

## 51. Processing of Human Body Odors

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Human chemosensory signals are able to transmit a wide range of social information to conspecifics. Resulting from the interaction of several genetic and physiological processes (e.g., metabolic, immune, nervous), each individual produces a unique odor signature. The central processing of such chemosignals by conspecifics modifies physiological, behavioral, and psychological responses. To illuminate the importance of this mode of communication, we describe how humans produce, decode, and respond to warning chemosignals. Behavioral evidence highlighting the cognitive and emotional consequences of body odor communication will be discussed. Special attention will be devoted to the current understanding of human body odor neural processing. After an overview on the topic, we discuss the role that social chemosignals may have in our everyday life in health and disease.

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Social communication is a central aspect in the life of animals and human beings alike. Despite the considerable research conducted on the topic of how social information is communicated among humans [51.1], the multisensory character of such communication has often been misrepresented. In humans, most of the literature is characterized by evidence originating from the visual and auditory modalities, uncovering how

facial expressions or body postures as well as linguistic features (e.g., prosody) affect social communication [51.2]. Although olfaction is widely used across species for social communication [51.3], little attention has been given to chemosensory communication in humans. This is even more surprising in light of the intrinsic and unique advantages of this form of communication. For instance, chemosignals can easily escape

the restrictions imposed by physical and time barriers where chemical molecules are able to freely disperse in air or water, and thus can be transported over long distances and remain a signal for several days. According to the physical features of the molecules, in particular volatility, chemical communication can outlast the presence of the sender (low volatile molecules) or quickly dissolve and facilitate the transmission of messages in a rapid time scale (highly volatile molecules) [51.4]. Among the far senses, olfaction remains functional when vision and audition are unavailable (e.g., in the dark, in noisy environments) and even when multiple chemosensory stimulations are simultaneously present. As an example, despite the efforts of western cultures to mask body odors with fragrances [51.5], chemosensory communication is still possible [51.6].

Aside from this ability of chemosignals to travel in space and time, and to persist within sensory overloaded environments, chemosensory communication is rather effortless for senders, as suggested by the low amount of energy required to produce and release a chemosignal [51.3]. The energy investment necessary during decoding is also limited, as suggested by the fact that receivers often elaborate the message outside of their conscious awareness [51.7–9].

This series of advantages is further strengthened by the specificity of the communication. Chemosignals transmit detailed social information related to both stable and transient states. Chemosignal communication successfully conveys information regarding personal identity [51.10–14], kins [51.15–17], partners [51.11, 12, 18], relatives [51.15, 17, 19, 20] and friends [51.15].

## 51.1 The Microsmatic Fallacy

Over the years, among both laymen and scientists, the concept of humans being microsmatic animals has wrongfully taken ground (Chap. 32). The term *microsmatic*, used in reference to primates and then extended to humans, traces back to *Turner* [51.40] who described animal species with differential olfactory skills ranging from acute in macrosmatic animals, such as dogs, to those without an olfactory system, i.e., anosmatic animals such as dolphins. Many authors have then characterized primates and humans as microsmatic in light of the concomitant increased emphasis on their use of vision [51.41–43] and based on morphological aspects. Often highlighted is the fact that the relative size of the olfactory epithelium and the olfactory bulb is reduced in primates as compared to other species [51.44, 45]. A direct comparison with vision has been gathered by the investigation of olfactory skills in nocturnal primates,

Furthermore, age [51.21], gender [51.21, 22], and personal predispositions [51.23] can be gleaned via human chemosignals. In addition, humans transmit information of transient states such as health status [51.24], sexual availability [51.25] and emotions [51.26–39] through chemosignals. This cumulative evidence suggests that the olfactory modality is a reliable medium through which social communication can occur among humans.

In the following sections, we will first briefly present the rationale for the terminology that we will be using throughout the chapter. Second, we will discuss the often mentioned, though questionable, concept of humans as microsmatic individuals, trying to review the basis for this belief, and the consequences for research and interpretation of data. Third, we will review how human chemosignals are produced and which are the experimental methods used during collection. Fourth, we will discuss the effects of chemosignal communication in recipients with special attention to central neural processing. Because such neural underpinnings are still incomplete and/or unaccounted for, we will advance speculative, yet fact-based, arguments in the hope of stimulating future discussion and research. Fifth, among all types of olfactory-mediated information, we will focus on the transmission of chemosignals promoting harm avoidance, for the critical survival benefits they serve. Please note that when using the word *signal* throughout the text we do not differentiate whether the signal is beneficial to the sender or not. Finally, challenges in the field as well as outstanding questions that warrant further investigations will be emphasized.

who – unable to rely on visual cues – show a greater portion of peripheral and central structures dedicated to the main olfactory system as compared to diurnal primates [51.46]. Such morphological approach, coupled with direct comparisons between vision and olfaction, has rendered the erroneous conclusion that animals primarily relying on vision exhibit a poor sense of smell. This notion has been extended to humans by Pierre Paul Broca, best known for his discovery of the speech processing area subsequently named after him. On the basis of the available measures of the relative sizes of the olfactory system and estimates of the centrality of olfaction in daily life, *Broca* and *Pozzi* [51.47] suggested that humans (as other mammals) were microsmatic. Data collected using more accurate techniques in the subsequent years deemed this classification system rather obsolete. *Keverne* [51.48–50] challenged the

concept that microsmia can be explained on the basis of a reduced number of olfactory receptors alone. Each receptor is part of a combinatorial code that can respond to different odors and even a limited number of receptors can therefore form many distinct patterns [51.51]. With respect to genetics, the biggest part of the human genome is dedicated to olfaction, with its approximately 400 olfactory receptors [51.52]. Besides functional genes, modern techniques have revealed that the number of pseudo-olfactory genes is higher in humans as compared to other species, macrosomatic included [51.53–55]. This notion, often used as an argument for human microsmia, does not, however, take into account the new discoveries that these *non-coding* regions have an essential role in gene regulation and ribonucleic acid (RNA) transcription [51.56]. The jury is still out on whether having more pseudogenes is advantageous or not.

Additionally, direct correlations between olfactory structures' morphology (e.g., anatomical size), the percentage of expressed olfactory genes, and olfactory performance cannot be found in either humans or other species investigated [51.57–61]. Direct behavioral testing of the human sense of smell also repeatedly contradicts the microsmia concept where humans have been demonstrated to possess a superbly keen sense of smell [51.62, 63], as confirmed by studies assessing detection thresholds and discrimination performance [51.58–60]. For example, ethyl mercaptan (or ethanethiol), an additive used to make odorless gases (such as propane) perceivable, can be detected by un-

trained humans at concentrations less than 1 ppb (part per billion) and perhaps as low as 0.2 ppb [51.64]. This ability was directly translated to a real-life example by *Yeshurun* and *Sobel* [51.65]: Humans can discriminate between two olympic-size swimming pools, of which only one contains three drops of ethyl mercaptan. Provided that the chemosensory message is of sufficient relevance, it appears that humans are able to detect very subtle olfactory cues [51.57].

A final testament towards the notion that odors indeed are important to us is the fact that a large portion of western countries' commercial interests revolves around the cosmetic, fragrance, and food industries. Capitalizing on the emotional advantages of odors to evoke memories and emotional transfer (Chap. 39), the fragrance industry has in 2015 a projected annual global sales revenue of approximately 29 billions US dollars [51.66], almost equivalent to the gross domestic product (GDP) of Paraguay in 2014 at USD market prices.

Altogether, these facts indicate that humans have a sense of smell that cannot be considered functionally microsmatic. Indeed, *Zelano* and *Sobel* [51.63] have even suggested that humans constitute an ideal model to study the olfactory system, providing access to introspective information that would be otherwise inaccessible in animals.

