Smelling human sex hormone-like compounds affects face gender judgment of men

Gyula Kovács, Balázs Gulyás,[1,CA] Ivanka Savic,[1] David I. Perrett,[2] R. Elisabeth Cornwell,[2] Anthony C. Little,[2] Ben C. Jones,[2] D. Michael Burt,[2] Viktor Gál[3] and Zoltán Vidnyánszky[4]

Center for Cognitive Sciences, Budapest University of Technology and Economics, Budapest, H-1111, Hungary; [1]Department of Neuroscience, Karolinska Institute, 171 77 Stockholm, Sweden; [2]School of Psychology, University of St. Andrews, KY16 9JU, St. Andrews, Scotland, UK; [3]Analogical and Neural Computing Systems Laboratory, Computer and Automation Research Institute of the Hungarian Academy of Sciences, Budapest, H-1111; [4]Neurobiology Research Group, Hungarian Academy of Sciences, Budapest, H-1094, Hungary

[CA]Corresponding Author: balazs.gulyas@neuro.ki.se

Received 23 January 2004; accepted 13 February 2004

DOI: 10.1097/01.wnr.0000130234.51411.0e

Although strong cross-sensory interactions between visual, tactile and auditory modalities have already been shown, we know little about how chemosensory information affects processing in other sensory modalities. We studied whether smelling gender-specific odorous sex hormone-like steroids: 5-α-androgenst-16-en-3-one (androgen) or oestra-1, 3, 5 (10), 16-tetraen-3-ol (estrogen) can bias face gender discrimination. We found that, as a result of inhalation of androgen, men perceive faces to be more masculine as compared to when they are exposed to estrogen. Our results provide evidence for specific cross-sensory effects of the gender-specific chemosensory cues on the categorization of visual face gender. *NeuroReport* 15:1275–1277 © 2004 Lippincott Williams & Wilkins.

Key words: Cross-modal interaction; Face gender discrimination; Pheromones

INTRODUCTION

Processing in a given sensory modality is affected by the information that is processed simultaneously in other modalities. Cues from different senses interact and are integrated by the brain to evoke the most efficient and appropriate behavioral responses. Intensive research has recently provided evidence that cross-sensory interactions between vision, audition and somatosensation occur at the early stages of sensory processing both in macaques [1] and in humans [2]. We know little, however, about how chemosensory information may affect sensory processing in other modalities. Although it has been shown that odors modulate the efficiency of learning and recall of sensory information provided by other modalities [3], evidence regarding the cross-sensory effects of odors on the sensory processing itself are lacking.

In the present study we investigated the effect of passive inhalation of sex hormone-like steroids 5-α-androgenst-16-en-3-one (androgen) and oestra-1, 3, 5 (10), 16-tetraen-3-ol (estrogen) on the visual face gender discrimination in men. There are two major reasons behind our choice of the specific chemosensory and visual stimuli. First, in a previous study by two of the present authors [4] it was found that smelling sex hormone-like compounds activates of the fusiform gyrus, a brain region that was shown to be involved in the processing of visual faces [for reviews see 5–7]. Second, our goal was to choose sensory modalities which may naturally be associated during ontogenesis. We selected female and male human faces and gender-specific odorous substances, based on the assumption that there is a prolonged and pronounced association between the gender-specific cues of different sensory modalities.

MATERIALS AND METHODS

Sixty-two healthy heterosexual male subjects (ranging from 19 to 45 years of age; mean 29.2 years) performed an interactive face gender categorization task [8]. All subjects had normal or corrected vision. No subject had any previous neurological or psychiatric history, olfactory disease or nasal congestion.

All testing was done in a designated room to prevent odor contamination. The room was equipped with a high volume ventilation and an additional adjustable vacuum hood was placed over the subjects head.

