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Emotional feeling and the orbitomedial prefrontal cortex: Theoretical and empirical considerations

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Emotional feeling can be defined as the affective constituent of emotions representing a subjective experience such as, for example, feeling love or hate. Several recent neuroimaging studies have focused on this affective component of emotions thereby aiming to characterise the underlying neural correlates. These studies indicate that the orbitomedial prefrontal cortex is crucially involved in the processing of emotional feeling. It is the aim of this paper to analyse the extent to which the present state of the art in neuroscience enables emotional feeling to be related to specific brain regions. In the first step, methodological and theoretical problems in the investigation of emotional feeling will be discussed leading to the characterisation of a "twofold gap." This gap represents (a) the theoretical difficulties encountered in transforming vivid subjective experience into a theoretical psychological concept, and (b) the problems of implementing such a concept by performing empirical studies. Based on these considerations we suggest approaches for future empirical studies. In the second step, a group of functional neuroimaging studies focusing on the affective constituent of emotions will be discussed in detail with regard to the theoretical problems outlined in the first step.

Keywords: Emotional Feeling; Functional Imaging; Orbitomedial Prefrontal Cortex

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1. Introduction

'Emotion' can be defined as an umbrella concept that includes various different components such as affective, cognitive, behavioural, expressive, and physiological changes (Lambie & Marcel, 2002; Panksepp, 2005). For instance, when I am happy, the cognitive component may be related to the reason why I am happy (e.g., I won the lottery). This happiness may be expressed by behavioural and mimic changes (e.g., smiling and jumping for joy), my heart rate and my blood pressure may increase representing the physiological changes. Moreover, there may be an overwhelming feeling of happiness.

This paper focuses on the feeling component of emotions.[1] Emotional feeling has been characterised predominately by qualitativeness, referring to the experiential quality of the subjective experience, i.e. what it is like to experience an emotion. (Chalmers, 1996; Jackson, 1986, 1990; Nagel, 1974, 1979; Northoff, 2003).

The aim of this paper is to analyse the extent to which results from functional neuroimaging studies on emotions permit emotional feeling to be related to specific brain regions. Such an enterprise has to face two fundamental problems: Firstly, the transformation of the subjectively experienced emotional feeling into a theoretical and thus objective conception, and secondly, the operationalisation of such a conception in empirical studies. These two problems may be considered as two parts of a twofold gap that extends between subjectively experienced emotional feeling and empirical results on emotional feeling. Usually, the first part of the twofold gap is considered to be a theoretical problem, which is dealt with in the philosophy of emotion but is rather neglected in empirical psychology and neuroscience. Unlike the first part, the second part of the gap is regarded as a purely empirical problem and is therefore often neglected in theoretical conceptions of emotion.

In contrast, we believe that a comprehensive consideration of both parts of the twofold gap may contribute to a broader understanding of emotional feeling. Additionally, we assume that the two parts of the gap are related to each other. That means, for example, that unsolved problems in the transformation of subjective emotional feeling into a theoretical conception (first part of the gap) may influence the possibilities of empirical realisation (second part of the gap).

The twofold gap can also be considered to be induced by the two subsequent points of view of theoretical and empirical psychology. The perspective of theoretical psychology (including a more objective point of view) leads to an objectified image of the emotional experience that may differ with regard to the subjective character of the emotional experience itself. The empirical measurement relying on the theoretical concept (not directly on the emotional feeling) again presupposes a different point of view, which may result in further changes of the original emotional feeling (see also figure 1).

It is intended to give equal consideration to the methodological problems of both parts of the twofold gap for emotional feeling. In the following, the first part of the twofold gap will be considered by discussing how subjectively experienced emotional feeling may be conceptualised in an empirical framework. Then the second part of

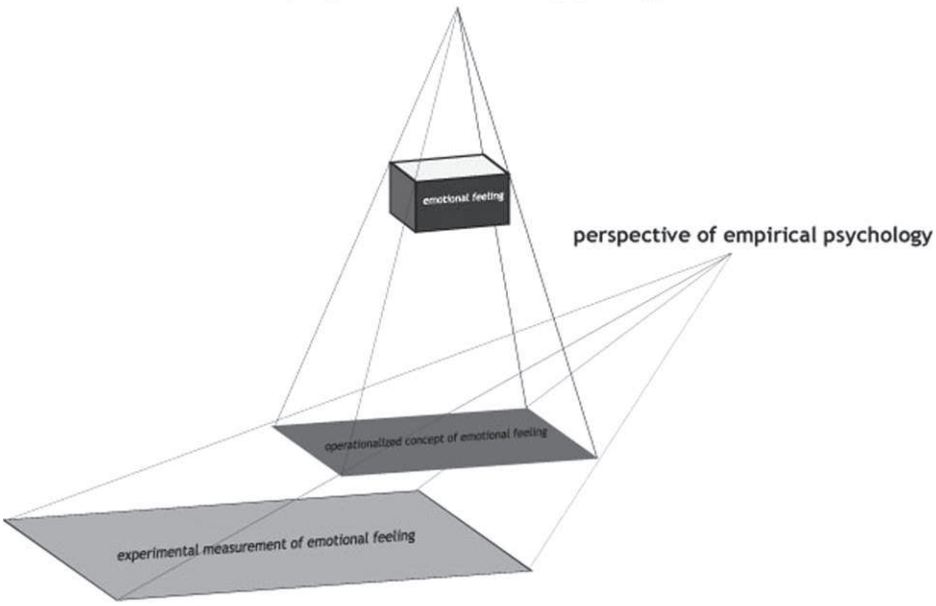

Figure 1 The twofold gap as induced by the two subsequent points of view of theoretical and empirical psychology. The box (emotional feeling) represents the subjective experience of emotional feeling. The perspective of theoretical psychology (including a more objective point of view) leads to an objectified image of the emotional experience that may differ with regard to subjective character of the emotional experience (theoretical concept of emotional feeling). The empirical measurement relying on the theoretical concept (not directly on the emotional feeling) presupposes again a new point of view, which may result in further changes of the original emotional feeling (experimental measurement of theoretical concept of emotional feeling).

