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Exploring the fMRI based neural correlates of the dot probe task and its modulation by sex and body odor

Jonas Hornung[a,*], Hannes Noack[a,c], Lydia Kogler[a], Birgit Derntl[a,b,c]

[a] Department of Psychiatry and Psychotherapy, Medical School, University of Tübingen, Tübingen, Germany
[b] Werner Reichardt Centre for Integrative Neuroscience, University of Tübingen, Tübingen, Germany
[c] Lead Graduate School, University of Tübingen, Tübingen, Germany

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ABSTRACT

The dot probe task implicitly cues attention via emotional information, an effect which is especially pronounced for threat-related cues. However, several questions remain unexplored. The first one is whether chemosignals like the androgen-derivative androstadienone can influence such attentional biases. Second, few studies have addressed sex differences regarding attentional biases. Finally, the neural correlates of these potential behavioral effects based on functional magnetic resonance imaging (fMRI) are not known. In two experiments we aimed to answer these questions.

A total of 159 healthy individuals (58 oral-contraceptive-users, 42 luteal women, 59 men) were tested. In experiment 1 (behavioral study) we examined attentional biases behaviorally, while in experiment 2 (fMRI study) the dot probe task was complemented by fMRI.

Our results provide robust evidence that in healthy participants fearful but not angry or happy faces lead to a strong general attentional bias. Elucidating the neural basis of this effects points to an early processing advantage in bilateral thalamus for valid compared to invalid cued fear. However, this finding was limited to those participants with the strongest attentional biases and was not linked to behavioral measures. Furthermore, no consistent sex or group differences existed neither did the putative human chemosignal androstadienone reliably modulate attentional biases or change neural processing.

1. Introduction

Human attention is both stimulus and control driven, i.e. both the salience of stimuli and the motivation/goal of the perceiver have an impact in the control of attention (Yantis and Egeth, 1999; Corbetta and Shulman, 2002). To investigate such attention capture especially with respect to stimulus driven attention, the dot probe task (MacLeod et al., 1986) was developed which assesses attentional biases induced by the presence of emotional and non-emotional stimuli. Commonly, participants have to detect a non-emotional target (dot probe) which is preceded by irrelevant cues. These cues can either be at the same (valid) or at the opposite (invalid) location to the following probe. In previous studies, cues have included aversive words (Mogg et al., 1994; Koster et al., 2004) or faces with different emotional displays (e.g. Pfabigan et al., 2014). The central assumption behind this procedure is that emotional information shifts attention in space, thereby influencing subsequent performance in detecting the target probe. In this regard, Bar-Haim et al. (2007) have pointed out in a meta-analysis including dot probe and Stroop paradigms, that threat-related stimuli lead to stronger attentional biases in clinical samples compared to non-anxious healthy controls. However, the reliability of the dot probe task has been repeatedly disputed claiming either the complete absence of internal and test-retest reliability (e.g. Schmukle, 2005) or that many situational factors including cue presentation time or types of stimuli play a role in determining the magnitude of attentional biases (see van Rooijen et al., 2017 for a review of such influencing factors).

1.1. Neural correlates of the dot probe task

Despite extensive research on the dot probe task, few experiments have addressed the neural correlates underlying attentional biases. Electroencephalography-experiments have tracked the temporal dynamics of theses biases (Pourtois et al., 2004; Kappenman et al., 2014; Pfabigan et al., 2014; van Heck et al., 2017). For example, time-locking event-related potentials (ERPs) to the onset of the dot probe, Pourtois et al. (2004) found an increased P1-amplitude at bilateral occipital

* Corresponding author at: Department of Psychiatry & Psychotherapy, University of Tübingen, Calwerstrasse 14, 72076 Tübingen, Germany.
E-mail address: jonas.hornung@med.uni-tuebingen.de (J. Hornung).

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location when the probe followed a fearful rather than a neutral face, suggesting an early visual processing advantage when no reallocation of attention was needed (valid > invalid location). Furthermore, in an fMRI study, Pourtois et al. (2006) showed a stronger activation of the bilateral intraparietal sulcus during invalid compared to valid fear-cue trials. This adds to other neuroimaging studies (comparing invalid to valid threat/fear) implicating the inferior frontal gyrus in healthy adolescents (White et al., 2016) or the anterior cingulate cortex in youth with anxiety disorder (Price et al., 2014) as the neural basis of reallocating attentional resources. The diversity of such results is somewhat surprising but is often attributed to the heterogeneity of modulatory factors, e.g. the use of differently aged participant samples and emotional displays (van Rooijen et al., 2017).

1.2. Sex-specific effects relating to emotion processing and attentional bias

Also emotional processing seems to be susceptible to the influence of a number of situational factors. Especially within women, hormonal fluctuations have been shown to influence reactions to emotional stimuli: women during their follicular cycle phase (low levels of endogenous female sex hormones) show better general emotion recognition than women during their luteal cycle phase (Derntl et al., 2008, 2013) whereas the intake of oral contraceptives (OCs) may lead to impaired recognition for sad, angry and disgusted faces (Hamstra et al., 2014) and reduced affective responsiveness (Radke and Derntl, 2016). Mechanistically, such associations are far from understood. However, it is known that sex hormones pass the blood brain barrier to act on sex steroid receptors in the brain. For example, progesterone can be metabolized into neuroactive steroids such as allopregnanolone and pregnanolone which potentiate the inhibitory $GABA_A$-receptor comparable to the action of benzodiazepines (Melcangi et al., 2011). Thus, high levels of progesterone can have an anxiolytic effect which speculatively could also spill over and affect the processing of emotional displays.

