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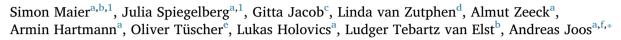
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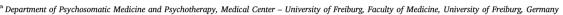
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Neural correlates of intimate picture stimuli in females





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ABSTRACT

Jacob et al. (2011) previously reported on intimate picture stimuli for emotion research in females in Psychiatry Research. Difficulties to engage in intimate relations constitute problems of many mental disorders, and intimacy must be differentiated from pure sex drive. Functional neuroimaging is an important tool to understand the pathophysiology of psychiatric disorders. We now studied cerebral activation in response to intimate stimuli in 35 healthy women. Comparison stimuli were taken from the International Affective Picture System. Neuroimaging revealed increased activation in bilateral occipitotemporal, parietal and anterior cingulate cortices extending to the orbitofrontal area. These data reflect cognitive, emotional and motivational compounds congruent with previous neuroimaging data of attachment and long term romantic relationships. Lateral prefrontal, posterior insular regions and the fusiform face area were more active during control images. Our data present a solid basis for use in psychiatric samples.

1. Introduction

Previously we reported on intimate stimuli for emotion research in healthy females in Psychiatry Research (Jacob et al., 2011). Psychological problems regarding intimate relationships represent central features of many psychiatric diseases, like borderline personality disorder, somatoform and eating disorders (Brockmeyer et al., 2013; Jacob et al., 2011; Oldershaw et al., 2015; Waller et al., 2004). Studying clinical populations provide clues on the pathophysiology, e.g. whether more top-down cortical or more bottom-up subcortical neural networks are disturbed in mental disorders. Furthermore studying recovered patients will give hints, if neural aberrations also normalize, or if there is an indication of neural endophenotypes (Gottesman and Gould, 2003; Kanakam et al., 2017).

The stimuli tested showed couples in romantic and tender interactions. In the previous study the pictures were evaluated by scoring the emotional experience with respect to the dimensions arousal, valence and dominance (Jacob et al., 2011); however, other physiological responses like skin conductance or neural correlates were not obtained. Since explicit sexual behavior was not the content of the pictures, these

stimuli represent examples of intimate relationships.

A small set of pictures showing single males used in the previous study were not considered in the current study, as we focused on the portrayal of intimate situations. Additionally, the previous study also included negative and positive non-erotic emotional stimuli. These items were not the focus of the current study; and it was not our intention to include a high variety of various emotional themes in this neuroimaging study. In effect we focused on the difference between intimate and control visual stimuli. In this respect we also used a robust block neuroimaging design (see below).

Intimacy is a complex emotion and there is no straightforward or unique definition. It is particularly related to attachment and sexual drives (Dekel and Farber, 2012; Fisher et al., 2006a, 2006b; Yoo et al., 2014). Intimacy involves cognitive, interpersonal, affective and physical aspects of close relationships Fisher et al. (2006a), (2006b); Yoo et al. (2014). A key feature of intimacy is its interpersonal and reciprocal nature (Vaillant, 2002). In this respect – and with regard to its differentiation from love – one can *love an object*, while one can only *be intimate with another person*. Intimacy is closely related to attachment, though intimacy involves the reciprocal exchange of feelings as well as

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thoughts; while attachment can be more "one-sided" and expressed more on bodily and emotional levels, like the attachment of a parent to a baby. Therefore, intimacy generally involves views and considerations of adults and adolescents, i.e. linguistic, emotional and mental organizations form the basis of intimacy (Buchheim et al., 2006b). In this respect it is worth noting that intimacy is an important maturation step in young adulthood according to Erikson's model of human development (Vaillant, 2002). In contrast attachment, a biologically based behavioral system, is already formed in infancy and certainly lays the foundation for intimacy in later human development. Early attachment experiences are internalized and form mental representations of interpersonal (conscious and unconscious) relationships. In effect, adults might not need the continuous physical closeness of another nurturing person as opposed to infants (Buchheim et al., 2006b). It is sufficient to say that emotional neglect and abuse in infancy can lead to negative representations, forming the basis of mental disease - and often with the vicious circle of reinstalling abusing interpersonal relationships in adolescence and adulthood. Buchheim and colleagues were among the first to try to disentangle neural correlates of attachment by using personal narratives induced by simple standardized drawings (Buchheim et al., 2006a). They found increased frontotemporal, cingular and occipital activations as well as subcortically in the basal ganglia.

