals that are often characterized by a typical odor, such as gasoline, diesel fuel, and solvents. In addition, workers who experience exposure to chemicals in the workplace, as well as residents who live near live stock farms or chemical industry have reported feeling sick as a result of the odorous emission (Schiffmann et al., 2000). The results from a recent review of 37 laboratory exposure studies in MCS sufferers supported the conclusion that cognitive factors, in the form of learning by classical conditioning, may give rise to expectations that (certain) odors will elicit health effects (Das-Munshi, Rubin & Wessely, 2006). In the present study we explored whether expectations that a target odor may be hazardous versus expectations that a target odor may be healthful caused differences in sniffing of the target.

Previous studies on the effect of expectations about health effects related to odor exposure by Dalton and colleagues (Dalton et al., 1997; Dalton, 1999) have involved assessments of perceived intensity, irritation, and annoyance, as well as of symptom reports. It was shown repeatedly that inducing beliefs that consequences of exposure to certain odorants might be harmful, as opposed to beliefs consequences might be healthful, resulted in both increased intensity and irritancy perception of those odorants as well as enhanced frequency and intensity of symptom reports. These findings led Dalton to propose that cognitive or emotional factors modulate the sensory response (Dalton, 2002; 2003). In recent studies by our own group, we investigated this hypothesis using the technique of Event Related Potentials (ERPs) in a within-subject design. ERPs reflecting olfactory processing of the odor of H_2S was compared across conditions that involved expecting sensory irritation (e.g. feelings of burning or stinging in the nose, often experienced while being exposed to high concentrations of volatile solvents; Shusterman, 2001) versus not expecting any irritation. We demonstrated that the early N1 peak of the olfactory ERP (associated with stimulus properties such as intensity and quality; Pause and Krauel, 2000; Lundström et al, 2006) had a shorter latency (Bulsing, Smeets, et al., 2007) and a higher amplitude (Bulsing et al., submitted) when participants expected the odor to be aversive. These results reflect faster and more intense processing of early olfactory information, confirming Dalton's hypothesis of a cognitive modulated sensory response.

The aim of the present study was to investigate whether believing that an odor may be unhealthy causes individuals to reduce sampling by shortening the duration and reducing the depth of the sniff as compared to believing that same odor is healthful or neutral. It was decided to manipulate beliefs regarding the health effects related to exposure to a target odor in a between-subjects design, using harmful, healthful and neutral cover stories as done by Dalton (1999). We chose not to test this by simply telling people that the odor they were about to smell might be dangerous, because such a procedure would likely create demand effects in the sense that individuals might not even try to sample the odor and simply hold their breath. Thus, we

devised a performance task in which sampling of the odor was mandatory in order to be able to complete the task. Participants received four descriptions of odors, which they had to study carefully. They were told they had to smell four odors and identify each by one of the descriptions. Participants were randomized across three groups. In each group all odors were identical, with the difference being only in the description of the target odor. In the negative group, the target was described as a chemical rest product, in the positive group it was described as an aromatherapy scent, and in the neutral group the target was described as a typical odor used in olfactory research. So, participants explored each odor stimulus by sniffing in order to be able to make the correct identification. It might be anticipated that individuals who expect an odor to be aversive to their health would sniff less vigorously in order to reduce exposure to the presumed harmful substance. Health symptoms were also assessed to explore effects of the cover story on the experience of health effects during or following the task.

Method

Participants

Sixty-three participants took part in this study. They were randomly assigned to either the negative bias group (n = 22, 18 females, Mean age = 22.91, *SD* = .51), the positive bias group (n = 20, 15 females, Mean age = 23.58, *SD* = 1.00) or the neutral bias group (n = 21, 17 females, Mean age = 22.62, *SD* = .43). All participants were students at Utrecht University. They were only allowed to take part if they did not smoke, did not have asthma, did not suffer from a cold, were not pregnant, and had a normal sense of smell (self-diagnosed). Participants received either course credits or financial remuneration for their participation. This study was performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki.

Odor stimuli

Four different odors were used in the study: "the odor of cookies and cake (commercial vanilla aroma, used for baking; Baukje), "tropical fruit (Peach Perfume Oil; Jacob Hooy), and "vomit" (ethylbutryrate;10% in Tec; Quest). Apart from these 3 "non-targets", participants were exposed to a target odor. Positive, negative and neutral expectations regarding the health effects from inhaling this target odor were induced, using various odor descriptions (see below). We aimed for the target odor to be unfamiliar (to avoid the influence of previous associations), and neutral in terms of perceived pleasantness, intensity, harmfulness, and naturalness. A pilot study (N = 19) demonstrated that the odorant that fit best to these requirements was Orange Flower Ether (Quest).

Of each odorous substance 0.5 ml was applied to a closable cylinder (about 3.5 cm high and 2 cm in diameter) filled with an absorbent material (cellulose acetate; "Sorbarods"; Ilacon Ltd, Kent, UK). After opening, the odor could be sampled from the cylinder.

Odor descriptions

The descriptions of vanilla, tropical fruit and vomit odor were the same for all bias groups. The only description that differed per group was the one describing the target odor.

Vanilla description: "**The odor of cookies and cake"** A sweet smelling odor, often smelled while eating a cookie or a piece of cake. This odor is perceived as very pleasant by almost everybody.

Tropical fruit description: **"Tropical fruit"** A very "fresh" smelling odor, often smelled while taking a bite from a juicy piece of fruit. This odor is often perceived as very pleasant.

Vomit description: **"Vomit"** A sour smelling odor, often smelled when someone has been unable to hold down their food. Most people consider this odor as extremely unpleasant. By inhaling the odor, you won't get sick yourself; perhaps you will only feel a bit nauseous.

Target description 1 (negative bias induction): **"Chemical rest product"** An artificial smelling odor, often smelled in the neighborhood of factories where chemical products are made, like paint. Residents living close to such factories perceive this odor as unpleasant and even report health symptoms, like headache and throat irritation.

Target description 2 (positive bias induction): **"Aromatherapy product"** A fresh smelling odor, often smelled during aromatherapy sessions. Volunteers undergoing aromatherapy perceive this odor as pleasant and even report a reduction of health symptoms, such as headache and stress.

Target description 3 (neutral bias induction): **"Standard odor for research"** This odor is often used for olfactory research. Usually, this odor is not perceived as particularly pleasant or unpleasant.

Ratings

Odor ratings – After the experiment, participants were asked to rate each odor ("I experience this odor as") on the following characteristics: pleasantness, intensity, artificialness, harmfulness, danger, and familiarity. Rating scales consisting of 7 response categories were used with bipolar descriptions ranging from "very pleasant" to "very unpleasant" for unpleasantness, "very weak" to "very strong" for intensity, "very natural" to "very artificial" for artificialness, "very beneficial" to "very harmful" for harmfulness, "very safe" to "very dangerous" for danger, and "very familiar" to "very unfamiliar" for unfamiliarity.

Health symptoms – In order to check the influence of our cognitive manipulation on perceived health, experienced health symptoms were monitored, after the experiment. We used the same list of symptoms as Dalton (1999) consisting of both solvent-related symptoms (e.g. headache and nose irritation), as well as control symptoms in order to check response tendencies (e.g. muscle pain, leg cramps; see Table 3). Participants were asked to indicate the intensity of the experienced symptoms on a 7 cm Visual Analogue Scale (VAS) with extreme categories "not at all" vs. "very much".

Sniff registration

During the entire experiment, participants wore a nasal pressure monitoring cannula (normally used to deliver oxygen to patients in hospitals or nursing homes), which was connected to a pressure transducer (PT; Slee*p* Sense). The PT registered sniffing behavior every 1 ms by measuring air

pressure in the nose (in a range of 0 - 40 cmH_2O): Air pressure rises can be observed during active inhalation through the nose, resulting in measurable sniff parameters (e.g. sniff amplitude and duration). The PT amplified the signal, which was in turn digitized using a 16 bit analog-digital converter (National Instruments, type NI-USB 6259).

The sniffing data was analyzed using a computer program (Sniff Pressure Analyzer, version 3.10), which was developed in our lab. The program was capable of automatically scanning the data in search for sniff pulses. Only periods ("blocks") were analyzed in which a stimulus was presented. The start and end of each block was automatically marked in the data: As soon as participants placed their head in a chin rest (the only manner to approach the small stimulus cylinder), a micro switch was activated. The switch was released as soon as participants voluntarily withdrew their head. A baseline was determined as the modus of the interval starting 5 seconds before until 10 seconds following stimulus presentation. Because baselines fluctuated throughout the experiment, separate baselines were calculated for each block. The period between the moment at which the air pressure level fell below the baseline, until the moment where it reached the baseline again was interpreted as a sniff. In order to minimize the noise in the data, only pulses which took at least 400 ms (Laing, 1983) were recognized as sniffs. In anticipation of stimulus presentation, some participants already sniffed before the actual onset of a block. Therefore, if a sniff started before onset, but ended within a block, it was included in the analyses. The total number of sniffs per block, sniff amplitudes, sniff durations, and area under the sniff curves (AUC) were analyzed. These parameters were used previously for describing sniffing behavior (e.g. by Sobel et al., 2007).

Procedure

After it was determined whether participants were allowed to take part in the experiment, they were informed about the procedure, and signed informed consent. First, the nasal cannula was inserted into the nose. Participants were told that it measured odorant concentrations in the nose, to allow the researcher to check the order of presentation of the odor stimuli. Next, participants were trained on how to place their chin in a chin rest and activate the microswitch as soon as the odor cylinder was placed in the holder attached to the chin rest. They were told to sample the odor as soon as their head was in place. This was practiced a few times with a cylinder containing no odor. The word "sniffing" was not used during the instructions.

In addition to the sniff training, participants were told that they would be presented with various odors during the experiment and that they had to identify each odor. They were given four descriptions to choose from: vanilla, tropical fruit, vomit and one of the following: a chemical rest product, an aromatherapy scent or a standard odor for research. Participants were instructed to carefully read each odor description before the start of the experiment.

During the experiment the odors were presented in a random order. Between each odor presentation a 45 to 60 s inter stimulus interval was used to prevent adaptation. They were asked to identify the odor by pointing to one of the odor descriptions that were presented on the computer screen in front of them. All odors were presented 2 times, whereby the first presentation of each

odor was intended to familiarize the participants with the range of odors. Participants were given feedback on the first trails, in order to make sure they would identify the target odor correctly during the second presentation. During the ISI participants were allowed to read a magazine.

