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The Feeling of Anxiety

Phenomenology and neural correlates

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The Feeling of Anxiety: Phenomenology and neural correlates

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Abstract

The feeling of anxiety, a conscious experience, is associated with uneasiness, painfulness, or disturbing suspense. The current paper presents the phenomenology of anxiety disorders based on diagnostic criteria and reviews neuroimaging studies on anxiety including dissociation studies. Activity in the anterior cingulate cortex, medial prefrontal cortex, insula, temporal poles and amygdala suggest neural correlates of anxiety. The relevance of the neural correlates, how the feeling of anxiety differs from fear and worry, and the construct validity of anxiety are addressed. Anxiety and pain correlate with activity in the anterior cingulate cortex, which warrants further studies on the painfulness–anxiety relationship.

Keywords: anxiety, phenomenology, neural correlates, construct validity

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Introduction

This paper presents a literature review of the feeling of anxiety in general, in anxiety disorders in particular and how the feeling of anxiety correlates with activity in the brain. Research in neuropsychology on anxiety has focused mainly on behavior that is accessible to external observers. This in spite of that the diagnostic criteria that are used to distinguish different anxiety disorders clearly indicate that subjective experience is central to anxiety. The concept of subjective experience emphasizes that access to the experience is private to the person undergoing the experience, but inaccessible to external observers. The purpose of the current paper is to present a literature review of the feeling of anxiety in general, as it appears in anxiety disorders, and possible neural correlates.

Anxiety may refer to a feeling of uneasiness, painful or disturbing suspense about some uncertain event, according to the *Oxford English Dictionary* (OED) (1989). A feeling is an experience of a mental state of pleasure, pain (OED, 1989) or motivation and is always conscious (Damasio, 2000). Anxiety is often described as a complex phenomenon, with interactions between bodily arousal (e.g. cardiac response), feelings of anxiety, cortical activation (Dalton et al., 2005), behavior (Kalish et al., 2005) and neurochemistry (Bishop, 2007). Anxiety enables avoidance of aversive events (Gray & McNaughton, 2000), for example, the presence of predators, the smell of a burning forest and the lurking of criminals in unlit streets. Humans may appear to be equipped with fear to tackle obstacles such as predators, fires, and criminals; however, fear is not always applicable to threats.

Anxiety is sometimes confused or equalized with fear (see Zinbarg, Barlow, Brown & Hertz, 1992) or worry (see Perkins et al., 2007). Fear is an emotion caused by apprehension of pain, of uneasiness or of anxiety (OED, 1989). Although there are similarities (e.g. Zinbarg et al., 1992), anxiety differs from fear (see also Barlow, 1988, 1991a,b in Zinbarg et al., 1992; Gray & McNaughton, 2000; Perkins et al., 2007). The uncertainty of an event is

characteristic to anxiety (Krain et al., 2008). Whether a person will feel anxiety or fear depends on the certainty of the event. In other words, if a subject knows what to expect when facing a threat, the subject will experience fear—if not, the subject will experience anxiety due to the suspense. Another way to distinguish anxiety from fear is to consider anxiety as a mood, a prevailing state of mind or feeling (OED, 1989), while fear is nothing but an emotion. According to the OED (1989) an emotion is a mental state that is neither cognitive nor volitional (volition—"the action of consciously willing or resolving" [OED, 1989]).

Anxiety is distinguishable from worry (Zebb & Beck, 1998), which is a thought pattern associated with some anxiety disorders (Fricchione, 2004; Jenike, 2004; Katon, 2006). Whereas a feeling is a lived emotion (Damasio, 2000), worry is a cognitive state (Zebb & Beck, 1998). The definition of anxiety differs from those of worry and fear.

The current literature review proceeds by combining findings from phenomenology and cognitive neuroscience. Phenomenology (in psychology) is the description and analysis applied to subjective experience of phenomena (OED, 1989). Phenomenological approaches to anxiety are sparse and are only present in the anxiety literature in reports relying on questionnaires or in diagnostic criteria, of which the latter is the focus of this essay. Cognitive neuroscience studies mental states (WordNet, 2006) and assumes that these states are features of the brain (Searle, 2004).