Other aspects of intimacy, i.e. romantic love and in particular sex drive have been studied with neuroimaging much more extensively in humans (for review, see e.g. Fisher et al., 2006a, 2006b and Stoléru et al., 2012). Subcortical reward related regions like the right ventral tegmental area and ventral striatum were activated as well as the hypothalamus, amygdala, together with anterior cingulate (ACC), medial prefrontal (PFC), orbitofrontal (OFC), ventrolateral occipitotemporal (vIOTC), insular and parietal cortices (Fisher et al., 2006a, 2006b; Karama et al., 2002; Stoléru et al., 2012). Georgiadis and Kringelbach reviewed data on cerebral responses with respect to various phases of the sexual responses pointing to similar subcortical and cortical cerebral regions in the so called "wanting phase", i.e. during motivation to mate triggered by various biological and psychological cues (Georgiadis and Kringelbach, 2012). Importantly, most studies so far were carried out in men (Georgiadis and Kringelbach, 2012; Stoléru et al., 2012). In the few studies considering males and females no fundamental differences were reported, though there seem to be some differences within female groups according to the menstrual cycle (Stoléru et al., 2012); and there is a difference of representation within the primary somatosensory cortex when explicitly showing genitalia, as might be expected (Cazala et al., 2015). Stoleru interestingly points to associations with Freud's theories in the context of neuropsychoanalysis (Stoléru, 2014) which is of interest as psychodynamic ideas still form the basis of the psychological treatment of many mental disorders. In the context of neuroimaging he differentiates cognitive, emotional, motivational and autonomic components of sexual drives.

One study of a small set of males and females is of note, which assessed neural correlates of long-term intense romantic love (Acevedo et al., 2012). In general though, only a minority of couples experience intense erotic attraction in the long term, while in most other couples other factors become more dominant over time, such as a companionate marriage (with considering careers and a balance with relationship issues), the rescue marriage ("healing" of early emotional traumata as central themes) or the traditional marriage (the woman takes charge of home while the man is the primary wage earner) (Wallerstein and Blkeslee, 1995). Acevedo et al. (2012) report subcortical (in particular the dopamine-rich ventral tegmental area), insular and cingular activations - quite similar to studies of early-stage romantic love; furthermore they report activations of "attachment related regions" like basal ganglia, insular and cingular regions when contrasting cerebral responses to facial images of their partner versus control images (like a close, long-term friend).

With respect to our current data on intimacy it is essential to note

that the study of sexual responses and sexual drive usually used explicit sexual scenes as well as genitals, which was not the case in our experiment.

The study of neural signatures of intimate stimuli and their alteration in disorders is an important tool in emotion research. In this study we investigated the neural response of these stimuli by functional magnetic resonance imaging (fMRI). As comparison stimuli we used pictures of the International Affective Picture System (IAPS) (Lang et al., 2008). To our knowledge this is the first fMRI report on a set of intimate picture stimuli in healthy females. Therefore, cerebral regions of in- or decreased activations are hypothetical. With respect to the aforementioned studies on sex drive and attachment, we expected activation differences of the vlOTC, frontocingular, parietal and insular cortices as well as basal ganglia. Data of our current study are thought to represent a solid basis for comparisons with female patients with emotional disturbances assumed to be related to problems of intimate relationships.

2. Methods

2.1. Participants

Thirty-five heterosexual females (mean age 23.1 years) without any current psychiatric or neurological disorder were recruited through advertisement in various institutions. All study participants were screened with the SCID I and II-Interview (Fydrich et al., 1997; Wittchen et al., 2004) to exclude participants with psychiatric disorders.

Furthermore we used various self-questionnaires with respect to common emotional problems in clinical population including indices of emotion regulation, trauma and intimacy. Therefore, these data can be used in future studies for comparison purposes. These were as follows: *anxiety*: State-Trait Anxiety Inventory (Laux et al., 1981), *depression*: Beck Depression Inventory-II (Hautzinger et al., 2006), *emotion regulation*: Difficulties in Emotion Regulation (Ehring et al., 2009; Gratz and Roemer, 2004), *trauma*: Childhood Trauma Questionnaire (Wingenfeld et al., 2010) and *relationships*: Experiences in Close Relationships – Revised (Ehrenthal et al., 2009).

We further evaluated if participants were in stable and positive relationship versus no partnership or a partnership with strong tensions: Twenty-six participants were in a stable, close partnership.

In order to be in a comparable hormonal state, participants had to be in the luteal phase of the ovarian cycle, or accordingly in the second half of the cycle when taking hormonal contraceptives. Twenty-one participants were on hormonal contraceptives.

After oral and written information, written informed consent was obtained by all participants. The study was approved by the Ethics Committee of the Albert-Ludwigs-Universität Freiburg (EK 520/13).

2.2. Stimuli

Sixty pictures showing couples in intimate interaction were chosen from the original set. These were compared to 60 pictures from the IAPS. The images were selected by our group with respect to the visual structures to resemble those of the intimacy stimuli, showing people, though not closely related, and partly including faces as main subject (see Fig. 1 for examples). As noted in our previous paper the intimate pictures can be used for noncommercial educational and research purposes (Jacob et al., 2011). Valence ratings of IAPS pictures had to be above 4 (out of 9, mean = 5.5) of the original female ratings (Lang et al., 2008) and arousal ratings less than 5 (mean = 3.6). The selected 60 intimacy pictures had valence ratings between 5.6 and 7.7 (mean = 6.9) while arousal was between 3.6 and 5.8 (mean = 4.5) (Data taken from the original study of Jacob et al., 2011). Twenty intimacy pictures were rated post scanning during the current study using "manikin ratings".

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