the twofold gap will be considered by reviewing recent neuroimaging studies on emotional feeling. We focus on the involvement of the orbitomedial prefrontal cortex. It should be noted that we do not rule out the fact that other regions may be involved in neural processing of emotional feeling. In this paper we specifically focus on these regions to analyse their significance for emotional feeling without evaluating a possible influence of further regions.

2. Subjectively Experienced Emotional Feeling and Theoretical Concepts of Emotional Feeling

Subjective experience in general and subjectively experienced emotional feeling in particular has been characterised phenomenologically by qualitativeness (Chalmers, 1996; Jackson, 1986, 1990; Nagel, 1974, 1979; Northoff, 2003; Searle, 2000).[2]

Qualitativeness refers to the special way in which emotions are experienced, i.e., the qualitative feel of emotions. The experience of being frightened by a dangerous situation is very different from falling in love, and both of those have a different qualitative character from sadness due to the death of a close friend. These examples illustrate different qualitative states of emotional feeling.

These emotional feelings have to be transformed into an empirical concept capable of possible empirical testing. There is a gap that such a conceptualisation has to overcome. The reason for this gap originates in the contrasting conception of the properties of emotional feeling (i.e., qualitativeness) and objective conceptualisation as presupposed by empirical theories. The more general problem of relating any kind of subjective experience to empirical concepts is a long-standing subject in the philosophy of mind. Historically, it can be traced back to Descartes' classical distinction of res extensa and res cogitans. 'Res extensa' refers to the physical world and 'res cogitans' denotes the subjective mental world. This distinction leads to the ontological gap between res cogitans and res extensa, raising the question of their possible interaction. One of the most influential contemporary formulations was put forward by Chalmers (1996) who called it the "hard problem." It refers to phenomenal experience, which may be considered a part of the Cartesian res cogitans. It comprises the problem why we have qualitative phenomenal experience and how they may be related to our brain. In contrast, the "easy problems" deal, for example, with explaining the ability to process information or to focus attention. These problems are considered easy because their solution only requires specifying a mechanism that can perform the function. However, according to Chalmers, the "hard problem" persists even if all the relevant functions are explained.

It is important to distinguish between the pure emotional feeling (i.e., the pure experience), on the one hand, and being aware of this feeling (i.e., reflection on this experience) on the other hand. In this paper we aim to focus predominately on pure emotional feeling: how this pure emotional feeling is related to consciousness is a matter of debate. For example, Rolls (1999, 2000) assumes that higher-order linguistic thought processing is essential for the establishment of consciousness and consequently for the emergence of feelings. LeDoux (1996, 2002) considers working memory to be crucial for consciousness, which in turn allows feelings to occur. Analogously, Damasio (1999) characterises consciousness by a meta- or second-order representation of contents, such as for example emotion, thereby giving rise to feeling. He considers the distinct types of emotions as contents that can be represented on a higher level, i.e., meta-represented thereby inducing feeling. Though these approaches differ in various aspects, they all have in common the fact that they account for emotional feeling by higher-order processing. Emotions as lower-order (and unconscious) processes are supposed to be represented on a higher level on a second or even third order that makes us conscious of them and gives us the ability to report and thus to know them as such.In contrast, Panksepp argues that the possibility of emotional feelings is a fundamental property of the evolutionarily ancient emotional action apparatus. These feelings do not require higher order thoughts. It is the pure emotional feeling that constitutes the basis for any reflective

higher order emotional processing (Panksepp, 1998). Proponents of this approach distinguish between "affective consciousness" and "cognitive consciousness" (Panksepp, 2003a, 2003b) or "first-order phenomenology" and "second-order awareness" (Lambie & Marcel, 2002). For example, it is argued that even though people may repress awareness of their emotional feelings at the level of second-order awareness, they may retain affective feelings at the level of first-order phenomenology. The present paper does not aim to make a decision on this matter. However, it should be noted that both approaches may imply different interpretations of emotional feelings and related research.

The fundamental challenge for the investigation of emotional feeling is based on the problems discussed above. The systematic examination of emotional feeling must preserve its qualitativeness on the one hand, but objectify and quantify it on the other hand. Although this seems to come close to a contradiction, one way out of the dilemma is to objectify and quantify the main phenomenal features of emotional experience. Objectification and quantification of phenomenal features can provide valid and reliable data resulting in a "science of experience" (Jack & Roepstorff, 2002; Lutz, Lachaux, Martinerie, & Varela, 2002; Varela, 1996; Varela & Shear, 1999). For example, one approach is to let the subjects evaluate their own subjective experience by using visual analogue scales, idiographic instruments, or scripts with semi-structured interviews (Jack & Roepstorff, 2002). These data about subjective experience can then be related to data about neuronal measures of the brain. The recently proposed concepts of "neurophenomenology" (Varela, 1996; Varela et al., 1999) and first-person neuroscience (Northoff & Heinzel, 2006; Panksepp, 1998, 2005) provide methods for systematically linking subjective and neuronal data: "it would be futile to stay with first-person descriptions in isolation. We need to harmonize and constrain them by building the appropriate links with third-person studies. ... To make this possible we seek methodologies that can provide an open link to objective, empirically based description" (Varela et al., 1999).