In the next sections we will provide evidence that human behavior – and in particular social behavior – cannot be fully understood without having a good knowledge of olfactory functioning.

## 51.2 Human Chemosignals

Chemosignals in social communication often comprise complex molecular mixtures, some of which are volatile and produce an odor [51.3]. These chemicals are interpreted as a signal actively conveying information from a sender and potentially influencing the behavior of receivers, rather than a cue, a passive biological trait that provides an observer with information [51.67]. In light of the still unresolved debate on whether human chemosignals transmitting social information should enter the domain of pheromones [51.3,

68], we will use the terms chemosensory signals, social chemosignals or body odors interchangeably in the present chapter (Chap. 52). Such signals are produced by the human body, making an individual the sender of a message. They are made of chemicals, part of which are characterized by odorous substances and contain socially relevant information. These chemical messages can be transmitted to a human receiver, who decodes the message and uses that information to adjust his/her responses in the environment.

## 51.3 How do Human Senders Produce Chemosignals?

Several systems across the human body can produce volatile odorous chemosignals with communicative potential. Here, we briefly present known chemical pathways that have been suggested to be involved

in communicating social information in humans. For a more detailed overview of the chemical composition and production of human body odors, please see Chap. 49.

### 51.3.1 The Axillary Glandular System

The majority of studies on human body odors to date have been conducted using axillary secretions with a few noticeable exceptions [51.69–75]. Besides the increase in experimental feasibility, the biological reason for such over-representation is that the glandular system contained in the axillary area contributes consistent secretions.

Most of the social communication mentioned in the literature is thought to derive from the activity of apocrine glands, found in the ano-genital and underarm areas or its specialized variations, among which we can count mammary glands (producing milk), ciliary glands in the eyelids (Moll's gland, responsible for lacrimal secretions), and ceruminous glands (which produce ear wax) [51.76]. The number of apocrine glands changes in relationship with the specific area of the body in which they are retrieved. However, the number of glands seems to be unrelated to the ability to produce signals with socially relevant information. The areas of the cutaneous gland system, in which the number of apocrine glands are most prolific, are the axillae [51.76]. Besides apocrine glands, the axillary skin contains eccrine, apoeccrine, and sebaceous glands. In light of this diversity, the glandular system of the axillary region constitutes a specific habitat, differing from most other body parts, because it harbors hair follicles with sebaceous glands and a high density of sweat glands [51.77].

*Apocrine glands*, inactive before puberty, increase in size under hormonal influence and begin functioning [51.78]. Their secretions are characterized by milky odorless solutions, consisting of electrolytes, steroids, proteins, vitamins, and a variety of lipid compounds [51.71, 73–75]. The activity of apocrine sweat glands is pronounced during eustressing and distressing situations and reduced during emotionally neutral physical exercise [51.79].

*Eccrine glands* are located throughout the body, with only a few exceptions [51.76]. In the armpit areas, they coexist with apocrine glands. The clear secretion produced by eccrine glands is thinner as compared to that of apocrine glands, mainly consisting of water and electrolytes, derived from blood plasma, and sodium chloride [51.76]. The amount of sweat depends on the number of functional glands and the size of the surface opening. Neural and hormonal mechanisms are responsible for the total volume of secretions. When all of the eccrine sweat glands are working at maximum capacity, the rate of perspiration for a human being may exceed 31/h [51.80].

*Apoeccrine glands*, comprising up to 50% of all axillary glands, share features of both apocrine and eccrine glands, as the name suggests. They produce wa-

ter secretions, in higher quantity as compared to both apocrine and eccrine glands, thus playing a primary role in axillary sweating [51.81].

*Sebaceous glands* are responsible for the discharge of an oily, waxy substance called sebum, mainly involved in the waterproofing and lubrication of the human skin [51.82].

Altogether, these glands contribute with their activity to the production of water-based secretions, involved in thermoregulation processes and skin protection [51.77, 83]. Such secretions are initially near odorless and the characteristic sweat odor is the product of the incubation with the bacteria residing in the armpit area [51.84–88].

### 51.3.2 The Axillary Microbiome

The moist environment created by the glandular secretions in the axillary areas represents a moderately diverse ecological niche hosting specifically adapted organisms establishing a distinct microbial profile [51.89]. The presence of hair follicles and sebum creates a rather occluded environment in which nutrients are readily available at a temperature that facilitates bacterial colonization [51.85]. The dominant resident flora is composed of *Corynebacterium*, *Staphylococcus*, *Streptococcus* and *b-Proteobacteria* [51.85, 89–93]. Combined, this flora is responsible for the microbial biotransformation of the nutrients secreted in the human axilla [51.94, 95]. Specifically, the axillary *Corynebacteria* and cocci (e.g., *Staphylococcus epidermidis*) are largely responsible for the production of odorous substances, such as androgen steroids [51.96] and aliphatic acids (e.g., isovaleric acid [51.97]). Furthermore, they contribute to the conversion of weakly odorous steroids (androstadienone) into more intensely smelling androstenes with urineous and musky notes (androstenone and androstenol, respectively [51.98, 99]).

Even though it is well established that the microbial activity is responsible for body-odor formation, the active metabolic processes are still unknown [51.100]. Obtaining axillary meta-transcriptomics is necessary to identify how endogenous characteristics (e.g., sex, age, handedness, ethnicity, and individual host factors) in combination with exogenous features (use of cosmetics, detergents, etc.) contribute to the definition of individual chemosignals, opening up a better understanding of body odors in a personalized manner.

### 51.3.3 What is in a Chemosignal?

The combination of a personalized axillary microbiome [51.100] and both exogenous and endogenous

factors of the donor (or sender of the chemical message) interact to form a unique production that constitutes the individual's body odor; an end product that lies behind the notion that each individual possesses an *odor print* [51.22, 101] (Chap. 50). (The term *odor print* should not be confused with the newly coined term *olfactory fingerprint* [51.102]; the former relates to a biomarker for identification of an individual and the latter is related to the characterization of an individual's olfactory perception.)

The high chemical variability needed to allow such a large degree of individualization does not necessarily rely on different chemical compounds to form this signature. Rather, it seems like a greater dependence is put on a differential quantitative composition of similar compounds, thus creating a complex code consisting of both chemical components and magnitudes of each individual component present [51.103]. Four classes of chemical compounds have been consistently associated with the characteristic sweaty odor of axillary secretions [51.104]: unsaturated or hydroxylated branched fatty acids, thio-alcohols, short chain fatty acids, and volatile steroids. For a more specific overview of the chemical composition, please refer to Chap. 49.

Additional variability in the production of axillary body odor is associated with sexual dimorphism, which strictly interacts with genetic makeup, the endocrine system, the immune system, microflora peculiarities, and diet. Men and women show dynamic structural and functional differences at the level of the glandular system. As alluded to above, during puberty, apocrine glands grow and mature [51.105], eccrine glands' production increases [51.106–108] and the axillary microbiome augments and differentiates across genders [51.109–111]. This results in substantial differences in the olfactory profiles of axillary sweat in men and women, such as different concentrations of fatty acids (e.g., 3M2H), isomers (e.g., Z-isomer), thiol and acid precursors [51.86, 95], as well as androgen steroids in male odor samples as compared to women [51.99, 112]. Furthermore, differences in the genetic makeup alter the olfactory characteristics of the body odor. Here, we bring forth the examples of

the impact of a gene (ABCC11) and of a gene cluster: The major histocompatibility complex (MHC), or in humans, the human leukocyte antigen (HLA) system. The ABCC11 gene, in its homozygous variant, is expressed by the apocrine glands and produces a very mild body odor [51.113] as an effect of a reduced production of odoriferous molecules [51.114]. MHC/HLA are the main determinants of immunological individuality and may contribute to the uniqueness of each *odor print* [51.115, 116]. For instance, as well demonstrated by transplant studies, different polymorphisms of the MHC/HLA between donor and receiver increase organ rejection rates. This rate is reduced when the similarity of the MHC/HLA is high, as among relatives [51.117].

