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Review

Emotion processing deficits: A liability spectrum providing insight into comorbidity of mental disorders

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ABSTRACT

Epidemiological studies have revealed that mental disorders are highly comorbid; almost half of the people with a mental disorder also meet the criteria of another disorder. The explanation of this high comorbidity has remained a scientific puzzle. We propose 'disrupted emotion processing' as a liability spectrum that underlies many different mental disorders. Emotion processing deficits have been reported in different disorders and result in difficulties in regulating emotions and at the perceptual level in attentional biases and impaired recognition of emotional expressions. This article provides a detailed overview of the literature on disrupted emotion processing in clinical groups on the behavioral and neurological level. In the discussion, the similarities and differences between these disorders are discussed in the context of common neuro-endocrine, genetic and environmental factors and ideas are put forward on how future research may advance. Most importantly, more interdisciplinary research is needed in which different techniques, tasks and clinical populations are combined to get a better understanding of disrupted emotion processing as a liability spectrum underlying various different mental disorders.

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1. Introduction

Epidemiological studies have revealed that up to 30% of the adult population in the United States has a mental disorder (e.g., Kessler et al., 1994). Interestingly, many people meet the criteria of more than a single mental disorder. In a large survey, it was found that 55% of the clinical population has a single disorder; 22% has two, and 23% has three or more disorders (Kessler et al., 2005). The cause of this high prevalence of comorbidity remains a scientific puzzle. Several explanations have been given. For example, comorbidity may represent different manifestations or two stages of the same underlying condition; there may be the same or correlated risk factors; or one condition predisposes to another disorder (for a review, see Rutter, 1997). It is also possible that it is an artifact of the diagnostic systems that are widely used, such as the *Diagnostic and Statistical Manual of Mental Disorders-5* (DSM-5, American Psychiatric Association, 2013). The DSM is constructed in such a way that symptoms cannot appear in the diagnostic criteria of more than one disorder. Moreover, it is possible that the divisions made in the DSM do not exist in nature and that the complexity and heterogeneity of mental disorders cannot be covered in a fixed, rigid diagnostic system (Maj, 2005; Panksepp, 2004a).

Recently, a network approach to psychopathology has been proposed (Borsboom et al., 2011; Borsboom and Cramer, 2013; Bringmann et al., 2013), where it is argued that symptoms of a disorder can be the direct cause of the arising of other symptoms. For example, symptoms of a major depressive episode, such as sleep deprivation, may easily cause symptoms of generalized anxiety disorder, such as irritability and fatigue (Borsboom et al., 2011). In addition, several other approaches are possible, such as a range of different bivariate and multivariate comorbidity models (Krueger and Markon, 2006). Based on their meta-analysis, Krueger and Markon concluded that most evidence points into the direction of a liability-spectrum model of comorbidity. The assumption of this model is that comorbidity reflects the existence of a smaller number of liability constructs that underlie multiple disorders. Krueger and Markon propose a broad internalizing liability and a broad externalizing liability. The internalizing liability underlies disorders such as major depression, generalized anxiety disorder and specific phobias, whereas the externalizing liability underlies disorders such as addictions and antisocial behavior.

In the present article, while fully acknowledging the complexity of comorbidity, we follow the liability-spectrum model, but we propose a broader liability spectrum. We argue that a broader liability spectrum is necessary in order to explain the comorbidity of internalizing and externalizing disorders. The liability spectrum we propose is disrupted emotion processing, which underlies a wide range of mental disorders, including anxiety and mood disorders, but also schizophrenia, autism spectrum disorders, borderline personality disorder and eating disorders. In this article we review the evidence for this proposal, and in addition, we review the evidence for neural correlates underlying disrupted emotion processing in different mental disorders.

We start this article by defining what emotion processing is and by addressing different theories that attempt to explain the nature of emotions. Then we briefly introduce the main neural correlates of emotion processing in healthy individuals. The main body of this article is a review of studies on emotion processing in several mental disorders, including anxiety disorders, mood disorders, schizophrenia, autism, borderline personality disorders, and eating disorders. We finish the article with a discussion about the implications of this literature review for the proposal that disrupted emotion processing is a plausible liability spectrum to explain the comorbidity of mental disorders.

1.1. What is emotion processing?

Emotion processing is a broad term that refers to a complex of affective, behavioral and cognitive mechanisms that underlie our emotions. Given the impact of our emotions on a wide range of mental processes (e.g., memory, decision making) and manifest behaviors (e.g., helping behavior, drug use), being able to recognize and regulate our emotions is of crucial importance and an essential feature of mental health. It is notable that different emotion regulation strategies have been shown to impact the subjective, physiological, and behavioral components of negative emotion in distinct ways. For example, cognitive reappraisal and suppression have been shown to decrease the behavioral expression of negative emotion, but only reappraisal decreases subjective distress (Gross, 1998). Moreover, emotion regulation strategies have varying effects on the temporal course of emotions. Rumination has been shown to prolong episodes of sadness, whereas distraction appears to shorten them (Nolen-Hoeksema and Morrow, 1993). Finally, habitual use of certain emotion regulation strategies is meaningfully associated with interpersonal functioning and well-being (Gross and John, 2003), suggesting that some emotion regulation strategies may be "healthier" than others (John and Gross, 2004). What emotions are and how they arise has been a matter of ongoing debate (e.g., Ekman and Cordaro, 2011; Panksepp and Watt, 2011).

Theories on emotions can be roughly categorized into two main approaches. The discrete emotion approach posits that there are empirically distinguishable basic emotions, such as happiness, sadness, fear, anger, disgust, and surprise. These emotions are biologically inherited and cannot be broken down in smaller components (e.g., Ekman, 1992). The dimensional approach proposes

that emotions can be defined according to one or more dimensions, such as valence (pleasantness) and arousal (strength) (e.g., Barrett, 1998).

In addition, the brain basis of emotions has been widely disputed (e.g., Hamann, 2012; Lindquist et al., 2012). Models following a locationist approach to emotion hypothesize that all emotions can be specifically localized to either a distinct brain region or a defined network of brain regions (Ekman and Cordaro, 2011; Izard, 2011; Panksepp and Watt, 2011). In contrast, the psychological constructionist approach to emotion hypothesizes that distinct emotions are constructed mental states that occur when many different systems in the brain act together (Barrett and Wager, 2006).

Another debate concerns the question how many 'roads' or pathways the brain uses to process emotions (Pessoa and Adolphs, 2010). In his famous two route model of emotion processing, LeDoux (1996) theorized that evolution has equipped the brain with a shortcut to rapidly analyze potentially threatening elements in a visual scene (the 'low road'). This subcortical pathway involves the superior culliculi, the pulvinar, and the amygdala, and can detect stimuli that potentially require a fight or flight response, such as snakes, spiders, and fearful faces (see also Panksepp, 2004b). Next to the low road, there is a 'high road', involving several cortical areas and the amygdala, for the more deliberate processing of emotions, such as the recognition of emotional expressions and the differentiation between several emotions. The current debate is about the number of pathways that the brain uses to process emotion. Recently, Pessoa and Adolphs (2010, 2011) proposed a model with multiple pathways, rather than a dichotomy between a 'low road' and a 'high road'. They argued that the primary function of the amygdala is to coordinate the activity of multiple cortical networks during emotion processing.

In sum, the exact nature of emotions and the underlying brain mechanisms are currently unknown. It is beyond the scope of the present article to resolve any of these debates. However, what is well-known is that emotions play a major role in mental disorders. Problems with emotions in mental disorders may relate to emotional intensity, emotional duration, emotion frequency, emotion type, emotional awareness, emotion-regulation goals, and emotion-regulation strategies (Gross and Jazaieri, 2014). We refer to these problems with the term disrupted emotion processing. In this review, our emphasis will be on two main parts of disrupted emotion processing. First, it includes 'emotion perception', which is the attention toward emotional cues in the environment, the accurate recognition of the emotion, and the adequate response toward it. Second, it includes 'emotion regulation', which is the management and control of one's own emotions. We review evidence of studies on both emotion perception and emotion regulation deficits in a broad range of mental disorders, and the underlying neural correlates.

1.2. Neural correlates of emotion processing in healthy individuals

When observing another person who experiences an emotion, humans pay attention to the facial expression and to the body posture (Ekman and Cordaro, 2011; De Gelder et al., 2010). The neural network underlying face perception is well known and includes the occipital face area (Gauthier et al., 2000; Puce et al., 1996), the fusiform face area (Kanwisher et al., 1997), the superior temporal sulcus and the amygdala (Haxby et al., 2000). Most of these areas are also involved in processing *emotional* faces. The human amygdala plays a key role in attending to and recognizing emotional expressions and interacts with higher order brain areas involved in inhibition and social decision making (Adolphs, 2010). Activity in the fusiform face area increases when faces turn emotional, and this increased activity also correlates with increased amygdala activity (Vuilleumier and Pourtois, 2007). The anterior cingulate cortex is a region within the medial prefrontal cortex that coordinates synchronized, multisystem emotional responses to salient environmental stimuli including emotional expressions of others (Patterson et al., 2002). Perceiving emotional expressions can be rewarding, especially when they express a positive emotion and computing the salience value of social stimuli rests on strong interactions with the ventral striatum and orbitofrontal cortex with which the amygdala also shares dense connections and which both respond to socially reinforcing stimuli (Ghashghaei et al., 2007).

Considering emotion regulation in healthy individuals, Frank et al. (2014) conducted a meta-analysis on emotion regulation fMRI studies and revealed signal change in bilateral amygdala/parahippocampal gyrus that decreased in down-regulated states and increased in up-regulated states, while regions including superior frontal gyrus, cingulate, and premotor areas exhibited enhanced activity across all regulation conditions. These results provide consistent evidence for the role of the amygdala in experienced emotional intensity, where intentional dampening and exaggeration are clearly expressed. However, as Frank et al. (2014) conclude, the execution of emotional up-regulation and down-regulation may involve distinct subsets of fronto-cortical structures. Kohn et al. (2014) developed a model for the core brain network involved in emotion regulation of emotional reactivity. According to this model, the superior temporal gyrus, angular gyrus and (pre) supplementary motor area should be involved in the execution of regulation initiated by frontal areas. The dorsolateral prefrontal cortex may be related to the regulation of cognitive processes such as attention, while the ventro-lateral prefrontal cortex may not necessarily reflect the regulatory process per se, but signals salience and therefore the need to regulate. The authors also identified a cluster in the anterior middle cingulate cortex as a region, which is anatomically and functionally in an ideal position to influence behavior and subcortical structures related to affect generation. Hence, this area may play a central, integrative role in emotion regulation. The authors argue that focusing on regions commonly active across multiple studies, their model may provide important à priori information for the assessment of dysregulated emotion regulation in psychiatric disorders.

1.3. Comorbidity, emotion processing and the brain

In this article, we review the evidence for emotion processing deficits and their neural correlates in a broad range of mental disorders, with the aim to provide evidence for the hypothesis that disrupted emotion processing is a plausible liability spectrum to help explain comorbidity in mental disorders. The role of emotions and their brain basis in different disorders has been noticed before (e.g., Davidson, 1998; Davidson et al., 1999; Nesse and Ellsworth, 2009; Panksepp, 2006). Many psychiatric patients have difficulties in identifying and describing one's own and other people's emotions. This is a typical characteristic of 'alexithymia' (Sifneos, 1973). This personality construct is marked by dysfunction in emotional awareness, social attachment, empathy and interpersonal relating (Feldmanhall et al., 2013; Bird and Viding, 2014), linked with differences in anterior cingulate and mediofrontal activity during emotional stimuli processing (Berthoz et al., 2014; Van der Velde et al., 2013) and creates interpersonal problems due to the avoidance of emotionally close relationships (Vanheule et al., 2007). Alexithymia can be seen as a "dimensional trait" and is prevalent in approximately 10% of the general population. However, prevalence rates are much higher in psychiatric disorders including eating disorders, autism, depression and anxiety disorders (Shipko et al., 1983; Taylor et al., 1999; Hill et al., 2004; Frith, 2004; Leweke et al., 2012). Alexithymia is a fundamental construct in the emotion regulation field and will therefore be discussed in more detail

within the individual sections for the different disorders and in the discussion.

Also Panksepp (2006) noted similarities in emotion processing across different disorders and defined different types of emotional systems (e.g., lust, care, panic, play, fear, rage, seeking) that can be related to different brain areas and neuromodulators, and to different mental disorders. He proposed the term 'emotional endophenotype' for the neuroanatomical, neurophysiological, neurochemical, emotional, motivational, cognitive or simple response tendencies (which have also been called 'biomarkers' or 'vulnerability traits'). Nesse and Ellsworth (2009) argued that emotions are the result of appraisals of the situation. For example, when seeing a dog, a person with positive experiences with dogs will show different emotions from someone with negative experiences, because of different situational appraisals. For someone who likes dogs, the dog provides pleasant feelings, including predictability and control of the situation. For someone who dislikes dogs, the opposite pattern will emerge. This approach can explain the experience of both positive and negative emotions, and individual differences in emotions. Mental disorders emerge through exaggerated experiences of emotions due to aberrant or maladjusted appraisals of situations. We call this disrupted emotion regulation.

In the present article we build upon these approaches to explain the comorbidity of mental disorders. In the present article, we argue that people with mental disorders share their disrupted emotion processing, including both emotion regulation and emotion perception. We review empirical evidence reported in studies on differences between people diagnosed with mental disorders and healthy controls on emotion processing, in particular emotion perception, emotion regulation and the underlying neural correlates. Because this would imply a tremendous number of studies, we chose to emphasize studies reporting meta-analyses on fMRI studies in clinical and control groups. We start with addressing anxiety disorders.

1.4. Anxiety disorders

In the USA, the lifetime prevalence of an anxiety disorder in adults is 33.7%. Anxiety disorders are characterized by feelings of anxiety and fear, where anxiety is a worry about future events and fear is a reaction to current events and is accompanied by physical symptoms, such as a racing heart and shakiness. There are various forms of anxiety disorders, including post-traumatic stress disorder, social phobia or other phobias, generalized anxiety disorder, and panic disorder. Research shows some overlap between anxiety disorders and alexithymia. Alexithymia has a higher prevalence in patients with anxiety disorders (30–40%) than in the healthy population (~10%) (Zahradnik et al., 2009; for a review, see De Berardis et al., 2008), and a higher prevalence in patients with panic disorder as compared to obsessive-compulsive disorder (Zeitlin and McNally, 1993). To date, it is unsure whether alexithymia is state-dependent or not and therefore an important measure to include in any anxiety study. Anxiety disorders are partly genetic but may also be due to drug use including alcohol and caffeine, as well as withdrawal from certain drugs. They often occur with other mental disorders, particularly major depressive disorder, bipolar disorder, certain personality disorders, and eating disorders (Kessler et al., 2012).

1.4.1. Emotion processing deficits in anxiety

A normative function of the mechanisms underlying fear is to facilitate detection of danger in the environment and to help the organism respond effectively to threatening situations. Anxiety or fear can thus be adaptive healthy responses, but can also become debilitating and maladaptive. Biases in emotion processing of threat-related information have been assigned a prominent role in the etiology and maintenance of anxiety disorders (Bar-Haim et al., 2007; Bell et al., 2011) and may reflect the influence of neuromodulatory factors in the formation and expression of cognitive-emotional biases such as those seen in anxiety and depression (Harmer et al., 2011).

Exactly *how* the deficits in the fear mechanism cause biases in the processing of threat-related information is a matter of current debate. The vigilance hypothesis postulates that individuals with anxiety disorders detect threat more rapidly and more often. This theory is supported by research on dichotic listening (McNally and Foa, 1986), signal detection (Wiens et al., 2008) and spatial attention (Mogg and Bradley, 2002). The maintenance hypothesis suggests that attentional biases may increase state anxiety by *maintaining* cognitive resources on threat (Fox et al., 2001). In addition to the facilitated detection of threat and the difficulty disengaging from it, studies that utilized longer stimulus exposures also observe anxiety-related biases in attention away from threat (Koster et al., 2005) that prevents reappraisal of threatening stimuli and thereby maintains harm associations (Mogg et al., 1987). Armstrong and Olatunji (2012) reviewed the application of eye tracking methodology in the study of attentional biases for threat in anxiety and depression and argued that these hypotheses are not mutually exclusive. They observed that relative to controls, anxious individuals showed increased vigilance for threat during free viewing and visual search, and showed difficulty disengaging from threat in visual search tasks, but not during free viewing.