However, the crucial point about qualitativeness of feeling is that there is no trivial way to directly access it through associated cognitive capacities allowing reflection and introspection. Instead, we have only indirect access through introspection and verbal reports. Introspection and verbal reports involve cognitive abilities like attention, working memory, linguistic functions, which are distinct from emotional feeling. These cognitive and reflective processes may influence and modulate the qualitative aspect of feeling (Lambie & Marcel, 2002). This could make complete isolation of qualitativeness from other components of emotions impossible. It is therefore important to note that what we obtain in introspection and verbal reports may reflect cognitively modulated qualitativeness rather than qualitativeness per se.

The presented phenomenal account of qualitativeness of emotional feeling is obviously not isomorphic with any concept underlying current brain imaging studies.

The approach which may be considered most common in empirical research is the conceptualisation in terms of valence referring to various feelings of goodness and badness as well as positive and negative affects. This concept has its origin in the

research of Wundt (see Feldmann Barrett & Russell, 1999, for an overview) and has recently been widely applied in functional imaging studies on the affective component of emotions (see below).

In this conception, valence is regarded as a dimension of emotion that refers to hedonic tone (i.e., pleasure versus displeasure). However, it remains unclear to what extent emotional valence shares exactly the same properties as the qualitativeness of emotional feeling with respect to the special way emotions are experienced. It has to be noted that emotional valence may contain additional properties with regard to the qualitativeness of emotional feeling and may also neglect certain components of qualitativeness of emotional feeling. However, due to the above-discussed problems it is unclear how controls can be established for such a difference.

It has been shown that the operationalisation of emotional feelings is linked to the problem of avoiding the influence of accompanying cognitive processing. To succeed completely in this endeavour may be impossible for theoretical reasons. Nonetheless, it may be assumed that such a possible difference between the qualitativeness of emotional feeling and the cognitively modulated variant is within tolerable limits. For example, Chalmers (1996) suggests that our cognitively accessible information and verbal reports on emotional feeling correspond to the emotional feeling itself, which he termed "structural coherence." According to this principle, the emotional feeling is accompanied by corresponding cognitive processing, which permits the investigation of emotional feeling.

Chalmers (1996) holds that the emotional feeling is mirrored in the corresponding cognitive processing, since otherwise the mutual influence may be not explained. For example, he states that differences in the intensity of the emotional feeling are obviously reflected in differences in our cognitive information on the emotional feeling. Thus such a co-occurrence of emotional feeling and the related cognitive processing may very well allow for empirical investigation. However, it has to be considered that there is still the problem of distinguishing between emotional feeling and accompanying cognitive processing, since, although the later may help to indicate the presence of the former, they cannot be considered as identical.

Whether these problems can be completely overcome by future conceptual and empirical approaches remains an open question. However, it is important to recognise these problems since they represent basic methodological limitations in the investigation of emotional feeling. They therefore limit any conclusions on emotional feelings based on empirical studies. Additionally, one important quality factor for empirical studies on emotional feeling should be how they address the above-mentioned problems.

An innovative approach for resolving this dilemma has been put forward by Panksepp (2001, 2004, 2005). Based on the results of animal experiments, Panksepp suggests adopting the perspective of "Spinozan dual aspect monism." From this point of view, pure emotional feelings and the neurodynamics of instinctual emotional action systems are considered to be the same entity. If Panksepp's assumptions are correct, the twofold gap (as illustrated in figure 1) can be considered

as bridged. There would be no basic difference between the subjective experience of emotional feeling and neural processing. However, Panksepp's theory remains to be proven. His data from animal experiments are exciting because they offer the possibility of establishing causal relationships. In contrast, in functional imaging on human subjects this is a very difficult task. Most of the results consist in a mere correlation of neural processing on the one hand and emotional feeling on the other hand. Animal research allows scientists to interfere directly with the neural dynamics and the associated emotional feelings. However, causality is not the same as identity. Even if we assume a causal link between neural processing and emotional experience, from a logical point of view a Cartesian dualism as opposed to a Spinozan dual aspect monism is still conceivable. For example, the causal link may be interpreted as mind-body interaction. Thus, even if a causal relationship between subjective emotional feeling and neural processing has been established, it still has to be shown that they are the same entity. Furthermore, the exact relationship of human and animal emotional feeling remains to be elucidated. Apart from these theoretical considerations, Panksepp's account provides the basis for promising new experimental approaches in human function imaging (see below).

3. Methodological Considerations in the Empirical Investigation of Emotional Feeling

The subjective aspects of emotions are usually operationalized based on the dimensional concept of emotional experience. In addition to valence (see above) it contains the dimensions arousal and some "power" or "surgency" (see e.g., Watson, Wiese, Vaidya, & Tellegen, 1999). Since valence is typically considered as the most important aspect of distinct types of emotional feelings we will focus on valence in this paper. The other dimensions will rather be considered as control variables.