After the experiment participants rated odor characteristics and health symptoms. While rating odor characteristics, they were allowed to sample the odors again (sniffs were not registered). After asking the participants what they thought the test purpose was, they received participant remuneration and were debriefed.

Analyses

Odor ratings

A Manova, with between-subjects factor Bias Group (3 levels: Negative, Positive, Neutral) was conducted on the six ratings (pleasantness, intensity, artificialness, harmfulness, danger, and familiarity) as a manipulation check. It was expected that the negative bias group would rate the target odor as less pleasant, more intense, less safe etc. compared to the positive and neutral bias groups.

Health symptoms

An Anova, with between-subjects factor Bias Group (3 levels: negative, positive, and neutral) was conducted on the two dependent variables mean solvent-related symptoms and mean somatic control symptoms. It was expected that the negative bias group would report more intense solvent related and control health symptoms compared to the positive and the neutral bias groups.

Sniffing data

Sniff data (amplitudes, duration, and AUC) per sniff pulse were converted to a SPSS data file. Sniffing data related to the familiarization trial were not included in the analyses. The reason was that participants often did not select the correct label that matched the odor during this trial, suggesting that participants' actual cognitions did not match the intended ones. Data of the second odor presentation when labels were almost always matched correctly to the target odor were analyzed. For the dependent variables (sniff amplitude, AUC and duration) a Manova was conducted, with between-subjects factor Bias Group (3 levels: negative, positive, and neutral). It was expected that the negative bias group would demonstrate lower sniff amplitudes, smaller AUCs, and shorter sniff durations compared to the positive and the neutral bias groups.

Results

Odor ratings

In Table 1 mean ratings for each of the six target odor ratings are displayed. The multivariate test showed a significant effect of bias group: $F(12,110) = 4.96$, $p < .001$, $\eta^2 = .35$. Results from the univariate tests and post-hoc comparisons are displayed in the table. As can be derived from this table, the groups rated all odor characteristics differently, except for intensity. Strictly speaking, it

would be expected that scores associated with the negative bias group are highest, those associated with the positive bias group lowest, and that scores from the neutral bias group would lie somewhere in between scores from the other two groups. However, a closer inspection of Table 1 reveals that scores from the neutral bias group are in fact closer to the scores from the negative bias group than the positive bias group: mean scores are all above 4 on the 7 point rating scale. Superscript numbers in Table 1 reflecting the results for post-hoc testing support this: in many comparisons, the neutral group scores are not significantly different from the negative bias group scores. This observation is not novel as similar findings were observed by Dalton and colleagues (Dalton, Wysocki, Brody, & Lawley, 1997; Dalton, 1999). This is not surprising since our study was modeled after these studies. Apparently, participants in the neutral group, on average, did not perceive the target odor as neutral, but as somewhat unpleasant, harmful and dangerous. Perhaps the neutral group is better characterized as ambiguous: if there is no explicit information on how to interpret the situation, participants impose their own interpretations onto the one suggested by the experimenter. In conclusion, the experimental manipulation was not completely successful. We will return to this point later.

Table 1

Mean target odor ratings (SD between parentheses) by bias

	Bias group			
Rating	**Negative**	**Positive**	**Neutral**	**F**
Unpleasantness	4.95[a] (1.09)	3.20 (1.40)	4.52[a] (1.21)	11.34**
Intensity	5.55[a] (1.18)	5.80[a,b] (.52)	5.81[a,b] (1.12)	.48
Artificialness	5.91[a] (1.06)	4.10 (1.74)	5.67[a] (.97)	11.86**
Harmfulness	5.45 (.86)	3.20 (1.06)	4.62 (1.07)	27.20**
Danger	5.09[a] (.81)	3.35 (1.14)	4.52[a] (.87)	18.31**
Unfamiliarity	3.91[a] (1.60)	3.20[a] (1.15)	4.67[a] (1.80)	4.61*

Note. * $p < .05$; ** $p < .01$. *F*-values refer to univariate tests. Ratings that have superscript letters in common are not significantly different from each other on a Fischer LSD post-hoc comparison ($p<.01$).

We checked whether there was any carry-over of the instructions pertaining to the target odor to any of the other three odors, by performing Manova's with between-subject factors Bias Group on the six ratings belonging to each of the three odors. Effects of Bias Group were non-significant for ratings of vomit odor, $F(12,110) = 1.14$, $p = .33$ and vanilla odor $F(12,110) = 1.62$, $p = .10$, but significant for tropical fruit, $F(12,110) = 2.03$, $p = .03$. There were differences between groups with respect to unpleasantness and unfamiliarity, with the negative bias group scoring higher on unpleasantness than the positive and neutral group, and the negative bias group scoring higher on unfamiliarity of tropical fruit. It was concluded that carry-over of the instructions on ratings of the other odors was minimal. In Table 2 mean ratings for the other three odors are displayed.

Table 2

Mean ratings of "vomit", "vanilla" and "tropical fruit" (SD between parentheses)

Rating	Vomit	Vanilla	Vomit
Unpleasantness	6.52 (.73)	2.43 (1.04)[a]	2.27 (1.17)[a]
Intensity	5.84 (1.17)[a]	3.67 (1.43)	4.81 (1.26)
Artificialness	3.32 (1.61)[a]	3.32 (1.41)[a,b]	3.29 (1.52)[a,b]
Harmfulness	5.06 (.91)	3.25 (1.00)[a]	3.14 (1.08)[a]
Danger	4.56 (1.00)[a]	2.43 (1.09)[b]	2.44 (1.12)[b]
Unfamiliarity	2.56 (1.04)[a]	2.67 (1.16)[a,b]	2.43 (1.07)[a,b]

Note. *p<.001. Pairs that have a superscript letter in common are not significantly different from each other on a Fischer LSD post-hoc comparison (p<.05).

Health symptom reports

In Table 3 mean intensity ratings of experienced health symptoms (solvent associated and somatic control symptoms) are shown. On the mean solvent symptoms a significant effect of Bias group was found: $F(2,62) = 3.33$, $p = .04$. Post-hoc tests with Fischer LSD corrections demonstrated that the neutral bias group reported more intense solvent associated health symptoms compared with the positive bias group ($p = .02$), and compared with the negative bias group ($p = .05$). There was no effect of bias group on the control symptoms, $F(2,62) = 1.46$, $p = .24$.

Table 3

Mean health symptom ratings (SD between parentheses) by bias group

Symptoms	Negative	Positive	Neutral
Solvent-associated symptoms			
Throat irritation	5.05 (7.05)	4.20 (5.06)	10.67 (13.19)
Eye irritation	5.82 (10.82)	4.50 (7.27)	9.52 (16.08)
Nose irritation	15.27 (16.71)	9.70 (11.73)	22.38 (20.02)
Dizziness	6.23 (7.73)	8.45 (10.36)	9.57 (12.15)
Headache	10.55 (12.61)	6.90 (7.41)	13.71 (15.36)
Nausea	4.72 (5.35)	5.60 (9.01)	11.43 (15.85)
Drowsiness	12.18 (12.10)	12.15 (12.94)	14.76 (16.29)
M	*8.55 (6.07)*	*7.36 (6.48)*	*13.15 (9.99)*
Somatic (control) symptoms			
Skin irritation	3.68 (6.68)	3.40 (3.75)	6.19 (11.82)
Bad taste	5.27 (6.93)	4.90 (3.97)	11.10 (14.73)
Nasal congestion	8.91 (14.05)	10.60 (12.80)	9.29 (15.20)
Cough	5.09 (9.30)	7.30 (12.07)	11.90 (16.56)
Sneeze	5.86 (7.85)	4.75 (5.45)	9.57 (15.73)
Stomachache	3.95 (6.30)	4.10 (5.10)	6.62 (8.98)
Shortness of breath	5.82 (9.16)	4.65 (5.85)	5.86 (8.70)
Heart palpitations	3.91 (7.57)	4.40 (4.85)	4.57 (5.99)
Numbness or tingling	4.86 (5.94)	4.35 (5.77)	11.86 (16.70)
Ear ringing	3.91 (6.51)	3.20 (2.61)	4.14 (6.58)
Leg cramps	2.73 (4.78)	3.10 (2.65)	3.57 (5.51)
Back pain	4.05 (6.01)	7.50 (12.29)	8.05 (9.22)
Sweating	7.09 (10.42)	5.30 (6.67)	6.43 (8.34)
Itching	3.45 (7.73)	4.60 (7.71)	4.19 (5.20)
Current irritation	4.05 (4.99)	3.65 (3.31)	8.70 (12.49)
M	*4.84 (4.93)*	*5.05 (3.47)*	*7.46 (7.60)*

Sniffing

Familiarization trial - Of the 63 participants, 20 participants made incorrect identifications of the target odor during the familiarization trial (6 in the negative bias group, 3 in the positive bias group and 11 in the neutral bias group). Of the 43 participants who made correct identifications, 35 participants sniffed only once, 2 sniffed twice, 4 sniffed three times, 1 sniffed four times and 1 six times. The maximum number of sniffs was six (1 participant, neutral bias group). Since most participants sniffed only once, and one sniff results in enough information for detection (Laing, 1986), it was decided to only include the first sniff (of the second odor presentation; the identification trial) in the analyses.

Identification trial - In Table 4, the total number of sniffs, the mean sniff amplitude, the mean AUC and the mean sniff duration are displayed. Five participants still made incorrect identifications of the target odor (1 in the negative bias group, 3 in the positive bias group, and 1 in the neutral bias group), and were therefore excluded from the sniffing analyses.

Table 4.

Number of sniffs, mean sniff amplitude, mean area under the sniff curve (AUC), and mean sniff duration (SD between parentheses) in response to the target odor, by bias group

	Bias group		
	Negative	**Positive**	**Neutral**
Number of sniffs	1.10 (.07)	1.06 (.06)	1.25 (.14)
Amplitude	-6.75 (2.73)	-8.34 (6.66)	-7.80 (6.61)
AUC	7.70 (5.74)	9.77 (7.43)	10.89 (14.23)
Duration	2.17 (1.22)	2.29 (1.00)	1.97 (.91)

A Manova, with between-subjects factor Bias Group (3 levels: Negative, Positive, Neutral) was conducted on the variables amplitude, area and duration. The multivariate test showed no significant effect of bias group, $F(6,108)= 1.44$, $p = .21$, $\eta^2=.07$. In conclusion, the cover story did not have an effect on the way the target odor was sampled.