Visual stimuli and procedure: Participants sat 100 cm in front of a standard 17″ monitor. Stimuli occupied the central $10 \times 9^{\circ}$ of the screen (average luminance 8 cd/m^2) and were presented on a uniform black background (0.5 cd/m^2). Participants first viewed an animation morphing gradually from a face with reduced sex characteristics to an opposite sex face enhanced in sex characteristics (e.g. from a 25% male/75% female face through to a 100% male configuration [9,10] (Fig. 1). After determining the sex of the last face of the animation, participants were presented with sequences of the same morphed images along the gender axis one by one and were asked to report the face where the gender transition is first perceived. The instruction given to the subjects was: "Previously you determined the person on the last image as male/female. Please choose now the first face of the continuum

Fig. 1. A representative facial morph series. The numbers above each face represent the female/male ratio of the given composite face.

which matches your selection.'' Suppose, for example, that in Fig. 1 the center row right stimulus is reported as the face where the female to male transition occurs. In this case the percentage of sexual dimorphism, required for gender decision, is 62.5%. Four facial continua sequences (26 images each) were presented twice, starting either with 25% male/75% female (masculinisation) or with 75% male/25% female faces (feminisation), giving eight trials in all. Raw gender transition data were entered into a one way ANOVA with the applied odorant as factors (3: water, androgen and estrogen). Fisher LSD tests were used for *post-hoc* comparisons of pairs of odorants (Fig. 2).

Odorants and exposure: During testing subjects were set into three groups randomly and they were exposed birhinally either to water (n=38) or to one of the odorous sex-hormone-like steroids, androgen (n= 10) or estrogen (n=14) in powder form. To avoid possible learning effects each subject was tested only once with only one type of odorant. Each subject was tested only once with only one of the odorants. To prevent adaptation effects, the odorants were presented to the subjects only during the animation movie (exposure time 5 s). Subjects were instructed to ignore the odorant exposure, to breathe normally, and to keep their attention on the visual stimulation. The odorants were kept at room temperature in a separate ventilation chamber.

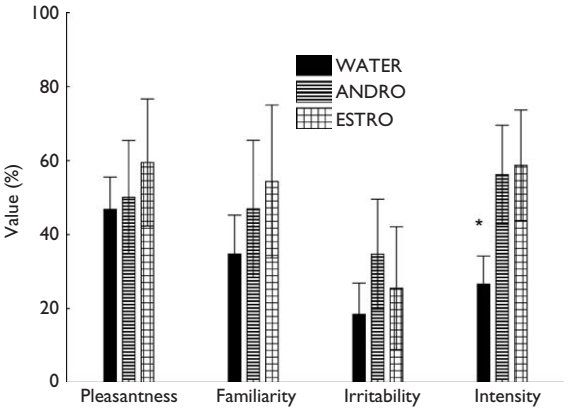

Fig. 2. Average (±s.e.m.) ratings of subjects regarding the pleasantness, familiarity, irritability and intensity of the three applied odorous substances. Asterisks indicates significant difference between water and androgen and estrogen ($p < 0.005$, *t*-test for independent samples).

At the end of the 8 trial blocks subjects rated the odorant on a 0-100 bipolar visual scale according to their subjective pleasantness (0, unpleasant; 100, pleasant), familiarity (0, unfamiliar; 100, very familiar), irritability (0, neutral; 100, very irritating) and intensity (0, weak; 100, intense). The experiments were conducted with the understanding and the written consent of each participant. The work was conducted in accordance with the Declaration of Helsinki and was approved by the ethical committee of the Karolinska Institutet.

RESULTS

Figure 2 shows data for the subjective odorant ratings. The odorants differed only in intensity with androgen and estrogen being significantly more intense than water (*t*-test for independent samples, $t = -3.8$ and -3.9 for androgen and estrogen, respectively; $p < 0.005$). Importantly, there was no significant difference between androgen and estro in the tested properties.