Recently, Plana et al. (2014) conducted a meta-analysis on forty studies including anxiety patients and their performance on behavioral social cognition tasks. Results showed that people with a post-traumatic stress disorder have deficits in mentalizing and emotion recognition while those with social phobia showed attributional biases. Unfortunately, for the other two social cognition domains that the authors defined, mentalizing and social perception/knowledge, the number of studies was insufficient to draw solid conclusions. Given that the emotional avoidance and numbing symptoms characteristic of PTSD suggest problems with affect regulation, and that cognitive factors are thought to contribute to the development and maintenance of PTSD, numerous studies have linked both alexithymia and anxiety-sensitivity to PTSD (e.g., Zahradnik et al., 2009).

1.4.2. fMRI research on emotion processing deficits in anxiety

Meta-analyses of neuroimaging studies on people with anxiety disorders revealed consistent amygdala hyperactivity along with reduced activity in the ventromedial prefrontal cortex and thalamus, providing evidence for a neuro-circuitry model of anxiety that emphasizes alteration in neural networks important for salience detection and emotion regulation (Etkin and Wager, 2007; Hayes et al., 2012). The meta-analysis by Hattingh et al. (2013) confirms that increased activation of the amygdala is a prominent feature in social anxiety disorder, particularly in response to socially emotive stimuli. Similar patterns have been observed in physically healthy but anxiety-prone subjects (Kret et al., 2011). For example, Stein et al. (2007) showed that higher scores on several measures assessing anxiety proneness including neuroticism, trait anxiety, and anxiety sensitivity, were all associated with greater activation of the amygdala. The three meta-analyses also showed over-activation of the anterior cingulate cortex in comparison to healthy controls. In healthy individuals, the anterior cingulate cortex is highly activated during the anticipation of pain (Straube, 2009). Etkin and Wager (2007) directly compared post-traumatic stress disorder patients with social anxiety disorder patients and found that especially the former group showed marked hyperactivation in this area. A post-traumatic stress disorder often results from the experiencing or witnessing of a stressor event involving life-threatening situations. Activation of the anterior cingulate

cortex may point to compensatory efforts to regulate high anxiety states in anticipation of pain that are evoked by showing patients trauma-related or general emotional stimuli. Recently, Binelli et al. (2014) conducted a meta-analysis on fMRI studies including patients with Williams' syndrome and social anxiety. The findings show that although the amygdala was over-activated in socially anxious patients, patients with Williams' syndrome showed decreased activation of the limbic system and the inferior region of the parietal lobule as compared to controls. Altered activity in the fusiform gyrus was not observed.

The meta-analyses outlined above include both emotion perception and emotion regulation studies. However, several studies have also used neuroimaging methods specifically to identify neural change in brain networks associated to emotion regulation, for example with reappraisal methods. Goldin et al. (2009) examined cognitive reappraisal of social (harsh facial expressions) and physical (violent scenes) threat in social anxiety disorder patients and healthy controls. Regulation during social threat, but not physical threat, was associated with diminished recruitment of brain systems implicated in cognitive reappraisal (dorso-medial and dorsolateral prefrontal cortex, and attention modulation (medial cuneus, posterior cingulate cortex, and parietal cortex) in social anxiety disorder, compared to healthy controls. In another study by this group, using negative self-beliefs, the temporal dynamics of the BOLD response, in addition to its signal magnitude, were analyzed (Goldin et al., 2009). Findings revealed greater early activity in healthy controls during reappraisal of negative self-beliefs in brain networks implicated in reappraisal (dorsomedial, dorsolateral, and ventrolateral prefrontal cortex), language (left inferior frontal gyrus), and visual (precuneus, inferior parietal) processing, while social anxiety disorder patients had greater late responses in dorsomedial and ventrolateral prefrontal cortex, insula, and visual processing regions. These findings suggest a failure to recruit reappraisal-related prefrontal regions in social anxiety disorder.

In a study by Brühl et al. (2013), patients were instructed either to perform 'reality checking' or to simply anticipate and then look at negative, positive, and neutral pictures. Thus, in contrast to the first two studies, which compared patients to healthy controls, this study compared patients applying cognitive control with patients not using cognitive control. The authors found regulation-related reduced activity in emotion reactivity regions (amygdala, insula, thalamus), and in the dorsolateral prefrontal cortex and cingulated cortex, with no regions with increased activity due to cognitive control.

Finally, Ziv et al. (2013) also examined reappraisal-related behavioral and neural responses in generalized social anxiety disorder patients and healthy controls during different socio-emotional tasks. Their results suggest a dysfunction of cognitive reappraisal in social anxiety disorder patients, with overall reduced late brain responses in prefrontal regions, particularly when reappraising faces. Decreased late activity in the dorsomedial prefrontal cortex might be associated with deficient reappraisal and greater negative reactivity. Recently, new methodologies such as measures for functional connectivity have been developed. Brühl et al. (2014) provide a first comprehensive meta-analysis including these more recent techniques. Again, hyper-activation of the fear circuit was shown, but more interestingly, also reduced connectivity between parietal and limbic and executive network regions.

In sum, primarily the typical fear circuit is overactive in anxiety disorders and the emotion regulation areas do have insufficient control to dampen that activity. The disconnection of the medial parietal hub in social anxiety disorder shown by Brühl et al. (2014) extends current frameworks for future research in anxiety disorders. For an overview, see Table 1.

1.5. Mood disorders

In the USA, the lifetime prevalence of mood disorders is 21.4% (Kessler et al., 2012). Mood disorders are characterized by a regular depressed mood, and a loss of interest or pleasure in almost all activities. There are two groups of mood disorders and the division is based on whether a manic or hypomanic episode has ever been present. The most studied disorders are major depressive disorder and bipolar disorder, formerly known as manic depression and characterized by intermittent episodes of mania or hypomania, usually interlaced with depressive episodes. There are also psychiatric syndromes featuring less severe depression known as dysthymic disorder (similar to, but milder than major depressive disorder) and cyclothymic disorder (similar to, but milder than bipolar disorder). Mood disorders may also be substance-induced or occur in response to a medical condition. Nearly 70% of the people with a mood disorder meet the criteria for at least one other mental disorder, including anxiety disorder, substance use disorder and impulse control disorder (Kessler et al., 2003). As with anxiety disorders, there is a strong association between alexithymia and depression in adults (Honkalampi et al., 2000) and in adolescents (Ciarrochi et al., 2008; Honkalampi et al., 2009).

1.5.1. Emotion processing deficits in mood disorders

Mood disorders are characterized by impaired emotion regulation. Sustained negative affect and a persistent reduction in positive affect are the hallmark features of a diagnosis of a major depressive episode. Indeed, it has been suggested that depression vulnerable and non-vulnerable people do not differ primarily in their initial response to a negative event, but in their ability to recover from the ensuing negative affect (e.g., Teasdale, 1988). As compared to healthy individuals, patients more frequent use of certain strategies (e.g., expressive suppression, thought suppression, rumination, catastrophizing) and less frequent use of other strategies (e.g., reappraisal, self-disclosure) is related to levels of symptoms of depression and anxiety (e.g., Campbell-Sills et al., 2006; Garnefski and Kraaij, 2006; Gross and John, 2003). In addition, it has been suggested that impaired emotion regulation not only characterizes currently depressed people, but is also evident following recovery from this disorder (Ehring et al., 2008).

Impaired perception of expressions of emotion has been proposed as a candidate marker for depression that may contribute to the vulnerability for negative emotion and onset of depressive episodes (Chan et al., 2008; Mikhailova et al., 1996; Leppanen, 2006). Most frequently, individuals susceptible to depression have been characterized as exhibiting negative attentional biases toward emotional information (e.g., Atchley et al., 2003; Bradley et al., 1997; Siegle et al., 2002). This negative bias can be seen through increased attention directed at negative stimuli (Rottenberg et al., 2005), as a failure to attend sufficiently to positive information or been interpreted as failing to block negative information from interfering with a mental task (e.g., Joormann, 2004). The results and interpretation of results is somewhat mixed, and although researchers have tried to find evidence for a differential deficit for specific emotions that relate to clinical symptoms, i.e. happy and sad, a recent meta-analysis suggests that the impairment is more general (Kohler et al., 2011). This meta-analysis on emotion perception studies in bipolar disorder and major depressive disorder revealed a moderate deficit in emotion perception in both disorders, irrespective of the task, the specific emotion being shown, diagnosis, age of onset/duration of illness, sex, and hospitalization status. Several factors moderated the observed impairment including self-reported depression, age at time of testing, and years of education. It must be noted however, that the analysis of individual emotions was limited by small sample sizes and possibly therefore failed to reveal that mood disorders, both overall and according

Table 1
Meta-analyses on emotion processing in clinical groups vs. controls. See ref. Li et al., 2010.

2007-2014	Disorder	Stimuli	Analysis	Results
		Anxiety disorders		
Etkin & Wager, 2007	Post-Traumatic Stress Disorder Social anxiety Disorder Specific phobia	Emotional	Voxel-wise PET & fMRI N = 40	**Negative:** Amygdala; Insula **SAD and SP vs. Post-Traumatic Stress Disorder:** Amygdala; Insula; rostral ACC; VmPFC; d. ACC; Thalamus
Hayes et al., 2012	Post-Traumatic Stress Disorder	Cognitive–Emotional	ALE N = 26	r. Mid- / d. ACC; l. STG; l. SMA; Amygdala; r. MFG; r. vmPFC; Thalamus; r. IFG; l. MOG; r. MFG; r.MTG r. Precuneus; r. Cerebellum; r. MFG; l. Fusiform; l. STG; l. d. ACC; l. SFG [vmPFC-Amygdala]
Hattingh et al., 2013	Social Anxiety Disorder	Facial expressions and emotional statements	ALE N = 7	Amygdala, l. medial temporal lobe encompassing entorhinal cortex, l. medial inferior temporal lobe encompassing perirhinal cortex and parahippocampus, r. ACC, r. globus pallidus, r. postcentral gyrus
Brühl et al., 2013	Social Anxiety Disorder	Disorder -specific stimuli and general emotional stimuli	ALE N = 40	**Specific emotional stimuli:** Amygdala; Insula; MPFC; VLPFC; ACC; parC **General emotional stimuli:** Amygdala; Insula; l. DLPFC; temporal, parietal and occipital cortex; Thalamus **After vs. before Treatment**: decreased activation in occipital and temporal cortex
Binelli et al., 2014	Social Anxiety Disorder Williams syndrome	Facial expressions	ALE N = 22	**Social Anxiety Disorder > control:** l. Amygdala/parahippocampal gyrus; l. entorhinal cortex; r. globus pallidus; r. subcallosal gyrus; r. insula; mPFC; l. putamen; l. STG; l. cuneus **Williams > control**: r. IPL; r. amygdala; r. parahippocampal gyrus; r. globus pallidus
		Mood disorders		
Chen, et al., 2011	Bipolar Disorder	Cognitive–Emotional	ALE N = 65	**Emotion:** Medial Temporal Lobe, Putamen, Pallidum; IFG
Delvecchio et al., 2012	Bipolar Disorder Major Depressive Disorder	Facial expressions	ALE N = 20	**Fear:** Bipolar l. Parahippocampal Gyrus (BA 28/35), l. Putamen; Thalamus; IFG (BA47/45); l. anterior cingulate cortex (BA32) Major Depressive Disorder l. Precentral Gyrus **Happy:** Bipolar Caudate; l. Parahippocampal Gyrus; r. anterior cingulate cortex Major Depressive Disorder r. Thalamus
Diener, et al., 2012	Major Depressive Disorder	Cognitive–Emotional	ALE N = 40	**Emotional:** Mid Occipital (BA 19, 31) Posterior Lobe, Postcentral (BA 40), a. Insula (BA 13); l. Medial Frontal (BA 6); r. Paracentral (BA 31); anterior cingulate cortex (BA 32); r. IFG (BA9) r. SFG (BA6), Lateral Globus Pallidus; STG (BA39); Thalamus; Striatum; Caudate **Fear:** SFG (BA 6) **Sad:** Thalamus **Positive:** Thalamus; Caudate; Lateral Globus Pallidus **Negative:** Parahippocampal Gyrus
Groenewold et al., 2012	Depression	Positive-Negative valence face/no face	parametric voxel-based meta-analysis N = 44	**Negative:** Amygdala; Striatum, Parahippocampal Gyrus; Cerebellar; Fusiform; ACC; dlPFC **Positive:** Amygdala; Striatum; Parahippocampal Gyrus; Cerebellar; Fusiform; ACC; OFC
Hamilton et al., 2012	Major Depressive Disorder	Positive-Negative valence	Voxel-wise rCBF & fMRI N = 38	**Negative:** r. Amygdala; l. d. ACC; l. Insula; l. TG; l. Precentral Gyrus; l. Middle Temporal Gyrus **Positive:** r. subcallosal gyrus; d.l. PFC; l. parahippocampal gyrus; r. d. ACC; r. Caudate/putamen; l. Cerebellar Uvula
Zhang et al., 2013	Major Depressive Disorder	Reward	ALE N = 22	**Reward: depressed > control:** Caudate; l. Thalamus; Cerebellum; r. Putamen; l. ACC; r. Insula; Cuneus; r. frontal lobe; MFG; l. SFG; l. FG; r. lingual gyrus **Positive: depressed > control:** Cerebellum; l. ACC; r. lentiform nucleus; l. Caudate; r. Thalamus; l. lingual gyrus; l. parahipposcampal gyrus; FG

Table 1 (*Continued*)

Ma, 2014	Mood Disorder	Positive-Negative valence	ALE N = 60	**Positive, antidepressant > control:** Amygdala; r. dlPFC; l. Hippocampus; r. vmPFC; r. ACC; l. Fusiform; l. vmPFC; l. Precuneus; l. Insula; Insufficient studies for the opposite contrast **Negative, antidepressant > control:** l. dlPFC **Negative, antidepressant < control:** Amygdala; r. Hypothalamus; l. Putamen; l. Middle Temporal; r. ACC; r. Insula; l. Middle Frontal
Schizophrenia				
Li et al., 2010	Schizophrenia	Facial expressions	ALE N = 15	Parahippocampal gyrus/Amygdala; Fusiform; r. SFG, r. Lentiform Nucleus; l. Insula
Sugranyes et al., 2011	- Autism Spectrum Disorders - Schizophrenia	Facial expressions	ALE N = 33	**Autism** l. STG; l. Postcentral **Schizophrenia** r. IFG; r. PCC; l. Amygdala; r. Fusiform; l. Thalamus
Taylor et al., 2012	Schizophrenia	Emotion perception/ experience	ALE N = 26	**Emotion:** l. Amygdala; l. Hippocampus; Thalamus; r. anterior cingulate cortex (BA 24/32); r. Dorsolateral Frontal (BA 44), r. Medial Frontal (BA 8); r. a. TP (BA 38); r. Caudate; r. STG (BA 22); Midbrain; r. Fusiform (BA 37); OP.; l. Cerebellum; l. Cuneus (BA 19); l. Parietal Lobule (BA 2); r. Precentral Gyrus (BA 6); l. STG (BA 21)
Delvecchio et al., 2012	- Schizophrenia - Bipolar disorder	Facial expressions	ALE N = 29	**Schizophrenia:** r. Cuneus, l. Medial Frontal (BA 9), l. Precentral (BA 6), l. Parahippocampal (BA 28), l. anterior cingulate cortex (BA 32), r. Amygdala, r. Insula (BA 13) **Bipolar:** parahippocampus/Amygdala; l. Thalamus ventrolateral prefrontal cortex (BA 47, 44), l. anterior cingulate cortex (BA 32), r. Caudate
Autism				
Sugranyes et al., 2011	- Autism Spectrum Disorders - Schizophrenia	Facial expressions	ALE N = 33	**Autism** l. STG; l. Postcentral **Schizophrenia** r. IFG; r. PCC; l. Amygdala; r. Fusiform; l. Thalamus
Binelli et al., in press	Social Anxiety Disorder Williams syndrome	Facial expressions	ALE N = 22	**Social Anxiety Disorder > control:** l. Amygdala/parahippocampal gyrus; l. entorhinal cortex; r. globus pallidus; r. subcallosal gyrus; r. insula; mPFC; l. putamen; l. STG; l. cuneus **Williams > control**: r. IPL; r. amygdala; r. parahippocampal gyrus; r. globus pallidus
Borderline				
Ruocco et al., 2013	Borderline	Emotion	ALE N = 11	**Negative:** r. Amygdala; r. STG; DLPFC; r. ACC; r. Insula; r. PCC; l. DLPFC
Mitchell et al., 2014	Borderline	Facial expressions	N = 7	Amygdala, ACC, IFG, STS
Eating disorders				
Zhu et al., 2012	Eating disorders	Food, body, emotion	ALE N = 17	**Emotion:** - **Food:** r. Medial Frontal, r. Caudate, l. Inferior Parietal **Body:** l. Limbic, l. ST, postcentral parietal, l. Inferior Parietal

This table gives an overview of meta-analytical studies in different patient groups concerning fMRI studies on emotion processing. Results are grouped per disorder and presented in the order of year of publication.