As previously stated, the experimental manipulation was only partially successful, in that most of the odor attribute ratings from the neutral bias group resembled those from the negative bias group. We thereupon divided the entire group by means of a median split based on the participants' own perception of the odor in terms of danger, and assigned participants with a relative high score on this rating in the "danger" group, and participants with a relative low score in the "safe" group ($M_{danger} = 5.31$, $SD = .47$; $M_{safe} = 3.35$, $SD = .80$ vs.). In this manner, two novel groups with actual positive versus negative expectations were once again compared on all sniffing parameters and health symptoms in a post-hoc fashion. The danger group consisted of 32 participants, and the safe group of 31 participants. Again the 5 participants who were unable to correctly identify the target odor (2 in the danger group, 3 in the safe group) were excluded from the analyses.

A Manova, with between-subjects factor Danger (2 levels: Danger vs. Safe) was conducted on the variables amplitude, area and duration. The multivariate test showed a significant effect of Danger, $F(3,54)= 2.72$, $p = .05$, $\eta^2=.13$. Results from the univariate tests showed a trend of Danger on mean amplitude, $F(1,56) = 3.76$, $p = .057$, $\eta^2=.06$. By examining the group means, it is demonstrated that the Danger group sniffed less vigorously than the Safe group ($M_{danger} = -6.26$, $SD = 3.61$; $M_{safe} = -8.99$, $SD = 6.74$). There was a significant effect of Danger on AUC, $F(1,56) = 6.83$, $p = .01$, $\eta^2=.12$; The AUC of the Danger group was significantly smaller than the AUC of the Safe group ($M_{danger} = 6.31$, $SD = 4.63$; $M_{safe} = 12.73$, $SD = 12.58$). There was also a significant effect of Danger on duration, $F(1,56) = 5.13$, $p = .03$, $\eta^2= .08$, demonstrating that participants in the Danger group

sniffed shorter compared to participants in the Safe group (M_{danger} = 1.85, *SD* = .64; M_{safe} = 2.44, *SD* = 1.28). There was no effect of the novel groups on health symptoms (solvent associated and somatic control symptoms: $F(1,61) = 2.62$, $p = .11$, and $F < 1.0$, respectively).

These post-hoc analyses suggest that the expectation that an odor is dangerous, based on participants' own danger ratings of the target odor, leads to more careful sniffing behavior compared to the expectation that an odor is safe.

Discussion

Contrary to previous work on sniffing (e.g. the detection of malingering in the context of health claims; Frank, Dulay, and Gesteland, 2003, or controlling for possible differences in brain activity as a result of specific sniff patterns in fMRI studies; Gottfried & Dolan, 2003; De Araujo et al., 2005), the present study arose out of an interest in sniffing as an index of olfactory attention. Specifically, we investigated whether expectations about health effects attributed to odor exposure affected attention to that odor, by quantifying the number of sniffs in response to the odor, as well as duration, amplitude and AUC of respective sniffs. Different biases were induced by providing groups with a cover story about the nature and effects of the target odor (Orange Ether Flower), which were negative ("chemical rest product"), positive ("aromatherapy scent") and neutral ("standard odor stimulus"). We expected a negative expectation to be associated with fewer sniffs, and shallower and shorter individual sniffs.

Although the negative bias group rated the target odor as significantly more unpleasant, artificial, dangerous and harmful than the positive bias group, our cognitive manipulation was not entirely successful. The neutral group turned out to endorse a somewhat more negative interpretation of the target odor than originally intended. This may be causally related to the absence of statistical effects associated with original group assignment on the sniffing parameters. Consequently, we proceeded with an alternative analysis in which groups were created in a post-hoc manner, based on actual ratings, as opposed to a priori assignments to bias condition. Two groups (i.e. a "danger" vs. a "safe" group) were created by means of a median split based on their perceptions of danger of the target odor. The results revealed lower sniff amplitudes, smaller AUC, and shorter sniff durations in the danger group, compared to the safe group. These findings imply a shallower sniff while at the same time inhaling less odorous air when the odor was expected to be dangerous to one's health. So, expecting danger from exposure to a certain odor seems to affect sampling of that odor.

Health symptom ratings were also collected to explore effects of expectation on health symptoms reporting. Previously, Dalton et al. (1997) and Dalton (1999) reported effects of bias induction on health symptoms reporting in studies that involved ambient odor exposures in an exposure chamber for at least 20 minutes. No meaningful differences in health symptom reports across conditions were encountered in the present study, which is best explained by the fact that our exposures were localized at the nose, and involved only few trials lasting seconds.

Variations in sniffing may have profound effects on how the odor is processed peripherally and centrally. Shallower sniffing is associated with reduced airflow inside the nostrils allowing fewer odor stimuli to reach the olfactory receptors. Furthermore, and centrally, sniffing, and even nasal inhalations without a detectable odor has been related to different patterns of neural activity in the primary olfactory cortex (Sobel et al., 1998). This means that perceptions of odors may change when sniffing patterns change.

An interesting study in this context is the one by Fannes et al. (2008). In a fear conditioning paradigm, odor was conditioned as a conditional stimulus (CS) to the inhalation of CO_2-enriched air as an unconditional stimulus. The authors found lowering of ventilation during the learning trials- a sign of breathing inhibition-, to be followed later by extinction of breathing inhibition. Our findings reflect a similar tendency: reduced inhalation of odorized air when the odor is expected to be unhealthy so as to reduce exposure to the stimulus. We are presently investigating whether and how sniffing parameters to a target odor change over repeated presentations, and if sniffs to presumed unhealthy odors remain shallow. Perhaps, explanations of MCS should be sought in avoidance - or extended avoidance - of odorized air by reduced sniffing and reduced inhalation (see also Fannes et al., 2008).

Although sniffing as an index of attention has been compared to eye movement, there are also differences. For example, whereas eye movements afford information about spatial location by allowing orientation across the visual field, sniffing does not facilitate localization of the odor source, unless the head is moved while sniffing. On the other hand, more frequent and increased sniffing is a sure sign of attention being moved - either overtly or covertly - to the odor as part of the multimodal context. Furthermore, sniffing is likely to contribute to discrimination of the odor signal against the chemical background, as much as ocular movements enable fixation on a region of interest in the visual field to allow superior visual processing at the level of the fovea. Analogous to the "active vision" movement that focuses on *looking* as opposed to *seeing*, and considers eye-tracking as its principal measure (Findlay & Gilchrist, 2003), sniffing may be considered as the prime manifestation of actively gauging one's chemosensory environment, and thus, of a top-down perspective of olfaction advocated in the introduction - active olfaction. Borrowing from active vision (Findlay & Gilchrist, 2003), future research should focus on revealing how decisions are made to start and terminate a sniff, when not to sniff at all, or on how the act of sniffing helps to activate stored olfactory representations (e.g. see Bensafi et al., 2003). In the long run, a better understanding of individual differences in sniffing could help elucidate underlying mechanisms involved in onset and maintenance of MCS.

Acknowledgements

The authors would like to thank Gaby Jongenelen, Margreet Worm, Marloes van Iperen, Alexander Backus, Arne Leer, and Theo van Aerts for their contribution to this research. We are grateful to Quest for generously supplying us with stimulus materials. The study was funded by NWO 452-03-334 to M.A.M.S.

References

Bensafi, M., Porter, J., Pouliot, S., Mainland, J., Johnson, B., Zelano, C., Young, N., Bremner, E., Aframian, D., Khan, R., & Sobel, N. (2003). Olfactomotor activity during imagery mimics that during perception. *Nature Neuroscience, 6*, 1142-1144.

Bulsing, P. J., Smeets, M. A. M., Hummel, T., Van den Hout, M. A. (2007). Influence of chemosensory pain-expectancy on olfactory event-related potentials. *Neuroimage, 38*, 164-170.

Dalton, P. (1999). Cognitive influences on health symptoms from acute chemical exposure. *Health Psychology, 18*, 579-590.

Dalton, P. (2002). Odor, irritation, and perception of health risk. *International Archives of Occupational and Environmental Health, 75*, 283-290.

Dalton, P. (2003). Upper airway irritation, odor perception and health risk due to airborne chemicals. *Toxicology Letters, 140-141*, 239-248.

Dalton, P., Wysocki, C. J., Brody, M. J., & Lawley, H. J. (1997). The influence of cognitive bias on the perceived odor, irritation and health symptoms from chemical exposure. *International Archives of Occupational and Environmental Health, 69*, 407-417.

Das-Munshi, J., Rubin, G., & Wessely, S. (2006). Multiple chemical sensitivities: A systematic review of provocation studies. *Journal of Allergy and Clinical* Immunology, *118*, 1257-1264.

De Araujo, I. E., Rolls, E. T., Velazco, M. I., Margot, C., & Cayeux, I. (2005). Cognitive modulation of olfactory processing. *Neuron*, *46*, 671-679.

Fannes, S., van Diest, I., Meulders, A., de Peuter, S., Vansteenwegen, D., & van den Bergh, O. (2008). To inhale or not to inhale: Conditioned avoidance in breathing behavior in an odor-20% CO2 paradigm. *Biological Psychology, 78*, 87-92.

Findlay, J. N., & Gilchrist, I. D. (2003). *Active vision. The psychology of looking and seeing.* Oxford: Oxford University Press.

Frank, R. A., Dulay, M. F., & Gesteland, R. C. (2003). Assessment of the Sniff Magnitude Test as a clinical test of olfactory function. *Physiology & Behavior, 78*, 195-204.

Gottfried, J. A., & Dolan, R. J. (2003). The nose smells what the eye sees: crossmodal visual facilitation of human olfactory perception. *Neuron, 39*, 375–386.

Kosslyn, S.M. (1994). Image and Brain: The resolution of the imagery debate. Cambridge: MIT Press.

Krauzlis, R. J., & Adler, S. A. (2001). Effects of directional expectations on motion perception and persuit eye movements. *Visual Neuroscience, 18*, 365-376.

Labarge, A. S., & McCaffrey, R. J. (2000). Multiple Chemical Sensitivity: A review of the theoretical and research literature. *Neuropsychology Review, 10*, 183-211.

Laing, D.G. (1982). Characterisation of human behaviour during odour perception. *Perception, 11*, 221-230.

Laing, D. G. (1983). Natural sniffing gives optimum odour perception for humans. *Perception, 12*, 99-117.

Laing, D. G. (1983). Identification of single dissimilar odors is achieved by humans with a single sniff. *Psysiology & Behavior, 37*, 163-170.

