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Thresholds and chemosensory event-related potentials to malodors before, during, and after puberty: Differences related to sex and age

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A sex-related difference in olfactory sensitivity to androstadienone and androstenone has been reported to occur during puberty. The study reported here extends this work to investigate whether sex and age differences exist before, during, and after puberty for 2-methyl, 3-mercapto-butanol (2M3M; a malodorous component of human sweat), carbon disulfide/hydrogen sulfide (H2S), and androstadienone. A total of 121 participants took part in the study (58 females, 63 males; age range 9–20 years). Participants were divided into 3 groups (i) pre-puberty, (ii) puberty and (iii) post-puberty. Threshold measurements for (i) androstadienone, (ii) 2M3M and (iii) carbon disulfide were recorded. Chemosensory event-related potentials (CSERPs) were recorded using air-dilution olfactometry. The results revealed that female thresholds for the three odorants were stable between the three age groups. Pubescent males had higher thresholds (less sensitive) for all three odorants. In the post-puberty group, sex differences were only observed for 2M3M. These differences are mirrored by significant sex differences for CSERP latencies. The latency increase in male pubescents may be due to the production of sweat by the apocrine glands resulting in increased levels of 2M3M and androstadienone, resulting in adaptation. To conclude, based on the present study performed in a relatively large sample, the processing of malodors in males is different from that of females during puberty. This observation not only relates to a reduced sensitivity towards odors typially found in axillary sweat but also extends towards other malodors. While the underlying cause may be partly due to specific adaptation towards malodors present in axillary sweat it might also reflect hormonal changes modifying the perception of odors.

Keywords: Chemosensory event-related potentials (CSERPs); Olfaction; Sex; Age; Puberty; Malodor; Sweat; Androstadienone

Introduction

Empirical investigations of olfaction and age have predominantly focused on areas of neonatal health, odor preferences in infants and young children (Schaal, 1988; Schmidt and Beauchamp, 1988), the decline of olfactory acuity with age (Doty et al., 1984) and neurodegenerative disorders (Hawkes, 2008). In contrast, few studies have addressed alterations in olfactory ability before, during and after puberty.

Sex-related differences in odor perception were first reported at the end of the nineteenth century in terms of lower detection thresholds for the environmental agent camphor for females (Toulouse, 1899). Sex differences have since continued to be of immense interest. Numerous studies have demonstrated superior olfactory performance in females in olfactory discrimination (Schleidt et al., 1981; Wallace, 1977), identification (Cain, 1982; Doty et al., 1985; Ship et al., 1996) and sensitivity (Koelega, 1970, 1994; Koelega and Koster, 1974; Scheider and Wolf, 1955).

A sex–age-related difference in olfactory sensitivity to androstenone has been reported to occur during adolescence (Dorries et al., 1989). More males exhibited anosmia to androstenone than females. A similar sexually dimorphic sensitivity has been observed for androstadienone in adolescents (Hummel et al., 2005) and adult women and men (Lundstrom et al., 2003).

This sexual-dimorphism during adolescence could be related to hormonal alterations occurring during this period (Doty, 1986). Numerous studies have attempted to correlate olfactory function and hormonal status during pregnancy and menstrual cycle (Doty et al., 1981; Hummel et al., 1991). However, it remains unknown whether variation in hormone levels during pubescence affects olfactory sensitivity.

The present study assessed pre- to post-pubescents, psychophysical responses to three odors, two of which are present in pubescent/adult sweat: (i) 2-methyl-3-mercapto-butanol (2M3M; otherwise known as 2-methyl-3-sulfanylbutan-1-ol; Natsch et al., 2004), (ii) androstadienone (4-, 16-androstadien-3-one), and one odor which is not found in sweat (iii) carbon disulfide in liquid form as required for the psychophysics, and hydrogen sulfide (H_2S) in gas form, as required for the delivery in the olfactometer for the collection of electrophysiological data.

2M3M has been identified as a malodorous component of human sweat (Natsch et al., 2004). It is one of many sulfanyl alcohols described in human sweat (Starkenmann et al., 2005). Sweat is a

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highly complex mixture, the identity and composition of molecules in male and female sweat is unknown. Sex, age and emotional differences in the composition of sweat are currently being investigated, however due to the lack of appropriate analytical tools available this is proving to be a difficult task.

Androstadienone is a member of the odorous steroids family, which is found in sweat, axillary hair, blood and semen (Gower et al., 1994). In human males, androstadienone has been found at blood concentrations of 98 mg/100 ml (Brooksbank et al., 1969) and in axillary secretions with a mean value of 228 pmol/total axillary hair weight (Nixon et al., 1988). Androstadienone can also be found in women, but in a much smaller concentration (Brooksbank et al., 1969). The related steroid, androstenone (5α-androst-16-en-3-one) has also been found to be higher in men than women (Gower et al., 1985).

Carbon disulfide/H_2S was selected as a non-body-related malodor; however sulphur compounds are present in oral malodor and intestinal gases, therefore it does not represent a true non-body-related malodor. It is difficult to identify non-body unpleasant odors, however as carbon disulfide/H_2S is not a typical sweat odor it was selected as be a suitable control malodor.