Studies that include multiple disorders appear multiple times in the table (i.e. Delvecchio et al. (2012) appear under 'Schizophrenia', but also under 'Mood disorders'.

Clinical group > Control group Control group > Clinical group
Abbreviations of brain areas: anterior cingulate cortex = anterior cingulate cortex; IFG = inferior frontal gyrus; MFG = medial frontal gyrus; MOG = middle occipital gyrus; SFG = superior frontal gyrus; ST(G) superior temporal (gyrus); OP = occipital pole; parC = parietal cortex; PCC = posterior cingulate cortex; SFG = superior frontal gyrus; SMA = supplementary motor area; TP = temporal pole
Abbreviations of locations: a. = anterior; BA = Brodmann area; d. = dorsal l. = left hemisphere; r. = right hemisphere
Other abbreviations: ALE = Activation Likelihood Estimation; HC = healthy controls; N = number of studies included in the meta-analysis.

to separate groupings, may induce a perception bias of a specific emotion.

1.5.2. fMRI research on emotion processing deficits in mood disorders

In the past 5 years, different meta-analyses have been conducted on major depression and bipolar disorder in relation to emotion processing. These studies showed over-activation of the amygdala, along with the parahippocampal gyrus and striatum, especially when processing negative signals (Chen et al., 2011; Delvecchio et al., 2012; Diener et al., 2012; Groenewold et al., 2012; Hamilton et al., 2012). In response to positive expressions, or otherwise rewarding stimuli, under-activation is commonly observed (Zhang et al., 2013).

Different theoretical models have been proposed to account for these findings. In the limbic-cortical model of depressed mood, over-activity in limbic areas (including the hippocampus) is not adequately controlled by prefrontal areas (Mayberg et al., 1999). The rostral and subgenual regions of the anterior cingulate cortex are believed to play a key mediatory role in this network (Disner et al., 2011; Seminowicz et al., 2004). In an alternative model, more emphasis is laid on the role of subcortical structures in the etiology of depression. The concept of parallel, overlapping, cortico–striato–pallidal–thalamic loops was introduced by Alexander et al. (1986). Circuits extend from the striatum to prefrontal and limbic regions and are involved in distinct functions including cognitive and emotional processing and motor control. Striatal dysfunction in particular has been associated with symptoms of major depression including anhedonia and psychomotor retardation and gray-matter volume reductions have been shown throughout regions of this network in major depressive disorder (Bora, 2012).

Alterations in the default network (including medial prefrontal regions, precuneus, lateral parietal cortex and the lateral temporal cortex) has been proposed as yet another model for depression. Patients frequently score highly on scales of negative mood valent rumination (Mor and Winquist, 2002), with associated heightened depressive symptom load and hyperactivity in the default mode network (Pizzagalli, 2011). These areas show increased activity at rest in current major depressive disorder (Greicius et al., 2007) along with a failure to deactivate normally during task conditions (Shulman et al., 1997). This model, based on a cognitive rumination process, is thought to best represent a state-dependent feature and may, in part, account for the maintenance of an episode.

To get more insight into these different theoretical accounts, Graham et al. (2013) conducted a meta-analyses and included not only emotional, but also cognitive tasks which is important to ascertain that deficits are specific for processing emotions or are more general. The results of their meta-analysis support the limbic-cortical and cortico-striatal models but not the default mode network. The authors also note that treatment-sensitive regions were primarily in lateral frontal areas but did not further specify the type of treatment that was used. As antidepressants are widely used in the treatment of mood disorders and influence emotional processes, Ma (2014) conducted yet another meta-analysis including pharmacological neuroimaging studies to investigate the antidepressant effects on human brain activity underlying emotional processes. Specifically, results show that for both patients and healthy volunteers, the medial prefrontal and core limbic parts of the emotional network (anterior cingulate, amygdala and thalamus) were increased in response to positive emotions but decreased to negative emotions by repeated antidepressant administration. In patients, antidepressants increased activity in the dorsolateral prefrontal cortex, a key region mediating emotion regulation, during both negative and positive emotions. In healthy volunteers, repeated antidepressant administration decreased brain responses to positive emotions in the nucleus accumbens, putamen, medial prefrontal and midbrain. The author concludes that antidepressants can be administered to normalize neural responses in depressed patients by increasing brain activity to positive stimuli and decreasing activity to negative stimuli in the emotional network, and increasing engagement of the regulatory mechanism in the dorso-lateral prefrontal cortex. For an overview, see Table 1.

The meta-analysis by Ma (2014) was limited to regional activation changes (as revealed by task and antidepressant vs. control comparisons). Studies focusing on functional connectivity, structural, resting-state or brain–behavior correlations were excluded, but there are several of those studies that report on altered connectivity between different brain regions. For example, Anand et al. (2007) observed decreased cortico-limbic *connectivity* in people with mood disorders when observing emotional stimuli and that antidepressant treatment can re-establish this connectivity. In line with that study, Vizueta et al. (2012) observed that bipolar patients exhibited reduced negative functional connectivity between the right amygdala and the right orbitofrontal cortex as well as the right dorsolateral prefrontal cortex relative to healthy comparison subjects. A substantive meta-analysis of these connectivity findings related to emotion processing is still missing.

1.6. Schizophrenia

Schizophrenia is characterized by abnormalities in the perception or expression of reality, such as delusions and hallucinations. Onset typically occurs in young adulthood, with 0.4–0.6% of the population being affected (Bhugra, 2005). Genetics and early environment, as well as psychological and social processes, appear to be important contributory factors. Some recreational and prescription drugs appear to cause or worsen symptoms. The many possible combinations of symptoms have triggered a debate about whether the diagnosis represents a single disorder or a number of separate syndromes or even separate disorders, as is suggested by a recent genetic study (Arnedo et al., 2015). People with schizophrenia are likely to have additional disorders, including major depression and anxiety disorders; the lifetime occurrence of substance use disorder is almost 50% (Buckley et al., 2009).

1.6.1. Emotion processing deficits in schizophrenia

Distortions in perception most commonly manifest as auditory hallucinations, paranoia, and bizarre delusions, or disorganized speech and thinking and may lead to social withdrawal or isolation, sloppiness of personal hygiene, and loss of motivation. There is often an observable pattern of emotional difficulty, for example lack of responsiveness, impairment in social cognition and paranoia (Hirsch and Weinberger, 2003). However, although the expression of emotions is impaired in schizophrenia, evidence is accumulating that the subjective emotional experience may not be reduced and that even more intense negative emotions are experienced (Myin-Germeys et al., 2000). Van't Wout et al. (2007) observed that schizophrenic patients have difficulties identifying and verbalizing emotions, especially in the face of a higher subjective emotional arousal, which is a characteristic of alexithymia. Non-affected siblings showed comparable problems in verbalizing their emotions as the patients.

Kapur (2003) proposed that schizophrenia is a disorder of aberrant salience: psychosis often starts with a feeling of increased awareness and emotionality, due to an increased release of dopamine, followed by the assignment of salience to stimuli that other people perceive as normal. These aberrant saliences eventually lead to psychosis when they are maintained in the absence of the original stimuli.

This aberrant salience has been found in many different empirical tests, including those of emotion processing. People with schizophrenia often find facial emotion recognition difficult (Kohler et al., 2011). Impaired recognition of facial expressions (Edwards et al., 2001; Feinberg et al., 1986; Whittaker et al., 2001) and prosody (Edwards et al., 2001) and a correlation between emotion recognition accuracy and specific symptoms (Kohler et al., 2000) and the chronicity of illness have been reported (Mueser et al., 1997). Other studies have suggested a greater differential impairment in negative affect recognition (Bell et al., 1997) including a superior ability in paranoid as compared to non-paranoid groups in negative affect identification (Kline et al., 1992). People with persecutory delusions demonstrated specific abnormalities in their viewing strategies for social scenes, more often depicting ambiguous rather than explicitly threatening information (Phillips

et al., 2000). Moreover, people with schizophrenia show deficits in emotion identification from body shapes and movements (Bigelow et al., 2006).

Some studies have reported deficits in the categorization of emotional voices, and correlations between deficits in hearing and seeing emotions (De Gelder et al., 2003; De Jong et al., 2009; Hendrick et al., 2001; Suri et al., 2001). In the healthy population, a vocal emotional expression influences the categorization of a facial expression (De Gelder et al., 1995) and vice versa (De Gelder and Vroomen, 2000). In people with schizophrenia, the multisensory integration of facial and vocal emotional information is impaired (De Jong et al., 2009). Vaskinn et al. (2007) presented facial expressions and spoken emotional sentences for identification and discrimination in groups of participants with schizophrenia, bipolar disorder and healthy controls. Visual emotion perception was unimpaired in both clinical groups, but the schizophrenia sample showed reduced auditory emotion perception (Altshuler et al., 2004). In another study compared people with schizophrenia were compared with people with bipolar disorder and controls in an emotion and age facial recognition task. Results showed that people with schizophrenia had deficits in recognizing angry faces as compared to healthy controls and people with bipolar disorder. Compared to control participants, people with schizophrenia and bipolar disorder were more likely to mislabel facial expressions of anger as fear (Goghari and Sponheim, 2012).

Recently, Barkl et al. (2014) conducted a meta-analysis of studies of facial emotion identification in early-onset and first-episode psychosis. Findings suggest that patients with early-onset and first-episode psychosis have impairment in identifying facial expressions of emotion. Across the twelve studies that were included, the onset of psychosis was distinguished by a generalized effect of significantly poorer accuracy for identifying facial expressions of emotion than healthy controls. Moreover, some emotions were harder for patients to identify than others, with the magnitude of impairment found to be large for disgust, fear and surprise, and medium for sadness, and happiness. No between groups mean differences were found for anger or neutral facial expressions. In another recent meta-analysis encompassing a larger number of case–control studies with different emotion paradigms, O'Driscoll et al. (2014) found distortions in emotion management and cognitive reappraisal along with increased experiential avoidance, attentional deployment, dissociation and alexithymia.

However, it must be noted that these difficulties might not be specifically related to emotional expressions, as difficulties in working and long-term memory, attention, executive functioning, and speed of processing are also observed more generally (Van Os and Kapur, 2009). That notwithstanding, emotion processing has become a high priority area in schizophrenia research.

1.6.2. fMRI research on emotion processing deficits in schizophrenia

Three meta-analyses showed that compared to controls, people with schizophrenia showed less involvement of the fusiform gyrus, amygdala and basal ganglia during emotion processing, areas commonly activated in face perception (Li et al., 2009; Taylor et al., 2012; Delvecchio et al., 2012). These meta-analytical accounts suggest that schizophrenia is associated with functionally important abnormalities in face processing in the domains of emotion recognition and complex social judgments. For an overview, see Table 1.

Michalopoulou et al. (2010) aimed to identify brain regions associated with reality distortion syndrome reduction in a group of patients with schizophrenia during processing of emotionally salient stimuli. The distortion of reality is characterized by hallucinations and delusions. To this extent, authors analyzed BOLD responses during an implicit emotional task. Patients were scanned twice with an interval of 6–8 weeks. The results show that reality distortion syndrome reduction was associated with increases in the activation of the affective division of the anterior cingulate and lateral prefrontal cortices. These findings may indicate that changes in the activation of these regions during processing of emotionally salient stimuli may represent neural markers of patients' symptomatic improvement.

A recent study by Mukherjee et al. (2012) suggests that there are also impairments in brain-connectivity. When looking at fearful compared to neutral faces, people with schizophrenia showed significantly reduced effective connectivity from the amygdala to the theory-of-mind network (i.e., the network involved when attributing mental states to other people, which includes the precuneus and temporo-parietal lobe), compared to healthy controls. In addition, in comparison to control participants, individuals with schizophrenia over-activated the superior frontal gyrus and middle frontal gyrus when making judgments of approachability from faces. These are key brain regions involved in cognitive control. Both brain regions have frequently been implicated in the pathology of schizophrenia by both structural and functional studies (Honera et al., 2005; Barch and Ceaser, 2012; Callicott et al., 2003). Notably, previous studies have suggested that these regions may be linked to emotion regulation (Mak et al., 2009) and increased activation of regions, including the dorsolateral prefrontal cortex has been demonstrated in patients with schizophrenia when greater emotional load impacts on cognitive processing (Becerril and Barch, 2011). Mukherjee et al. (2012) therefore suggest that the greater activation of this cognitive network in patients with schizophrenia may reflect a compensatory response to the joint cognitive and emotional demands of the social task.

The majority of theory-of-mind studies asked participants to retrospectively attribute mental states to others. In addition, behavioral studies have revealed slower theory-of-mind performance reaction times in patients with schizophrenia, and it is possible that time may have an impact on fMRI activation patterns. Pedersen et al. (2012) used a novel animated task to investigate implicit mentalizing online. In their study, the authors applied the "Moving Shapes" paradigm, which involves two interacting triangles, to an fMRI block design and investigated the neural activation patterns of schizophrenia patients with matching healthy control subjects. The first and second halves of each video were analyzed separately to assess time-related differences. The results of this study showed that patients with schizophrenia had predominantly increased activation in theory-of-mind-related brain areas during the second half of the theory-of-mind paradigm, whereas the activation in areas of the theory-of-mind-network in healthy controls occurred during the first half of the presentation. This observation of slower cognitive processing in patients with schizophrenia during mentalizing might explain some of the contradictory imaging findings in these patients and have implications for cognitive remediation.

1.7. Autism spectrum disorders

Autism spectrum disorders are neurodevelopmental disorders that have an early onset and involve impairments in social and communication skills, as well as repetitive and stereotyped behaviors. The prevalence of autism spectrum disorders is approximately 1% and it occurs four to five times more often in boys than girls (Elsabbagh et al., 2012). Autism spectrum disorders often co-occur with other psychiatric disorders, including ADHD (Leyfer et al., 2006) and anxiety (Van Steensel et al., 2011) in children and anxiety and mood disorders in adults (Buck et al., 2014).

1.7.1. Emotion processing deficits in autism

People with autism spectrum disorders have severe problems in regulating their emotions and in recognizing emotions of

others. Research has shown that people with autism attend less to faces than controls, but when they do, perceptual processes and exploratory ocular movements focus much on irrelevant features (Senju and Johnson, 2009; Spezio et al., 2007). They have deficits in the recognition of emotion, identity, gender and age from faces (Celani et al., 1999) and emotion from bodies but have no difficulties in recognizing actions and object manipulations (Hubert et al., 2007). Riby and Hancock (2009) tracked eye gaze of children with autism and those with Williams' syndrome when they were looking at pictures and videos of socially relevant scenes. Children in the autism group spent less time looking at faces than normally developed children. On the contrary, children with Williams' syndrome spent more time than controls on looking at faces. The authors conclude that these different visual preferences for important social information might indicate that both groups interpret the social cues differently. In a study in which people with autism and schizophrenia were compared, it was observed that both attended less to faces than healthy controls. People with schizophrenia, like healthy controls, oriented to informative face regions but showed a delay in this orienting (Sasson et al., 2007). The abnormal viewing patterns in the autism group may be related to the complexity of the stimuli or the extent to which they contain socially relevant information. No looking pattern differences between individuals with autism and a control group were observed in an experiment in which both groups observed a non-emotional speaking face. Interestingly, whereas the control group blinked when the speaker blinked, such blink synchrony was absent in the autism group (Nakano et al., 2011). However, caution should be taken when addressing these deficits to autism directly, as a recent study found that the emotional symptoms of autism co-occur with alexithymia. It has even been suggested that the existing diagnostic criteria may need to be revised (Cook et al., 2013). Alexithymia clearly is a factor that should be taken into account when testing these patients.