Li, W., Howard, J. D., Parrish, T. B., & Gottfried, J.A. (2008). Aversive learning enhances perceptual and cortical discrimination of indiscriminable odor cues. *Science*, *319*, 1842-1845.

Lundström, J.N., Seven, S., Olsson, M.J., Schaal, B., Hummel, T., 2006. Olfactory Event-Related Potentials reflect individual differences in odor valence perception. Chem. Senses. 31, 705-711.

Mainland, J. & Sobel, N. (2006). The Sniff Is Part of the Olfactory Percept. *Chemical Senses, 31*, 181-196.

Pause, B. M., & Krauel, K. (2000). Chemosensory event-related potentials (CSERP) as a key to the psychology of odors. *International Journal of Psychophysiology, 36*, 105-122.

Schiffman, S. S., Walker, J. M., Dalton, P., Lorig, T. S., Raymer, J. H., Shusterman, D., & Williams, C. M. (2000). Potential health effects of odor from animal operations, wastewater treatment, and recycling of byproducts. *Journal of Agromedicine, 7*, 7-81.

Shusterman, D. (2001). Odor-associated health complaints: competing explanatory models. *Chemical Senses, 26*, 339-343.

Sobel, N., Thomason, M. E., Stappen, I., Tanner, C. M., Tetrud, J. M., Bower, J. M., Sullivan, E. V., & Gabrieli, D. E. (2001). An impairment in sniffing contributes to the olfactory impairment in Parkinson's disease. *Proceedings of the National Academy of Sciences of the United States of America, 98*, 4154-4159.

Sobel, N., Prabhakaran, V., Desmond, J. E., Glover, G. H., Goode, R. L., Sullivan, E. V., & Gabrieli, J. D. (1998). Sniffing and smelling: separate subsystems in the human olfactory cortex. *Nature, 392,* 282-286.

Wilson, D. A., Stevenson, R. J. (2006). *Learning to Smell*. Baltimore: The John Hopkins University Press.

Chapter 7

Summary and general discussion

The rationale for conducting the research presented in this thesis was to better understand mechanisms involved in why some people attribute health effects to low concentrations of odor exposures that are often well-tolerated by the majority of the population. To study this phenomenon, we adopted a top-down perspective, since both research on odor-induced health effects and olfactory perception in general suggest that analytical accounts of olfaction alone (i.e. bottom-up perspectives) cannot sufficiently explain behavioral and sensory responses, while models which incorporate the influence of contextual and experiential factors (i.e. top-down perspectives) are better equipped to do so. The focus was on perceptual endpoints rather than on health effects or symptom reports. This focus was chosen based on the fact that cognitions have been shown to penetrate phases of information processing that were believed to be completely stimulus-driven (e.g. encoding of basic stimulus characteristics). This led to the hypothesis that cognition modulates olfactory sensations and perceptions, and that altered perceptions, in turn, play a role in the initiation and persistence of somatic responses and health symptom reports.

The thesis is organized around two main objectives: Objective 1 involved the determination of the content of cognitions related to odors and health that are believed to have a top-down influence. Objective 2 concerned the determination of the nature and magnitude of the effects of top-down influences on odor sensation and perception. The objectives were tackled in five empirical chapters (Objective 1 in Chapters 2 and 3 and Objective 2 in Chapters 4, 5, and 6).

In this General Discussion main findings per empirical chapter will be summarized, and discussed in the context of Objectives 1 and 2. Implications of the findings will be discussed in relation to theoretical models of olfaction and health (see General introduction), and suggestions for future research will be offered. Finally, remaining issues such as limitations will be presented.

Objective 1: The content of cognitions associated with odors

Summary Chapters 2 and 3

With reference to the information processing model on Chemosensory Perception (Dalton & Hummel, 2000; Smeets & Dalton, 2005) top-down influences of cognitions should be interpreted broadly and refers to previously stored knowledge, beliefs about the relation between odors and health - whether appropriate or inappropriate - and even pre-existing personality traits and states. This has led to empirical studies focusing on the influence of explicit beliefs and cognitions (via manipulation of information: e.g. Dalton, 1999) and of personality characteristics such as negative affectivity (Smeets & Dalton, 2002) on health symptom reports. Little attention, however, has been paid to the influence of implicit attitudes about odors and health on behavior. In Chapters 2 and 3 we concentrated on implicit attitudes, by measuring automatically activated associations between odors and health that are not necessarily accessible to introspection but might still have an influence on behavior. To this end, we chose a method that enabled us to study cognitions related to olfaction that act on an implicit level: the Implicit Association Test (IAT; Greenwald et al., 1998). First, the valence of the concept odor as experienced by participants was explored, without taking

into account the association with the concept health (Chapter 2). Then, automatic health associations with the concept odor were investigated: We tested whether there are automatic odor-illness or automatic odor-healthiness associations (Chapter 3).

In Chapter 2, we demonstrated a robust positive attitude toward the concept odor: participants exhibited shorter reaction times during parts of the test where the concept odor had to be associated with the concept "good" compared to parts of the test where the concept odor had to be associated with the concept "bad". Additionally, the Odor-IAT distinguished between individuals with various odor-related behaviors; participants who preferred using scented consumer products demonstrated a clear positive attitude to the concept odor, whereas control participants (who did not have a specific odor preference) showed neither a positive nor a negative attitude toward that concept. This between-group distinction in implicit odor attitude was not observed in ratings of word valence (explicit odor attitudes), suggesting that the Odor-IAT was capable of measuring an implicit attitude that was different from explicit odor attitudes.

The study reported in Chapter 3 demonstrated that participants exhibited shorter reaction times when associating the concept odor with the concept sick as opposed to associating the concept odor with the concept healthy. Explicit ratings of the words that were used in the odor-IAT in terms of their healthiness (instead of their valence) indicated no illness association. Again, these results demonstrated that implicit evaluations did not simply reflect explicit ones.

Summarizing, we demonstrated an odor-good association in Chapter 2, and an odor-sick association in Chapter 3. Although this seems to be conflicting at first blush (a "positive" odor-good association, and a "negative" odor-sick association), this contradiction becomes understandable if the concept good is interpreted not as just a positive evaluation, but rather as referring to "useful" or "helpful". In other words, the robust odor-good association might indicate the awareness of the usefulness and trustworthiness of odors as indicators of danger, and odors are therefore classified as "good", and not as "bad"; the odor-good association may imply an appreciation of the sense of smell as information channel in this particular population. Moreover, the positive attitude toward the concept odor seems to reflect evaluations that were not tied to the concept of health or illness, as this concept was not given, and thus associations related to other contexts in which odors play a role might have become activated, such as pleasant food or perfume associations. These results imply that the concept odor elicits various different associations. However, as soon as the association of odor becomes tied to health, it leans over towards the negative.

Implications

The robust implicit odor-illness association, in the absence of a clear explicit odor-illness association, suggests that odors belong to the group of stimuli that have a certain biological "preparedness", i.e. a strong innate association with possible danger, even in the absence of actual threat. The term "preparedness" refers to the notion that certain stimuli which once posed serious threat to our early ancestors may still be easily experienced as harmful today (Öhman & Mineka, 2001). From an evolutionary perspective, this innate association leads to a well-adapted perceptual strategy.

Scanning the environment for possible danger in an automatic or implicit manner is more efficient than relying on a system which needs cognitive resources to make such evaluations[6].
Obviously, a common side-effect of an automatically operating detection system is the increased possibility of false alarms, as expressed by an exaggerated response to essentially harmless odors. A hypothesis which follows from this line of thought is that individuals with MCS and others who are suspicious of odor exposures in their environment have even stronger odor-illness associations, most likely resulting from previous experiences or beliefs, leading to faster reactions and maladaptive responses in new exposure situations.

In the cognitive-perceptual model of Chemosensory Perception by Dalton and Hummel (2000) and Smeets and Dalton (2005) emphasis is placed on the top-down influences on odor perception and somatic and behavioral responses to these odors (see General introduction). The results obtained in Chapter 3 imply that implicit beliefs should also be acknowledged in this theoretical model; especially since implicit odor associations did not completely match explicit associations. In other words, there may be influences on odor perception that act on a much more implicit level, and may run counter to what people state as their explicit beliefs.

Objective 2: To*p* –down influence of cognitions on perception

Summary results chapters 4-6

In a series of studies Dalton and colleagues observed that cognitive influences were not limited to behavioral endpoints (health symptoms reports), but were already reflected in sensory responses (intensity and irritancy perceptions; Dalton, Wysocki, Brody, & Lawley, 1997; Dalton, 1999) presumed to take place at earlier levels of information processing. This led Dalton to propose that health symptoms attributed to odor exposures could be modulated by such changes during basic perceptual processing (Dalton, 2002, 2003), meaning that if an odorant is *encoded* as much more intense or sensory irritating as a result of top-down influences of cognition, it will more likely elicit "corresponding" health effects. The research presented in the second part of this thesis tested whether health-related cognitions can indeed affect perception. To test this hypothesis, a cognitive neuroscience perspective was taken in Chapters 4 and 5: We employed olfactory Event-Related

[6] This apparently innate, automatic association between odors and illness is reflected by the ancient belief that odors themselves can influence health in a negative way. In fact, the tendency to attribute illness to odors in the air may reflect elements of the miasma theory (Corbin, 1986). According to this theory, inhalation of the odorous air emanating from toxic or spoilt foods or from open wounds causes illness. For centuries people adhered to this theory, until it was discovered that these odors are the byproducts of bacterial processes involved in decay, and that consumption of the toxic or rotten food products - the origins of the bad odor - themselves will make you sick, but not the inhalation of the accompanying odor. Nevertheless, the behavior or reactions of many people to odorous emissions still reflect these notions.

Potentials (OERPs), which enabled us to investigate whether top-down effects influenced earlier encoding phases rather than, or in addition to, later "higher order" cognitive stages of information processing. In addition to assessment of temporal processing of the odor stimulus, we studied the influence of cognitions on olfactory sampling, or sniffing behavior (Chapter 6). This endpoint provided us with a measure of olfactory attention (as an equivalent of attention-driven eye movements).