Every healthy human being experiences anxiety now and then. Some individuals experience anxiety more often or more intense. This has an aversive impact on those persons' quality of life. Reoccurring experiences of excessive or long-term anxiety characterize a set of psychiatric disorders known as anxiety disorders. These disorders all have the experience of anxiety in common. The phenomenology of the anxiety disorders, which consequently appear in diagnostic criteria (see Kearney, Albano, Eisen, Allan & Barlow, 1997; Yehuda, 2002; Neerakal & Srinivasan, 2003; Fricchione, 2004; Jenike, 2004; Katon, 2006; Schneier,

2006; Davey, 2007), will be shown here for each anxiety disorder: In generalized anxiety disorder (GAD), panic attacks, panic disorder (PD), post-traumatic stress disorder (PTSD), social anxiety disorder (SAD), obsessive-compulsive disorder (OCD) and phobia. Phenomenological approaches to emotions in relation to neurobiological processes have been reviewed recently (Feldman Barrett, Mesquita, Ochsner & Gross, 2007).

Activities in five regions of the brain have been suggested to correlate with the experience of anxiety: the insula, the anterior cingulate cortex (ACC), the orbitofrontal cortex (OFC), the temporal poles (Chua, Krams, Toni, Passingham & Dolan, 1999; see Olson, Plotzker & Ezzyat, 2007); the ACC together with the medial prefrontal cortex (mPFC) (e.g. Kalish et al., 2005); and the amygdala (see Anderson & Phelps, 2002). The studies mentioned here are either neuroimaging studies or dissociation studies. Dissociation studies study patients with neuropsychological deficits, where lesions of the brain are coupled with the loss of a psychological ability to form a dissociation analysis, dissociation meaning the break up of association (OED, 1989).

In excluding what may be referred to as behavioral neuropsychology, the current paper deviates from the mainstream neuropsychological approach to anxiety (cf. Gray & McNaughton, 2000). What levels of explanation are relevant to an understanding and study of anxiety is a controversial issue in the neuropsychology of anxiety (Gray & McNoughton, 2000). While a behavioristic agenda presupposes that subjective experience must be left out of the investigations in order not to hamper research on emotions (LeDoux, 2000), the approach of the current paper assumes that anxiety is a construct that cannot be defined by referring to behavior, in accordance with the definition provided by the OED (1989).

To emphasize the suspense about an uncertain event, researchers use the notion anticipatory anxiety (e.g. Chua et al., 1999; Kalish et al, 2005). Anticipatory anxiety is relevant because it is considered a very basic form of anxiety, because normal individuals

experience it (Chua et al., 1999). In a typical study of anticipatory anxiety, a cue is given prior to an aversive stimulus, signaling the appearance of the stimulus. Pain is sometimes used as a stimulus (Chua et al., 1999; Kalish et al, 2005). A study on the subjective experience of pain emphasizes anticipation and indicates that the subjective experience of pain correlates with activity in regions associated with anxiety (Koyama, McHaffie, Laurienti & Coghill, 2005).

The construct validity of anxiety is important for the choice of experimental design. Construct validity "is involved whenever a test is to be interpreted as a measure of some attribute or quality which is not 'operationally defined' " (Cronbach & Meehl, 1955, p.282). Operational definitions point to something concrete, which is publicly accessible, in order to define something abstract, which is publicly inaccessible (Houts & Baldwin, 2004). The subjective experience is publicly inaccessible, but behavior and images of the brain are publicly accessible. Operational definitions that were once behavioral are potentially replaceable by images through neuroimaging, which point to something concrete. The study on the subjective experience of pain, which includes neural correlates (Koyama et al., 2005) is an example where the relation between concrete images and abstract pain is present. Researchers use different constructs of anxiety. Thus, it is uncertain if the suggested correlates presented here are relevant to the feeling of anxiety.

The current paper starts out by presenting the phenomenology for each anxiety disorder, whereupon it reviews neuroimaging studies including dissociation studies on anxiety; then follows a discussion on limitations (including construct validity) and future applications. Finally, a conclusion summarizes the discussion and the paper.

The subject matter under investigation assesses the plausibility of one hypothesis: The construct of anxiety of the OED (1989) is valid and thus enables the prediction of necessary criteria for the anxiety phenomenon.

Phenomenology of Anxiety Disorders

The phenomenology of anxiety disorders can be found in the diagnostic criteria for each disorder. For example, a feeling of apprehensive expectation is experienced in GAD (Fricchione, 2004). The symptoms for any anxiety disorder must be severe enough to cause significant distress in the patient's life (e.g. Fricchione, 2004). Also, other illnesses—both psychiatric and somatic ones—must be discarded (e.g. Fricchione, 2004; Katon, 2006).