Yet, despite such theoretical considerations, few previous studies have investigated sex differences in attentional biases using the emotional dot probe task. In one study, Pfabigan et al. (2014) report no behavioral sex differences, whereas in another study, Tran et al. (2013) reported an interaction between sex and the level of individual anxiety. Here, high levels of anxiety favored a stronger attentional bias for angry faces in women, while hindering attentional disengagement from happy faces in men. Still, systematic studies exploring the impact of hormonal fluctuations on attentional biases and their neural underpinnings are missing.

1.3. Specific effects of androstadienone

Next to the potential influence of participant sex or hormonal fluctuations, another modulator of interest especially in social contexts may be the presence of chemosignals. One of such potential human chemosignals is the steroid 4,16-androstadien-3-one (AND) which has been identified in human axillary hair (Nixon et al., 1988; Gower et al., 1994). Thus, being present in human body secretions, AND has been considered a candidate for human pheromones. In this regard, research has revolved around the effects of AND on mood (Grosser et al., 2000; Jacob and McClintock, 2000; Villemure and Bushnell, 2007) and attractiveness of the opposite sex (Saxton et al., 2008; Ferdenzi et al., 2016; Hare et al., 2017). Of note, results of these studies have been mixed, sparking criticism (Wyatt, 2015) and asking for a better understanding of the basic psychological properties of AND. To help with this, a study by Hummer and McClintock (2009) investigated the effects of AND on attentional processes. Results of this study suggest that AND may strengthen attentional biases in an emotional dot probe task including happy and angry faces. In this experiment the authors showed that during the AND session participants took longer in detecting the dot probe when displayed at the invalid location compared to the control session. Thus, attention seemed to be more strongly captured by emotional cues under AND. However, this result has remained singular allowing not to derive a common theoretical background on the action of AND. This is due to the variety of experimental paradigms that have followed since Hummer & McClintock's study. For example, the presence of AND enhanced avoidance of angry faces in an approach and avoidance task (Frey et al., 2012) and, in male participants, it reduced interference-related costs in an emotional Stroop task with angry faces (Hornung et al., 2017). However, the neural underpinnings of these odor-dependent attention effects are almost unknown apart from a recent study by Hornung et al. (2018a) pointing to higher interference related brain activation in areas involved in the detection and resolution of emotional conflicts. In another experiment, Parma et al. (2012) provided a link that also hormonal fluctuations as occurring throughout the female menstrual cycle might have an impact on AND-action: here the authors reported that under AND exposure women during their luteal phase spent more time looking at other women's faces compared to women in their follicular phase. This result provided a potential link to the action of the human chemosignal AND when fertility is high in women.

Experimental questions. With the present set of experiments, we aimed at answering the following two main questions:

Sex and hormonal effects: Do hormonal differences as observed between men and women and within women (e.g. depending on the use of oral contraceptives) have an impact on attentional biases? We do not formulate clear behavioral expectations regarding this question as previous studies are scarce and results provided no consistent pattern. This is true both for sex differences in general and for differences in hormonal states (OC-use, menstrual cycle).

Odor effects: Does the putative human chemosignal AND affect attentional biases? As previous studies had indicated that AND might shift attention to emotional stimuli, we expected AND to increase attentional biases across all emotions in our dot probe paradigm. Importantly, we decided to refine this claim by incorporating participants with different hormonal states, by using various negative and positive emotions and to differentiate between orientation towards and disengagement from emotional cues which no previous experiment has provided. Furthermore, we were interested in the potential neural mode of such AND-action.

2. Methods

2.1. Participants

In two studies, a total of 159 female and male students at the University of Tübingen, Germany were recruited and measured twice (once under AND, once under placebo-exposure on two consecutive days). An initial behavioral study (n = 79, results are partially reported in Hornung et al., 2017) served to establish baseline effects and expectations for a subsequent fMRI study (n = 80). Female participants were either taking combined oral contraceptives (OC-users behavioral study: n = 29, fMRI study: n = 29; combination of ethinyl-estradiol and progestin) or were during their luteal cycle phase without taking any oral contraceptives (luteal women behavioral study: n = 21, fMRI study: n = 21). To maximize hormonal differences between our female groups, experimental dates were scheduled for luteal women between day 18–24 of the standardized 28 day cycle when endogenous female sex hormones are high in contrast to the low endogenous hormone profile that is normally observed during OC-use (Sundström-Poromaa and Gingnell, 2014). Exclusion criteria were any current or past psychiatric or neurological disorders as confirmed via structured clinical interview, SCID (DSM-IV; Wittchen et al., 1997) and depression inventory, BDI-II (Hautzinger et al., 2006). Furthermore, the intake of any other type of hormones or medication were exclusion criteria for both men and women. Both in the behavioral and fMRI study three subjects were excluded due to high depression scores resulting in 77 (fMRI