Some of the methodological problems concerning qualitativeness are equally relevant for the investigation of emotional valence. Similar to the investigation of qualitativeness, a major problem is to disentangle valence processing from other factors. Any attempt at investigating emotional valence inevitably involves accompanying factors. These concern, for example, the induction method as well as cognitive functions such as attention, working memory, and evaluation. Since it is difficult to establish controls for these accompanying factors, emotional factors of interest may potentially remain hidden. For example, if visual stimuli are used to test for emotional valence processing this may be confounded by the semantic content of the pictures and by the emotional arousal they induce. Establishing controls for the semantic content may appear relatively easy, for instance, by adjusting for semantic contents across valences. This might be realised by using pictures with similar content for emotional and non-emotional conditions. For example, the different conditions may use similar numbers of pictures showing people, faces, animals, objects and scenes (Heinzel et al., 2005). However, a relationship between content and valence can never be completely excluded even by using large samples of stimuli.

This problem becomes even more significant in the case of arousal. In general, negative stimuli are often more arousing than positive, which are, in turn, more arousing than neutral stimuli. In the visual modality, this problem can only partially be solved by adjusting photographs for colours, brightness, complexity, and composition, as accomplished, for example, in the IAPS (Centre for the Study of Emotion and Attention, 1999). Therefore differing arousal values may invalidate the comparison of negative with positive stimuli and to an even greater extent a comparison of negative with neutral stimuli. A possible solution to this problem may be to perform subject-specific arousal ratings of the stimuli and to include them in the statistical data analysis as ''covariates of no interest.'' However, due to the strong correlation with valence ratings such an analysis may not only reduce the possible influence of arousal, but also of the valence itself. Thus, it appears difficult to completely exclude any possible influence of arousal on emotional valence processing.

4. Empirical Findings

Although our analysis focuses predominately on the orbitomedial prefrontal cortex (OMPFC) we would like give a short overview of other brain regions that have been identified as playing a central role in emotional processing such as the amygdala, the anterior cingulate cortex, the insula, the dorsomedial thalamus, and the periaqueductal grey. These regions, and also the OMPFC, are characterized by their reciprocal anatomical connectivity with each other, with neuromodulatory systems (e.g., serotonergic dorsal raphe, cholinergic nucleus basalis of Meynert, and dopaminergic ventral tegmentum), and with other brain areas involved in sensory, motor, and cognitive functions (Szily & Keri, 2008). Using functional imaging these separate brain regions have been related to different aspects of emotion, but they are also assumed to contribute to the functional integration of emotional processing as a whole.

One of the major brain regions implicated in emotional processing is the amygdala. A meta-analysis showed that it is specifically associated with the induction of fear in various circumstances. Particularly, the amygdala is involved in the recognition of fearful facial expressions (consciously and unconsciously experienced), fear conditioning, evocation of fearful emotional responses from direct stimulation and the detection of environmental threat (Phan, Wager, Taylor, & Liberzon, 2002). Additionally, the amygdala has been associated with emotional intensity mainly based on studies implying gustatory or olfactory stimuli (Anderson et al., 2003; Small et al., 2003). Whether this also holds true for other emotional stimuli remains a matter of controversy (Grimm et al., 2006).

The anterior cingulate cortex is often described as part of the limbic system due to its connections to subcortical structures such as the amygdala. The anterior cingulate cortex is assumed to be functionally segregated. The more dorsal division is involved in cognitive tasks while the more rostral-ventral affective division serves emotional

functions (Phan, Wager, Taylor, & Liberzon, 2004). Especially activation in the perigenual anterior cingulate cortex (PACC) has been observed in paradigms that require the encoding and recall or recognition of emotions (Grimm et al., 2006). This is in accordance with the hypothesis that neural activity in the PACC accounts for the recognition of emotional salience (Mayberg et al., 1999; Phillips, Drevets, Rauch, & Lane, 2003). Moreover, one specific emotion, sadness, has been related to the subcallosal cingulate cortex (SCC). A meta-analysis demonstrated that especially sadness induction studies reported activation in this region. Additionally, alterations in SCC activity have been found in studies on clinical depression, a mood disorder characterised by sustained sadness (Phan et al., 2002).

The insula, especially the anterior part, has been related to olfactory and gustatory sensations induced by disgusting olfactory or gustatory stimulation. Additionally, it has been implicated in transforming unpleasant sensory input into visceromotor reactions and the accompanying feeling of disgust (Wicker et al., 2003). Other functional imaging studies showed that, in addition to disgust, the insula was activated in other types of emotions supporting a more general function in aversive or threat-related processing, including also fear (Phan et al., 2004). Furthermore, the insula plays an important role in Damasio's "somatic marker" hypothesis. According to this hypothesis, optimal decision making is not simply the result of rationality (i.e., cognitively calculated categorisation of gains and losses), but is also based on good or bad affective reactions and emotionally guided evaluation. Within this process, the insula might integrate emotionally relevant information on somatic internal feelings with external cues (Damasio, 1994).

The dorsomedial thalamus and the periaqueductal grey have been related to the human sadness system that also includes the anterior cingulate and insula (Panksepp, 2003a). Interestingly, the activation of the dorsomedial thalamus, the periaqueductal grey and the anterior cingulate show strong similarities between animals—feeling induced by separation distress (Panksepp, 1998)—and humans—feeling of sadness (Damasio et al., 2000). Panksepp emphasises the significance of subcortical regions, involved in emotional processing in animals, for human emotional processing. He assumes that the basic emotions are homologous in animals and humans implying that the core of human emotional feelings is contained within the evolved emotional action apparatus of mammalian brains. Therefore, according to Panksepp, a detailed neuroscientific understanding of human emotions may depend critically on understanding comparable animal emotions (Panksepp, 2005).