The GAD patient experiences difficulties in controlling worry and displays at least three of the following six symptoms: restlessness, being easily fatigued, difficulty concentrating, irritability, muscle tension, sleep disturbance (Fricchione, 2004).

The panic attack patient may experience up to twenty-six symptoms (Neerakal & Srinivasan, 2003). In one sample of patients experienced panic attacks, comprising more PD patients than depressed patients and more depressed patients than agoraphobic patients, over fifty percent reported eleven of these symptoms in descending order of percentage: anxiety, increased heart beat, panic, fear of dying, weakness, heart pounding, feeling depressed, trembling, sweating, shortness of breath and hot flushes (Neerakal & Srinivasan, 2003).

The PD patient experiences intense fear or discomfort, reaching a peak within ten minutes, including at least four of the following symptoms: palpitations (awareness of irregular, hard or rapid heartbeat); sweating; trembling or shaking; shortness of breath or choking; chest pain or discomfort; nausea or abdominal distress; dizziness, feeling light-headed or faint; derealization (loosing one's sense of reality) or depersonalization (loosing ones sense of personal identity); fear of loosing control or going crazy; fear of dying; chills or hot flushes; abnormal skin sensations (Katon, 2006). In addition, a worry about future attacks and their implications is necessarily a diagnostic criterion (Katon, 2006). Furthermore, some environmental settings may increase the likelihood of triggering a panic attack in patients diagnosed with PD (Kearney et al., 1997). The difference between the panic attack diagnosis

and the diagnosis of PD is that PD, not only includes the diagnostic criteria for panic attacks, but also the criterion of worry of a future attack.

Yehuda (2002) provides the following description of PTSD. The PTSD patient has been exposed to a traumatic event involving a threat, which the patient was unable to effectively cope with at the time. Reexperiences of the event occurs intrusively as flashbacks and nightmares. Remembering the trauma triggers panic responses (cf. description of panic attack above) and distress. PTSD includes feelings of detachment, estrangement from others and emotional numbness. The patient experiences a general lack of motivation in life and has at least two of the following arousal symptoms: insomnia or shallow sleep—sometimes because of anticipatory apprehension of nightmares; irritability and feelings of anger; difficulties concentrating; increased vigilance and concern about safety.

The SAD patient experiences a distinctive and prevailing apprehension in social or performance situations where unfamiliar people, or possibly the scrutiny of others, are present (American Psychiatric Association, 2000 in Schneier, 2006). Everybody feels performance or evaluation anxiety now and then, but in SAD the fear is excessive. The anxiety in social and performance situations may result in panic attacks (cf. description of panic attack above) (Schneier, 2006). Another characteristic feature of the disorder is that the patient apprehends humiliation or embarrassment (Schneier, 2006).

The OCD patient experiences intrusive and persistent thoughts, impulses or images that are perceived as inappropriate and which lead to excessive anxiety, worry or distress (Jenike, 2004). (Apart from this obsessive aspect there is a compulsive one, which is the resulting behavior involving repetition of certain acts and rigid rule-following [Jenike, 2004], exclusively characteristic of OCD.)

The phobia patient experiences unreasonable fear of a particular situation or object and may have irrational beliefs about the situation or object (Davey, 2007). The phobia may

even be triggered by a belief that a situation or an object is dangerous (Field, Argyris, & Knowles, 2001 in Davey, 2007). Phobia includes both anxiety and fear, as phobia patients become exaggeratedly frightened in the presence of the fear eliciting threat, and anticipation of the threat may result in avoidance behavior that is characteristic to anxiety. Apprehension in the phobia patient's fear requires the immediate presence of the specific phobogenic object or situation. Phobia patients experience both anticipatory anxiety and fear as two distinct affective states (Andrews, 1994).

Worry is a central construct to some clinical manifestations of anxiety, namely GAD (Fricchione, 2004), PD (Katon, 2006) and OCD (Jenike, 2004). A study on questionnaires used in the clinical assessment of anxiety and questionnaires used in the assessment of worry in educational test anxiety, indicate that worry and anxiety may be separate constructs (Zebb & Beck, 1998). On this interpretation worry is a purely cognitive mental state characterized by intrusions of "unrealistic concern about future events" (Borkovec, Robinson, Pruzinsky & DePree, 1983 in Zebb & Beck, 1998, p. 46) in the stream of thought and is thus a cognitive component of anxiety. In contrast, anxiety includes both somatic (pertaining to the body) and cognitive components (Zebb & Beck, 1998). Another definition states that worry is a troubled state of mind or a kind of harassing anxiety according to the OED (1989). Other cognitive aspects of anxiety, in anxiety disorders in particular, have been explored elsewhere (see Starcevic & Berle, 2006). Concluding the phenomenal analysis, the feeling of fear differs from anxiety in its phenomenology and worry is common to at least three anxiety disorders.