Odor variability is also influenced by ecological factors, such as the health status [51.24, 118] and diet features [51.119]. Indirect evidence of a change in the composition of body odor is gathered from the analysis of odor preferences in the recipients. Activating the innate immune system in healthy individuals via injection of lipopolysaccharide results in more aversive body odors as compared to controls within a few hours [51.24]. Analogously, red meat consumption seems to have a negative impact on perceived body odor hedonicity [51.120].

All in all, a combination of endogenous as well as exogenous factors within the sender dynamically impacts the activity of the glandular system and of the axillary microbiome, determining unique and complex olfactory outcomes of the body odor production. Such olfactory signatures are complex messages containing information of social relevance, reflecting the activity of all the systems of the senders specifically involved in the production of the body odor. Signature odors contain information about particular individuals and, as a result of the processing of such information, they modulate the activity of different systems in the perceiver, prominently, his/her perception, physiological and neurophysiological state and behavior. Also, the outcomes promoted by olfactory signatures reflect the high variability that characterizes body odor production, creating a complex and dynamic multivariate pattern of changes in the recipient.

## 51.4 Human Axillary Chemosignals for Experimental Purposes

Recent data suggest that humans spontaneously sample chemical signals from their own body parts that have been in close proximity with an unknown individual using what could be considered an intuitive sampling method. Individuals sniff their hand more often in the period following a handshake with a con-

specific relative to a similar timeframe lacking such contact [51.121]. However, in an experimental setup where temporal presentation is of importance, more controlled sampling methodologies, as those reviewed in the following paragraphs, are usually implemented. Unfortunately, even though different sampling methods

may have significant impact on the obtained results, the field still lacks a clear methodological systematization of the way odor stimuli are collected meaning that direct comparisons between individual studies are, at best, difficult.

We have characterized the methodological steps of sampling and preserving body odors by extending the framework proposed by Lenochnova et al. [51.122]. Each of these steps can influence the quality of the donated chemosignals, and – by extension – the experimental measures of interest:

1. The restrictions placed on body odor donors
2. The medium of sampling
3. The type of sampling
4. The time of the day and length of sampling, to
5. Sample storage.

#### 51.4.1 Restrictions on Body Odor Donors

Common lifestyle restrictions related to hygienic, dietary, and behavioral concerns are applied before and/or during body odor sampling. The stringency of such restrictions varies greatly across studies and research groups, but the rationale is always a reduction in the variability due to external factors of the body odor samples. Such external factors can be either removed (e.g., fragrance-containing body products, foods and drinks, etc.) or standardized (e.g., all donors are provided with the same odor-free products). As any contact of an exogenous material with the sampling area can be a source of contamination, it is nearly impossible to collect uncontaminated samples outside of the strictest laboratory settings. Therefore, standardization of inevitable contamination sources can be a valuable approach, provided that the experimental design is compatible (e.g., planned contrasts).

Hygienic restrictions combat the many fragranced products often applied to body odor sampling areas and to the materials that come into contact with those areas. Products (e.g., deodorants, antiperspirants, perfumes, etc.) usually applied to sampling areas, often the underarm or vicinities (e.g., trunk, face, hands) are often eliminated. Any materials that will contact sampling areas (e.g., clothes, bedding), are often selected with regard to minimizing contamination by exogenous chemicals. To address the variability of shower products, donors can be provided with a standard, odor-free body wash, shampoo [51.21], and – in some cases – deodorant. Hygiene restrictions are usually implemented before the sampling period starts and can last from a minimum of 1–2 days to as long as 10 days (especially in cases in which chemical analyses are performed [51.123]) presampling. Restriction involving

armpit shaving has only rarely been taken into account. Experimental evidence suggests that, even though odor preference increases for unshaved relative to shaved armpits [51.124], such differences are minimal and, when present, transient [51.125].

Dietary restrictions, the most commonly implemented type of restriction, include the elimination of a collection of food items that, when metabolized, leave detectable traces in bodily fluids. A few examples are garlic, fruits, and asparagus [51.126–128]; however, many other reports on this topic are either anecdotal or subjectively ascertained by the experimenters, and there is a lack of controlled studies in this area. Alcohol consumption is commonly eliminated during presampling and sampling periods despite the fact that the effects of alcohol on the perception of body odor is still lacking. To date, one of the few controlled studies of how diet modulates skin secretions comes from a study investigating the olfactory traces of a diet rich in red meat [51.120].

Behavioral restrictions are a catch-all category of nonhygienic and nondietary regulations aimed at eliminating exogenous contamination. Sporadic or social smoking as well as second-hand smoking is often eliminated due to its strong contamination potential. Levels of physical exercise and exposure to highly emotional situations are often regulated, especially in studies examining the emotional chemosignals. Sexual intercourse and sharing a bed with another person and/or pet are also commonly prohibited during presampling and sampling periods of nighttime-collection studies. For female donors, hormone-based contraception and menstrual phase are commonly recorded – if not actively controlled for – to detect or avoid their effects on body odor perception [51.129, 130].

The most common means of ascertaining the usability of each sample is to have a small (e.g., two to three) panel of trained people determine the presence of uncontaminated body odor. While chemical analysis (e.g., gas chromatography-mass spectrometry) would provide a means of detecting and quantifying a priori-defined contaminants, obstacles of cost and practicality concerns often make this impossible.

#### 51.4.2 Medium of Sampling

T-shirts alone, or cotton pads sewn into the armpit area of the T-shirt [51.131], are the most common means by which to collect body odor samples from the axillary areas. The T-shirts, with or without pads, are usually worn directly on the bare skin and are subsequently removed and subjected to olfactory ratings or additional analyses [51.13]. If the underarm area or cotton pad is not cut and separated from the rest of the T-

shirt, the ratings can be confounded by odors originating from extra-axillary areas, such as the torso [51.130]. The variability introduced by T-shirts can be counteracted by laundering each with the same odor-free detergent shortly before use and storing each in a similar manner until use. If the T-shirts are worn during the day without compensative strategies or are worn at any time with clothes laundered with a nonstandard or fragranced detergent, the odor variability of the sweat sample significantly increases. Prepared properly, T-shirts can serve as shields to external chemicals for cotton pads sewn to the T-shirt or anchored by other means to the underarm area. Cotton pads have also been used in isolation and fixed to the axillae with surgical tape [51.16, 130, 132]. This facilitates the adherence of the sampling medium to the collection area and maintains its position throughout the sampling period.

The large variability in sampling mediums and procedures has generated an equally wide array of criticisms. One common concern is with the use of tape as a means of securing pads to the underarm area, as the compounds found in the tape material and its adhesives pose a risk for contamination. Another concern is with the use of cotton as a sampling medium, which can trap the sulfurous compounds of axillary odors [51.133], removing the sulfurous compounds from the odor signature, when the collection is performed with cotton pads and/or T-shirts [51.95]. These concerns and others like it are important in that any sampling method that systematically alters body odor collection prevents studies from assessing the odor signature in its entirety. However, these concerns must also be balanced by feasibility considerations. In the case of cotton as a sampling medium, finding an alternative that simultaneously enables sample collection in situations mimicking day-to-day life and preserves the sample's sulfurous compounds has been very challenging. Furthermore, sulfurous compounds have been identified at very low concentrations; their detection required the collection of hundreds of milliliters of sweat in glass vials while participants were exercising in a sauna [51.95]. It seems therefore that although perceivable using a perceptual smell test – such as that performed by most behavioral and neuroimaging experiments – these molecules, by their own chemical nature, tend to disappear when extracted from a cotton medium and when chemically quantified in isolation. The chemical and physical considerations of the odorants, the materials and form of sampling media, as well as potential interactions are all questions ripe for systematic evaluations within future studies.