1.7.2. fMRI research on emotion processing deficits in autism

Research suggests that people with autism have reduced neural sensitivity to emotional cues such as facial expressions and abnormally localized regions of face sensitivity. A meta-analysis comparing autistic and schizophrenic patients with controls reported reduced activity in autistic individuals in the left amygdala, thalamus and the right fusiform and inferior frontal gyrus (Sugranyes et al., 2011). Earlier studies already hinted toward an under-recruitment of the fusiform gyrus during emotion perception and this meta-analysis partly supports that earlier work. More specifically, the results of several earlier studies suggested that a particular area within the fusiform gyrus, i.e., the fusiform face area is underdeveloped in autism (Critchley et al., 2000; Hubl et al., 2003; Pierce et al., 2001; Schultz et al., 2000). For an overview, see Table 1.

Several contradicting results have been published, which may be due to different tasks and differences in eye-gaze patterns in autism as compared to healthy controls. The relevance of this characteristic to fMRI studies of autism has been identified; a correlation has been observed between time spent fixating on the eyes and activation in the fusiform gyrus and amygdala (Dalton et al., 2005; see also Adolphs et al., 2005). Nonetheless, a recent study showed that people with autism failed to engage the subcortical brain regions involved in face detection while fearful faces were presented subliminally, which points to a core mechanism for impaired socio-emotional processing in autism, independent of looking patterns (Kleinhans et al., 2011).

Over the past three decades, a number of theories have been put forward to account for the pervasive social impairments found in autism. The idea of a core deficit in social cognition (theory-of-mind skills and accompanying neural networks) has become one of the most prominent accounts of this disorder. Concomitantly, the impact of motivational factors on the development of social skills and social cognition has received recent attention in 'the social motivation theory' of autism (Chevallier et al., 2012). According to this theory, autism can be construed as an extreme case of diminished social motivation. More specifically, they state that in autism, there appears to be an overall decrease in the attentional weight assigned to social stimuli in general. Diminished social orienting, social reward and social maintaining are all found in autism and can account for a range of behaviors, including cascading effects on the development of mature social cognitive skills. These deficits appear to be rooted in biological disruptions of the orbitofrontal-striatum circuitry. Decreased (motivated) attention to social stimuli such as emotional expressions of others might explain why individuals with autism find it difficult to understand the emotions of others.

1.8. Borderline personality disorder

With a prevalence ranging from 1.4% to 5.9% in the normal population (Aragones, 2012), borderline personality disorder is the most common personality disorder. Prevalence rates increase up to 20% for psychiatric outpatients (Korzekwa et al., 2008) and up to 40% for inpatient settings (Grilo et al., 1998). The most essential feature of this disorder is a pattern of marked impulsivity and instability of affects, interpersonal relationships and self-image. The pattern is present by early adulthood and occurs across a variety of situations and contexts (Leichsenring et al., 2011). Comorbidity with other mental disorders is high; nearly 85% of the patients meet the criteria of other disorders, especially substance use, mood and anxiety disorders (Grant et al., 2008).

1.8.1. Emotion processing deficits in borderline personality disorder

Borderline personality disorder is sometimes also being referred to as 'emotionally unstable personality disorder' or 'emotional intensity disorder' and is, as these alternative names already suggest, characterized by severe and persistent emotional, cognitive, behavioral and interpersonal impairments. People with this disorder feel emotions more easily, more deeply and for longer than others do. Emotions may repeatedly resurge and persist for a long time. Consequently, it may take much longer than normal before borderline personality disorder patients return to a stable emotional baseline following an intense emotional experience (Linehan, 1993). Their disrupted emotion regulation is linked to self-injurious and suicidal behavior and can radically impede treatment engagement (Brodsky et al., 2006).

This emotional hypersensitivity has been related to social-cognitive perceptual biases, including heightened sensitivity to social cues that might signal threat or rejection and impaired facial emotion recognition and may contribute to social disturbances in borderline personality disorder (Linehan, 1993). In accordance with this notion, a number of behavioral studies have revealed a pattern of alterations in facial emotion recognition associated with this disorder: subtle impairments in basic emotion recognition, a negativity or anger bias, and a heightened sensitivity to the detection of negative emotions. New et al. (2012) found that alexithymia is elevated in patients with borderline personality disorder. Daros et al. (2012) conducted a small meta-analysis on emotion perception studies in this patient group. They found that patients were less accurate than controls in recognizing facial displays of anger and disgust, although their most pronounced deficit was in correctly identifying neutral (no emotion) facial expressions. These results could not be accounted for by speed/accuracy in the test-taking approach of borderline personality disorder patients (Daros et al., 2012). Mitchell et al. (2014) conducted a somewhat larger meta-analysis of this literature and concluded that there is consistent evidence supporting a negative response bias

to neutral and ambiguous facial expressions in patients. However, findings for negative emotions were mixed with evidence from individual studies of an enhanced sensitivity to fearful expressions and impaired facial emotion recognition of disgust, while meta-analytically, no significant recognition impairments between borderline personality disorder and healthy controls were observed for any negative emotion. The authors recommend that future studies must address methodological inconsistencies between the experiments from all these different research groups, and in particular in the variations in patients' key clinical characteristics. In line with these recommendations, it has indeed been shown that participants with high borderline personality disorder *traits* identified more negative mental states to affective eye stimuli than those with low borderline personality disorder traits (Scott et al., 2011), a finding consistent with data from basic emotion recognition paradigms (Unoka et al., 2011). These data suggest that future studies should include and quantify degree of disorder-related dysfunction, including nonclinical populations with borderline personality disorder traits as this would allow a dose response relationship to be explored (Trull et al., 1997).

To conclude, it has been suggested that emotional hyperreactivity interferes with emotion perception including facial emotion recognition, thereby contributing to the specific pattern of altered emotion recognition in borderline personality disorder (Domes et al., 2009).

1.8.2. fMRI research on emotion processing deficits in borderline personality disorder

Early functional imaging work linked facial emotion processing deficits to heightened amygdala activity (Donegan et al., 2003; Minzenberg et al., 2007). More recent work also considers functional connectivity across distributed anatomical and functional networks that underpin the functional deficits in emotional processing in this disorder. Thus far, two meta-analyses have been conducted on the neural mechanisms underlying emotion perception deficits in people with borderline personality disorders. The first study, by Ruocco et al. (2013) showed that, compared to healthy control subjects, borderline personality disorder patients demonstrated greater activation within the insula and posterior cingulate cortex. Conversely, they showed less activation than control subjects in a network of regions that extended from the amygdala to the subgenual anterior cingulate and dorsolateral prefrontal cortex. Mitchell et al. (2014) come to a very different conclusion. Their meta-analysis shows that the underlying neural substrate involves *hyper*-activation in the amygdala to affective facial stimuli, and altered activation in the anterior cingulate, inferior frontal gyrus and the superior temporal sulcus particularly during social emotion processing tasks. This strikingly different effect, especially with regard to the amygdala is probably related to the huge varability in task designs and/or related to differences in sample characteristics. Ruocco et al. (2013) included a smaller number of studies, and only included those where emotional faces were compared with neutral faces, and not with alternative control conditions such as objects or shapes.

Several independent studies compared the connectivity between different brain areas in patient and control groups. The majority of these studies à priori focused on connections between the prefrontal cortex and limbic regions (Anand et al., 2009; Anticevic et al., 2013; Chai et al., 2011; Chepenik et al., 2010; Mamah et al., 2013; Torrisi et al., 2013) because aberrant frontal-limbic functioning has been repeatedly implicated in the pathophysiology of borderline disorder, and is thought to drive the resulting emotion dysregulation (Townsend and Altshuler, 2012). With a slightly different approach, Koenigsberg et al. (2014) examined the behavioral and neural correlates of habituation in borderline patients and observed that those with a borderline personality disorder exhibited smaller increases in insula–amygdala functional connectivity than healthy subjects and, unlike healthy subjects, did not show habituation in ratings of the emotional intensity of the stimulus material.

Hence, processing of negative emotions in borderline personality disorder might be subserved by an abnormal reciprocal relationship between limbic structures representing the degree of subjectively experienced negative emotion and anterior brain regions that support the regulation of emotion (Cullen et al., 2011). For an overview, see Table 1.

1.9. Eating disorders

Eating disorders are psychological illnesses defined by abnormal eating habits that may involve either insufficient or excessive food intake to the detriment of an individual's physical and mental health. The most common eating disorders are anorexia nervosa and bulimia nervosa. Anorexia nervosa is characterized by a classic triad of amenorrhea, weight loss, and psychiatric disturbance (Klein and Walsh, 2003). Bulimia nervosa is often related to previous anorectic behavior and is characterized by periods of severe food restriction and gorging. Some eating disorders are classified as an eating disorder not otherwise specified and may be associated with excessive exercise. The precise cause of eating disorders is not entirely understood, but there is evidence that it may be linked to other medical conditions and situations. Cultural idealization of thinness and youthfulness has contributed to eating disorders affecting diverse populations. Several studies suggested a relationship with post-traumatic stress disorder, especially due to a sexually related trauma (Reyes-Rodriguez et al., 2011). Comorbidity with other mental disorders is high, especially with impulse control, mood and anxiety disorders (Hudson et al., 2007).

1.9.1. Emotion processing deficits in eating disorders

Anorexia nervosa has been associated with impairments in emotion processing (Jansch et al., 2009; Joos et al., 2012) and with alexithymia (Bydlowski et al., 2005; Jansch et al., 2009; Kucharska-Pietura et al., 2004; Pollatos et al., 2008). Disordered eating behavior is often used as a maladaptive strategy to regulate emotion (Haynos and Fruzzetti, 2011). These include emotional avoidance and suppression strategies (Aldao et al., 2010) such as binge eating, excessive exercise, self-induced vomiting and caloric restriction. These strategies are positively reinforced as they lead to a temporary reduction in anxiety and therefore play a role in the disorder's maintenance (Fairburn et al., 2003; Harrison et al., 2009; Schmidt and Treasure, 2006).

A review of emotional processing in people with eating disorders (Oldershaw et al., 2011) concluded that women with anorexia nervosa have difficulties in their ability to infer emotional states in others. Attentional biases toward threatening faces have been reported (Cserjesi et al., 2011; Harrison et al., 2010a; Pollatos et al., 2008). However, conflicting evidence has been published too. In bulimia nervosa, some studies do demonstrate emotion perception difficulties (Harrison et al., 2010a; Pradas et al., 2012) but one study of women with a diagnostic mix of bulimia nervosa did not demonstrate any significant difficulties on the Reading the Mind in the Eyes test (Baron-Cohen et al., 2001) or on a more complex task of emotion recognition in films (Kenyon et al., 2012). Kessler et al., 2006 also did not find any difference between individuals with an eating disorder (either anorexia nervosa or bulimia nervosa) and healthy controls. Similarly, in an emotion decoding study, no significant differences were found between a currently ill (anorexic) and healthy participant group (Mendlewicz et al., 2005).

Kanakam et al. (2013) investigated the role of endophenotypes in emotional processing difficulties related to eating disorders. Twins with and without eating disorders were given the Reading

the Mind in the Eyes test, the Emotional Stroop task and the Difficulties in Emotion Regulation Scale. Results show that emotion recognition difficulties, attentional biases to social threat and difficulties in emotion regulation were greater in twins with vs. without eating disorders, and some were present in the unaffected twin siblings. Evidence for a possible genetic basis was highest for emotion recognition and attentional biases to social stimuli.

Harrison et al. (2010b) conducted a meta-analysis on self-report data regarding anomalies in sensitivity to reward and punishment in eating disorders. The authors found that patients with anorexia nervosa (restricting type) were less sensitive to reward than healthy controls, whereas patients with bulimia nervosa and anorexia nervosa (binge/purge) type were more sensitive. All eating disorder groups reported higher sensitivity to punishment than healthy controls.

1.9.2. fMRI research on emotion processing deficits in eating disorders

Differences in brain dynamics might contribute to difficulties in the recognition of facially expressed emotions, deficits in social functioning, and in turn the maintenance of eating disorders. Imaging studies have revealed different neural responses in visual attention networks and somatosensory areas in people with eating disorders versus controls following high caloric food pictures (Santel et al., 2006) and in the extrastriate body area when attending to photographs of one's own body versus other female bodies (Vocks et al., 2010). Few neuroimaging studies looked at how people with eating disorders process emotional expressions of others. One study showed that people with bulimia nervosa had a decreased neural response in the precuneus to facial expressions of both anger and disgust and a decreased neural response to angry facial expressions in the right amygdala (Ashworth et al., 2011). However, a meta-analytical study that included four fMRI studies on people with anorexia and controls found no difference in activation pattern between the two groups in the emotion perception domain, albeit differences were observed when food or body-related images were processed (Zhu et al., 2012). For an overview, see Table 1.

There are important confounding variables in studies of emotion processing in anorexia nervosa which may explain the conflicting results. One difficulty with anorexia nervosa is that it is difficult to pull apart the effects of underweight and the underlying disease without comparing the clinical group with control participants who also have underweight or with a control group who recovered from their eating disorder (Kaye et al., 2009). One study solved this problem by testing patients with anorexia nervosa who were weight recovered (Schulte-Rüther et al., 2012). In that study, a reduced activation in the middle and anterior temporal cortex and in the medial prefrontal cortex was observed when patients completed a theory-of-mind task. In addition, this hypo-activation of the medial prefrontal cortex was associated with clinical outcome at a 1-year follow up. Cowdrey et al. (2012) investigated whether people recovered from anorexia showed differential brain activation when categorizing the sex of fearful and happy faces than a control group, but did not find support for their prediction There is mixed evidence that patients with eating disorders process emotions differently and some positive findings might be explainable by other factors including, weight, depression, anxiety or social inhibition and isolation.

2. Summary of fMRI results

Emotion processing deficits have been reported in many different disorders and result in attentional biases and impaired recognition of emotional expressions related to problems in emotion regulation, general adjustment, emotional and social functioning, and well-being. On the neural level, research has consistently shown that in anxious and depressed individuals, the amygdala is over-activated and patients with these disorders show reduced coupling with the ventromedial prefrontal cortex when processing threatening information. In contrast, people with autism, schizophrenia and borderline personality disorder are marked by under recruitment of the amygdala. In schizophrenia, a substantial limitation in activation throughout the ventral temporal-basal ganglia-prefrontal cortex has been observed during emotion processing. For an overview of these fMRI results, see Table 1.

3. Discussion

The aim of this article was to provide evidence for the thesis that disrupted emotion processing is a broad liability spectrum which underlies a range of mental disorders and can possibly help to explain the high comorbidity between mental disorders. We found ample evidence for disrupted emotion processing in anxiety disorders, mood disorders, schizophrenia, autism spectrum disorder, borderline personality disorder, and eating disorders. We argue that disrupted emotion processing is a likely liability spectrum underlying these different mental disorders. The liability spectrum of disrupted emotion processing can explain why internalizing and externalizing disorders also show comorbidity. It is consistent with the view that disorders do not represent discrete disease entities, and with the view that the nature of psychopathology is intrincially heterogeneous (Cloninger, 2002; Maj, 2005).

Theoretically, we endorse an evolutionary perspective on emotion processing and its related disorders (e.g., Nesse and Ellsworth, 2009; Nettle and Bateson, 2012; Panksepp, 2010). One possible approach (among many others) has been called 'the smoke detector principle' (Nesse, 2001, 2005). Advocates of this approach argue that emotions serve as detectors. Organisms have to gain knowledge about their environment in order to be able to respond in an appropriate way. The information available is often incomplete or unclear, so organisms have to make decisions with possibly wrong outcomes. The possible wrong outcomes of any detection problem are a false positive and a false negative. It has been hypothesized that people with mental disorders (especially those anxious and/or depressed) have a low threshold for detecting information related to punishment (i.e. a negative outcome) and a high threshold for detecting information related to reward (i.e. a positive outcome). In other words, there is a bias away from positive aspects and toward negative aspects. This is in agreement with the liability spectrum of disrupted emotion processing.