The OMPFC seems to play a central role in general emotional processing (Davidson & Irwin, 1999; Lane, Reiman, Ahern, Schwartz, & Davidson, 1997; Phan et al., 2002). It was found to be involved in a variety of emotional paradigms concerning all kinds of emotions such as sadness, happiness, disgust, and fear (Canli, Desmond, Zhao, Glover, & Gabrieli, 1998; Elliott, Rubinsztein, Sahakian, & Dolan, 2000; Geday, Gjedde, Boldsen, & Kupers, 2003; Gusnard, Akbudak, Shulman, & Raichle, 2001; Paradiso et al., 1999; Wager, Phan, Liberzon, & Taylor, 2003). Additionally, various methods of induction of emotional experience (verbal and non-verbal; current external events and recall of past events) led to the involvement of the MPFC

(Frey, Kostopoulos, & Petrides, 2000; Geday et al., 2003; Hariri, Mattay, Tessitore, Fera, & Weinberger, 2003; Hariri, Tessitore, Mattay, Fera, & Weinberger, 2002; Lane et al., 1997; Reiman et al., 1997).

Moreover, based on observations from damage to the OMPFC, Damasio (1994) suggested a role in decision making within the context of his somatic marker hypothesis (see above). He holds that the OMPFC is crucially involved in the generation of somatic markers. Therefore patients with damage to the OMPFC perform their decision-making purely on the basis of logical analysis without any access to prior emotional experience.

It may therefore be suggested that the OMPFC might be implicated in processes that are common to various emotional tasks, such as the experiential aspect of emotional processing. The studies indicate a general function of the OMPFC in emotional processing and its engagement in both negative and positive emotional processing.[3] However, due to the above-mentioned problems this may only be considered as indirect support for a central role in emotional processing independent of the valence of the emotional stimuli presented. In order to isolate emotional valence processing from accidental accompanying processes, tasks are needed which exclusively vary the valence of the presented stimuli leaving all the confounding factors of the task as unaltered as possible.

One approach is to search for the correlation of signal intensity in specific brain regions with behavioural measures (e.g., the more positive a stimulus is judged to be the stronger is the signal intensity). This allows a differentiation to be made between regions that are involved in valence processing irrespective of the specific valence (i.e., the whole range from negative to positive stimuli) and those that only involved in the processing of specific valences (i.e., fear). In the following, we will only discuss studies that apply this approach for investigating emotional valence processing. The studies were identified by searching peer-reviewed journals indexed in MEDLINE and PsychInfo published between January 1998 and December 2006. Additionally, only studies on healthy adults performing whole brain analysis were included.

In the visual domain, Lane et al. (1998) investigated regional cerebral blood flow (rCBF) changes during film- and recall-induced emotion; these were related to scores on the Levels of Emotional Awareness Scale (LEAS), a measure of individual differences in the experience of emotion. Covariate analysis revealed a positive correlation between the neural activation in the anterior cingulate and the scores in the LEAS. It should, however, be noted that LEAS scores are judged by the observer rather than by the subjects themselves. LEAS scores may thus reflect objective data rather than subjective data. The results should therefore be considered carefully.

Heinzel et al. (2005) performed a parametric study on emotional stimulus processing (IAPS) by using individual valence ratings as regressor. They found that the OMPFC and other regions such as the DMPFC, medial parietal cortex, and insula show valence dependence during emotional stimulus processing. However, a possible problem involved in this and similar studies is the influence of cognitive processing. Although the subjects have been instructed not to perform any cognitive judgment during the stimulus presentation it cannot be excluded that the subjects performed

implicit judgments. Therefore the period of emotional stimulus processing may have involved various kinds of implicit cognitive processing. This is an important point, since there is empirical evidence demonstrating the influence of cognitive processing on emotional valence processing. Keightley et al. (2003) varied the judgment task related to emotional photographs and faces. Their results indicate that the ventral and dorsal prefrontal cortices both appear to be sensitive to changing task demands and stimulus features during emotional processing. Additionally, Simpson et al. (2000) reported that areas implicated in emotional processing paradigms, such as, for instance, the OMPFC, demonstrate decreased activity during more attentionally demanding cognitive tasks, consistent with these results. If it is true that explicit cognitive processing notably influences the processing of emotional valence, a similar influence of implicit cognitive processing cannot be excluded and should even be considered likely.

Grimm et al. (2006) aimed to avoid these problems by controlling for associated cognitive processing such as judgment and preceding attention. In a similar manner to the study by Heinzel et al. (2005), they performed emotional stimulus processing (IAPS) by using individual valence ratings as regressor. Additionally, they included the judgment of emotional pictures and an expectancy period (indicating the kind of IAPS picture) as control conditions. In accordance with Heinzel et al. (2005), valence correlated significantly with the functional response in OMPFC. However, it did not correlate positively with the DMPFC.

Additionally, they excluded any significant correlation between emotional valence processing in the OMPFC and associated cognitive processing such as judgment or attention. Thus the neural activity in the OMPFC seems to specifically reflect emotional valence processing independent of explicit cognitive processing.