Neuroimaging and Dissociation Studies

Dissociation studies are used to back up the hypothesis that the amygdala mediates experience of emotion, including both fear and anxiety, but this hypothesis has recently been challenged (Anderson & Phelps, 2002). In addition, dissociation studies of patients with

bilateral damage to the amygdala suggest that recognition of anxiety and fear are not unique to amygdala, but also recognition of positive emotions in faces are related to the amygdala (Siebert, Markowitsch & Bartel, 2003).

Apart from the amygdala, a handful of neural correlates of the experience of anxiety have been suggested: the ACC, the temporal poles, the insula, the OFC, and the mPFC. The ACC is presented in Figure 1. The remaining areas lack figures, but their locations are as follow: The temporal poles are located at the anterior-most part of the temporal lobes; The insula, also known as the insular cortex or the central lobe of the cerebrum, is located medial to the bilateral sulci; The OFC is located superior to the eye sockets, in the anterior-most part of the cortex. The mPFC, as the abbreviation specifies, is the medial portion of the prefrontal cortex, including the areas of the superior and medial frontal gyrus.

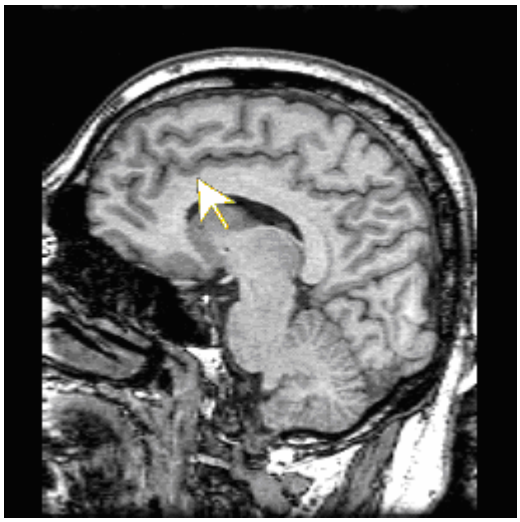

Figure 1. The arrow points toward the anterior cingulate cortex (ACC). Left corresponds to anterior and right to posterior. Image courtesy of Whole Brain Atlas (1999).

Two studies on anticipatory anxiety have focused on different, but overlapping, regions of interest (ROI:s). ROI:s, metaphorically speaking, resemble windows of the brain, which enclose isolated views where one is likely to find changes in neuronal activation. ROI-

based approaches constrain an area of the brain to the ROI, thus allowing for increased statistical sensitivity, because—somewhat simplified—there is less data to compare (Mitsis, Iannetti, Smart, Tracey & Wise, 2008) resulting in greater statistical power. The object of study in both anticipatory anxiety studies was the ACC, shown in Figure 1. In addition, the first study considered the insula, the OFC and to some extent the temporal poles (Chua et al., 1999), and the second study regarded the mPFC (Kalish et al., 2005). The authors of the former study note that the results only lend weak support to the activity in the temporal poles as correlates of anxiety, although they confirm this correlation with previous studies.

Another study of anticipatory anxiety claims to be the first neuroimaging study of anxiety regulation (Kalish et al., 2005). In the functional magnetic resonance imaging (fMRI) study, when participants were exposed to the suspense of experiencing painful stimuli, the ACC was found to be the site of modulation and mPFC its source. In other words, the hemodynamic response (i.e. the dynamic regulation of blood flow) in the mPFC modulates ACC in regulation of anticipatory anxiety. The relevance here is that regulation of anxiety through affirmations and mental imagery influences the degree of experienced anxiety. Participants of the control group were not instructed to regulate their anxiety. Thus, the experimental group experienced more anxiety than the control group. However, in the study under review, regulation of anxiety led only to moderately significant results. Nevertheless, regulation of emotion using the same techniques have shown to be successful as supported by earlier studies mentioned in the report under review. Conclusively, activity in the ACC and mPFC regions indicate increased anticipatory anxiety of pain. However, because studies of anticipatory anxiety frequently involve pain as stimulus, to what degree pain is necessary for anxiety remains obscured.