In the study reported in Chapter 4, cognitions were manipulated using instructional learning, i.e. by explicitly telling participants which is the good and which is the bad stimulus. In these studies, pain following sensory irritation (i.e. a sense of burning or stinging from stimulation of the nerve endings of the trigeminal nerve innervating among others the nasal cavity) was induced to model an adverse health effect. Sensory irritation seems to be ecologically valid with reference to MCS, since patients with MCS often report irritation of trigeminally innervated areas (Schiffman et al., 2000). Participants were told they would experience a chemical stimulus delivered to the nose that would be either painful or not painful. The painful stimulus was the trigeminal irritant CO_2; the non-painful stimulus was H_2S, which is not a trigeminal irritant. We compared OERPs in response to the "safe' odor H_2S under these two different expectancy conditions: when they were expecting to perceive pain versus no pain. An increase in processing speed was demonstrated when participants expected pain: N1 latencies were significantly shorter. In other words: when the participants expected to experience pain they were faster to process the presented chemical stimulus than when they did not expect to experience pain. Since the N1 peak has been related to the encoding of exogenous stimulus characteristics such as stimulus intensity and quality, we concluded that cognitions have an influence on information processing of chemosensory stimuli at a basic and early perceptual level. We did not find any effects on the later P2 peak, which, if they had been found, would have reflected effects of e.g. salience and emotionality involved in processing the chemical stimulus.

In Chapter 5 two OERP studies were presented. Here expectancies regarding health effects were induced by means of classical conditioning, whereby the odor acted as Conditioned Stimulus (CS) signaling the temporal proximity of pain from the Unconditioned Stimulus (US), the trigeminal irritant CO_2: An unpleasant odor (H_2S in Study 1) and a pleasant odor (PEA in Study 2) were used as the conditioned stimuli. Both odors were evaluated as more annoying after conditioning to sensory irritation. However, whereas all peak latencies and amplitudes associated with smelling of the odor were affected after conditioning when the odorant was H_2S, only the N1 peak amplitude was changed when the odorant was PEA. We concluded that the expection of pain following inhalation of an odor alters perception of that odor to a much greater extent when the odor is unpleasant than when the odor is pleasant (possibly as a consequence of "belongingness" of the unpleasant H_2S, see below).

All three OERP studies (the one study presented in Chapter 4 and the two studies presented in Chapter 5) underscore the hypothesis of influence of expectations on early perception. However, there are differences with respect to the effects of expectations on the more cognitive phases of ol-

factory information processing. In the study presented in Chapter 4, no effects of pain-expectancy on the P2 peak were observed. The absence of P2 changes may be explained by the fact that H_2S and CO_2 are easy to discriminate: the former being an odor stimulating the olfactory nerve, the latter being an irritant stimulating the trigeminal nerve. Therefore, as soon as participants identified the chemical as being the odor, they could immediately interpret it as "safe"; effects of expectation of pain may not have outlasted the early detection phase as the odor was no longer salient as soon as it had been detected as the safe chemosensory stimulus. Something similar was observed in the second study presented in Chapter 5, whereby the odor of PEA was conditioned to pain. Again, we did not observe any effect of e.g. salience on the P2 peak. The absence in this instance may again be explained by quick categorization of the odor as being safe, probably based on previous formed pleasant and safe associations with the odor of PEA (rose) that have a more profound impact on cognitive processing than newly formed associations between the odor and a trigeminal irritant. These results suggest that healthy individuals are capable of making very quick evaluations about the safety of a chemical. As soon as the signal is interpreted as "safe" (either because it is determined that the stimulus is not the harmful one [Chapter 4], or based on other, previous established, and perhaps stronger associations [Chapter 5]), the odor is no longer salient, and extra cognitive resources are no longer needed after detection phases, resulting in P2 peaks that remain unchanged.

In Chapter 6, we again used instructional learning to induce the expectation that inhalation of an odor may be followed by adverse health consequences, to investigate the effects of this expectation on sniffing of the odor. We demonstrated a shallower sniff, and less inhaled odorous air when participants believed an odorant to be dangerous to their health, although this was irrespective of the manipulation. In other words, the effects were only found for those individuals who after smelling of the odor indicated they believed the odor to be potentially dangerous. So, expecting danger from exposure to a certain odor affected olfactory attention, or sampling of that odor.

Summarizing, in this second part of the thesis, it was shown that health-related cognitions related to odors and their effects not only affect the more interpretational stages of information processing of the odor, but specifically affect those stages of information processing associated with (early) perception (e.g. encoding of basic stimulus characteristics). This was specifically the case for the unpleasant odor when compared to the pleasant odor in Chapter 5. Additionally, cognitive influences were observed during sampling of the odor. This was interpreted as reflecting an attentional effect.

Implications

The profound effects of negative health consequences that become associated with olfactory stimuli on early olfactory processing goes against traditional perspectives of perception, in which earlier stages were believed to be inaccessible to top-down influences. Moreover, the findings obtained in Chapters 4 and 5 confirm that the *expectation* that an odor is harmful may change *perception* of that odor. In turn, health effects as a consequence of odor exposures could be modulated by these sen-

sory changes as proposed by Dalton (2002, 2003), although this hypothesis still remains to be tested by including endpoints that measure such health effects (e.g. ocular hyperemia, nasal secretion; Smeets et al., 2002). An interesting hypothesis that follows our findings is that perceptual changes as a consequence of cognitive interference may be more profound in individuals who suffer from odor-induced health effects.

The fact that cognitive influences on OERPs are larger when the odor has an unpleasant hedonic value, suggest that belongingness of H_2S plays a role in our results. Belongingness refers to the fact that associations are easier established when the CS and US are similar in affectivity. We indeed observed larger effects of conditioning on OERP when the CS and US were affectively congruent (the odor of H_2S and the CO_2 pulses, both unpleasant), as opposed to instances where the CS and US were affectively incongruent (the pleasant odor of PEA and the unpleasant CO_2). Apparently, in healthy individuals, previously established associations between pleasant odors and safe situations are hard to overcome, resulting in less extensive conditioning effects. However, since some people with MCS report health symptoms even after exposure to pleasant odors, such as the odors of perfume or deodorizers, the present results give rise to the hypothesis that in these individuals congruency effects have lesser or no impact. That is, learning of incongruent CS-US associations may be as effective as learning of congruent CS-US associations in individuals experiencing odor-induced illness.

Additionally, and related to the previous argument, we observed that participants in our studies could very quickly determine whether they were exposed to a safe or a potentially harmful stimulus (reflected by less extensive effects of conditioning on later phases of processing as soon as the stimulus was categorized as safe). A hypothesis that follows is that individuals who experience health effects as a consequence of odor exposure might be unable to make such quick evaluations, or are uncertain about their evaluations, and react as a consequence in a hypersensitive manner to a large number of (or even to all) chemical stimuli they encounter (see for instance: Anderson, Nordin, Millqvist, & Bende, 2009).

In Chapter 6, we presented results that demonstrated that believing that an odor can be harmful affected sampling of that odor. It is not surprising that people who believe that an odor can induce negative health effects try to avoid inhalation of that odor as much as possible. An interesting study in this context is the one by Fannes et al. (2008). They demonstrated that participants lowered their ventilation during the learning trials of a fear conditioning experiment whereby an odor was conditioned as a CS to the inhalation of CO_2. This lowering of ventilation, a sign of breathing inhibition, was in turn followed by extinction of breathing inhibition. Our findings show a similar pattern: reduced inhalation of odorized air when the odor is expected to be unhealthy in order to avoid exposure to the stimulus as much as possible. A hypothesis that follows our findings and the ones obtained by Fannes et al. (2008) is that explanations of MCS might be sought in avoidance – or sustained avoidance - of odorized air by reduced inhalation. Alterations in normal breathing might in turn induce the experience of various health effects, such as dizziness and increased heart rate (Van den Bergh et al., 1995, 1997, 1998). In turn, these health effects may be misdiagnosed as consequences of odor exposure.

All findings in this second part of the thesis support an information processing system that aims to determine as quickly as possible whether an encountered chemical is either a safe or a harmful one, in which top-down influence of health-related cognitions adds to the speed of this process. That is, expecting potential harm from an odor accelerates early olfactory information processing. Adding top-down influences to bottom-up processing contribute to perception efficacy in most instances. The downside however, is that a system that does not only rely on "objective" stimulus characteristics, but also allows "subjective" interpretations is sensitive to misclassifications of harmless odors as dangerous chemicals, leading to hypersensitivity for olfactory cues and maladaptive behavioral responses.

Final Remarks

Limitations

The research presented in this thesis provides new insights in the phenomenon of health effects ascribed to low-levels of odorous chemicals. However, some limitations need to be recognized.

All studies have been conducted in healthy participants, mostly young students (recruited from the Universities of Utrecht and Dresden). It therefore remains unknown whether the findings can be generalized to the population of interest; people who suffer from odor-induced health effects. Yet, we demonstrated innate odor-illness associations and perceptual alterations after learning even in healthy participants, which give rise to the assumption that cognitive influences and perceptual changes might play an even more profound role in individuals with MCS-like health symptoms. This theory, however, still remains to be fully investigated.

Furthermore, and related to the former argument, most individuals who participated in our studies were female. In the OERP studies, only females were recruited, to exclude as much unrelated variability in brain responses as possible (Lundström & Hummel, 2006). In the other studies, more females were willing to participate. That male participants were not well represented in our studies should be taken into account when interpreting the results, although it should also be acknowledged that the majority of individuals who suffer from odor-induced health effects is female (estimations vary from 68% to 88%; Labarge & McCaffrey, 2000).

The research in this thesis focused on perception and not on health effects as endpoints. That is, we demonstrated alterations in perception, modulated by top-down influences of cognitions, but we have not investigated to what extent such changes in perception affect health symptom experiences. This is an important step that should be taken next.

Finally, other OERP studies already demonstrated the impact of cognitions on early information processing, by manipulation participants' attention to the odorant. More attention resulted in shorter latencies (but not in increased N1 amplitudes; Krauel et al., 1998; Pause & Krauel, 2000; Pause, 2002). In that sense, we replicated a phenomenon that was demonstrated before: the possibility of affecting early perceptual processing. The studies in this thesis specifically and systematically show that manipulations of expectancies about the harmfulness of a stimulus have a similar or even a larger effect on early processing, and that influences of cognitions differ for different odorants.

To conclude

In this thesis we investigated whether expectations concerning odors and health are capable of affecting perception of odors using experimental manipulations of these cognitions. We indeed demonstrated such effects in healthy participants. The findings demonstrate that top-down influences of health-related cognitions speed up early olfactory information processing. Whereas beneficial in most instances, the interference of "subjective" factors in a perceptual system increases the likelihood of misclassifications of harmless odors as dangerous chemicals. This could in turn elicit hypersensitivity for odors and maladaptive behaviour. The obvious next step would be to test the influence of health cognitions in populations in which cognitions may be assumed to play such a role, such as in MCS patients and others bothered by environmental odors, using cross-sectional methods.