#### 51.4.3 Type of Sampling

An additional factor that is seldom factored into experimental designs as a source of experimental variation is the direct comparison of different activities performed during collection. Recent research on the emotional effects of body odor communication raises this issue. Some experimenters used video clips with specific emotional content (e.g., horror clips for fear/anxiety, splatter video for disgust, cheerful videos for happiness [51.26–28]) to induce a vicarious experience of a transient emotional state. Other experimenters prefer more ecologically relevant conditions and collect emotional chemosignals of acute stress responses at an important examination [51.134], during a first-time skydiving event [51.33], or during a high-ropes course experience [51.30]. As a control condition for emotionally induced axillary secretions, groups have used sweat collected from participants at rest or during performance of aerobic or anaerobic physical exercise. The use of physical exercise might be experimentally problematic due to the increase in secretions originating from the eccrine glands (as opposed to the apocrine glands), which serve to cool the body during exercise. Published evidence from chemical analyses characterizing the differences between these control conditions is lacking [51.135].

#### 51.4.4 Time of the Day and Length of Sampling

Various studies sample body odors at different times of the day – some daytime, others nighttime, and still others, both. Considering the differences in level of activity in many systems (skin microbiome, metabolic, immune, autonomic, and central nervous) during wakefulness and sleep [51.136], it is possible that such differences are reflected in the sampled body odors. However, no experimental evidence contrasting daytime and nighttime collection has been published. Furthermore, regardless of sampling time (of day), body odor samples can be affected by the length of the collection. Large disparities in collection duration have been reported across studies, ranging from 20 min [51.26] to 7 nights [51.11]. Considering sampling time and duration in conjunction, samples collected during the day for longer periods of time are likely to be more emotionally variable and more likely to include a greater variety of exogenous, contaminant compounds that nighttime samples do not share. Despite limitations in the control over activities performed by daytime donors, our own experience is that daytime-collected samples are more intense. Aside from the interference of night-

mares and other emotionally vivid dreams, nighttime-collected samples are considered less variable due to the decreased variability in participants' emotional and physical states and greater control over sampling conditions. To reach supra-threshold detection levels, multiple-night sampling periods or highly controlled daytime samplings are often used. One method of characterizing sample quantity is to weigh the pads used during collection and compare this weight to unused pads [51.26–28]. This method is particularly useful to determine the presence of chemosignals collection over short sampling periods. These differences in sampling time of day and length might lead not only to differences in the intensity of the chemosignals but also to differences in the co-varying odor pleasantness [51.132, 137, 138].

#### 51.4.5 Sample Storage

Post-collection methodologies are another critical variable affecting the preservation of body odor samples. After sampling, bacteria transferred to the sampling medium will continue metabolizing the sample, thereby continually altering the chemical substrate over time. In an effort to limit this confound, some groups use freshly collected samples for each rating session [51.132, 139–141]. This approach prevents us from studying longitudinal effects of specific olfactory signatures. The most commonly used storage method is freezing [51.21, 142–144], though, like so many other aspects of sampling methodology, there is a great degree of variability; across studies and research groups, samples are frozen

at variable temperatures in different types of containers for a variable amount of time and are thawed (and re-frozen for re-use) a variable number of times in different types of containers. A study conducted by *Lenochova et al.* suggests that freezing at  $-32^{\circ}\text{C}$ , the lowest temperature achievable with a regular freezer, for relatively long periods of time (up to four months was assessed) and repeated freeze-thaw cycles do not affect perceptual ratings of body odor samples [51.122]. However, the freezing temperature is relevant in maintaining the integrity of a chemosignal, as it is for other types of bodily secretions. Storing milk at temperatures around  $-20^{\circ}\text{C}$  resulted in degradation after a few months of storage, whereas conserving the samples at  $-80^{\circ}\text{C}$  did not change the chemical profile of the milk [51.145, 146]. Other parameters, such as whether the thawing is done within the storage container (e.g., a ziplock bag) or within a delivery container (e.g., a glass or plastic jar), are still untested. It is important that future studies consider the absorptiveness and permeability of the storage and delivery containers to limit both the loss of volatiles as well as the acquisition of exogenous contamination.

Finally, it is important to note that the aforementioned experiments assessed the effects of these freezing parameters only on the perceptual characteristics of the body odor stimuli, not on whether the chemical structure or composition, and therefore the chemosignals themselves, may have been altered. Moreover, it is not clear what the link is between perceptual ratings and chemosensory signal strength.

### 51.5 Central Processing of Human Chemosignals

Ever since the first olfactory neuroimaging study was published over 20 years ago [51.147], a plethora of studies have demonstrated the involvement of a range of brain areas in the processing of olfactory stimuli. Areas consistently reported as involved in processing of common odors are the piriform cortex, amygdala, entorhinal cortex, hippocampus, hypothalamus, thalamus, orbitofrontal cortex, and the insula [51.148]. For a detailed overview of the cerebral processing of olfactory stimuli, please see Chap. 38.

Stimuli with ecological relevance presented in other sensory modalities, such as vision [51.149–151] and audition [51.152], are processed via dedicated brain pathways outside of the main sensory system. The range of behavioral studies presented above supports the claim that human chemosignals are salient carriers of information about other individuals, along the

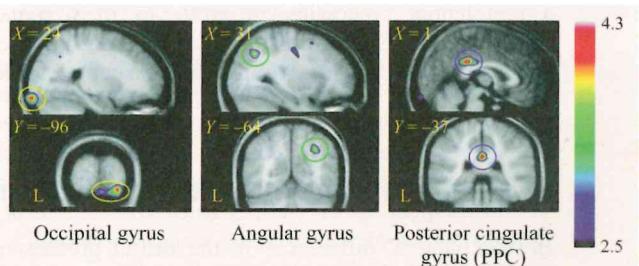
same lines as visual and auditory stimuli. Empirical validation of this claim has been corroborated by a study by *Lundström et al.* [51.131]. To assess whether human body odors are subjected to non-olfactory processing recruiting a separate network from common odors, *Lundström et al.* [51.131] exposed recipients to different body odors as well as to a fake body odor, namely a mixture of common odorants (including cumin oil, anise oil, and indole) with perceptual characteristics similar to real social chemosignals. Direct comparisons of neural processing between the two perceptually similar stimuli, real and fake body odors, demonstrated that real body odors selectively activate a neural network located predominantly outside the main olfactory system and composed of the occipital cortex, the angular gyrus, and the anterior and posterior cingulate cortex (Fig. 51.1).

#### 51.5.1 Occipital Cortex

The occipital gyrus is an area located within the primary visual cortex, responsible for the processing of visual information. Activations at the level of the occipital gyrus following exposure of body odors suggest that this area has a multimodal character. Indeed, rather than activating at the presentation of purely visual stimuli, it responds to the social relevance of the stimuli presented in different modalities [51.153]. It has previously been demonstrated that olfactory cues are able to activate visual processing areas in the absence of visual stimulation [51.154–158] and that emotional highly relevant stimuli induce increased activations in the primary visual cortex [51.159]. In the study by *Lundström et al.* [51.131] activations in primary visual areas are retrieved from participants who were not able to distinguish between real and fake body odors. This is in line with the fact that activations in the occipital cortex are commonly found in olfactory neuroimaging studies [51.145–149], and it suggests that the observed activity is not completely attributable to the social content of chemosignals. In other words, olfactory stimuli – independent of their social value – activate this visual area. Therefore, this finding has been interpreted as indicative of a preparedness mechanism [51.131]. An odor (as well as an image), whether ecologically relevant or not, indicates the presence of an object in the immediate vicinity and may trigger the visual system to be prepared for the entrance of a stimulus in the visual field, therefore requiring special attention.