Peaks in the hemodynamic response in the study of the mPFC (Kalish et al., 2005) were located to one area at the superior frontal gyrus in the right hemisphere and one area

located at the medial frontal gyrus in the left hemisphere. (The current paper derived these anatomical labels from the coordinates in Kalish et al. using the Talairach Client software version 2.4 [Lancaster et al., 2000] with the Single point option selected, i.e. null deviation: +/- 0 mm.)

The amygdala has been suggested to correlate with the experience of emotions, including anxiety and fear (see Anderson & Phelps, 2002). The ability to recognize fearful expression, both in faces of others (Adolphs, Tranel, Damasio & Damasio, 1994) and in music (Gosselin, Peretz, Johnsen & Adolphs, 2007), is impaired in people with damage to the amygdala. An alternative role of the amygdala in facial recognition of emotions has been proposed suggesting that the amygdala may not be relevant to fear as such, but to overt attention of gaze (Adolphs, Gosselin, Buchanan, Tranel, Schyns & Damasio, 2005).

Neuropsychological findings suggest that lesions to the amygdala hinder the ability to recognize expressions of fear (Adolphs et al., 1994; Gosselin et al., 2007), although these findings are not uncontroversial (Adolphs et al., 2005). A study with 20 patients with unilateral damage and one patient with bilateral damage to the amygdala revealed that the amygdala is not necessary for the production of mental states of experience (Anderson & Phelps, 2002). The sudden impact of this finding can be explained on the basis that earlier studies did not justify the connection between subjective experience and the amygdala. When only behavioral accounts of the functions of amygdala were present, researchers simply assumed this association to be valid. If anxiety is defined behaviorally then support for the necessity of the association between subjective experience and the amygdala is superfluous. The locations of the amygdalae are depicted in Figure 2.

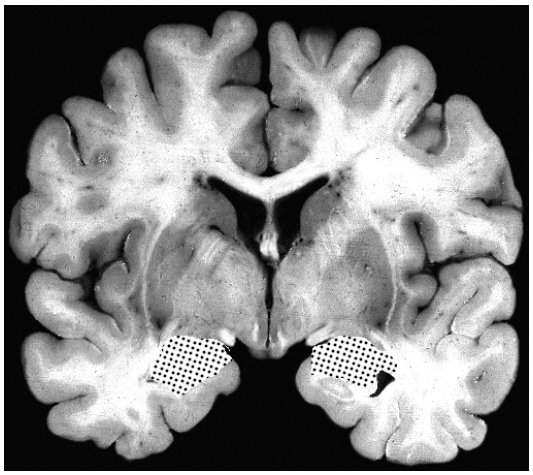

Figure 2. Coronal section of human brain showing the locations of amygdalae represented as computer rendered spotted areas. Original image courtesy of BrainInfo (2007).

Discussion

The construct of anxiety in the OED (1989) is valid and thus enables the prediction of necessary criteria for the anxiety phenomenon, with one exception: The relationship between painfulness and anxiety is unclear. The phenomenological descriptions of the current paper provide that feeling is a necessary and valid component of the construct, and that three anxiety disorders include worry. That feeling is valid justifies the approach taken in the current paper, although it could be argued that taking a phenomenological approach, which results in the importance of experience, is to reason circularly.

If worry is a kind of uneasiness or disturbance, then these latter concepts will be valid for the construct as well. However, their necessity can be challenged on the basis that worry is only present in three anxiety disorders according to the current phenomenological analysis. Conversely, Krain et al. (2008) claim that worry is a key characteristic of anxiety disorders. Nevertheless, the researchers base this conclusion on a cognitive model of adolescent worry. Whether such a model generalizes to adults is uncertain.