One-way ANOVA showed a significant effect of the applied compounds on the perceived gender transition ($F(2,58) = 5.23$, $p = 0.008$, Fig. 3a). With exposure to androgen, less masculinised features were required before subjects judged an image to be male. In turn, subjects expressed to estrogen required more maculinized features to make the same judgement. Fisher LSD *post hoc* analysis showed that responses to androgen differed significantly from estrogen ($p < 0.002$) and from water ($p < 0.016$), while estrogen and water did not differ significantly ($p < 0.15$). Interestingly, the effects of androgen or estrogen exposure were present only in masculinisation trials (effect of applied compound in feminisation trials: $F(2, 59) = 0.02$, n.s., Fig. 3b), which led to a significant interaction between the direction along gender axis (within subject factor: masculinisation/feminisation) and the applied odorant (between subject factor): two-way ANOVA, $F(2,249) = 7.2$, $p < 0.0009$).

DISCUSSION

The results provide evidence that passive inhalation of sex hormone-like compounds can bias men's face gender judgments. An intriguing property of our findings is that cross-sensory effects were found only in those trials where female faces were masculinised. When faces were femininised, face gender categorization was not effected by the presence of

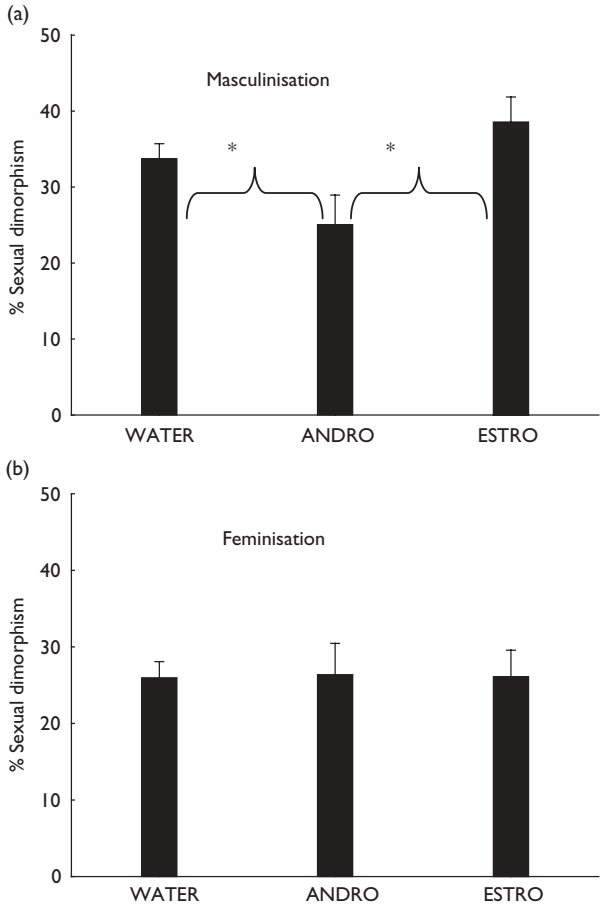

Fig. 3. Mean sexual dimorphism required to judge a face as being male (**a**, masculinisation) or female (**b**, feminisation) in the presence of water, androgen and estrogen. Zero percentage sexual dimorphism refers to the initial female face (a, masculinisation trials) or the initial male face (b, feminization trials). Asterisks indicate significant difference ($p < 0.01$; Fisher's LSD test).

steroid. The fact that cross-sensory effects were found to be highly specific for the direction of morphing on the gender axis has two important implications. First, these findings are not explained by a differential effect of androgen and estrogen on the autonomic nerve functions, mood or general arousal that were previously shown to be effected by sex hormone-like compounds (for a review see [11]). Second, it suggests that a cross-sensory chemosensory-to-visual modulation occurs at the stage where gender specific facial attributes are processed. This conclusion is supported by the results of a recent PET study [4] showing that the fusiform gyrus, where face gender processing is assumed to be taking place [12], is strongly activated by sex hormone-like steroids (estrogen and the androgen precursor 4,16-androgenstadien-3-one). Further studies are required to uncover the exact neural mechanisms that mediate the observed chemosensory–visual cross-sensory effects and the selective directionality of these effects along the gender axis.