#### 51.5.2 Angular Gyrus

Located in the posterior part of the inferior parietal lobule, the angular gyrus activates in response to information related to the human body. Indeed, the functional role of the angular gyrus has been associated with a variety of tasks, including those involving social cognition [51.160] and multisensory integration if we also include the overlapping area of the intraparietal sulcus. Please refer to Fig. 51.1 [51.161]. Overall, recent meta-analytic evidence suggests that the angular gyrus is involved in the processing of concepts during tasks in which the simultaneous interface of perception/recognition and action is required [51.160]. Specifically, lesions at the level of this area alter (or fully impair) the ability to interpret the perception of one's and other individuals' bodies [51.162–165] and evidence indicates the angular gyrus serves as a cross-modal hub in which converging multisensory information is combined and integrated, including that relating to body



**Fig. 51.1** Comparing the group-averaged regional cerebral blood flow (rCBF) responses to the processing of body odors versus fake body odors produced the depicted statistical parametric maps of  $t$  values thresholded at 2.5 superimposed on group-averaged anatomical magnetic resonance imaging (MRI). The top panels show a lateral view and the lower panels show a coronal view of the same areas. Coordinates refer to the center of activation and slice expressed according to the Montreal Neurological Institute (MNI) world coordinates system. From left to right, the colored circles mark an increased rCBF response in the right occipital cortex (yellow), in the left angular gyrus (green) and in the posterior cingulate cortex (blue) (after [51.131])

representations [51.165]. Given its multisensory nature, the role of the angular gyrus in the chemosensory context cannot be appreciated in isolation and requires the simultaneous account of the contribution of the connected regions.

#### 51.5.3 Anterior and Posterior Cingulate Cortex

Smelling a body odor in contrast to common odors increases activity in both the anterior cingulate cortex (ACC) and the posterior cingulate cortex (PCC), which have been linked to the implementation of attentional, mnemonic templates [51.166–168], emotion regulation [51.169, 170] and regulation of emotional actions [51.171, 172], respectively. Moreover, a recent meta-analysis identified ACC and PCC as critically involved in self-reflective processes [51.173]. PCC elaborates not only self-relevant information, but it is also included in the evaluation and decision-making process of whether a certain stimulus is applicable to the self, therefore in line with autobiographical memories [51.173]. In contrast, the ACC activity underpins the emotional aspects of the processing of self-relevant information [51.174] and it is involved in the comparison with other-reflective processes, to indicate self-specificity [51.173].

Although a definite mechanism of body odor communication has not been established, it may be that body odors, in contrast with common odors, receive

a preferential processing in virtue of their signal value [51.131]. Seen from an evolutionary perspective, signals carrying important information, such as those related to threats, might have been selected by evolutionary pressure to receive preferential processing (i.e., emotional and attentional prioritization).

## 51.6 Human Chemosignals of Harm Avoidance

Besides general differences in the neural processing of common and body odors, the body odor literature has focused on the characterization of the neural underpinnings of different messages with social relevance. These specific areas of social communication via chemosignals can be distinguished in two macro areas: chemosignals related to reproduction and chemosignals involved in harm avoidance. We will refer to the excellent review by *Liibke and Pause* [51.104] in reference to an analysis on the chemosignals of reproduction and we will here focus our attention on the chemosignals sustaining harm avoidance.

Harm avoidance is an umbrella term used to refer to all adjustments made in response to stressful events, involving demanding environments and/or dangerous individuals [51.90]. Stress is a response based on fight, flight, or tend-and-befriend behaviors, that occurs following the perturbation of an organism's homeostasis [51.175]. If stress requires severe adjustments over long periods of time, such as in the case of chronic stress, the organism faces collapse and eventually death [51.176]. Given the life-threatening power of stress, it is not surprising that mechanisms of harm avoidance have been favored during evolution and are presently used by the vast majority of animal species [51.3] as well as by plants [51.177]. Chemosensory signals have all the characteristics to act as efficient warning signals, as overviewed in the introduction of this chapter. Below, we will review chemosensory harm avoidance mechanisms, including strategies capitalizing on self-other recognition, discrimination among different types of *others* and transient harm-related signals.

### 51.6.1 Self-Other Recognition

The first step to identify what is safe and what is potentially harmful is the recognition of something different from oneself. Disposing of a system able to differentiate self from others might capitalize on the decoding of social information related to threat, including that coming from body odors. A self-reference mechanism, such as that used by rodents and referred to as the *armpit effect* [51.178], is supposed to be at the basis of the ability of people to identify their own body odor by sniffing [51.179]. However, *Pause* et al. [51.180]

could not reveal a similar pattern of results when testing males and females with self and non-self odors. In the authors' words, the low accuracy in the identification performance might be a result of the low odor concentration. Alternatively, it might indicate that the ability to discriminate between subtle body odors does not necessarily involve conscious processing [51.131].

### 51.6.2 Different Types of Others: From Kin to Strangers

Recognizing whether a signal is similar or different to oneself is a binary decision. However, what is *other* can be categorized in many different ways. Other can be a kin, with whom the receiver shares genetic features; the individual can be a friend, with no genetic relationships with the donor of the chemosignal, yet familiar due to exposure to that individual; or the individual can be a stranger, with no genetic or learned connections and, given the lack of additional information besides the odor, considered potentially dangerous.

Recognition of kin via chemosignals is an important mechanism that is manifested very early in life. In virtue of the pre-post birth continuity of the chemosensory experience [51.69], body odors are supposedly the first signals used to prevent the occurrence of stress situations. In situations of high vulnerability, such as early in life when a newborn is totally dependent on maternal care to survive [51.181], olfactory cues from the mother and the newborn become the basis of parent-infant interactions, and they constitute a foundation of the development of the parent-child relationship and secure attachment [51.182, 183]. Besides the ability of newborns to recognize and prefer the odor of their mother's amniotic fluid and breast body odor, mothers – who have an active role in the protection of their offspring from stress and harm – are able to discriminate and prefer the odor of their own baby [51.139, 184, 185].

However, as mentioned above, experience has an impact on the processing of human social chemosignals. Evidence to this claim is suggested by *Lundström* et al. [51.131], who asked their participants to smell the odor of highly familiar individuals such as long-time friends. Interestingly, duration of friendship – which correlates with the neural activity in the right occipito-temporal cortex – did not increase the identification rate

or the confidence in the recognition of the kin's body odors, supporting the notion that social chemosignal communication is primarily mediated by nonconscious processes. This view of a specific reaction to familiar body odors and their relationship with the duration of friendship suggests that exposure to a specific body odor in the context of long-lasting positive experiences will specifically impact the social chemosignal communication. In the study the odors of some sisters were also included [51.131]. When compared to friends, no differences in the identification of body odors were found, suggesting a complex interplay between learned and genetic cues. This would be in line with evidence found in mice, for whom a common odor (e.g., peppermint odor) can produce the same social behavior as a kin's odor (i.e., maternal odor), when previously associated with care and protection [51.181].

How is chemosignal communication modulated by the origin of the body odor? Such highly relevant stimuli seem to embed a threatening message, as suggested by the perceptual ratings collected in the *Lundström* et al. study [51.131]. Body odors were rated as being more intense and less pleasant when rated by individuals to whom these donors were a stranger to than when the very same odors were presented as the body odors of kins, indicating that the relationship to the rater, and not the chemical composition of the odor, was responsible for the perceptual differences found across conditions.