The uncertainty in the suspense of anxiety might be a characteristic to anxiety, because of two reasons: Researchers claim anticipatory anxiety to be basic to anxiety and anticipation emphasizes suspense; Without the concept of uncertainty, anxiety would not be distinguishable from fear. However, some researchers suggest that it is possible to differentiate anxiety from fear through a temporal (pertaining to time) criterion, because fear occurs more rapidly than anxiety (e.g. Chua et al., 1999). Another difference between anxiety and fear often provided is that whereas fear is stimulus-bound, anxiety is less stimulus-bound (e.g. Chua et al., 1999). From the current phenomenological description of the anticipatory anxiety experienced in specific phobia, which requires a specific object as stimulus, this distinction does not seem valid. Although anxiety is triggered by a cue that refers to a stimulus, for example, in the anticipatory studies under review, the cue is nevertheless stimulus-bound. Thus, anxiety is not less stimulus-bound. In addition, although the cues represent stimuli, the cues are stimuli in themselves, because they are perceived. Uncertainty may be a necessary criterion to distinguish anxiety from fear, as well as elapsed time between stimulus and response (Chua et al., 1999).

Concerning phenomenology, one need to take into consideration that patients may display different symptoms across different cultures (Neerakal & Srinivasan, 2003). Thus, one should be careful to generalize from a single study to what extent patients diagnosed with an anxiety disorder experience different symptoms.

On one hand, the phenomenology presented here is not rich in its description as it relies on the diagnostic criteria of the anxiety disorders and not on a systematic phenomenology. On the other hand, some researchers explicitly do not consider richness to be an ideal in phenomenological analyses of feelings (Feldman Barrett et al., 2007). Even so, the phenomenological descriptions are not rich enough to describe painfulness. Because the lack of descriptions of painfulness, the phenomenological analysis is unable to assess the

presence of painful experience in anxiety disorders. However, the painfulness criterion can be evaluated on a cognitive neuroscientific basis. The neural correlate ACC was found to response in both studies of anticipatory anxiety (Chua et al., 1999; Kalisch et al., 2005). ACC has also been implied together with the insula and the prefrontal cortex among other brain areas in the subjective experience of pain (Koyama et al., 2005). The insula was also responsive in the findings by Chua et al. and the medial aspect of the prefrontal cortex (i.e. the mPFC) was responsive in the findings by Kalisch et al. It is possible to take the following into consideration:

a) Both anticipatory anxiety studies by Chua et al. and Kalish et al. used pain as stimulus
b) Several researchers assume that there is interaction between different components such as behavior, feeling and autonomic arousal in anxiety(e.g. Chua et al., 1999; Bishop, 2007; Dalton et al., 2005)
c) Anxiety was not present in the experience of pain, because the participants did not respond with autonomic arousal in the findings by Koyama et al.

From the above, this paper suggests that the use of pain as stimulus in anticipatory anxiety paradigms may obscure neural correlates of anxiety. Nevertheless, it is possible that responsive ACC, insula, and perhaps the prefrontal cortex, somehow indicate correlates of anticipation or suspense. Suspense or that "anxiety... is not closely bound in time to the actual stimulus" (Chua et al., 1999, p. 569) may render the uncertainty criterion obsolete. It is possible that suspense or anticipation are sufficient criteria and that uncertainty is unnecessary. Construct validity seems to be challengeable through the current assessment of the validity of the painfulness criterion.

Activity in the ACC was found in two anticipatory anxiety studies. However, comparisons between studies may reflect overlaps of ROI. In other words, if one correlate is found in one study but not another, it is possible that the studies did not consider the same ROI, that is researchers expected activity in different parts of the brain. The downside with ROI-based approaches is that strong hypotheses are required in order to take advantage of the increased statistical sensitivity (Mitsis et al., 2008). Thus, one might speculate on the possibility why several correlates have been proposed. This might explain why this literature review was unable to locate explanatory studies, which by their nature need not to be ROI-based. Whether such explanatory studies do exist or not, studies that aim to achieve statistical power and to test strong hypotheses dominate the neuroscience of anxiety domain. The consequence is that certainty is gained in testing individual hypotheses, but alternate hypotheses are likely to be fewer.

Activity in the temporal poles have been supported as correlates in earlier anticipatory anxiety studies, but received weak support in the most recent of selected studies (Chua et al., 1999). Because the temporal poles have not been studied extensively (Olson et al, 2007), more research is needed on their role in the feeling of anxiety.

On the basis that the amygdala is not necessary for subjective experience, activity in this structure is deemed implausible as a correlate (Anderson & Phelps, 2002). The single case dissociation study of the amygdala (Adolphs et al., 1994) suggests that activity in the amygdala is a neural correlate for recognition of expressions of fear, but recognition does not imply experience (Anderson & Phelps, 2002) and fear does not imply anxiety (see also Chua et al., 1999). The latter implication follows from the difference between the definitions of anxiety and fear: The uncertainty of an event is characteristic to anxiety, but not to fear (cf. OED, 1989). Other researchers have reached similar conclusions, although with different starting points (e.g. Barlow, 1988, 1991a,b in Zinbarg et al., 1992; Bishop, 2007) including

justification through empirical observations (Gray & McNaughton, 2000; Perkins et al., 2007). Not all researchers accept the fear–anxiety dichotomy. Admittedly, their reports were excluded from the current literature review because they lacked both explicit statements concerning the dichotomy and empirical support against it.