Evidence for the evolutionary roots of emotions as signal detectors comes from a recent comparative fMRI study (Birn et al., 2014). Both children with anxiety disorder and young monkeys (*Macaca mulatta*) showed reduced functional connectivity between the amygdala and the dorsolateral prefrontal cortex, an area associated with the cognitive control of emotions. This study shows that prefrontal-amygdala dysfunction is associated with an evolutionary conserved brain circuit that probably has played an important role in signal detection in a distant evolutionary past. Future studies could investigate the role of this conserved brain circuit in relation to different mental disorders.

3.1. Mechanisms underlying emotion processing deficits across clinical populations

The focus of the current article lies on fMRI research in different patient groups. However, differences between patients and controls have also been observed in brain anatomy, genetics and

hormone levels. We here first provide a short summary of examples of this literature and later on integrate this research and highlight future directions for research.

3.1.1. Anatomical differences between patient groups and healthy controls

Researchers agree that there is no one-to-one mapping between neuronal structures and cognitive functions, and that multiple neuronal systems are capable of producing the same behavioral response. However, functionality does not stand completely separate from anatomy and it is possible that functional differences in brain activity between patient groups are in part reflections of anatomical alterations. For example, Koelkebeck et al. (2013) investigated the association between cerebral gray matter volumes and performance on a theory-of-mind task using voxel-based morphometry in patients with schizophrenia and matching healthy controls. The authors observed that performance deficits in patients on this task were positively correlated with gray matter volume reductions in the superior temporal sulcus and medial prefrontal cortex. These findings suggest that volume reductions impact behavioral deficits in patients with schizophrenia.

Volumetric changes have also been observed following interventions. For example, Messina et al. (2013) conducted a meta-analysis to identify neural change in brain networks associated to emotion regulation after psychotherapy for anxiety and depression. The authors showed that studies on anxiety and depression gave partially consistent results for changes in the dorsomedial prefrontal cortex and in the posterior cingulated gyrus/precuneus. Furthermore, the authors suggest that the cluster of change in the prefrontal cortex may refer to increased recruitment of control processes, as hypothesized by influential models of emotion regulation changes due to psychotherapy.

3.1.2. Genetic predispositions

Epidemiological and genetic studies support the hypothesis that the commonalities in the neurological underpinnings of emotion processing deficits may be related to common genetic factors. The serotonergic system has been widely implicated in stress related psychiatric disorders such as depression and anxiety (Canli and Lesch, 2007). For example, Mekli et al. (2011) observed that the serotonin-1A receptor conveys vulnerability to these disorders by modulating threat-related information processing. The tendency to interpret events negatively has been observed in different clinical populations and is enhanced in those with the serotonin transporter (5-HTT-LPR) short allelic variant. For those with the 5-HTT-LPR short allele, the addition of early life stress contributed to an enhanced negativity bias and effects on heart rate and neural activation for unconscious fear (Williams et al., 2009).

In a review article, Ivleva et al. (2008) focus on psychosis, which is common not only in schizophrenia, but also in other disorders such as bipolar disorder. Psychosis strongly aggregates in families and twin studies suggest high heritability. Whole-genome linkage studies have identified chromosomal loci that influence susceptibility to psychosis, independent of diagnostic categories. Detailed studies of linked genomic regions have identified several putative candidate genes (NRG 1, dysbindin, DISC 1, COMT, G72/G30, BDNF, RGS 4), which appear to be involved in schizophrenia and affective psychoses.

Understanding the biological effect of risk genes is complex. Even though several genes have been found to be implicated in several disorders or symptoms, it is difficult to determine the disease mechanism of each risk gene. Interactions between risk genes and environmental factors add to the complexity of the picture. Future genetic studies, focusing on the symptom dimensions across disorders, are urgently needed and a dimensional approach may help improve understanding the mechanisms of psychiatric illnesses.

3.1.3. Effects of hormones and neuropeptides

Some psychiatric disorders have a different prevalence across males and females. This suggests that deficits in emotion processing are also related to the sex chromosomes (Harmer et al., 2011). Changes in emotion processing abilities across the menstrual cycle and/or in response to ovarian hormone modulation may inform our understanding of the differing prevalence of psychiatric disorders in men and women. Research suggests that ovarian hormones play a crucial role in social cognition including emotional processing (Little et al., 2013). In addition, varying associations between ovarian hormone levels and emotion recognition have been reported, with progesterone levels being negatively correlated with emotion recognition accuracy (Derntl et al., 2008) and estradiol being more specifically associated with anger recognition accuracy (Guapo et al., 2009). Related studies have focused on the role of progesterone in emotion evaluation or attentional bias (Maner and Miller, 2014; Conway et al., 2007). Emotion recognition accuracy is generally lowest during that phase (Derntl et al., 2008; Guapo et al., 2009).

To date, models of psychological disorders have tended to sidestep the influence of ovarian hormones in the development and expression of psychiatric symptoms. Yet it is difficult to ignore epidemiological data showing dramatically increased risk of psychiatric disorders at stages of the reproductive life-cycle associated with sudden and dramatic changes in ovarian hormone levels: adolescence, pregnancy, post-partum and menopause (McEwen, 2002; Carretti et al., 2005). The hormone withdrawal hypothesis of postpartum depression attributes the onset of depressive symptoms to the rapid postpartum withdrawal of the ovarian hormones estradiol and progesterone that occurs during the first five days following childbirth. Indeed, approximately 50–80% of women experience increased mood symptoms during the postpartum period (Bloch et al., 2005). These findings suggest that periods associated with changes in ovarian hormone levels, rather than their absolute circulating levels may be important in the development of psychiatric symptoms. Epidemiological research suggests that the latter part of the luteal phase is associated with a variety of psychological and physical premenstrual symptoms in the majority (up to 75%) of healthy women sampled from the general population (Moran et al., 1998). These symptoms are usually mild, although a proportion of women (up to 18%) suffer significant disruption and impairment associated with Premenstrual Dysphoric Disorder symptoms (Steiner, 1997). Since progesterone levels rise in the early luteal phase, and then fall precipitously in the late phase, the latter epoch may recapitulate the neuroendocrine changes that have been proposed to contribute to symptoms of depression and anxiety (Brummelte and Galea, 2010; Bloch et al., 2000).

A growing body of research has investigated the possible involvement of cortisol, vasopressin, testosterone and oxytocin in the pathophysiology of neuropsychiatric disorders that affect social functioning including emotion processing, such as autism, schizophrenia, anxiety and depression (i.e. De Winter et al., 2003; Goldman et al., 2008; Hammock and Young, 2006). A complete overview of this large literature is beyond the scope of this article. However, it is worthwhile mentioning that there are numerous studies linking oxytocin to the pathophysiology of autism and suggestions have been made to use intranasal administration of oxytocin as a potential therapeutic target for this and other disorders (for a review, see Kret and de Dreu, under review). Cochran et al. (2013) reviewed the literature and conclude that the evidence for the role of oxytocin in a broad range of neuropsychiatric disorders is accumulating, and that further research is needed to

determine the exact nature of its role and to translate these findings into a better understanding of the underlying pathophysiology of the disorders and effective treatment strategies targeting the oxytocinergic system.

3.2. Future directions

In this section, we briefly outline our suggestions for future research. We highlight the question of causality, the relationship between lab studies and emotion processing in daily life, and the clinical relevance of our findings.

3.2.1. Causality

Despite considerable evidence that patients with different disorders have emotion processing deficits that are reflected in certain disrupted brain activity patterns, controversy often persists over what the role of disrupted processing is in our understanding of these diseases. Are connectivity problems or hyper-activation of the amygdala best seen as central, core or primary, or are they one of numerous downstream features of disrupted system performance? Attempts to answer this question have been frustrated by the considerable difficulties involved in studying early development in these disorders, prior to diagnosis. Subjects are often diagnosed long after they developed their symptoms, making causal pathways hard to untangle. Adding genetic analyses might solve part of the puzzle. And as noted earlier, research may be enhanced by comparing different clinical groups with different recovered groups and when on and off medication on the same tasks. Many of the people who were tested in the above studies were taking medication. It is surprising that the majority of studies do not take this into account, considering the effects of antidepressant medication on emotion processing in healthy and depressed participants (Harmer et al., 2008, 2009) and people with eating disorders (Jansch et al., 2009). In addition, other common factors such as physical fitness and environmental factors might be generally different in clinical as compared to control groups. Failure to assess or control for these factors could confound results when comparing emotion processing between clinical and control groups.

3.2.2. Do observations in the lab correspond to emotion processing deficits as observed in real life?

How do emotion processing deficits as observed in a lab-setting translate to deficits during real-world interactions? The majority of studies on emotion processing are emotion perception studies, mostly with a facial expression recognition task. Only a handful of these studies pulled apart emotion perception and emotion regulation or emotional experience. In real life, patients do not get confronted with isolated facial expressions. In real encounters, they observe other people in their natural context, including the whole body context. Very little research has been conducted on the recognition of alternative emotional signals (for example bodily expressions and vocalizations).

In real life, patients are seldom explicitly asked to label emotional expressions of others, yet this is what is most commonly asked during lab experiments. So the majority of tasks were emotion recognition tests, but still with great variety in the specific task settings (the specific emotions, presentation duration of the stimulus material etc.), which makes comparing emotion perception deficits across different disorders difficult. It is therefore recommended that researchers compare the performance of patients versus controls (or other patient groups) on different emotional tasks within a single study. In addition, a comparison on a non-emotional control tasks should be made, in order to rule out or control for general cognitive impairments.

3.2.3. Clinical relevance

Our proposal may have far reaching implications for the clinical practice. An obvious implication is that clinicians should not only use the DSM or other systems for diagnoses, but in addition should look for disrupted emotion processing and alexithymia as clear indicators of mental problems. They may shift their focus to emotion processing and the underlying causes of the deficits. Considering the neural correlates of emotion processing, recently the new clinical approach of neurofeedback has revealed promising results (Johnston et al., 2010; Kim and Birbaumer, 2014). For example, Zotev et al. (2013) found that real-time fMRI neurofeedback resulted in stronger connectivity between prefrontal areas and the left amygdala in healthy participants. In a neurofeedback study with a group of patients with major depressive disorder, it was found that they could self-regulate their amygdala activity, which resulted in a better mood (Young et al., 2014). Positive results with neurofeedback by using quantitative EEG have been reported in children and adolescents with anxiety disorders, depressive disorders, comorbid addiction and ADHD (for a review, see Simkin et al., 2014).

4. Conclusion

Disrupted emotion processing is an important liability spectrum which underlies different mental disorders and can help to explain the high comorbidity between different mental disorders. Advances in our understanding of the features of responding to emotions that are shared across versus unique to specific disorders will require more dimensional approaches. Therefore, future research should attempt to compare the severity and nature of the abnormalities in emotion processing and their neural basis across different clinical groups and integrate new findings with human lesion, genetic and developmental studies. Thus, among the many future avenues, perhaps the most important one right now is to integrate the observations acquired with different paradigms, measurements techniques and clinical samples. To this extent, the field could benefit from an extensive meta-analysis on emotional processing deficits and subsequent brain activity patterns that cover different clinical groups. Such a meta-analysis would not only allow for direct comparisons between patient groups but will also give more insight into effects of certain environmental factors, medication and physical health. Finally, investigations of commonalities and differences in emotion processing across different clinical groups can lead to the development of new diagnostic tools.

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References

Adolphs, R., 2010. What does the amygdala contribute to social cognition? Ann. N. Y. Acad. Sci. 1191 (1), 42–61.

Adolphs, R., Gosselin, F., Buchanan, T.W., Tranel, D., Schyns, P., Damasio, A.R., 2005. A mechanism for impaired fear recognition after amygdala damage. Nature 433 (7021), 68–72.

Aldao, A., Nolen-Hoeksema, S., Schweizer, S., 2010. Emotion-regulation strategies across psychopathology: a meta-analytic review. Clin. Psychol. Rev. 30 (2), 217–237.

Alexander, G.E., DeLong, M.R., Strick, P.L., 1986. Parallel organization of functionally segregated circuits linking basal ganglia and cortex. Annu. Rev. Neurosci. 9, 357–381.

Altshuler, Dudley, R., McGuire, J.A., 2004. Resolution of a paradox: hummingbird flight at high elevation does not come without a cost. Proc. Natl. Acad. Sci. U.S.A. 101 (51), 17731–17736.