References

Anderson, L., Nordin, S., Millqvist, E., & Bende, M. (2009). On the relation between capsaicin sensitivity and responsiveness to CO_2: detection sensitivity and event-related brain potentials. *International Archives of Occupational and Environmental Health, 82*, 285-290.

Dalton, P. (1999). Cognitive influences on health symptoms from acute chemical exposure. *Health Psychology, 18*, 1-12.

Dalton, P. (2002). Odor, irritation, and perception of health risk. *International Archives of Occupational and Environmental Health, 75*, 283-290.

Dalton, P. (2003). Upper airway irritation, odor perception and health risk due to airborne chemicals. *Toxicology Letters, 140-141*, 239-248.

Dalton, P., & Hummel, T. (2000). Chemosensory function and response in idiopathic environmental intolerance. *Occupational Medicine*, *15*, 539-556.

Dalton, P., Wysocki, C. J., Brody, M. J., & Lawley, H. J. (1997). The influence of cognitive bias on the perceived odor, irritation and health symptoms from chemical exposure. *International Archives of Occupational and Environmental Health*, 69, 407-417.

Fannes, S., van Diest, I., Meulders, A., de Peuter, S., Vansteenwegen, D., & van den Bergh, O. (2008). To inhale or not to inhale: Conditioned avoidance in breathing behavior in an odor-20% CO2 paradigm. *Biological Psychology, 78*, 87-92.

Greenwald, A. G., McGhee, D. E., & Schwartz, J. L. K. (1998). Measuring individual differences in implicit cognition: The implicit association test. *Journal of Personality and Social Psychology, 74*, 1464-1480.

Krauel, K., Pause, B. M., Sojka, B., Schott, P., & Ferstl, R. (1998). Attentional modulation of central odor processing. *Chemical Senses, 23*, 423-432.

Labarge, A. S., & McCaffrey, R. J. (2000). Multiple Chemical Sensitivity: A review of the theoretical and research literature. *Neuropsychology Review, 10*, 183-211.

Lundström, J. N, & Hummel, T. (2006). Sex-specific hemispheric differences in cortical activation to a bimodal odor. *Behavioural Brain Research, 166*, 197-203.

Öhman, A., & Mineka, S. (2001). Fears, phobias, and preparedness: Toward an evolved module of fear and fear learning. *Psychological Review, 108*, 483-522.

Pause, B. M. (2002). Human brain activity during the first second after odor presentation. In: Rouby, C., Schaal, B., Dubois, D., Gervais, R., Holley, A. (Eds), *Olfaction, taste, and cognition*. University Press, Cambridge, pp. 309-323.

Pause, B. M., & Krauel, K. (2000). Chemosensory event-related potentials (CSERP) as a key to the psychology of odors. *International Journal of Psychophysiology, 36*, 105-122.

Schiffman, S. S., Walker, J. M., Dalton, P., Lorig, T. S., Raymer, J. H., Shusterman, D., & Williams, C. M. (2000). Potential health effects of odor from animal operations, wastewater treatment, and recycling of byproducts. *Journal of Agromedicine, 7*, 7-81.

Smeets, M. A.. M., & Dalton, P. H. (2002). Perceived odor and irritation of isopropanol: a comparison between naïve controls and occupationally exposed workers. *International Archives of Occupational and Environmental Health, 75,* 541-548.

Smeets, M. A. M., & Dalton, P. H. (2005). Evaluating the human response to chemicals: Odor, irritation and non-sensory factors. *Environmental Toxicology and Pharmacology, 19*, 581-588.

Van den Bergh, O., Kempynck, P. J., Van de Woestijne, K. P., Baeyens, F., & Eelen, P. (1995). Respiratory learning and somatic complaints: A conditioning approach using CO2-enriched air inhalation. *Behaviour Research and Therapy, 33*, 517-527.

Van den Bergh, O., Stegen, K., & Van de Woestijne, K. P. (1997). Learning to have psychosoamtic complaints: Conditioning of respiratory behavior and complaints in psychosomatic patients. *Psychosomatic Medicine, 59*, 13-23.

Van den Bergh, O., Stegen, K., & Van de Woestijne, K. P. (1998). Memory effects of symptom reporting in a respiratory learning paradigm. *Health Psychology, 17*, 241-248.

Samenvatting
(Summary in Dutch)

Geuren signaleren de aanwezigheid van chemicaliën in de lucht, waarvan sommige (meestal in hoge concentraties) directe gezondheidseffecten kunnen initiëren. Voorbeelden van directe gezondheidseffecten zijn irritatie aan de slijmvliezen in de neus en keel, ademhalingsproblemen of zelfs schade aan het zenuwstelsel. Geuren kunnen ook de aanwezigheid van bacteriën aanduiden, bijvoorbeeld in geval van rotting of slechte hygiëne. In deze gevallen dient contact met de geurbron vermeden te worden, maar de geur zelf geeft niet een directe aanleiding tot gezondheidsproblemen en kan gezien worden als een waarschuwingssignaal. Echter, er zijn mensen die gezondheidseffecten rapporteren, niet als gevolg van inhalatie van hoge concentraties aan toxische chemicaliën of door contact met bijvoorbeeld rottend voedsel, maar in reactie op het waarnemen van onschadelijke, vaak dagelijks voorkomende geurstoffen, zoals de geur van parfum, deodorant, schoonmaakmiddelen of geuruitstoot door verkeer of fabrieken. De meest extreme variant van geurgerelateerde gezondheidsproblemen is Meervoudige Chemische Overgevoeligheid (MCO). Mensen met MCO kunnen klachten hebben in reactie op blootstelling aan vrijwel alle geuren. Het onderzoek dat wordt beschreven in dit proefschrift had als doel om dit fenomeen beter te begrijpen. Waarom rapporteren sommige mensen gezondheidsproblemen nadat zij bloot hebben gestaan aan vaak onschuldige en lage concentraties aan geurstoffen, geuren die geen lichamelijke effecten initiëren in de rest van de populatie?

Om geurgerelateerde gezondheidseffecten te bestuderen, werd een psychologische benadering gekozen. Er werd onderzocht welke rol *cognitieve invloeden* mogelijk spelen in het ontstaan van gezondheidsproblemen na blootstelling aan geur. In de context van dit proefschrift wordt met 'cognitieve invloeden' of 'cognities' eerder opgeslagen kennis, ideeën en verwachtingen over de relatie tussen geur en gezondheid bedoeld. Deze cognitieve benadering werd gekozen nadat gebleken is dat analytische modellen van geurperceptie onvoldoende in staat bleken om waarneming van geur en gedrag in reactie op geur te verklaren en te voorspellen. Hiermee wordt bedoeld dat kennis over bijvoorbeeld de moleculaire structuur van geurmoleculen enerzijds en receptoreigenschappen anderzijds (beschreven in zogenaamde stimulus-respons modellen) niet genoeg is om de ervaring die we hebben wanneer we iets ruiken te begrijpen. Het bestuderen van psychologische processen die hierbij komen kijken is dan noodzakelijk.

In dit proefschrift lag de focus op de bestudering van de *waarneming* van geur en niet zozeer op het ontstaan van gezondheidseffecten of op de rapportage van symptomen. Deze focus werd gekozen omdat steeds meer onderzoek laat zien dat cognitieve invloeden niet alleen bewuste waarnemingen of gedragingen kunnen beïnvloeden, maar reeds doordringen tot fasen van informatieverwerking waarvan gedacht werd dat ze volledig bepaald werden door de stimulus zelf. Met andere woorden, langzaam wordt duidelijk dat psychologische processen zelfs de codering van basale stimuluseigenschappen kunnen moduleren. In dit proefschrift werd dit onderzocht binnen de context van geurgerelateerde gezondheidseffecten: Kunnen cognities over geur en gezondheid de basale waarneming van geur veranderen, waardoor deze veranderde waarneming wellicht de aanleiding voor gezondheidsproblemen wordt? Wanneer het brein een geur als veel intenser codeert, zullen 'corresponderende' somatische reacties wellicht het gevolg zijn. Nogmaals, de focus

lag op het eerste deel van deze vraagstelling, de invloed van cognities op waarneming, en niet op het effect daarvan op lichamelijke reacties.

Het onderzoek beschreven in dit proefschrift besloeg twee hoofddoelen. Het eerste doel betrof het bestuderen van *de inhoud* van geurgerelateerde cognities. Doel 2 betrof het onderzoeken van *de invloed van cognities op de waarneming* van geur. Deze twee doelen werden behandeld in vijf empirische hoofdstukken (Doel 1 in Hoofstuk 2 en 3; Doel 2 in Hoofdstuk 4, 5 en 6).

Doel 1: De inhoud van geurgerelateerde cognities

Voorgaand onderzoek liet zien dat cognities over geuren en gezondheid de frequentie en de intensiteit van gerapporteerde gezondheidsklachten kan beïnvloeden. Proefpersonen aan wie verteld werd dat een bepaalde geur schadelijk voor de gezondheid zou kunnen zijn, rapporteerden meer gezondheidssymptomen na blootstelling aan deze geur dan proefpersonen aan wie verteld werd dat dezelfde geur gezondheidsbevorderend zou kunnen zijn. In dit experiment werd dus expliciet informatie aangereikt over de geur waaraan men bloot stond. Echter, cognities over geur en gezondheid kunnen ook op een impliciet niveau invloed uitoefenen. Dat wil zeggen dat cognities niet per definitie toegankelijke en duidelijke denkbeelden in het bewustzijn moeten zijn om waarneming en gedrag te beïnvloeden, maar ook kunnen bestaan uit snelle, automatisch geactiveerde en mogelijk onbewuste associaties. Tot nu toe is er weinig aandacht geweest voor impliciete of automatisch geactiveerde cognities in de context van geur. Het eerste deel van het proefschrift beschrijft onderzoek dat zich hierop richtte.

In de Hoofdstukken 2 en 3 werden impliciete associaties ten aanzien van geur en gezondheid bestudeerd: Associëren mensen het concept geur makkelijker met een positief of met een negatief concept en relateert het concept geur eerder aan ziekte of juist aan gezondheid? Deze automatische associaties werden gemeten met behulp van een reactietijdentaak; de Implicit Association Test (IAT).