In addition to psychophysical thresholds chemosensory event-related potentials (CSERPs) were measured from the scalp. CSERPs offer a relatively unbiased and quantitative method for studying changes in olfactory function due to age or sex in humans. This method allows the investigation of the sequential, early processing of olfactory information (Hummel and Kobal, 2002). The early N1 peak of the CSERP reflects stimulus characteristics such as intensity and quality; the late positivity, referred to as the P2 peak, is associated with more cognitive aspects of perception, such as stimulus salience or novelty (Lundstrom et al., 2006; Pause and Krauel, 2000). Among other relations, changes in latencies are associated with processing speed (shortened latencies relate to faster processing; Hummel and Kobal, 2002), changes in early component amplitudes are associated with attention (Pause and Krauel, 2000) and changes in P2 amplitude are associated with changes in expectation, familiarity, or pleasantness (Pause et al., 1996). CSERPs also reflect sex-related differences in the perception of odors. Although sex-related differences are not frequently found, some studies have observed that women exhibit larger responses and shorter latencies (Becker et al., 1993; Stuck et al., 2006) which is also found for responses to trigeminal stimuli (Lundstrom et al., 2005; Stuck et al., 2006). It also appears that men and women process chemical stimuli differently with regard to hemispheric activation (Yousem et al., 1999). Specifically, with regard to event-related potentials (ERPs) in response to mixed trigeminal-olfactory stimuli, women generally expressed larger amplitudes and longer latencies over their left hemisphere, whereas men demonstrated a similar pattern over their right hemisphere (Lundstrom and Hummel, 2006).

Based on previous investigations on changes of olfactory sensitivity towards androstadienone during puberty (Hummel et al., 2005), the current study addressed the question whether similar, sexually dimorphic effects of aging during puberty can also be observed for 2M3M. It was hypothesised that male sensitivity would decrease during puberty for androstadienone and 2M3M and that these differences would be reflected in the electrophysiological data, in that there would be increased latencies for the early sensory components (P1 and N1) and the later phase of processing (P2) reflecting stimulus evaluation and a reduced P2 amplitude in male pubescents for 2M3M and androstadienone reflecting the hormonal alterations during puberty and increased levels of sweat in males. It was expected that there would be less age-related changes for females and for the control malodor H_2S.

Methods

Participants

A total of 121 volunteers participated in the study and were divided into 3 groups (i) pre-puberty (17 females, 21 males; age 9–11, mean age 9.4 years), (ii) puberty (25 females, 19 males; age 12–14, mean age 13.7 years) and (iii) post-puberty (18 females, 21 males; age 17–20, mean age 18.5 years). The grouping of participants was based on the assumption that the average onset of puberty occurs at around 12 years of age for females (menarche; Whincup et al., 2001) and males (stage 2 genital growth; Villarreal et al., 1989).

Pre-puberty and puberty participants were recruited from a primary and secondary school respectively, and some of the post-puberty participants were students at the Technical University of Dresden. Participants' medical history and consent to the study was obtained prior to testing. Parental consent was obtained for participants under the age of 18. Participants were all free from nasal congestion, acute infection, and head trauma. The study was carried out in accordance with the Helsinki Declaration and had been approved by the Ethics Committee at the Technical University of Dresden Medical School.

Screening

All participants initially completed the German "Wortschatztest" (Schmidt and Metzler, 2000) for verbal abilities. This test cosists of 42 rows, each consisting of 5 nonsense words and 1 actual word which the participants were instructed to identify. The difficulty of the task increased throughout the test. The test score was used as an indicator of general verbal abilities.

Olfactory function of the participants was assessed using the odor identification "Sniffin Sticks" test (Hummel et al., 1997; Kobal et al., 2000).

Psychophysical testing

Stimuli

Participants' sensitivity were assessed with a three-alternative forced-choice test consisting of 12 concentration steps to (i) androstadienone (Steraloids Inc., UK; 2.25 mM, 0.5 mM, 0.25 mM, 50 μM, 22.5 μM, 5 μM, 2.25 μM, 0.5 μM, 0.225 μM, 0.05 μM, 0.0225 μM, 0.005 μM), (ii) 2M3M (Unilever Research & Development, UK; 5.12 mM, 1.28 mM, 0.32 mM, 80 μM, 20 μM, 5 μM, 1.25 μM, 0.313 μM, 0.078 μM, 0.019 μM, 0.0048 μM , 0.0012 μM) and (iii) carbon disulfide (Sigma-Aldrich, Germany; 0.33 mM, 0.11 mM, 37 μM, 12 μM, 4.11 μM, 1.7 μM, 0.46 μM, 0.15 μM, 0.051 μM, 0.017 μM, 0.0056 μM, 0.0019 μM). Odorants were dissolved in propylene glycol (Sigma-Aldrich, Germany). Solutions were stored in brown glass bottles (volume 62 cm^3, diameter of opening 2.3 cm) with 5 ml of odorant.

Procedure

Three bottles were presented to the participant, starting with the lowest concentration; participants were asked to identify which of the 3 bottles smelled differently. One bottle contained the odor, the