American Psychiatric Association, 2013. Diagnostic and Statistical Manual of Mental Disorders (DSM-5), 5th ed. APA, Washington, DC.
Anand, A., Li, Y., Wang, Y., Gardner, K., Lowe, M.J., 2007. Reciprocal effects of antidepressant treatment on activity and connectivity of the mood regulating circuit: an fMRI study. J. Neuropsychiatry Clin. Neurosci. 19 (3), 274–282.
Anand, A., Li, Y., Wang, Y., Lowe, M.J., Dzemidzic, M., 2009. Resting state corticolimbic connectivity abnormalities in unmedicated bipolar disorder and unipolar depression. Psychiatry Res. 171, 189–198.
Anticevic, A., Brumbaugh, M.S., Winkler, A.M., Lombardo, L.E., Barrett, J., et al., 2013. Global prefrontal and fronto-amygdala dysconnectivity in bipolar I disorder with psychosis history. Biol. Psychiatry 73, 565–573.
Aragones, E., 2012. Registered prevalence of borderline personality disorder in primary care databases. Gac. Sanit. 77 (2), 171–174.
Armstrong, T., Olatunji, B.O., 2012. Eye tracking of attention in the affective disorders: a meta-analytic review and synthesis. Clin. Psychol. Rev. 32 (8), 704–723.
Arnedo, J., Svrakic, D.M., Del Val, C., Romero-Zaliz, R., Hernández-Cuervo, H., Molecular Genetics of Schizophrenia Consortium, et al., 2015. Uncovering the hidden risk architecture of the schizophrenias: confirmation in three independent genome-wide association studies. Am. J. Psychiatry 172 (2), 139–153, http://dx.doi.org/10.1176/appi.ajp.2014.14040435.
Ashworth, F., Pringle, A., Norbury, R., Harmer, C., Cowen, P.J., Cooper, M.J., 2011. Neural response to angry and disgusted facial expressions in bulimia nervosa. Psychol. Med. 41 (11), 2375–2384.
Atchley, R.A., Ilardi, S., Enloe, A., 2003. Hemispheric asymmetry in theprocessing of emotional content in word meanings: the effect of currentand past depression. Brain Lang. 84, 105–119.
Bar-Haim, Y., Lamy, D., Pergamin, L., Bakermans-Kranenburg, M.J., Van IJzendoorn, M.H., 2007. Threat-related attentional bias in anxious and nonanxious individuals: a meta-analytic study. Psychol. Bull. 133 (1), 1–24.
Barch, D.M., Ceaser, A., 2012. Cognition in schizophrenia: core psychological and neural mechanisms. Trends Cogn. Sci. 16, 27–34.
Barkl, S.J., Lah, S., Harris, A.W., Williams, L.M., 2014. Facial emotion identification in early-onset and first-episode psychosis: a systematic review with meta-analysis. Schizophr. Res. 159 (1), 62–69.
Baron-Cohen, S., Wheelwright, S., Hill, J., Raste, Y., Plumb, I., 2001. The "reading the mind in the eyes" test revised version: a study with normal adults, and adults with Asperger syndrome or high-functioning autism. J. Child Psychol. Psychiatry 42, 241–251.
Barrett, L.F., 1998. Discrete emotions or dimensions? The role of valence focus and arousal focus. Cogn. Emot. 12 (4), 579–599.
Barrett, L.F., Wager, T., 2006. The structure of emotion: evidence from the neuroimaging of emotion. Curr. Dir. Psychol. Sci. 15, 79–85.
Becerril, K., Barch, D., 2011. Influence of emotional processing on working memory in schizophrenia. Schizophr. Bull. 37, 1027–1038.
Bell, C., Bourke, C., Colhoun, H., Carter, F., Frampton, C., Porter, R., 2011. The misclassification of facial expressions in generalised social phobia. J. Anxiety Disord. 25 (2), 278–283.
Bell, M., Bryson, G., Lysaker, P., 1997. Positive and negative affect recognition in schizophrenia: a comparison with substance abuse and normal control subjects. Psychiatry Res. 73 (1–2), 73–82.
Berthoz, S., Artiges, E., Van de Moortele, P., Poline, J., Rouquette, S., Consoli, et al., 2014. Effect of impaired recognition and expression of emotions on frontocingulate cortices: an fMRI study of men with alexithymia. Am. J. Psychiatry 159 (6), 961–967.
Bhugra, D., 2005. The global prevalence of schizophrenia. PLoS Med. 2 (5), e151.
Bigelow, N.O., Paradiso, S., Adolphs, R., Moser, D.J., Arndt, S., Heberlein, A., et al., 2006. Perception of socially relevant stimuli in schizophrenia. Schizophr. Res. 83 (2–3), 257–267.
Binelli, C., Subirà, S., Batalla, A., Muñiz, A., Sugranyés, G., Crippa, J.A., et al., 2014. Common and distinct neural correlates of facial emotion processing in social anxiety disorder and Williams syndrome: a systematic review and voxel-based meta-analysis of functional resonance imaging studies. Neuropsychologia.
Bird, G., Viding, E., 2014. The self to other model of empathy: providing a new framework for understanding empathy impairments in psychopathy, autism, and alexithymia. Neurosci. Biobehav. Rev. 47, 520–532.
Birn, R.M., Shackman, A.J., Oler, J.A., Williams, L.E., McFarlin, D.R., Rogers, G.M., Shelton, S.E., Alexander, A.L., Pine, D.S., Slattery, M.J., Davidson, R.J., Fox, A.S., Kalin, N.H., 2014. Evolutionarily conserved prefrontal-amygdalar dysfunction in early-life anxiety. Mol. Psychiatry 19 (8), 915–922.
Bloch, M., Rotenberg, N., Koren, D., Klein, E., 2005. Risk factors associated with the development of postpartum mood disorders. J. Affect. Disord. 88, 9–18.
Bloch, M., Schmidt, P.J., Danaceau, M., Murphy, J., Nieman, L., Rubinow, D.R., 2000. Effects of gonadal steroids in women with a history of postpartumdepression. Am. J. Psychiatry 157 (6), 924–930.
Bora, E., 2012. Meta-analysis of volumetric abnormalities in cortico–striatal–pallidal–thalamic circuits in major depressive disorder. Psychol. Med. 42, 671–681.
Borsboom, D., Cramer, A.O.J., 2013. Network analysis: an integrative approach to the structure of psychopathology. Annu. Rev. Clin. Psychol. 9, 91–121.
Borsboom, D., Cramer, A.O.J., Schmittmann, V.D., Epskamp, S., Waldorp, L., 2011. The small world of psychopathology. PLoS ONE 6 (11), e27407.
Bradley, B.P., Mogg, K., Millar, N., Bonham-Carter, C., Fergusson, E., Jenkins, J., et al., 1997. Attentional biases for emotional faces. Cogn. Emot. 11, 25–42.
Bringmann, L.F., Vissers, N., Wichers, M., Geschwind, N., Kuppens, P., Peeters, F., et al., 2013. A network approach to psychopathology: new insights into clinical longitudinal data. PLoS ONE 8 (4), e60188.
Brodsky, B.S., Groves, S.A., Oquendo, M.A., Mann, J.J., Stanley, B., 2006. Interpersonal precipitants and suicide attempts in borderline personality disorder. Suicide Life-Threat. Behav. 36 (3), 313–322.
Brühl, A.B., Delsignore, A., Komossa, K., Weidt, S., 2014. Neuroimaging in social anxiety disorder—a meta-analytic review resulting in a new neurofunctional model. Neurosci. Biobehav. Rev. 47, 260–280.
Brühl, A.B., Herwig, U., Delsignore, A., Jäncke, L., Rufer, M., 2013. General emotion processing in social anxiety disorder: neural issues of cognitive control. Psychiatry Res. 212 (2), 108–115.
Brummelte, S., Galea, L.A., 2010. Depression during pregnancy and postpartum: contribution of stress and ovarian hormones. Prog. Neuropsychopharmacol. Biol. Psychiatry 34 (5), 766–776.
Buck, T.R., Viskochil, J., Farley, M., Coon, H., McMahon, W.M., Morgan, J., et al., 2014. Psychiatric comorbidity and medication use in adults with autism spectrum disorder. J. Autism Dev. Disord. 44 (12), 3063–3071.
Buckley, P.F., Miller, B.J., Lehrer, D.S., Castle, D.J., 2009. Psychiatric comorbidities and schizophrenia. Schizophr. Bull. 35, 383–402.
Bydlowski, S., Corcos, M., Jeammet, P., Paterniti, S., Berthoz, S., Laurier, C., et al., 2005. Emotion-processing deficits in eating disorders. Int. J. Eat. Disord. 37 (4), 321–329.
Callicott, J.H., Mattay, V.S., Verchinski, B.A., Marenco, S., Egan, M.F., Weinberger, D.R., 2003. Complexity of prefrontal cortical dysfunction in schizophrenia: more than up or down. Am. J. Psychiatry 160, 2209–2215.
Campbell-Sills, L., Barlow, D., Brown, T., Hofmann, S., 2006. Acceptability and suppression of negative emotion in anxiety and mood disorders. Emotion 6 (5), 87–595.
Canli, T., Lesch, P.T., 2007. Long story short: the serotonin transporter in emotion regulation and social cognition. Nat. Neurosci. 10 (9), 1103–1109.
Carretti, N., Florio, P., Bertolin, A., Costa, C.V.L., Allegri, G., Zilli, G., 2005. Serum fluctuations of total and free tryptophan levels during the menstrual cycle are related to gonadotrophins and reflect brain serotonin utilizaton. Hum. Reprod. 20 (6), 1548–1553.
Celani, G., Battacchi, M.W., Arcidiacono, L., 1999. The understanding of the emotional meaning of facial expressions in people with autism. J. Autism Dev. Disord. 29 (1), 57–66.
Chai, X.J., Whitfield-Gabrieli, S., Shinn, A.K., Gabrieli, J.D.E., Nieto-Castanon, A., McCarthy, J.M., et al., 2011. Abnormal medial prefrontal cortex resting-state connectivity in bipolar disorder and schizophrenia. Neuropsychopharmacology 36 (10), 2009–2017.
Chan, S.W., Harmer, C.J., Goodwin, G.M., Norbury, R., 2008. Risk for depression is associated with neural biases in emotional categorisation. Neuropsychologia 46 (12), 2896–2903.
Chen, C.H., Suckling, J., Lennox, B.R., Ooi, C., Bullmore, E.T., 2011. A quantitative meta-analysis of fMRI studies in bipolar disorder. Bipolar Disord. 13 (1), 1–15.
Chepenik, L.G., Raffo, M., Hampson, M., Lacadie, C., Wang, F., Jones, M.M., et al., 2010. Functional connectivity between ventral prefrontal cortex and amygdala at low frequency in the resting state in bipolar disorder. Psychiatry Res. 182 (3), 207–210.
Chevallier, C., Kohls, G., Troiani, V., Brodkin, E.S., Schultz, R.T., 2012. The social motivation theory of autism. Trends Cogn. Sci. 16 (4), 231–239.
Ciarrochi, J., Heaven, P.C.L., Supavadeeprasit, S., 2008. The link between emotion identification skills and socio-emotional functioning in early adolescence: a 1-year longitudinal study. J. Adolesc. 31 (5), 565–582.
Cloninger, C.R., 2002. Implications of comorbidity for the classification of mental disorders: the need for a psychobiology of coherence. In: Maj, M., Gaebel, W., López-Ibor, Sartorius, N. (Eds.), Psychiatric Diagnosis and Classification. Willey & Sons, Chichester, UK, pp. 79–105.
Cochran, D.M., Fallon, D.F., Hill, M., Frazien, J.A., 2013. The role of oxytocin in psychiatric disorders: a review of biological and therapeutic findings. Harv. Rev. Psychiatry 21 (5), 219–247.
Conway, C.A., Jones, B.C., DeBruine, L.M., Welling, L.L.M., Law Smith, M.J., Perrett, D.I., et al., 2007. Salience of emotional displays of danger and contagion in faces is enhanced when progesterone levels are raised. Horm. Behav. 51, 202–206.
Cook, R., Brewer, R., Shah, P., Bird, G., 2013. Alexithymia, not autism, predicts poor recognition of emotional facial expressions. Psych. Sci. 24 (5), 723–732.
Cowdrey, F.A., Harmer, C.J., Park, R.J., McCabe, C., 2012. Neural responses to emotional faces in women recovered from anorexia nervosa. Psychiatry Res. Neuroimaging 201 (3), 190–195.
Critchley, H.D., Daly, E.M., Bullmore, E.T., Williams, S.C., Van Amelsvoort, T., Robertson, D.M., et al., 2000. The functional neuroanatomy of social behaviour: changes in cerebral blood flow when people with autistic disorder process facial expressions. Brain 123 (11), 2203–2212.
Cserjesi, R., Vermeulen, N., Lenard, L., Luminet, O., 2011. Reduced capacity in automatic processing of facial expression in restrictive anorexia nervosa and obesity. Psychiatry Res. 188 (2), 253–257.
Cullen, K.R., Vizueta, N., Thomas, K.M., Han, G.J., Lim, K.O., Camchong, J., et al., 2011. Amygdala functional connectivity in young women with borderline personality disorder. Brain Connect. 1, 61–71.
Dalton, K.M., Nacewicz, B.M., Johnstone, T., Schaefer, H.S., Gernsbacher, M.A., Goldsmith, H.H., et al., 2005. Gaze fixation and the neural circuitry of face processing in autism. Nat. Neurosci. 8 (4), 519–526.
Daros, A.R., Zakzanis, K.K., Ruocco, A.C., 2012. Facial emotion recognition in borderline personality disorder. Psychol. Med. 43 (9), 1953–1963.
Davidson, R.J., 1998. Affective style and affective disorders: perspectives from affective neuroscience. Cogn. Emot. 12 (3), 307–330.