The criteria for including the neuroimaging studies were two: A study should measure the subjective experience in anxiety prior to or during the experimental phase, and the study should use one of the methods of cognitive neuroscience. The studies on the insula, ACC, OFC and the temporal poles (Chua et al., 1999), and the ACC and mPFC (Kalish et al., 2005) were included on this basis. However, also certain studies that are representative to an argument for a neural correlate of the feeling of anxiety were included: The amygdala studies (Adolphs et al., 1994, 2005; Gosselin et al., 2007) were included on the basis that the amygdala has been associated with the subjective experience of anxiety (Anderson & Phelps, 2002).

Single-case studies of lesion patients require that the patient carries out the task procedure without using a different strategy than normal individuals usually do, for example, in pure alexia—the inability to read words—a patient may sound each letter in turn and attempt to combine them into a word (Shallice, 2002) thereby using another faculty. To recognize fear in faces, a normal individual attends the eyes whereas in the case of the patient with bilateral damage to the amygdala, the eyes in the faces of others are not attended (Adolphs et al., 2005). This suggest, in a similar vein to the type of limitation presented above, that the cognitive association between amygdala and fear might rest on the ability to direct gaze—toward the eyes (Gosselin et al., 2007).

It is doubtful that the neuropsychological studies here mentioned elicited threat. Possibly, the facial expression study may have provoked fear in normal subjects through some empathical reaction; however, this involves empathic ability as an intermediate

variable, which may act as a confound if not controlled for. Moreover, the patient with bilateral damage to the amygdala may have experienced anticipatory anxiety since the experimenters briefed the participant about the nature of stimuli prior to experimentation, which may have influenced the recognition task. Thus, whether fear or anxiety was studied in the two experiments is not entirely clear, because correlations of anxiety tend to linger more than correlations of fear (Chua et al., 1999). The direct perception of a threat differs from the perception of an emotional expression of a person's face. Moreover, fear and anxiety do not require a social context, except in particular anxiety disorders such as SAD, and thus face recognition studies are not necessary to explain anxiety.

The problem with the many definitions in relation to anxiety and fear is that they may end up in a circular referral to each other. For example, worry describes a characteristic of three anxiety disorders, however, it is per definition a kind of anxiety (OED, 1989).

It is unknown whether the feeling of anticipatory anxiety generalizes to feelings of anxieties experienced in all anxiety disorders, which warrants further studies into the differences between anxiety disorders and anticipatory anxiety regarding their phenomenology.

Cognitive regulation of anxiety through mental imagery and inner voice affirmation is possible, without relying on external stimuli or behavioral responses, and may influence autonomic responses. These findings suggest that trying to escape from cognition and the subject in anxiety research might hamper an understanding what anxiety is about. Operational definitions of anxiety have paved the way for research of animal models of anxiety, which may be relevant to understanding autonomic response, however, there is no need to "escape from the shackles of subjectivity" (LeDoux, 2000, p. 156).

The following recommendations for future research should only be considered as tentative, and should only be regarded if the conclusion is deemed valid. The

recommendations are based on the discussion above. More research is needed on the relationship between uncertainty, worry and anxiety in adults. Further research is needed to distinguish between anticipation of pain and other aversive events. The relationship between painfulness and the feeling of anxiety needs to be clarified. The role of the temporal poles should be further investigated (see also Olson et al., 2007) now that advancements in neuroimaging have been made.

Conclusion

The resulting thesis statement is that more cognitive neuroscience research is needed to establish the neural correlates of the experience of anxiety, and that the present construct of anxiety is valid, but with one exception: The unclear relationship between painfulness and anxiety warrants further investigation. This conclusion is founded on the observation that the studies presented herein on neural correlates of anxiety, diverge. As long as the construct validity of anxiety definitions is continuously reevaluated, and the subject's feeling is not neglected, the prospects of reaching a consensus on a definition of anxiety hinges on the horizon of a future for a comprehensive theory of anxiety.

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