Gender specific secretion is an essential condition for sex hormone-like compounds used in the present study to function as chemosensory gender cues. In fact, it has been shown that the concentration of androgen in the axillary sweat of males is significantly higher than that of females [13]. An important question concerns the minimal concentration of these sex hormone-like steroids that is required to evoke the observed cross-sensory effects. A previous imaging study indicates that estrogen evokes significant brain activations even at subliminal concentration, without conscious perception [14]. Whether the cross-sensory effects of the sex hormone-like compounds on face gender judgement found in the present study are an automatic process which does not require awareness of the chemosensory signal is an intriguing question that remains to be explored.

CONCLUSION

This study provides behavioural evidence for specific cross-sensory interactions between human chemo-sensation and vision, by showing that gender specific chemosensory cues can affect men's face gender judgment when the visual cues alone are ambiguous.

REFERENCES

1. Schroeder CE. The timing and laminar profile of converging inputs to multisensory areas of the macaque neocortex. *Cogn Brain Res* 2002; **14**:187–198.
2. Molholm S, Ritter W, Murray MM, Javitt DC, Schroeder CE and Foxe JJ. Multisensory auditory-visual interactions during early sensory processing in humans: a high-density electrical mapping study. *Cogn Brain Res* 2002; **14**:115–128.
3. Walla P, Hufnagl B, Lehrner J, Mayer D, Lindinger G, Imhof H *et al.* Olfaction and face encoding in humans: a magnetoencephalographic study. *Brain Res Cogn Brain Res* 2003; **15**:105–115.
4. Savic I, Berglund H, Gulyás B and Roland P. Smelling of odorous sex hormone-like compounds causes sex-differentiated hypothalamic activations in humans. *Neuron* 2001; **31**:661–668.
5. Haxby JV, Hoffman EA and Gobbini MI. The distributed human neural system for face perception. *Trends Cogn Sci* 2000; **4**:223–233.
6. Kanwisher N. Domain specificity in face perception. *Nature Neurosci* 2000; **3**:759–763.
7. Tarr MJ and Gauthier I. FFA: a flexible fusiform area for subordinate-level visual processing automatized by expertise. *Nature Neurosci* 2000; **3**: 764–769.
8. Penton-Voak IS, Perrett DI, Castles DL, Kobayashi T, Burt DM, Murray LK and Minamisawa R. Menstrual cycle alters face preference. *Nature* 1999; **399**:741–742.
9. Frigerio E, Burt DM, Montagne B, Murray LK and Perrett DI. Facial affect perception in alcoholics. *Psychiatry Res* 2002; **113**:161–171.
10. Tiddeman BP, Burt DM and Perrett DI. Prototyping and transforming facial textures for perception research. *IEEE Comp Graphics Appl* 2001; **21**:42–50.
11. Kohl JV, Atzmueller M, Fink B and Grammer K. Human pheromones: integrating neuroendocrinology and ethology. *Neuroendocrine Lett* 2001; **22**:309–321.
12. Gorno-Tempini ML, Pradelli S, Serafini M, Pagnoni G, Baraldi P, Porro C *et al.* Explicit and incidental facial expression processing: an fMRI study. *Neuroimage* 2001; **14**:465–473.
13. Gower DB, Bird S, Sharma P and House FR. Axillary 5 alpha-androst-16-en-3-one in men and women: relationships with olfactory acuity to odorous 16-androstenes. *Experientia* 1085; **41**:1134–1136.
14. Sobel N, Prabhakaran V, Hartley CA, Desmond JE, Glover GH, Sullivan EV and Gabrieli JD. Blind smell: brain activation induced by an undetected air-borne chemical. *Brain* 1999; **122**:209–217.

Acknowledgements: This work was supported by grants from the Hungarian National Research and Development Program: 5/0079/2 to G.K. and 2/035 to Z.V. and by grants from the Royal Swedish Academy of Sciences and Hungarian Academy of Sciences as well as the Swedish Institute (HÖI07) to BG. We express our gratitude to Dr David Schmitt for his advice during the preparation of the manuscript.