Davidson, R.J., Abercrombie, H., Nitschke, J.B., Putnam, K., 1999. Regional brain function, emotion and disorders of emotion. Curr. Opin. Neurobiol. 9 (2), 228–234.
De Berardis, D., Campanella, D., Nicola, S., Gianna, S., Alessandro, C., Chiara, C., et al., 2008. The impact of alexithymia on anxiety disorders: a review of the literature. Curr. Psychiatry Rev. 4, 80–86.
De Gelder, B., van den Stock, J., Meeren, H.K.M., Sinke, C.B.A., Kret, M.E., Tamietto, M., 2010. Standing up for the body. Recent progress in uncovering the networks involved in processing bodies and bodily expressions. Neurosci. Biobehav. Rev. 34 (4), 513–527.
De Gelder, B., Vroomen, J., 2000. Bimodal emotion perception: integration across separate modalities, cross-modal perceptual grouping or perception of multimodal events? Cogn. Emot. 14 (3), 321–324.
De Gelder, B., Vroomen, J., Annen, L., Masthof, E., Hodiamont, P., 2003. Audio–visual integration in schizophrenia. Schizophr. Res. 59 (2–3), 211–218.
De Gelder, B., Vroomen, J., Teunisse, J.P., 1995. Hearing smiles and seeing cries. The bimodal perception of emotion. Psychonom. Bull. Rev. 29, 309.
De Jong, J.J., Hodiamont, P.P., Van den Stock, J., De Gelder, B., 2009. Audiovisual emotion recognition in schizophrenia: reduced integration of facial and vocal affect. Schizophr. Res. 107 (2–3), 286–293.
De Winter, R.F.P., Van Hemert, A.M., De Rijk, R., Zwinderman, K.H., Frankhuijzen-Sierevogel, Wiegant, V.M., Goekoop, J.G., 2003. Anxious–retarded depression: relation with plasma vasopressin and cortisol. Neuropsychopharmacology 28, 140–147.
Delvecchio, G., Fossati, P., Boyer, P., Brambilla, P., Falkai, P., Gruber, O., et al., 2012. Common and distinct neural correlates of emotional processing in bipolar disorder and major depressive disorder: a voxel-based meta-analysis of functional magnetic resonance imaging studies. Eur. Neuropsychopharmacol. 22 (2), 100–113.
Derntl, B., Kryspin-Exner, I., Fernbach, E., Moser, E., Habel, U., 2008. Emotion recognition accuracy in healthy young females is associated with cycle phase. Horm. Behav. 53, 90–95.
Diener, C., Kuehner, C., Brusniak, W., Ubl, B., Wessa, M., Flor, H., 2012. A meta-analysis of neurofunctional imaging studies of emotion and cognition in major depression. Neuroimage 61 (3), 677–685.
Disner, S.G., Beevers, C.G., Haigh, E.A., Beck, A.T., 2011. Neural mechanisms of the cognitive model of depression. Nat. Rev. Neurosci. 12, 467–477.
Domes, G., Schulze, L., Herpertz, S.C., 2009. Emotion recognition in borderline personality disorder – a review of the literature. J. Pers. Disord. 23 (1), 6–19.
Donegan, N.H., Sanislow, C.A., Blumberg, H.P., Fulbright, R.K., Lacadie, C., Skudlarski, P., et al., 2003. Amygdala hyperreactivity in borderline personality disorder: implications for emotional dysregulation. Biol. Psychiatry 54 (11), 1284–1293.
Edwards, J., Pattison, P.E., Jackson, H.J., Wales, R.J., 2001. Facial affect and affective prosody recognition in first-episode schizophrenia. Schizophr. Res. 48 (2–3), 235–253.
Ehring, T., Fischer, S., Schnülle, J., Bösterling, A., Tuschen-Caffier, B., 2008. Characteristics of emotion regulation in recovered depressed versus never depressed individuals. Pers. Indiv. Differ. 44, 1574–1584.
Ekman, P., 1992. An argument for basic emotions. Cogn. Emot. 6 (3–4), 169–200.
Ekman, P., Cordaro, D., 2011. What is meant by calling emotions basic. Emot. Rev. 3 (4), 364–370.
Elsabbagh, M., Divan, G., Koh, Y.-J., Kim, Y.S., Kauchali, S., Marcin, C., et al., 2012. Global prevalence of autism and other pervasive developmental disorders. Autism Res. 5 (3), 160–179.
Etkin, A., Wager, T.D., 2007. Functional neuroimaging of anxiety: a meta-analysis of emotional processing in PTSD, social anxiety disorder, and specific phobia. Am. J. Psychiatry 164 (10), 1476–1488.
Fairburn, C.G., Cooper, Z., Shafran, R., 2003. Cognitive behaviour therapy for eating disorders: a "transdiagnostic" theory and treatment. Behav. Res. Ther. 41 (5), 509–528.
Feinberg, T.E., Rifkin, A., Schaffer, C., Walker, E., 1986. Facial discrimination and emotional recognition in schizophrenia and affective disorders. Arch. Gen. Psychiatry 43 (3), 276–279.
Feldmanhall, O., Dalgleish, T., Mobbs, D., 2013. Alexithymia decreases altruism in real social decisions. Cortex 49 (3), 899–904.
Fox, E., Russo, R., Bowles, R., Dutton, K., 2001. Do threatening stimuli draw or hold visual attention in subclinical anxiety? J. Exp. Psychol. Gen. 130, 681–700.
Frank, D.W., Dewitt, M., Hudgens-Haney, M., Schaeffer, D.J., Ball, B.H., Schwarz, N.F., et al., 2014. Emotion regulation: quantitative meta-analysis of functional activation and deactivation. Neurosci. Biobehav. Rev. 45, 202–211.
Frith, U., 2004. Emanuel Miller lecture: confusions and controversies about Asperger syndrome. J. Child Psychol. Psychiatry 45 (4), 672–686.
Garnefski, N., Kraaij, V., 2006. Relationships between cognitive emotion regulation strategies and depressive symptoms: a comparative study of five specific samples. Pers. Individ. Dif. 40, 1659–1669.
Gauthier, I., Tarr, M.J., Moylan, J., Skudlarski, P., Gore, J.C., Anderson, A.W., 2000. The fusiform "face area" is part of a network that processes faces at the individual level. J. Cogn. Neurosci. 12, 495–504.
Ghashghaei, H.T., Hilgetag, C.C., Barbas, H., 2007. Sequence of information processing for emotions based on the anatomic dialogue between prefrontal cortex and amygdala. Neuroimage 34 (3), 905–923.
Goghari, V.M., Sponheim, S.R., 2012. More pronounced deficits in facial emotion recognition for schizophrenia than bipolar disorder. Compr. Psychiatry 54 (4), 388–397.
Goldin, P.R., Manber, T., Hakimi, S., Canli, T., Gross, J.J., 2009. Neural bases of social anxiety disorder: emotional reactivity and cognitive regulation during social and physical threat. Arch. Gen. Psychiatry 66, 170–180.
Goldman, M., Marlow-O'Connor, M., Torres, I., Carter, C.S., 2008. Diminished plasma oxytocin in schizophrenic patients with neuroendocrine dysfunction and emotional deficits. Schizophr. Res. 98 (1–3), 247–255.
Graham, J., Salimi-Khorshidi, G., Hagan, C., Walsh, N., Goodyer, I., Lennox, B., Suckling, J., 2013. Meta-analytic evidence for neuroimaging models of depression: state or trait? J. Affect. Disord. 151 (2), 423–431.
Grant, B.F., Chou, S.P., Goldstein, R.B., Huang, B., Stinson, F.S., Saha, T.D., et al., 2008. Prevalence, correlates, disability, and comorbidity of DSM-IV Borderline Personality Disorder: results from the Wave 2 National Epidemiologic Survey on Alcohol and Related Conditions. J. Clin. Psychiatry 69 (4), 533–545.
Greicius, M.D., Flores, B.H., Menon, V., Glover, G.H., Solvason, H.B., Kenna, H., Schatzberg, A.F., 2007. Resting-state functional connectivity in major depression: abnormally increased contributions from subgenual cingulate cortex and thalamus. Biol. Psychiatry 62 (5), 429–437.
Grilo, C.M., McGlashan, T.H., Quinlan, D.M., Walker, M.L., Greenfeld, D., Edell, W.S., 1998. Frequency of personality disorders in two age cohorts of psychiatric inpatients. Am. J. Psychiatry 155, 140–142.
Groenewold, N.A., Opmeer, E.M., De Jonge, P., Aleman, A., Costafreda, S.G., 2012. Emotional valence modulates brain functional abnormalities in depression: evidence from a meta-analysis of fMRI studies. Neurosci. Biobehav. Rev. 37 (2), 152–163.
Gross, J.J., 1998. Antecedent- and response-focused emotion regulation: divergent consequences for experience, expression, and physiology. J. Pers. Soc. Psychol. 74, 224–237.
Gross, J.J., John, O.P., 2003. Individual differences in tow emotion regulation processes: implications for affect, relationships, and well-being. J. Pers. Soc. Psychol. 85, 348–362.
Gross, J.J., Jazaieri, H., 2014. Emotion, emotion regulation, and psychopathology: an affective science perspective. Clin. Psychol. Sci. 2 (4), 387–401.
Guapo, V.G., Graeff, F.G., Zani, A.C.T., Labate, C.M., dos Reis, R.M., Del-Ben, C.M., 2009. Effects of sex hormonal levels and phases of the menstrual cycle in the processing of emotional faces. Psychoneuroendocrinology 34, 1087–1094.
Hamilton, J.P., Etkin, A., Furman, D.J., Lemus, M.G., Johnson, R.F., Gotlib, I.H., 2012. Functional neuroimaging of major depressive disorder: a meta-analysis and new integration of base line activation and neural response data. Am. J. Psychiatry 169 (7), 693–703.
Hamann, S., 2012. Mapping discrete and dimensional emotions onto the brain: controversies and consensus. Trends Cogn. Sci. 16 (9), 458–466.
Hammock, E.A.D., Young, L.J., 2006. Oxytocin, vasopressin and pair bonding: implications for autism. Phil. Trans. R. Soc. B 361 (1476), 2187–2198.
Harmer, C.J., Cowen, P.J., Goodwin, G.M., 2011. Efficacy markers in depression. J. Psychopharmacol. 25 (9), 1148–1158.
Harmer, C.J., Heinzen, J., O'Sullivan, U., Ayres, R.A., Cowen, P.J., 2008. Dissociable effects of acute antidepressant drug administration on subjective and emotional processing measures in healthy volunteers. Psychopharmacology 199 (4), 495–502.
Harmer, C.J., O'Sullivan, U., Favaron, E., Massey-Chase, R., Ayres, R., Reinecke, A., et al., 2009. Effect of acute antidepressant administration on negative affective bias in depressed patients. Am. J. Psychiatry 166 (10), 1178–1184.
Harrison, A., O'Brien, N., Lopez, C., Treasure, J., 2010a. Sensitivity to reward and punishment in eating disorders. Psychiatry Res. 177 (1–2), 1–11.
Harrison, A., Sullivan, S., Tchanturia, K., Treasure, J., 2010b. Emotional functioning in eating disorders: attentional bias, emotion recognition and emotion regulation. Psychol. Med. 40 (11), 1887–1897.
Harrison, A., Sullivan, S., Tchanturia, K., Treasure, J., 2009. Emotion recognition and regulation in anorexia nervosa. Clin. Psychol. Psychother. 16 (4), 348–356.
Hattingh, C.J., Ipser, J., Tromp, S.A., Syal, S., Lochner, C., Brooks, S.J., et al., 2013. Functional magnetic resonance imaging during emotion recognition in social anxiety disorder: an activation likelihood meta-analysis. Front. Hum. Neurosci. 6, 347.
Haxby, J.V., Hoffman, E.A., Gobbini, I.M., 2000. The distributed human neural system for face perception. Trends Cogn. Sci. 4, 223–233.
Hayes, J.P., Hayes, S.M., Mikedis, A.M., 2012. Quantitative meta-analysis of neural activity in posttraumatic stress disorder. Biol. Mood Anxiety Disord. 2 (1), 9.
Haynos, A.F., Fruzzetti, A.E., 2011. Anorexia nervosa as a disorder of emotion dysregulation: evidence and treatment implications. Clin. Psychol. Sci. Prac. 18, 183–202.
Hendrick, V., Stowe, Z.N., Altshuler, L.L., Mintz, J., Hwang, S., Hostetter, A., et al., 2001. Fluoxetine and norfluoxetine concentrations in nursing infants and breast milk. Biol. Psychiatry 50 (10), 775–782.
Hill, E., Berthoz, S., Frith, U., 2004. Brief report: cognitive processing of own emotions in individuals with autistic spectrum disorder and in their relatives. J. Autism Dev. Disord. 34 (2), 229–235.
Hirsch, S.R., Weinberger, D.R. (Eds.), 2003. Schizophrenia. , 2nd ed. Wiley-Blackwell, Malden, MA.
Honera, R., Crow, T.J., Passingham, D., Mackay, C.E., 2005. Regional deficits in brain volume in schizophrenia: a meta-analysis of voxel-based morphometry studies. Am. J. Psychiatry 162, 2233–2245.
Honkalampi, K., Hintikka, J., Tanskanen, A., Lehtonen, J., Viinamäki, H., 2000. Depression is strongly associated with alexithymia in the general population. J. Psychosom. Res. 48 (1), 99–104.
Honkalampi, K., Tolmunen, T., Hintikka, J., Rissanen, M.-L., Kylmä, J., Laukkanen, E., 2009. The prevalence of alexithymia and its relationship with Youth Self-Report problem scales among Finnish adolescents. Compr. Psychiatry 50 (3), 263–268.
Hubert, B., Wicker, B., Moore, D.G., Monfardini, E., Duverger, H., Da Fonseca, D., et al., 2007. Brief report: recognition of emotional and non-emotional biological motion in individuals with autistic spectrum disorders. J. Autism Dev. Disord. 37 (7), 1386–1392.

Hubl, D., Bolte, S., Feineis-Matthews, S., Lanfermann, H., Federspiel, A., Strik, W., et al., 2003. Functional imbalance of visual pathways indicates alternative face processing strategies in autism. Neurology 61 (9), 1232–1237.
Hudson, J.I., Hiripi, E., Pope Jr., H.G., Kessler, R.C., 2007. The prevalence and correlates of eating disorders in the National Comorbidity Survey Replication. Biol. Psych. 61 (3), 348–358.
Ivleva, E., Thaker, G., Tamminga, C.A., 2008. Comparing genes and phenomenology in the major psychoses: schizophrenia and bipolar 1 disorder. Schizophr. Bull. 34 (4), 734–742.
Izard, C.E., 2011. Forms and functions in emotions: matters of emotion–cognition interactions. Emot. Rev. 3 (4), 371–378.
Jansch, C., Harmer, C.J., Cooper, M.J., 2009. Emotional processing in women with anorexia nervosa and healthy volunteers. Eat. Behav. 10 (3), 184–191.
John, O.P., Gross, J.J., 2004. Healthy and unhealthy emotion regulation: personality processes, individual differences, and life span development. J. Pers. 72, 1301–1333.
Johnston, S.J., Boehm, S.G., Healy, D., Goebel, R., Linden, D.E.J., 2010. Neurofeedback: a promising tool for the self-regulation of emotion networks. Neuroimage 49 (1), 1066–1072.
Joormann, J., 2004. Attentional bias in dysphoria: the role of inhibitory processes. Cogn. Emot. 18 (1), 125–147.
Joos, A.A., Gille, M., Hartmann, A., Unterbrink, T., Wetzler-Burmeister, E., Scheidt, C., et al., 2012. Emotional perception in patients with eating disorders in comparison with depressed patients. Eur. Eat. Disord. Rev. 20 (6), 468–475.
Kanakam, N., Krug, I., Raoult, C., Collier, D., Treasure, J., 2013. Social and emotional processing as a behavioural endophenotype in eating disorders: a pilot investigation in twins. Eur. Eat. Disord. Rev. 21 (4), 294–307.
Kanwisher, N., McDermott, J., Chun, M.M., 1997. The fusiform face area: a module in human extrastriate cortex specialized for face perception. J. Neurosci. 17 (11), 4302–4311.
Kapur, S., 2003. Psychosis as a state of aberrant salience: a framework linking biology, phenomenology, and pharmacology in schizophrenia. Am. J. Psychiatry 160, 13–23.
Kaye, W.H., Fudge, J.L., Paulus, M., 2009. New insights into symptoms and neurocircuit function of anorexia nervosa. Nat. Rev. Neurosci. 10 (8), 573–584.
Kenyon, M., Samarawickrema, N., DeJong, H., Van den Eynde, F., Startup, H., Lavender, A., et al., 2012. Theory of mind in bulimia nervosa. Int. J. Eat. Disorder. 45 (3), 377–384.
Kessler, H., Schwarze, M., Filipic, S., Traue, H.C., Von Wietersheim, J., 2006. Alexithymia and facial emotion recognition in patients with eating disorders. Int. J. Eat. Disord. 39, 245–251.
Kessler, R.C., Berglund, P., Demler, O., Jin, R., Koretz, D., Merikangas, K.R., et al., 2003. The epidemiology of major depressive disorder: results from the National Comorbidity Survey Replication (NCS-R). JAMA 289 (23), 3095–3105.
Kessler, R.C., Chiu, W.T., Demler, O., Merikangas, K.R., Walters, E.E., 2005. Prevalence, severity, and comorbidity of 12-month DSM-IV disorders in the National Comorbidity Survey Replication. Arch. Gen. Psychiatry 62 (6), 617–627.
Kessler, R.C., McGonagle, K.A., Zhao, S., Nelson, C.B., Hughes, M., Eshleman, S., et al., 1994. Lifetime and 12-month prevalence of DSM-III-R psychiatric disorders in the United States: results form the National Comorbidity Survey. Arch. Gen. Psychiatry 51 (1), 8–19.
Kessler, R.C., Petukhova, M., Sampson, N.A., Zaslavsky, A.M., Wittchen, H.U., 2012. Twelve-month and lifetime prevalence and lifetime morbid risk of anxiety and mood disorders in the United States. Int. J. Meth. Psych. Res. 21 (3), 169–184.
Kim, S., Birbaumer, N., 2014. Real-time functional MRI neurofeedback: a tool for psychiatry. Curr. Opin. Psychiatry 27 (5), 332–336.
Klein, D.A., Walsh, B.T., 2003. Eating disorders. Int. Rev. Psychiatry 15 (3), 205–216.
Kleinhans, N.M., Richards, T., Johnson, L.C., Weaver, K.E., Greenson, J., Dawson, G., et al., 2011. fMRI evidence of neural abnormalities in the subcortical face processing system in ASD. Neuroimage 54 (1), 697–704.
Kline, J.S., Smith, J.E., Ellis, H.C., 1992. Paranoid and nonparanoid schizophrenic processing of facially displayed affect. J. Psychiatr. Res. 26 (3), 169–182.
Koelkebeck, K., Hirao, K., Miyata, J., Kawada, R., Saze, T., Dannlowski, U., et al., 2013. Impact of gray matter reductions on theory of mind abilities in patients with schizophrenia. Soc. Neurosci. 8 (6), 631–639.
Koenigsberg, H.W., Denny, B.T., Fan, J., Liu, X., Guerreri, S., Mayson, S.J., et al., 2014. The neural correlates of anomalous habituation to negative emotional pictures in borderline and avoidant personality disorder patients. Am. J. Psychiatry 171 (1), 82–90.
Kohler, C.G., Bilker, W., Hagendoorn, M., Gur, R.E., Gur, R.C., 2000. Emotion recognition deficit in schizophrenia: association with symptomatology and cognition. Biol. Psychiatry 48 (2), 127–136.
Kohler, C.G., Hoffman, L.J., Eastman, L.B., Healey, K., Moberg, P.J., 2011. Facial emotion perception in depression and bipolar disorder: a quantitative review. Psychiatry Res. 188 (3), 303–309.
Kohn, N., Falkenberg, I., Kellermann, T., Eickhoff, S.B., Gur, R.C., Habel, U., 2014. Neural correlates of effective and ineffective mood induction. Soc. Cogn. Affect. Neurosci. 9 (6), 864–872.
Korzekwa, M.I., Dell, P.F., Links, P.S., Thabane, L., Webb, S.P., 2008. Estimating the prevalence of borderline personality disorder in psychiatric outpatients using a two-phase procedure. Compr. Psychiatry 49, 380–386.
Koster, E.H., Verschuere, B., Crombez, G., Van Damme, S., 2005. Time-course of attention for threatening pictures in high and low trait anxiety. Behav. Res. Ther. 43 (8), 1087–1098.
Kret, M.E., Denollet, J., Grèzes, J., de Gelder, B., 2011. The role of negative affectivity and social inhibition in perceiving social threat: an fMRI study. Neuropsychologia 49 (5), 1187–1193.
Kret M.E., de Dreu, C.K.W., under review. Oxytocin conditions intergroup relations through up-regulated in-group empathy, cooperation, conformity, and defense. Biol. Psychiatry.
Krueger, R.F., Markon, K.E., 2006. Reinterpreting comorbidity: a model-based approach to understanding and classifying psychopathology. Annu. Rev. Clin. Psychol. 2, 111–133.
Kucharska-Pietura, K., Nikolaou, V., Masiak, M., Treasure, J., 2004. The recognition of emotion in the faces and voice of anorexia nervosa. Int. J. Eat. Disord. 35 (1), 42–47.
LeDoux, J., 1996. The Emotional Brain: The Mysterious Underpinnings of Emotional Life. Simon & Schuster, New York.
Leichsenring, F., Leibing, E., Kruse, J., New, A.S., Leweke, F., 2011. Borderline personality disorder. Lancet 377, 74–84.
Leppanen, J.M., 2006. Emotional information processing in mood disorders: a review of behavioral and neuroimaging findings. Curr. Opin. Psychiatry 19, 34–39.
Leweke, F., Leichsenring, F., Kruse, J., Hermes, S., 2012. Is alexithymia associated with specific mental disorders? Psychopathology 45 (1), 22–28.
Leyfer, O.T., Folstein, S.E., Bacalman, S., Davis, N.O., Dinh, E., Morgan, J., et al., 2006. Comorbid psychiatric disorders in children with autism: interview development and rates of disorders. J. Autism Dev. Disord. 36 (7), 849–861.
Li, H., Chan, R.C.K., McAlonan, G.M., Gong, Q.Y., 2009. Facial emotion processing in schizophrenia: a meta-analysis of functional neuroimaging data. Schizophr. Bull. 36 (5), 1029–1039.
Li, H., Chan, R.C., McAlonan, G.M., Gong, Q.Y., 2010. Facial emotion processing in schizophrenia: a meta-analysis of functional neuroimaging data. Schizophr Bull. 36 (5), 1029–1039, http://dx.doi.org/10.1093/schbul/sbn190.
Lindquist, K.A., Wager, T.D., Kober, H., Bliss-Moreau, E., Barrett, L.F., 2012. The brain basis of emotion: a meta-analytic review. Behav. Brain Sci. 35 (3), 121–143.
Linehan, M.M., 1993. Cognitive-Behavioral Treatment of Borderline Personality Disorder. Guilford Press, New York.
Little, A.C., Burriss, R.P., Petrie, M., Jones, B.C., Roberts, S.C., 2013. Oral contraceptive use in women changes preferences for male facial masculinity and is associated with partner facial masculinity. Psychoneuroendocrinology 38, 1777–1785.
Ma, Y., 2014. Neuropsychological mechanism underlying antidepressant effect: a systematic meta-analysis. Mol. Psychiatry, http://dx.doi.org/10.1038/mp.2014.24 [Epub ahead of print].
Maj, M., 2005. 'Psychiatric comorbidity': an artefact of current diagnostic systems? Br. J. Psychiatry 186, 182–184.
Mak, A.K., Hu, Z.G., Zhang, J.X., Xiao, Z.W., Lee, T.M., 2009. Neural correlates of regulation of positive and negative emotions: an fMRI study. Neurosci. Lett. 457, 101–106.
Mamah, D., Barch, D.M., Repovs, G., 2013. Resting state functional connectivity of five neural networks in bipolar disorder and schizophrenia. J. Affect. Disord. 150 (2), 601–609.
Maner, J.K., Miller, S.L., 2014. Hormones and social monitoring: menstrual cycle shifts in progesterone underlie women's sensitivity to social information. Evol. Hum. Behav. 35, 9–16.
Mayberg, H.S., Liotti, M., Brannan, S.K., McGinnis, S., Mahurin, R.K., Jerabek, P.A., et al., 1999. Reciprocal limbic-cortical function and negative mood: converging PET findings in depression and normal sadness. Am. J. Psychiatry 156 (5), 675–682.
McEwen, B., 2002. Estrogen actions throughout the brain. Recent Prog. Horm. Res. 57, 357–384.
McNally, R.J., Foa, E.B., 1986. Preparedness and resistance to extinction to fear-relevant stimuli: a failure to replicate. Behav. Res. Ther. 24 (5), 529–535.
Mekli, K., Payton, A., Miyajima, F., Platt, H., Thomas, E., Downey, D., et al., 2011. The HTR1A and HTR1B receptor genes influence stress-related information processing. Eur. Neuropsychopharmacol. 21 (1), 129–139.
Mendlewicz, L., Linkowski, P., Bazelmans, C., Philippot, P., 2005. Decoding emotional facial expressions in depressed and anorexic patients. J. Affect. Disord. 89 (1–3), 195–199.
Messina, I., Sambin, M., Palmieri, A., Viviani, R., 2013. Neural correlates of psychotherapy in anxiety and depression: a meta-analysis. PLoS ONE 8 (9), e74657.
Michalopoulou, P.G., Giampietro, V.P., Morley, L.A., Azim, A., Kapur, S., Lykouras, L., et al., 2010. The effects of reality distortion syndrome on salient stimuli processing in patients with schizophrenia: an fMRI study. Psychiatry Res. 183, 93–98.
Mikhailova, E.S., Vladimirova, T.V., Iznak, A.F., Tsusulkovskaya, E.J., Sushko, N.V., 1996. Abnormal recognition of facial expression of emotions in depressed patients with major depression disorder and schizotypal personality disorder. Biol. Psychiatry 40 (8), 697–705.
Minzenberg, M.J., Fan, J., New, A.S., Tang, C.Y., Siever, L.J., 2007. Fronto-limbic dysfunction in response to facial emotion in borderline personality disorder: an event-related fMRI study. Psychiatry Res. 155 (3), 231–243.
Mitchell, A.E., Dickens, G.L., Picchioni, M.M., 2014. Facial emotion processing in borderline personality disorder: a systematic review and meta-analysis. Neuropsychol. Rev. 24 (2), 166–184.
Mogg, K., Bradley, B.P., 2002. Selective orienting of attention to masked threat faces in social anxiety. Behav. Res. Ther. 40, 1403–1414.
Mogg, K., Mathews, A., Weinman, J., 1987. Memory bias in clinical anxiety. J. Abnorm. Psychol. 96 (2), 94–98.
Mor, N., Winquist, J., 2002. Self-focused attention and negative affect: a meta-analysis. Psychol. Bull. 128, 638–662.