In contrast, Anders, Lotze, Erb, Grodd, and Birbaumer (2004), also using the IAPS, did not observe any correlation of neural activity in the OMPFC with emotional valence. They recorded startle reflex modulation and skin conductance responses in healthy volunteers during fMRI while they viewed a set of emotional pictures and took verbal ratings of the emotional valence and arousal elicited by each picture after scanning. The discrepancy of their results compared to those of the other studies appears difficult to account for since they used the same stimuli and applied a similar paradigm. It may be speculated that there is a relation to the application of the startle reflex recording, which may interact with the neural activity in OMPFC. However, due to the lack of empirical data this remains unclear.

Lewis, Critchley, Rotshtein, and Dolan (2006) applied words from the standardised list of affective norms for English words (ANEW) (Bradley & Lang, 1999) that provides valence and arousal attributes similar to the IAPS ratings. They reported significant activation for valence processing in the orbitofrontal cortex and the anterior cingulate. However, unlike Heinzel et al. (2005) and Grimm et al. (2006), they did not report a bipolar relationship representing activation changes from most negative to most positive. They found the positive and negative valences to be independent of each other. This difference may be due to the abstract representative nature of word stimuli. It may be speculated that there are different ways of valence

coding as represented by bipolar, independent and U-shaped models for negative and positive valences. It is conceivable that these different ways of valence processing may be related to different tasks or to different brain regions. Further studies are needed to directly compare the different ways of valence processing in different tasks and different brain regions. It has to be noted that in contrast to the other studies Lewis et al. (2006) did not include individual ratings of valence for the correlation with the fMRI data. They relied on the ratings from the ANEW database. Therefore it cannot be excluded that individual ratings implicitly made by the subjects differ from those given by the ANEW.

The studies reported so far relied on visual emotional stimulation. Other studies inducing emotional feeling in different sensory modalities using non-visual tasks revealed similar regions with predominant involvement of the OMPFC.

In a gustatory whole-food experiment, Kringelbach, O'Doherty, Rolls, and Andrews (2003) determined the subjective pleasantness ratings when a liquid food was eaten to satiety. These ratings mirroring the feeling of satiety correlated with the activation of a region in the left OMPFC cortex. By this means they were able to demonstrate a direct correlation between a subjective state of pleasure induced by a primary (unlearned) reinforcer and the activation of a brain area measured in an event-related fMRI design where individual activations are produced each time the stimulus is delivered.

In the study by Small et al. (2003), the subjects had to sample and rate the intensity and pleasantness/unpleasantness of five concentrations of sucrose and quinine sulfate using an 11 point scale. This design permitted controls to be incorporated for the influence of emotional intensity by equating intensity in pleasant and unpleasant gustatory stimuli.

They demonstrated regional dissociation between subjective intensity and subjective affective valence during the presentation of unpleasant and pleasant taste in fMRI. Subcortical regions including the amygdala, pons and cerebellum correlated with intensity irrespective of valence. In contrast, valence-specific modulation was observed in the orbitofrontal cortex, the anterior cingulate and the anterior insula.

An analogous dissociation between intensity and valence was obtained in the case of olfaction. Making use of olfactory stimuli, Anderson et al. (2003) aimed to distinguish valence processing especially from arousal processing by applying a parametric design. They observed that the two odours citral and valeric acid are associated with signal changes in the posteromedial orbitofrontal cortex. These signal changes correlated positively with the evaluation of the pleasantness of the stimuli. They also observed amygdala activation to be associated with intensity of odours, whereas activity in OMPFC cortical regions was independent of intensity.

In addition to emotional feeling the OMPFC has also been implicated in self-related processing (e.g., David et al., 2006, Ochsner et al., 2004, Vogeley et al., 2004). The exact relationship of emotions and self remains a matter of debate. However, based on the empirical results, it may be speculated that they hint at a close relationship of emotions and the self. For example, it has been argued that, when

objects and events are viewed through the "eyes of the self," stimuli become emotionally coloured. They are no longer simply objective aspects of the world, but they become more intimately, related to one's sense of self (Northoff et al., 2006). On the other hand emotional stimuli may be considered as implicitly self-referential, since they are crucial to the individual in that they guide decision-making and efficient behavioural responses (Northoff & Bermpohl, 2004). Moreover, according to Damasio, they are mentally significant for a person, since one cannot formulate and use adequate theories of one's own mind if something like the somatic markers fails (Damasio, 1999).

5. Conclusions and Strategies for Further Empirical Testing

The reviewed studies provide evidence for the involvement of the OMPFC in emotional feeling as characterised by qualitativeness. Due to the empirical results it may be assumed that the OMPFC plays an important role as a neural correlate of the qualitativeness of emotional feeling.

However, these assumptions are far from being conclusive due to the twofold gap, which has to be considered for the interpretation of the empirical results. We discussed various methodological difficulties of the presented studies. These difficulties demonstrate that the empirical results cannot be identified with the psychological concept they intend to realise. One of the main problems in the studies targeting emotional valence processing is the possible influence of confounding factors such as arousal or cognitive processing. It is not clear whether such influence might not be avoided as a matter of principle. However, as long as these confounding factors exist, there is still a gap between the data and the concept they aim to investigate.

Furthermore, the other part of the twofold gap has to be considered. Emotional feeling as characterised by qualitativeness cannot be equated with emotional valence processing. Some of these problems are reflected in the second part of the gap as described above. Some are of a completely different nature, such as the basic problem of obtaining data on emotional feeling although any introspection or reflection on the emotional feeling may alter or even fundamentally change these data. At present it is not clear whether such problems may be overcome by new innovative empirical or conceptual approaches.

In the following section, we will briefly address some points related to the empirical studies discussed above that might be considered for future studies. Additionally, a different experimental approach based on the conception of Panksepp will be discussed in more detail.