### 51.6.3 Transient Harm-Related Chemosignals: Behavioral Evidence

Besides stable traits, more transient information related to harmful situations can be communicated via body odors. For instance, *Shirasu and Touhara* [51.118] reviewed a number of infectious diseases as well as metabolic disorders, toxins and poisons that had been associated with either a volatile organic compound and/or a more or less specific odor label. *Olsson* et al. [51.24] have recently demonstrated that healthy individuals use chemosensory cues to evaluate the health status of individuals in their surroundings. Indeed, the body odor of senders undergoing an innate immune response induced by a lipopolysaccharide injection is rated as more intense, unpleasant and unhealthy (in other words, aversive) than that of individuals exposed to a placebo. This finding, in line with the idea that perceived disgust promotes avoidance behavior [51.28], suggests that olfaction plays an important role in reducing the risk of contagion, thereby maintaining an individual in good health. This is in line with the idea that behavioral avoidance is a first-line defense against disease; which of course is more cost efficient than to involve the organism's immune system.

Other types of situational danger can also be communicated via chemosignals. When an individual faces the need to implement a fight or flight response, and therefore experiences a stress situation, it is of value for potential conspecifics in the surrounding to be warned that a critical event is occurring. A series of studies have recently explored the chemosensory communication of stress by using axillary sweat samples. Stress is a complex response characterized by an increase in physiological arousal associated with the experience of a variety of emotions, ranging from those related to eustress (e.g., excitement and surprise) to those coupled with distress (e.g., fear and disgust) [51.186]. The literature on chemosensory communication of stress includes chemosignals collected within a wide range of situations, potentially affecting the quantity and the quality of the axillary sweat samples donated. The less intense stress sampling conditions consist of a person watching movies with a predominant emotional character and vicariously experiencing the situation visualized, while the body odor sampling occurs. Although this method induces relatively weak stress responses, the advantage is in providing a rather precise characterization of the emotions experienced by the donor, and that can be mediated to recipients via chemosignals, of anxiety and disgust [51.27, 28, 37, 187] (for positive accounts see [51.26]). In an attempt to keep the emotional specificity of the body odor donation stable and to specifically focus on the collection of chemosignals in highly anxious situations – thus, increasing the intensity of the signal – *Pause* et al. [51.134, 188] collected the body odor from donors waiting for an examination needed to complete their academic degree. Other groups increased the intensity of the stress response at the expense of emotional specificity by collecting body odors in extreme conditions, such as a first-time parachute jump [51.31] and high-rope courses [51.30, 38]. These chemosignals were subsequently presented to receivers and the effects of the exposure were quantified. It was reliably demonstrated across studies that chemosensory sweat stimuli are difficult to detect perceptually [51.33, 134, 188] and as a result, participants have difficulties in reliably verbally reporting the emotions experienced by sweat donors during collection [51.31, 32, 37, 187]. However, there is mounting evidence suggesting that adults, and in particular women, are more accurate than chance in identifying the emotion of the donor during collection [51.37, 187], in visually evaluating facial expressions on the basis of the chemosensory prime [51.32], and in discriminating between emotional expressions especially when body odor samples from donors experiencing fear are the target [51.31]. Altogether these data suggest that the effects of chemosensory stress signals are largely

unknown to the perceiver and that perceptual acuity mechanisms specific for social information are at play. Indeed, detection of safety signals (e.g., positive emotions, [51.38, 134]) is reduced in favor of an increased prevalence of detecting threatening stimuli [51.31, 32]. This is in line with the idea that body odors originating from fearful individuals, in virtue of the highly relevant message they convey, receive prioritized processing [51.189, 190]. Indeed, anxiety chemosignals, but not emotionally neutral body odors, affect the acoustic startle reflex [51.36], an evoked preattentive reflex modulated by the affective and relevance value of the stimulus [51.191].

Further, the association between a neutral body odor and a threatening situation can facilitate the processing of body odors. *Alho* et al. [51.192] tested the idea that an offender, in parallel to eyewitness lineup identification tests, could be identified by their odor alone. Participants could do this fairly well. It was also demonstrated that when the encoding of a body odor is associated with the simultaneous presentation of threatening information (e.g., authentic and arousing videos of criminal activities), they were subsequently identified well above chance in body odors lineup tests and considerably better as compared to the body odors associated with neutral videos. In other words, a body odor of a threatening stranger was remembered significantly better than a nonthreatening stranger.

So far, the evidence suggests that the responses to threatening body odors are in line with the elicitation of the automatic, and rather nonconscious, responses to fearful stimuli [51.193]. In contrast with this view, *Chen* et al. [51.35] found that smelling threatening body odor stimuli increased the response time and response accuracy of participants in processing words with fearful content in a word association task. This finding, interpreted as the ability of body odors to modulate cognitive processes, could be seen as counterintuitive. In contrast to carefully deliberated, but not timely reactions, rapid and automatic reactions to threatening situations are thought to increase the chances of survival. In other words, the promotion of mechanisms facilitating fast detection of threat, possibly high in false positives, would maximize survival rates as compared to a precise and slow processing. Threatening stimuli commonly enhance speed (that is, lower reaction times) at the cost of accuracy, as previously demonstrated for fearful multimodal stimuli [51.189, 194–196]. Because few studies have investigated the trade-off between speed and accuracy in response to threatening body odors, it is too early to say whether the detection of these chemosignals is governed by other processing principles than visual signals of threat.

Besides the cognitive consequences of body odor communication, emotional information processing is also affected. Evidence suggests that threatening body odors are sufficient to induce – particularly in female receivers [51.31] – a reflection of the emotional state of the sender [51.28, 197]. This is particularly true for fear-related odors, which have been demonstrated to quickly establish (and maintain) synchrony between sender and receiver. Sweat samples, produced with the involvement of the sympathetic-adrenal medullary system contain a distinctive signature (not yet chemically specified), which triggers in receivers fearful facial expressions (i.e., co-contraction of corrugator supercilii and medial frontalis muscle) and vigilant behavior (faster reaction times when classifying facial expressions) [51.27].

Emotional synchronization also occurs in the presence of chemosignals of disgust [51.28]. Indeed, a body odor from a person experiencing disgust while watching a disgusting movie will induce in the recipient an experience of disgust, revealed via the analysis of sniff patterns and facial electromyogram [51.198]. As demonstrated by *de Groot* et al. [51.28], the chemosignal communication of different forms of harm is specific and therefore can be discriminated. On the one hand, fear chemosignals generate a fearful facial expression and promote sensory acquisition (increased sniff magnitude and eye scanning); on the other hand, disgust chemosignals evoke a disgusted facial expression and sensory rejection (decreased sniff magnitude, target-detection sensitivity, and eye scanning) [51.28].

One of the theories mainly used to explain the transmission effects from sender to receiver via chemosignals involves the idea of emotional contagion, a basic mechanism promoting coordinated thoughts and actions, mutual understanding, and interpersonal closeness [51.199, 200]. However, as demonstrated in other types of social interactions [51.201], the simple emulation of a social percept is not the only possible adaptive response. Indeed, complementary states can be triggered. Emotional complementarity occurs when one person's emotions evoke different (yet corresponding) emotions in others. A classic example is the fact that a person's distress triggers compassion in another [51.202]. In the domain of social chemosignals of harm avoidance, emotional complementarity can acquire different meanings. Let's imagine the example of an individual who donates his/her body odor while involving in an act of aggression, characterized by anger. Rather than the implementation of an emotional contagion mechanism, i.e., the social chemosignal triggers anger feelings in the recipient, it is also plausible that a fear reaction is experienced by the recipient. This

would be in line with the fact that angry expressions are perceived as threatening [51.203, 204] and are known to trigger adaptive actions in the observers [51.205]. Future research extending the limited knowledge of chemosignals of aggression, now mostly performed

with indirect measures (e.g., competitiveness, dominance, [51.23, 206]) or limited to one odorous compound (e.g., androstenone) and not to a more complex odor signature [51.4], will shed further light on the issue.