In Hoofdstuk 2 staan drie experimenten beschreven die een robuuste, positieve associatie met het concept geur demonstreren: proefpersonen hadden minder moeite met delen van de IAT waar het concept geur moest worden geassocieerd met een positief concept, vergeleken met delen van de test waar het concept geur geassocieerd diende te worden met een negatief concept. Daarnaast maakte de IAT onderscheid tussen proefpersonen met verschillend geurgerelateerd gedrag: proefpersonen die een voorkeur hadden voor het gebruik van geurende producten lieten een duidelijke positieve impliciete associatie met het concept geur zien, terwijl proefpersonen die niet per definitie een voorkeur voor geurende producten hadden bleken noch een positieve, noch een negatieve associatie met geur te hebben. Dit onderscheid tussen groepen in impliciete associatie werd niet zichtbaar in de expliciete evaluatie van de concepten. Dit suggereert dat de IAT in staat was om impliciete associaties met geur te meten die verschilden van expliciete associaties.

Het onderzoek in Hoofdstuk 3 demonstreerde een robuuste associatie tussen het concept geur en ziekte. Proefpersonen hadden kortere reactietijden tijdens delen van de IAT waar zij het con-

cept geur moesten associëren met het concept ziek, vergeleken met delen van de taak waar zij geur moesten associëren met het concept gezond. Wanneer dit verband op een expliciete wijze onderzocht werd, werd geen associatie tussen geur en ziekte gevonden. Wederom laat dit zien dat de IAT in staat was om impliciete associaties met geur te meten die anders waren dan expliciete associaties.

De resultaten beschreven in de Hoofdstukken 2 en 3 demonstreren duidelijk dat het concept geur verschillende associaties kan oproepen. Deze associaties kunnen zowel een positief als een meer negatief karakter hebben. Tevens laten deze studies zien dat zodra het concept geur binnen een gezondheidscontext geplaatst wordt, associaties een negatieve richting opgaan.

De robuuste impliciete associatie tussen geur en ziekte, in de afwezigheid van een duidelijke expliciete associatie tussen deze twee concepten, suggereert dat geuren tot een groep stimuli behoren die mogelijk een aangeboren relatie hebben met potentieel gevaar (geuren als waarschuwingssignalen). Vanuit een evolutionair perspectief is dit een handige strategie. Het automatisch en onbewust scannen van de omgeving om mogelijk gevaar te herkennen is veel efficiënter dan een systeem dat veel cognitieve capaciteit nodig heeft om gevaar te detecteren. Echter, het nadeel van een automatisch opererend systeem is de toegenomen kans op *false alarms*; het systeem kan ongevaarlijke geuren, mogelijk onder invloed van cognitieve invloeden, gaan classificeren als toxische chemicaliën, waardoor een overdreven lichamelijke reactie een gevolg zou kunnen zijn.

Doel 2: Invloed van cognities op waarneming

Zoals hierboven al beschreven toonde eerder onderzoek aan dat de verwachting dat een geur schadelijk kan zijn voor de gezondheid tot een toename leidde van waargenomen gezondheidssymptomen na blootstelling aan deze geur. Deze cognitieve invloed bleef niet beperkt tot de rapportage van symptomen, maar had tevens een effect op de manier waarop basale stimuluseigenschappen ervaren werden. Proefpersonen aan wie verteld werd dat zij blootstonden aan een potentieel gevaarlijke geur gaven aan de geur sterker en meer prikkelend en irriterend te vinden. Dit in tegenstelling tot proefpersonen aan wie verteld was dat zij blootstonden aan een gezondheidbevorderlijke geur. Het onderzoek in het tweede deel van dit proefschrift richtte zich op de vraag of cognities over geur en gezondheid inderdaad de waarneming van basale stimuluseigenschappen kan beïnvloeden. Hier werd echter niet alleen aan proefpersonen gevraagd om stimuluskarakteristieken te beoordelen; er werd tevens gebruik gemaakt van olfactorische Event Related Potentials (OERPs; Hoofdstukken 4 en 5), waarbij hersensignalen in reactie op het aanbieden van een stimulus geregistreerd worden (door middel van elektrodes op het hoofd). Door deze techniek konden de verwerkingsintensiteit en de verwerkingssnelheid van een geur onderzocht worden. Daarnaast kon door het registeren van OERPs bekeken worden of de invloed van cognities zich voornamelijk manifesteerde in de relatief late fasen van informatieverwerking (de P2 piek in het OERP signaal; samenhangend met de interpretatie en de betekenis van de geurstimulus) of juist ook in de 'vroege' coderingsfasen van stimulusverwerking (de N1 piek van het OERP signaal). Wanneer cognities

over geur en gezondheid daadwerkelijk basale coderingsfasen zouden beïnvloeden, zouden we dus een veranderde N1 piek in het OERP signaal moeten registreren.

In Hoofdstuk 4 wordt een OERP-studie beschreven waarbij proefpersonen vooraf informatie kregen over de chemische stimulus die zij toegediend zouden krijgen in de neus (met behulp van een zogenaamde olfactometer). Er werd gedurende verschillende perioden van het experiment expliciet verteld dat zij ofwel telkens alleen een geur zouden ruiken (H_2S), of dat zij naast het ruiken van een geur ook zo nu en dan 'een pijnlijke prikkel' in de neus aangeboden zouden krijgen. De pijnlijke prikkel werd veroorzaakt door de aanbieding van een korte CO_2 puls welke sensorische irritatie opwekte (een gevoel van prikkeling of branden in de neus als gevolg van de stimulatie van de zenuwuiteinden van de trigeminale zenuw). Patiënten met MCO rapporteren geregeld sensorische irritatie in de neus, wat deze stimulus dus ecologisch valide maakte. Door het design van dit experiment ontstonden er twee cognitieve condities: één waarbij men geen pijn verwachtte tijdens het ruiken van de geur en één waarbij men juist wel pijn verwachtte tijdens het ruiken van de geur. OERPs in reactie op H_2S werden vergeleken tussen de twee condities. Dit experiment liet zien dat de verwerkingssnelheid van de vroege coderingsfase van een geur toeneemt wanneer men pijn verwacht. Met andere woorden, wanneer de proefpersonen pijn verwachtten, verwerkten zij de chemische stimulus sneller dan wanneer zij geen pijn verwachtten. Cognities hebben dus invloed op de vroege en basale delen van de waarneming. Er werd geen effect van cognities op de P2 piek gevonden.

In Hoofdstuk 5 worden twee experimenten beschreven. Hier werden cognities over geuren en gezondheid geïnduceerd met behulp van klassiek conditioneren. In het eerste experiment werd een onplezierige geur (H_2S) geconditioneerd aan sensorische irritatie door de aanbieding van CO_2 in de neus (de geur raakte dus geassocieerd met de pijnlijke prikkel). In het tweede experiment werd ditzelfde gedaan met een plezierige geur (PEA). Beide geuren werden minder prettig ervaren na conditionering aan CO_2. Bovendien veranderde zowel de verwerkingssnelheid als de verwerkingsintensiteit van de N1 en de P2 piek na conditionering, maar alleen wanneer het de onplezierige geur betrof. Voor de plezierige geur gold dat alleen de verwerkingsintensiteit toenam van de N1 piek. Dit resulteerde in de conclusie dat de verwachting van pijn na de inhalatie van een geur de waarneming van die geur verandert, maar vooral wanneer dit een onplezierige geur betreft (mogelijk vanwege de overeenkomst in valentie tussen de geur en de daaropvolgende pijnlijke prikkel: beiden zijn onprettig, waardoor deze geur wellicht makkelijker geassocieerd raakt met CO_2).

Het onderzoek in Hoofdstuk 6 richtte zich niet op het temporele aspect van geurwaarneming zoals in de Hoofdstukken 4 en 5, maar op de invloed van cognities op olfactorisch bemonsteren of snuffelen. Deze maat gaf een indicatie van attentie voor geur (als een equivalent van attentiegestuurde oogbewegingen). Een veranderde bemonstering zou kunnen betekenen dat de geur onder invloed van cognities reeds anders het lichaam binnenkomt, wat weer een effect zou kunnen hebben op de waarneming en verwerking van de geur. Proefpersonen werden ingedeeld in één van drie experimentele condities: een conditie waarin proefpersonen het idee hadden dat

zij aan een 'chemisch product' roken ("een geur die vaak geroken wordt in de buurt van fabrieken en waar mensen vaak hoofdpijn van krijgen"), een conditie waarin proefpersonen dachten aan een 'aromatherapiegeur' te ruiken ("een geur die vaak gebruikt wordt tijdens aromatherapiesessies, waar mensen zich vaak beter door gaan voelen") en een conditie waarin proefpersonen geloofden dat ze blootstonden aan een 'standaard geur' ("een geur die geregeld gebruikt wordt voor geuronderzoek"). In werkelijkheid besnuffelde iedere groep dezelfde geur. De resultaten van dit experiment lieten zien dat de verwachting dat een geur schadelijk kan zijn voor de gezondheid inderdaad een effect op snuffelgedrag heeft. Er werd met minder kracht geïnhaleerd en er kwam minder lucht de neus binnen. Dit effect was niet afhankelijk van de experimentele conditie, maar van het feit of proefpersonen daadwerkelijk geloofden dat de geur potentieel schadelijk kon zijn. Er werd geconcludeerd dat cognities over geur en gezondheid invloed hebben op olfactorisch bemonsteren.

In het tweede deel van dit proefschrift werd dus aangetoond dat cognities over geur en gezondheid inderdaad een effect hebben op basale en vroege fasen van de informatieverwerking van geur; de resultaten van drie experimenten geven convergerend bewijs dat de vroege delen van stimulusverwerking onder invloed van cognities anders verlopen (intenser en/of sneller). Dit geldt vooral wanneer het een onplezierige geur betreft. Tevens werd een effect van cognities op bemonstering geobserveerd, wat als een aandachtseffect geïnterpreteerd kan worden; wanneer men de verwachting heeft dat een geur schadelijk zou kunnen zijn voor de gezondheid, wordt er op een voorzichtigere manier aan deze geur gesnuffeld. De manier waarop de geur het lichaam binnenkomt, wordt dus mede gestuurd door cognities.

Conclusie

Het onderzoek beschreven in dit proefschrift liet zien dat automatisch geactiveerde cognities over geur en gezondheid een negatieve connotatie hebben. Geur lijkt een sterke (en zelfs een mogelijk aangeboren) relatie te hebben met ziekte en gevaar. Hoewel een automatisch opererend systeem een handige strategie is vanuit een evolutionair perspectief, neemt de kans op *false alarms* toe; het systeem kan ongevaarlijke geuren, mogelijk onder invloed van cognitieve invloeden, gaan classificeren als gevaarlijke stimuli, met een overdreven lichamelijke reactie tot gevolg.