Firstly, due to the possible interference between valence and other rather cognitive components of emotions discussed above, complete isolation of feeling from associated cognitive function may remain impossible in experimental paradigms. All neuronal measures during feeling must be interpreted with respect to the exact origin of neuronal activity because it could be associated with both components.

Secondly, one might try to rely more on indirect measures such as behavioural or somatic markers indicating feeling. One example is the study by Bechara and Damasio (2002), who investigated skin conductance response as a somatic marker of feeling. Most interestingly, it was possible to modulate such somatic markers during emotional-cognitive interference. The study by Anders et al. (2004) represents one interesting way of how to perform such a study. However, it has to be taken into account that the measurement of the somatic marker itself may interfere with the neural processing.

Thirdly, the way to model valence processing remains a matter of debate. Assumption of a bipolar model as recently reported by Grimm et al. (2006) is challenged by the results of Lewis et al. (2006). In contrast to Grimm et al. (2006) they observed orbitofrontal activities in association with independent and U-shaped, but not bipolar, models. Therefore, it would be highly interesting to compare the different models of valence processing for different kinds of emotional tasks. For example, a combination of emotional scenes and emotional words may be conceivable where the valence processing is modulated by shifting attention between the different modalities. The investigation of the possible ways of valence processing may contribute to a greater understanding of general principles of neural coding.

Fourthly, most of the above-mentioned studies used individualized ratings of subjective experience serving as parametric or modulating regressors fitted to the changes in neural activity as observed in functional imaging. This enables one to determine whether the signal changes (i.e., BOLD signal in the case of fMRI) in any brain region are correlated with the changes in subjective experience. However, those studies tend to objectify the received subjective data to adapt them to the data from functional imaging. An interesting alternative approach may be to analyse the imaging data with respect to the characteristics obtained in first-person reports. Varela (1996) suggested that the imaging data should be grouped and contrasted along the lines of these "phenomenological clusters": "thus, for example, a large-scale integration mechanism in the brain such as neural synchrony in the gamma band should be validated also on the basis of its ability to provide insight into first-person accounts of mental contents such as duration. The empirical questions must be guided by first-person evidence" (Varela, 1996, p. 343). From a theoretical point of view, this is an important suggestion though it remains unclear how it could be realised in the case of emotional feeling especially with regard to valence processing and qualitativeness. Maybe a completely new type of experimental paradigm will be needed.

The most promising approach possibly consists in the combination of data from animal experiments with functional imaging studies on human. There might still be some theoretical problems to overcome (see above), but this approach provides several advantages. Imaging studies yield predominantly correlational rather than causal data. Following Panksepp (1998, 2005), causal data on feelings can only be obtained by studying emotions in animals, which provides insight into the causal mechanisms underlying the generation of emotions. For example, the use of localized electrical stimulation of the brain allows identifying brain systems

for specific emotions. Such artificially evoked instinctual arousals provide not only distinct emotional displays but also clear indications that animals like or dislike such brain states. Therefore, it seems possible that the spontaneous emotional vocalizations of animals yield strong evidence of their emotional feelings.

However, we remain unable to obtain verbal subjective data in animals. Therefore, ideally, animal and human studies on emotions should be combined working with complementary methods on the same question. The observed experiences of the animals may be validated by human studies. Humans have comparable emotional feelings and can additionally provide self-reports with full felt ownership of such experiences.

An interesting example is the study by Gordon, Panksepp, Dennis, & McSweeny (2005) on laughter and crying. Instead of inducing emotional feeling by visual stimuli they trained the subjects to perform internal imagery of laughter and crying to evoke joy and sadness. Other ways of inducing emotional feelings are also conceivable. Especially, powerful affects, such as homeostatic feelings (e.g., hunger and thirst that can easily be evoked hormonally), or even more precisely certain sensory affects such as nausea, are of interest. They can be modelled in animals using a simple conditioned taste aversion (CTA) procedure, where there is already a massive database (Riley & Freeman, 2004) and a rich animal literature (for recent reviews, see: Mediavilla, Molina, & Puerto, 2005; Sandner, 2004; Sewards, 2004), including a fairly precise understanding of the underlying neuroanatomies in other mammals (de la Torre-Vacas & Agüero-Zapata, 2006; Jiménez & Tapia, 2004; Ramírez-Lugo, Núñez-Jaramillo, & Bermúdez-Rattoni, 2007; Reilly, 1999; Reilly & Bornovalova, 2005; Yamamoto, Shimura, Sako, Yasoshima, & Sakai, 1994). This affect has widespread implications for human nutritional habits (Gietzen & Magrum, 2001; Scalera, 2002).

Another feature of this model is that it has immediate implications for medical treatments and the development of new and even more precise therapeutics, as well as a highly replicable and simple learning paradigm where novel tastes that are not intrinsically nauseating can be imbued with this affect through simple classical conditioning principles (i.e., the pairing of a new taste with a nausea-producing manipulation; lithium chloride is commonly used, even though there are an enormous number of more precise manipulations such as stimulation of 5HT3 and substance p receptors (vide infra).