## 51.7 Central Processing of Human Chemosignals Involved in Harm Avoidance

Behavioral and psychophysiological data suggest that chemosignals involved in harm avoidance can be preferentially processed. To further characterize this idea, the neural underpinnings of such body odor communication are explored below.

### 51.7.1 Self Body Odor Activates Areas in the Self-Other Recognition System

*Lundström* et al. [51.15] uncovered the neural mechanism of human self-recognition mediated by chemosignals, in line with the *armpit effect* [51.178]. They compared the body odor of oneself to the odor of a known friendly person and did not find any difference in cerebral activity. They suggested that humans, as had been suggested for rodents, use their own body odor as a template to assess the identity of another individual [51.178]. Further support to this interpretation seems to come from the neural underpinnings elicited by body odors when contrasted with common odors. As suggested, the PCC processes emotional stimuli via interaction with the ACC using *self* as reference frame [51.173]. Furthermore, the activity in the angular gyrus can be put in the context of self-referential space. Indeed, patients with an epileptic focus in the angular gyrus are known to report out-of-body experiences or perceptual distortions of other people's bodies [51.164, 165]. The self-reference matching mechanism is in line with results from studies using chemosensory event-related potentials, a temporally specific technique based on the averaged epochs of the electroencephalogram occurring in association with the presentation of chemosensory stimuli [51.180, 207]. These studies reveal that the human brain is able to discriminate between body odors coming from different sources, irrespective of conscious awareness of such differences. Specifically, the odor originating from oneself can be discriminated and processed faster as compared to the odor originating from someone else [51.180]. Further evidence reveals that more neural resources are required to process the body odors more similar to oneself (e.g., with similar HLA) [51.207], indicating a preferential neural processing for self-matching chemosignals.

The lack of conscious awareness, present in both the behavioral and neural correlates of chemosignal self-other recognition [51.15, 18], might be explained by a unique anatomical feature of the olfactory system. Olfaction is the only sense characterized by the lack of a mandatory thalamic relay, meaning that the olfactory receptors project directly to the olfactory bulb and primary olfactory cortical areas [51.208]. Given that thalamic processing has been implied in conscious awareness [51.209], it seems likely that the contribution of this structure to the olfactory percept might make it more weakly associated with conscious processing. However, the thalamic involvement in conscious and unconscious olfactory perception has not yet been fully clarified [51.210].

### 51.7.2 The Neural Encoding of Familiarity in Someone Else's Body Odor

The first chance to use odors to recognize others comes as early as in utero [51.69]. The evidence on the behavioral preference of infants for their mother's odors and for parents of their baby's odor is also reflected at the neural level. Indeed, the odor of the mother and the child are both subjected to preferential processing, a strategy that in evolutionary terms facilitates the survival of the individual and of the species. Mothers exposed to the body odor of newborns, including their own infant, show selective activation of the thalamus [51.211] and of the orbitofrontal cortex [51.212]. Interestingly, the orbitofrontal cortex is activated in both mothers and nulliparous women when smelling body odors originating from men [51.212]. Moreover, as demonstrated by *Lundström* et al. [51.211], both mothers and nulliparous women respond with neuronal activity within the reward system to the exposure to unfamiliar baby odors. The authors interpret this finding in light of evolutionary theories suggesting that the general ability of infant chemosensory cues to prime affection in adult women serves the purpose to motivate them to care for the infant, i.e., an indication of attachment mechanisms at play [51.213]. Although untested, the fact that fathers are also able to identify

the odor of their infant's amniotic fluid and judge it as qualitatively similar to their infant's and mother's body odor [51.214], suggests that fathers too can present specific neural pathways elaborating body odors.

The individual learning history seems to modulate signal processing, especially in brain areas with social roles [51.215]. Smelling a friend [51.15] activates, among other areas, the occipital cortex including posterior parts of the retrosplenial cortex, previously involved in the processing of familiar faces and voices [51.216]. Furthermore, the duration of friendship – an indirect index of the familiarity of the body odor – significantly correlates with increased regional cerebral blood flow in the extrastriate body area, a region implicated in the multimodal processing of information related to the human body [51.217, 218]. In other words, the more familiar the smell of the body odor, the greater the neuronal involvement to process body-related information [51.15].

With respect to unknown individuals, *Lundström* et al. [51.15] demonstrated that smelling a stranger's body odor evokes cortical activations (i.e., inferior frontal gyrus and amygdala) similar to those described in response to viewing negative stimuli [51.219–221], including masked fearful faces [51.220]. This supports the idea that a body odor never encountered before is treated like any other highly relevant (and potentially dangerous) stimuli [51.222] and differently from perceptually comparable common odors.

In line with the idea that the strangers' body odors conveys a threat sociochemosignal is the activation of the insula, implicated in the processing of unpleasant chemosensory stimuli [51.223] as well as in the recognition of fearful and disgusting objects [51.150]. The simultaneous activation of amygdala and insula, two highly interconnected areas [51.224], suggests that the body odor of a stranger induces separate, yet related, activations of fear and disgust [51.222]. This reaction is not, however, specific to body odors, but is shared with all novel and suddenly presented stimuli [51.225].

In addition, the body odor of a stranger elicits activations at the level of the supplementary motor area and, right below threshold of significance, of the premotor area [51.15]. These structures are known to be part of a hierarchical executive network involved in the adaptation and optimization of motor behaviors [51.226]. The involvement of such a network suggests that the body odor of a stranger by communicating fear or disgust information prepares the recipient to react to the potential presence of an unknown individual in the vicinity. Such motor preparation involves fight or flight responses: basic reactions critically involved in the survival process of the individual.

### 51.7.3 Threatening Body Odors and Their Neural Correlates

In line with the idea of a preferential processing of chemosignals indicating threat or harm, smelling the body odor collected in anxious situations increased neuronal processing from medial frontal brain areas (P3 amplitude) [51.188]. This effect was more pronounced in women than in men, which is in accordance with the findings that females show a processing advantage for social emotional stimuli [51.227] and for perceptually weak threatening stimuli [51.228]. Preferential processing can also be inferred by the allocation of early attentional resources to threatening stimuli [51.229] and to ambiguous stimuli (e.g., neutral facial expressions [51.29]).

Studies conducted with body odor samples collected from individuals experiencing anxiety activate brain areas involved in the processing of social emotional stimuli (fusiform gyrus), and in the regulation of empathic feelings (insula, precuneus, cingulate cortex; [51.33]). This evidence is used in support of the idea that fear-related chemosignals produce emotional contagions [51.28], and increase the level of situational anxiety [51.30] in the receivers.

When the sweat presented in the scanner comes from individuals experiencing high levels of stress, it being eustress or distress, such as in the case of the parachute jump [51.31], activations were mainly demonstrated within the amygdala, a center encoding the relevance of a situation and stimulus, in a non-specific fashion. This is indeed related to a negative affect compatible with fear. The amygdala has long been known to process negative emotional stimuli [51.150, 220, 221] including threat [51.230], although non-selectively [51.231]. In mice, the amygdala has been specifically identified as the main processing center of threat-related endogenous odors [51.232]. This might be taken as an indication of the fact that the amygdala should also be involved in the detection of threat-related olfactory stimuli in humans and not in the processing of fear itself [51.230]. As suggested by *Pause* et al. [51.188], amygdala activations are more pronounced in women than in men [51.233], indicating that stress-related chemosensory cues are more relevant to women.