Daarnaast werd aangetoond door middel van OERP studies dat cognities over geur en gezondheid niet alleen de meer bewuste fasen van geurwaarneming kunnen beïnvloeden (b.v. "vind ik deze geur lekker of niet?"), maar juist van invloed lijken op fasen van informatieverwerking waarvan altijd gedacht werd dat psychologische factoren er geen toegang tot hadden (het coderen van basale stimuluseigenschappen, zoals intensiteit). De geur wordt intenser verwerkt en sneller gedetecteerd wanneer deze samenhangt met de verwachting van pijn; de geur lijkt meer negatieve lading gekregen te hebben. Dit proces vindt vooral plaats wanneer de geur een onplezierig karakter heeft. Tevens werden effecten van cognities op het bemonsteren van geuren

geobserveerd. Cognities over geur en ziekte zorgden ervoor dat er minder intensief gesnuffeld werd.

Het onderzoek in dit proefschrift laat zien dat ziek worden van geur niet tussen de oren zit, maar in de hersenen. Toekomstig onderzoek zal verder moeten uitwijzen hoe impliciete cognities en een veranderde waarneming door cognitieve invloeden bijdragen aan de totstandkoming en instandhouding van geurgerelateerde gezondheidseffecten.

Dankwoord
(Acknowledgements)

Graag wil ik een aantal mensen bedanken voor hun bijdrage aan mijn (werk)plezier van de afgelopen vierenhalf jaar.

Monique Smeets, uiteraard begin ik bij jou. Terwijl ik dit schrijf, zit je naast me in het vliegtuig, terwijl we op weg zijn naar een congres in Florida. Je nam me al mee naar ditzelfde congres toen ik pas een paar maanden werkzaam was bij de UU en dit is precies zoals je bent als aio-begeleider: je hebt me direct overal bij betrokken en me overal mee naartoe genomen (de waarde hiervan merk ik vooral nu ik een volgende stap gezet heb). Daarnaast heb je me enthousiast gemaakt voor het doen van goed en eerlijk onderzoek. Toekomstige aio's van 'The Smeet Lab' mogen in hun handen knijpen met een begeleider zoals jij. Bedankt voor alles!

Marcel van den Hout, achteraf bezien had ik vaker met je willen praten; onze gesprekken over onderzoek heb ik als zeer waardevol en leerzaam ervaren. Grazie!

Marga Veldhuizen, bedankt voor je goede adviezen, onze brainstormsessies en onze vriendschap. Ik ben blij als je straks weer iets dichter in de buurt bent.

I would like to thank the entire *Dresden family*, but especially Thomas Hummel: Thank you very much for giving me the opportunity to do research in the famous 'Hummel Lab'; I learned a lot from that! Furthermore, I would like to thank Simona Negoias, Inga Gartz, and Pia Rother for the wonderful time in Dresden. Christian Gemeinhardt and Benno Schuster, thanks for helping me with the data acquisition and analyses.

Voor de technische ondersteuning wil ik graag Theo van Aerts en Martin Laverman bedanken. Martin, er staat bijna geen enkel experiment in dit proefschrift waar je niet aan bijgedragen hebt. Fijn dat ik hiervoor altijd bij je terecht kon.

Ik wil verder al mijn collega's van Klinische en Gezondheidspsychologie bedanken, waarvan in het bijzonder Iris Engelhard, Paul Boelen, Jaap Lancee en Henriet van Middendorp en in het *zeer* bijzonder Karolijne van der Houwen en Joanne Gerrits. Karolijne en Joanne, straks zijn we er alledrie vanaf! Hoera!

Elske Salemink, jij krijgt een eigen alinea. Bedankt voor al die leuke jaren samen in H205 (of was het nu toch H201??). Ik mis ons dagelijks opstartkwartiertje waarbij we even onze avonturen van de dag ervoor doornamen. Leuk dat je mijn paranimf wilt zijn!

Ik wil alle aio's van EPP symposia bedanken voor de leerzame (!) bijeenkomsten, en dan vooral Johan Verwoerd, Tim Schoenmakers, Kim de Jong en natuurlijk Patricia Bakvis.

I would also like to thank my new colleagues of Sensation, Perception, and Behaviour at Unilever, who helped me through the final, and perhaps the heaviest months of writing!

Gelukkig bestaat er naast het werk nog een heel andere wereld!

Ik wil ten eerste mijn ouders bedanken. Lieve pap en mam, fijn dat jullie altijd zo meegeleefd hebben en interesse getoond hebben in mijn werk. Bedankt voor jullie steun bij alles wat ik doe!

Maurice Bulsing en Carl Stolz, bedankt dat jullie me standaard de slappe lach bezorgen; een goede manier om een proefschrift even te vergeten. Maurice, enorm bedankt voor de mooie omslag van dit proefschrift.

Ik wil ook Frans, Nelly, Martine, Mattijs, Joost en Simone van der Knaap bedanken voor hun interesse in de totstandkoming van dit boekje. Simone, zoals je weet ben jij de geheime derde of vierde paranimf!

Martijn Veltkamp, waar ben je?? Nadat we eerst onze studie samen volbrachten en daarna dit klusje geklaard hebben in hetzelfde gebouw is de tijd aangebroken dat we niet meer op dezelfde plek aanwezig zijn. Gelukkig bestaat er telefoon en email.

Thijs Ruhrup, bedankt voor alle muziek- en levenslessen tijdens de afgelopen jaren. Erg fijn om naast het schrijven bezig te zijn met (andere) belangrijke zaken!

Sander en Christa van Rijswijk, bedankt dat ik zo vaak even bij jullie aan kon schuiven 's avonds!

Verder mogen in dit dankwoord de volgende mensen zeker niet ontbreken: Kim Weverling (de andere geheime derde of vierde paranimf), Ashwien Bisnajak en Mark Wortman (bedankt lieve Ash, dat je tijdens de verdediging naast me wilt staan!), Lennart Lieffering (jij kunt ook wel een boek schrijven), Kushik Marhe (jij ook!), Arthur en Hanneke Valstar (dit jaar wel wintersport!) en Gaby Jongenelen (je bent me d'r eentje!). De meeste van jullie vormen al jaren 'mijn harde kern' en hopelijk blijft dit ook nog jaren en jaren hetzelfde!

En Remko van der Knaap, jou wil ik echt overal voor bedanken. Vooral je eeuwige vrolijkheid is fantastisch en zeker tijdens het schrijven van een boekje! xxx

Patricia Bulsing was born on April 11, 1980 in The Hague, the Netherlands. In 1999 she graduated from secondary school (Interconfessionele Scholengemeenschap Het Westland in Naaldwijk). In 2004 she obtained her Master's degree in Cognitive Psychology at the University of Leiden, with a specialization in Neuropsychology. Between 2004 and 2009 she worked on her PhD project at the department of Clinical and Health Psychology at the University of Utrecht. She conducted part of her project at the University of Dresden Medical School, Germany. Currently, she works as a researcher at the department of Sensation, Perception and Behaviour of Unilever Research and Development in Vlaardingen.

Publications

Bulsing, P.J., Smeets, M.A.M., & van den Hout, M.A. (2009). The implicit association between odors and illness. *Chemical Senses, 34,* 111-119.

Bulsing, P.J., Smeets, M.A.M., & van den Hout, M.A. (2007). Positive implicit attitudes toward odor words. *Chemical Senses, 32,* 525 – 534.

Bulsing, P.J., Smeets, M.A.M., Hummel, T., & van den Hout, M.A. (2007) Influence of chemosensory pain-expectancy on olfactory event-related potentials. *NeuroImage, 38,* 164 -170.

Smeets, M.A.M., **Bulsing**, P.J., Van Rooden, S., Steinmann, R., de Ru, S., Ogink, N., Van Thriel, C., & Dalton, P. (2007) Odor and lateralization thresholds for ammonia: A comparison between static and dynamic olfactometry. *Chemical Senses, 32,* 11- 20.

Submitted manuscripts & manuscripts in preparation

Bulsing, P.J., Smeets, M.A.M., Gemeinhardt, C., Laverman, M., Schuster, B., Van den Hout, M.A., & Hummel, T. Conditioning odor to trigeminal irritations alters odor perceptions: Evidence from Olfactory Event Related Potential research (submitted).

Bulsing, P.J., Smeets, M.A.M., Lorig, T., & Van den Hout, M.A. Hold that sniff: Effects of health-related cognitions on sniffing of an environmental odor (submitted).

Smeets, M.A.M., **Bulsing**, P.J., Gemeinhardt, C., Negoias, S., Laverman, M., Van den Hout, M.A, & Hummel, T. Effects of expectation of adverse health effects on the perception of odor: an fMRI study (in preparation).

Published conference abstracts

Bulsing, P.J., Smeets, M.A.M., Hummel, T., & van den Hout, M.A. (July, 2008). Expecting negative effects of odor exposure influences various stages of olfactory information processing: an unpleasant odor associated with sensory irritation. Part I. *Chemical Senses, 33,* S116.

Smeets, M.A.M., **Bulsing**, P.J., Hummel, T., & van den Hout, M.A. (July, 2008). Expecting negative effects of odor exposure influences various stages of olfactory information processing: a pleasant odor associated with sensory irritation. Part II. *Chemical Senses, 33,* S116.

Bulsing, P.J., Smeets, M.A.M., Hummel, T., & van den Hout, M.A. (2007). Expectancies about harmfulness influence early odor sensations. *Chemical Senses, 32, 6,* A101.

Smeets, M.A.M., **Bulsing**, P.J., Ogink, N., van Thriel, C., & Dalton, P. (2006). Odor and lateralization threshold for ammonia: a comparison across static and dynamic olfactometry. *Chemical Senses, 31, 5*, A56.

Bulsing, P.J., Smeets, M.A.M., & van den Hout, M.A. (2006). Measuring odor attitudes in an implicit way. *Chemical Senses, 31, 5*, A143.

Bulsing, P.J., Smeets, M.A.M., & van den Hout, M.A. (2006). Odor attitudes uncovered implicitly. *Chemical Senses, 31, 8* ,E62.

Smeets, M.A.M., & **Bulsing**, P.J. (2005). Measuring implicit beliefs about odors and health: the "Mysterious Machine" task. *Chemical Senses, 30,* 6, A208.