Besides the ability to control this powerful affect experimentally with a large number of distinct manipulations, the CTA paradigm provides a variety of controls that would be desirable to pursue both raw affective as well as learned-cognitive interactions (e.g., Hall & Symonds, 2006; Welzl, D'Adamo, & Lipp, 2001) that reflect true life experiences but are also capable of tight experimental control.[4]

These approaches apply in the first place to primal emotional feelings as those described above. It has to be acknowledged that the investigation of more complex human emotions such as love, hate or jealousy might be more difficult to address. However, the combination of animal and human research may yield fundamental principals of emotional processing which constitute a basis for those more complex

emotional feelings. Such innovative paradigms might help to further elucidate the role of the OMPFC in emotional feeling.

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Notes

[1] In contrast, the proponents of cognitive theories of emotions do not consider emotional feeling as a necessary property of emotions. They hold that emotions are mainly characterised by their relationship with cognitions (Bedford, 1957; Kenny, 1963; Solomon, 1980).

[2] The unique character of subjective experience (including the subjective experience of emotions) has been put forward by various arguments in the philosophical debate. Some of the most famous are the "knowledge argument" and the "what it is like to be argument." The "knowledge argument" deals with the brilliant neuroscientist Mary who perceives the world only from a black and white room. She knows everything there is to know about color perception (i.e., all physical and neural information) without having seen colors herself. "What will happen when Mary is released from her black and white room or is given a color television monitor? Will she *learn* anything or not? It seems just obvious that she will learn something about the world and our visual experience of it. But then it is inescapable that her previous knowledge was incomplete" (Jackson, 1990, p. 442). A similar kind of knowledge argument could be deployed for emotional experience. Let's imagine, for example, a patient suffering from severe depression for many years or indeed since birth. Let's imagine further that despite his depression he has become a brilliant neuroscientist who has learned everything there is to know about feeling happy. It seems obvious that, as soon as he experiences for the first time what it is like to be happy (e.g., after successful treatment of his depression), he will learn something new about the feeling of happiness. Likewise it seems impossible even for the best psychiatrists to know what a patient suffering from severe depression actually experiences. It is difficult to imagine how deeper insight into the neural basis of depression may solve this problem. Thus, it appears that only those who have themselves already suffered from depression may completely understand this state.

Nagel underlines the extraordinary character of subjective experience by asking what it is like to be a bat. He argues that no amount of information provided by neuroscientific research can answer this question since this knowledge is linked to the specific point of view of a bat. Likewise any human subjective experience requires a specific point of view. However, such a point of view is negated by objective neuroscience thereby leading to a distorted image of human experience. "Certainly it appears unlikely that we will get closer to the real nature of human experience by leaving behind the particularity of our human point of view and striving for a description in terms accessible to beings that could not imagine what it was like to be us. If the subjective character of experience is fully comprehensible only from one point of view, then any shift to greater objectivity—that is, less attachment to a specific viewpoint—does not take us nearer to the real nature of the phenomenon: it takes us farther away from it." (Nagel, 1974, p. 441).

In contrast to the hypotheses of Nagel and Jackson other authors oppose the notion of subjective experience (see Metzinger, 1995, for an overview). Probably the most radical

attack is put forward by Churchland's conception of eliminative materialism. He argues that subjective experience is part of a wrong theory called "folk psychology," which will be replaced by the future results of scientific neuroscience (Churchland, 1981, 1985).

[3] Several authors suggested a functional subdivision in the orbitofrontal cortex, with different regions specialized to process different components of positive or negative valence. Some observed left lateralization of orbitofrontal responses to negative stimuli and right lateralization of orbitofrontal responses to positive stimuli (Anderson et al., 2003; Small et al., 2003; Zald & Pardo, 2000). Others demonstrated differential responses in medial and lateral orbitofrontal cortex for positive versus negative or rewarding versus punishing stimuli. (Gottfried, Deichmann, Winston, & Dolan, 2002; Northoff et al., 2000, O'Doherty, Rolls, Francis, Bowtell, & McGlone, 2001; Small et al., 2003).

[4] An overwhelming benefit of this model is that an abundance of neurochemical manipulations are available to directly modify specific neurochemical aspects of the underlying affect-generating circuitry. This has arisen largely because of the medical importance of controlling nausea and malaise following chemo and radiation therapy for cancers. Among the most commonly used agents—prochlorperazine, ondansetron, and apreptitant—mechanisms of action are distinct and well characterized both pharmacologically, neurochemically, and functionally, especially for the last two items, where ondansetron is a specific serotonin 5-HT3 receptor antagonist, and aprepitant selectively blocks the NK1 tachykinin (i.e., substance P) receptor. The former generally has a more restricted therapeutic profile (McAllister & Pratt, 1998). Although ondansetron can reverse classic LiCl-induced CTAs (Balleine, Gerner, & Dickinson, 1995) as well as aversions induced by imbalanced amino acid diets (Terry-Nathan, Gietzen, & Rogers, 1995), there are many nausea-provoking emetics that are not effectively reversed by ondansetron (Rudd, Ngan, & Wai, 1998).

The fact that there are such a large number of convergent manipulations for generating nausea, from apomorphine to 5-HT3 and substance P receptor agonists (Ciccocioppo, et al., 1998; Landauer, Balster, & Harris, 1995) provides an armamentarium of convergent manipulations taking the analysis of at least this affect to a fine circuit level. At present, there is, to our knowledge, not a single brain imaging study that has sought to study this as a model system—one that has all the advantages that are desirable for a thorough scientific analysis and none of the disadvantages of weak and ephemeral affects that are commonly used in human brain imaging of affective processes. The disadvantage is that these are experiments that one would not want to impose on non-medically sophisticated volunteer subjects. But this may also be a blessing in disguise in order to obtain the highest quality data from professionally qualified individuals.

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