However, not all evidence points towards a preferential processing of threatening human chemosignals. Indeed, the cognitive modulation induced by smelling threatening body odors suggests that smelling anxiety chemosignals makes the receiver more accurate and less fast in using that information [51.31, 32, 35], thus raising the issue of intermodal differences in the processing

of threatening stimuli. If, on the one hand, threatening visual and auditory stimuli are processed fast [51.195, 196], this is not in accordance with how the olfactory system generally works. Indeed, chemosensory stimuli take longer to be processed as compared to visual or auditory stimuli [51.234]. Furthermore, the estimated time difference between the onsets of the first perceptual and the first cognitive processing is approximately 200 ms in vision, and it is approximately doubled for olfactory stimuli [51.235, 236]. This evidence highlights a downside of olfaction as a warning signal: early detection of alarming olfactory stimuli might be delayed by the slower central processing that olfactory signals undergo. Nevertheless, the possibility of using such mechanisms in critical conditions (e.g., in the absence of visual and auditory functioning, at a distance), makes the olfactory warning system a good addition to the survival kit mechanisms, by allowing chemosensory stimuli to shape the slower and more deliberate processing rather than the initial and more rapid detection phase [51.35].

Interestingly, none of the published functional neuroimaging studies including threat-related body odors in their paradigms has reported activations at the level of the primary or secondary olfactory cortices [51.15, 31, 33]. When extending the search including studies incorporating body odors of any sort [51.15, 34], only one of the two remaining experiments reveals activations at the level of the lateral orbitofrontal cortex. *Zhou* and *Chen* [51.32] recorded increased neural activity in that structure when participants were smelling the body odors sampled from donors watching erotic videos. Because the activation of the lateral orbitofrontal cortex is determined in *Zhou* and *Chen* [51.34] by contrasting

body odors with a common odor (phenylethyl alcohol (PEA)) but a similar activation is also obtained when discriminating odors within a mixture [51.228], whether the lateral orbitofrontal cortex activity is a clear demonstration of differential body odor processing still remains to be determined. What can be safely concluded though is that five neuroimaging studies, which have included different types of body odors and were performed by independent laboratories, have not been able to report activations located within the olfactory areas even though participants are presented with clearly perceivable odors. This phenomenon can have a series of explanations, for which direct experimental proof is still lacking. It is possible that the conscious perception of body odors is too transient to be detected at the level of the olfactory cortices, possibly due to the high susceptibility to habituation of such areas [51.237, 238] and activity is therefore only demonstrated in less habituating areas of the social brain [51.239]. If this were to be true, non-endogenous control odors (i.e., the fake body odors), should have not generated clear activations in olfactory cortices [51.15, 18]. One might also claim that the lack of olfactory activations depends on the neuroimaging analyses applied, which only correct for false positive errors but do not account for false negative errors. Therefore, lack of significant activity in a neuroimaging study cannot be taken as evidence for the hypothesis that a specific area is not involved in a task. However, if the lack of activation in olfactory cortices is due to cognitive processing, no differences should be found between real and fake body odors [51.131]. Finally, it is unlikely that five independent neuroimaging studies would produce five sets of results with similar false negative errors.

## 51.8 A Clinical Perspective on Human Chemosignals

The research on how a social message is transmitted from a sender to a receiver through body odors has mostly been conducted on healthy human participants. However, health and mental issues modify brain processing and experience [51.240] (Chap. 50). Given the social relevance of body odor communication, differences in the processing of such signals according to baseline social skills are expected. Only a few studies have empirically tested this assumption and demonstrated that socially skilled versus socially unfit individuals use body odor information differently. For instance, emotional competence facilitates the identification of familiar body odors [51.32] and highly sociable and assertive individuals process body odors within the central nervous reward system, as well as in structures involved

in social cognition and in synchronization processes (inferior frontal gyrus) [51.241]. In other words, higher social emotional competence facilitates the transmission of socioemotional messages via chemosignals. This powerful feature of chemosensory stimuli, along with the automatic processing of these stimuli, might offer an opportunity for individuals with reduced social skills. This hypothesis has been tested in a group of children with autism spectrum disorders (ASD), a series of disorders known for their core deficits in social information processing [51.242]. When exposed to their mother's body odor, high-functioning children with ASD can readily start and conclude basic social actions [51.243, 244]. With specific reference to harm avoidance, individuals with high social anxiety quickly elaborate the

presence of body odors of anxiety, yet subsequent attentional processing is blocked, possibly reflecting a mechanism of perceptual defense [51.188]. Furthermore, individuals with high social anxiety show greater startle responses under the exposure of chemosignals of anxiety as compared to neutral chemosignals [51.245] and respond with heightened sensitivity to such chemosensory contextual information [51.229].

Recent studies in rodents indicate that a single receptor is involved in the transmission of warning chemosignals and, when blocked, the warning signal (predator odor) loses its threatening power [51.246].

## 51.9 Conclusions

The evidence reviewed in this chapter suggests that humans do use chemosignals as a form of social communication [51.248]. A chemosensory signal conveying a social message is generated by the coactivation of the systems maintaining the homeostasis in the sending individual. In healthy individuals, genetics, the immune system, metabolism, hormones, and the autonomic and central nervous systems work in concert to determine the chemical composition of body secretions. With respect to the axillary sweat, such systems affect the apocrine and apoeccrine secretions. These secretions will be converted by the resident flora into a joint result.

Such a chemosignal, conveyed from the sender to the receiver via airborne molecules, carries a variety of information, among which is that promoting survival. Suggested to date are chemosignals can communicate self-other information (e.g., kin recognition), emotional messages (e.g., chemosignals of anxiety), and those that inform the receiver about the presence of potential threats in the environment (presence of an unknown or sick individual). As noted by *Liibke* and *Pause* [51.104], the receiver's responses constitute the only unspecific step in the social chemosignal communication process, as outlined here. This would be in line with the need of receivers to adaptively respond to the presence of situations challenging survival. In the case of danger perceived through different sensory modalities, the same type of fight, flight, or tend-and-befriend responses would be required to handle the threat. Importantly, receivers can implement those responses without conscious awareness of having smelled the chemosignal [51.131].

With respect to methodology, researchers have not yet agreed upon guidelines for body odor collection, reducing the comparability across databases. In this respect, it is worth noting that the choice of the experi-

Should a similar mechanism be proved in humans, it could be used as a therapeutic strategy for patients suffering from social anxiety.

Overall, these results show that socioemotional skills and human communication mediated via chemosignals are intrinsically interwoven. In light of the ability to sensitively detect, accurately process, and show appropriate responses based on relevant chemosensory social information, it is plausible that chemosignal communication critically contributes to the formation and maintenance of social groups [51.247], an essential condition for human evolution.

mental control conditions is of primary importance. To avoid confounders in the perceivers' responses, secretions from the same glands should be sampled across conditions. Stringent control conditions can separately account for several significant factors and it is advisable to include common odors to reveal further distinctions and similarities across olfactory functional subsystems. However, the extensive time required to collect usable body odors, as well as the fast central habituation to olfactory stimuli [51.237], constrains the number of olfactory conditions and trials possibly included in one experimental session.

Delivery techniques have also been one of the major causes limiting the exploration of the field. Indeed, olfactometers – dedicated computer-controlled delivery systems, with rapid onset-offset stimulus release – are machines not widely commercialized and relatively expensive. Nevertheless, they are necessary for the study of the temporal dynamics and the neural underpinnings of body odor communication.

With regards to the neural bases of social chemosignal communication, future efforts should focus on increasing our knowledge of the neural bases of social chemosignal communication and further our understanding of the functional separation between pathways processing common and body odors. Furthermore, the neural underpinnings of chemosignals with different emotional characterizations should be included to assess emotion-specific dissociations. This would open the discussion on the communication strategies used by emotional chemosignals.

Finally, a better understanding of how social aspects of life are transmitted through chemosensory stimuli can provide additional insights on clinical populations struggling with social information processing (e.g., ASD, schizophrenia, social phobia).

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