Moran, M.H., Goldberg, M., Smith, S.S., 1998. Progesterone withdrawal: II: insensitivity to the sedative effects of a benzodiazepine. Brain Res. 807 (1), 91–100.
Mueser, K.T., Penn, D.L., Blanchard, J.J., Bellack, A.S., 1997. Affect recognition in schizophrenia: a synthesis of findings across three studies. Psychiatry 60 (4), 301–308.
Mukherjee, P., Whalley, H.C., McKirdy, J.W., McIntosh, A.M., Johnstone, E.C., Lawrie, S.M., et al., 2012. Lower effective connectivity between amygdala and parietal regions in response to fearful faces in schizophrenia. Schizophr. Res. 134 (2–3), 118–124.
Myin-Germeys, I., Delespaul, P., deVries, M.W., 2000. Schizophrenia patients are more emotionally active than is assumed based on their behavior. Schizophr. Bull. 26, 847–854.
Nakano, T., Kato, N., Kitazawa, S., 2011. Lack of eyeblink entrainments in autism spectrum disorders. Neuropsychology 49 (9), 2784–2790.
Nesse, R.M., 2001. The smoke detector principle: natural selection and the regulation of defensive responses. Ann. N.Y. Acad. Sci. 935, 75–85.
Nesse, R.M., 2005. Natural selection and the regulation of defenses: a signal detection analysis of the smoke detector principle. Evol. Hum. Behav. 26 (1), 88–105.
Nesse, R.M., Ellsworth, P.C., 2009. Evolution, emotions, and emotional disorders. Am. Psychol. 64, 129–139.
Nettle, D., Bateson, M., 2012. The evolutionary origins of mood and its disorders. Curr. Biol. 22, 712–721.
New, A.S., aan het Rot, M., Ripoll, L.H., Perez-Rodriguez, M.M., Lazarus, S., Zipursky, E., et al., 2012. Empathy and alexithymia in borderline personality disorder: clinical and laboratory measures. J. Pers. Disor. 26 (5), 660–675.
Nolen-Hoeksema, S., Morrow, J., 1993. Effects of rumination and distraction on naturally occurring depressed mood. Cognit. Emot. 7, 561–570.
O'Driscoll, C., Laing, J., Mason, J., 2014. Cognitive emotion regulation strategies, alexithymia and dissociation in schizophrenia, a review and meta-analysis. Clin. Psychol. Rev. 34 (6), 482–495.
Oldershaw, A., Hambrook, D., Stahl, D., Tchanturia, K., Treasure, J., Schmidt, U., 2011. The socio-emotional processing stream in anorexia nervosa. Neurosci. Biobehav. Rev. 35, 970–988.
Panksepp, J., 2004a. Biological psychiatry sketched–past, present, and future. In: Panksepp, J. (Ed.), Textbook of Biological Psychiatry. Wiley, Hoboken, NJ, pp. 3–32.
Panksepp, J., 2004b. Emerging neuroscience of fear and anxiety: therapeutic practice and clinical implications. In: Panksepp, J. (Ed.), Textbook of Biological Psychiatry. Wiley, Hoboken, NJ, pp. 489–519.
Panksepp, J., 2006. Emotional endophenotypes in evolutionary psychiatry. Prog. Neuropsychopharmacol. Biol. Psychiatry 30 (5), 774–784.
Panksepp, J., 2010. Affective neuroscience of the emotional BrainMind: evolutionary perspectives and implications for understanding depression. Dialogues Clin. Neurosci. 12, 533–545.
Panksepp, J., Watt, D., 2011. What is basic about basic emotions? Lasting lessons from affective neuroscience. Emot. Rev. 3 (4), 387–396.
Patterson, J.C., Ungerleider, L.G., Bandettini, P.A., 2002. Task-independent functional brain activity correlation with skin conductance changes (an fMRI study). Neuroimage 17, 1797–1806.
Pedersen, A., Koelkebeck, K., Brandt, M., Wee, M., Küppers, K., Kugel, H., et al., 2012. Theory of mind in patients with schizophrenia: is mentalizing delayed? Schizophr. Res. 137 (1–3), 224–229.
Pessoa, L., Adolphs, R., 2010. Emotion processing and the amygdala: from a 'low road' to 'many roads' of evaluating biological significance. Nat. Rev. Neurosci. 11 (11), 773–782.
Pessoa, L., Adolphs, R., 2011. Emotion and the brain: multiple roads are better than one. Nat. Rev. Neurosci. 12 (7), 425-U72.
Phillips, M.L., Senior, C., David, A.S., 2000. Perception of threat in schizophrenics with persecutory delusions: an investigation using visual scan paths. Psychol. Med. 30 (1), 157–167.
Pierce, K., Muller, R.A., Ambrose, J., Allen, G., Courchesne, E., 2001. Face processing occurs outside the fusiform 'face area' in autism: evidence from functional MRI. Brain 124 (10), 2059–2073.
Pizzagalli, D.A., 2011. Frontocingulate dysfunction in depression: toward biomarkers of treatment response. Neuropsychopharmacology 36, 183–206.
Plana, I., Lavoie, M., Battaglia, M., Achim, A.M., 2014. A meta-analysis and scoping review of social cognition performance in social phobia, posttraumatic stress disorder and other anxiety disorders. J. Anxiety Disord. 28 (2), 169–177.
Pollatos, O., Herbert, B.M., Schandry, R., Gramann, K., 2008. Impaired central processing of emotional faces in anorexia nervosa. Psychosom. Med. 70 (6), 701–708.
Pradas, C.M., Navarro, J.B., Alvarez-Moya, E.M., Grau, A., Obiols, J.E., 2012. Emotional theory of mind in eating disorders. Int. J. Clin. Health Psychol. 12 (2), 189–202.
Puce, A., Allison, T., Asgari, M., Gore, J.C., McCarthy, G., 1996. Differential sensitivity of human visual cortex to faces, letterstrings, and textures a functional magnetic resonance imaging study. J. Neurosci. 16, 5205–5215.
Reyes-Rodriguez, M.L., Von Holle, A., Ulman, T.F., Thornton, L.M., Klump, K.L., Brandt, H., et al., 2011. Posttraumatic stress disorder in anorexia nervosa. Psychosom. Med. 73 (6), 491–497.
Riby, D., Hancock, P.J., 2009. Looking at movies and cartoons: eye-tracking evidence from Williams syndrome and autism. J. Intellect. Disabil. Res. 53 (2), 169–181.
Rottenberg, J., Gross, J.J., Gotlib, I.H., 2005. Emotion context insensitivity in major depressive disorder. J. Abnorm. Psychol. 114, 627–639.
Ruocco, A.C., Amirthavasagam, S., Choi-Kain, L.W., McMain, S.F., 2013. Neural correlates of negative emotionality in borderline personality disorder: an activation-likelihood-estimation meta-analysis. Biol. Psychiatry 73 (2), 153–160.
Rutter, M., 1997. Comorbidity: concepts, claims and choices. Crim. Behav. Ment. Health 7 (4), 265–285.
Santel, S., Baving, L., Krauel, K., Munte, T.F., Rotte, M., 2006. Hunger and satiety in anorexia nervosa: fMRI during cognitive processing of food pictures. Brain Res. 1114 (1), 138–148.
Sasson, N., Tsuchiya, N., Hurley, R., Couture, S.M., Penn, D.L., Adolphs, R., et al., 2007. Orienting to social stimuli differentiates social cognitive impairment in autism and schizophrenia. Neuropsychology 45 (11), 2580–2588.
Schmidt, U., Treasure, J., 2006. Anorexia nervosa: valued and visible. A cognitive-interpersonal maintenance model and its implications for research and practice. Br. J. Clin. Psychol. 45 (3), 343–366.
Schulte-Rüther, M., Mainz, V., Fink, G.R., Herpertz-Dahlmann, B., Konrad, K., 2012. Theory of mind and the brain in anorexia nervosa: relation to treatment outcome. J. Am. Acad. Child Adolesc. Psychiatry 51 (8), 832–841.
Schultz, R.T., Gauthier, I., Klin, A., Fulbright, R.K., Anderson, A.W., Volkmar, F., et al., 2000. Abnormal ventral temporal cortical activity during face discrimination among individuals with autism and Asperger syndrome. Arch. Gen. Psychiatry 57 (4), 331–340.
Scott, L.N., Levy, K.N., Adams Jr., R.B., Stevenson, M.T., 2011. Mental state decoding abilities in young adults with borderline personality disorder traits. Personal Disord. 2 (2), 98–112, http://dx.doi.org/10.1037/a0020011.
Seminowicz, D.A., Mayberg, H.S., McIntosh, A.R., Goldapple, K., Kennedy, S., Segal, Z., Rafi-Tari, S., 2004. Limbic-frontal circuitry in major depression: a path modelling metanalysis. Neuroimage 22, 409–418.
Senju, A., Johnson, M.H., 2009. Atypical eye contact in autism: models, mechanisms and development. Neurosci. Biobehav. Rev. 33 (8), 1204–1214.
Shipko, S., Alvarez, W.A., Noviello, N., 1983. Towards a teleological model of alexithymia: alexithymia and post-traumatic stress disorder. Psychother. Psychosom. 39 (2), 122–126.
Shulman, G.L., Fiez, J.A., Corbetta, M., Buckner, R.L., Miezin, F.M., Raichle, M.E., Pertersen, S.E., 1997. Common blood flow changes across visual tasks: II. Decreases in cerebral cortex. J. Cogn. Neurosci. 9, 648–663.
Siegle, G.J., Ingram, R.E., Matt, G.E., 2002. Affective interference: an explanation for negative attention biases in dysphoria? Cognitive Ther. Res. 26, 73–87.
Sifneos, P.E., 1973. The prevalence of 'alexithymic' characteristics in psychosomatic patients. Psychother. Psychosom. 22 (2), 255–262.
Simkin, D.R., Thatcher, R.W., Luber, J., 2014. Quantitative EEG and neurofeedback in children and adolescents: anxiety disorders, depressive disorders, comorbid addiction and attention-deficit/hyperactivity disorder, and brain injury. Child Adol. Psychiatr. Clin. N. Am. 23 (3), 427–464.
Spezio, M.L., Adolphs, R., Hurley, R.S., Piven, J., 2007. Analysis of face gaze in autism using "Bubbles". Neuropsychology 45 (1), 144–151.
Stein, M.B., Simmons, A.N., Feinstein, J.S., Paulus, M.P., 2007. Increased amygdala and insula activation during emotion processing in anxiety-prone subjects. Am. J. Psychiatry 164, 318–327.
Steiner, M., 1997. Premenstrual syndromes. Annu. Rev. Med. 48 (1), 447–455.
Straube, T., 2009. Dynamic activation of the anterior cingulate cortex during anticipatory anxiety. Neuroimage 44, 975–981.
Sugranyes, G., Kyriakopoulos, M., Corrigall, R., Taylor, E., Frangou, S., 2011. Autism spectrum disorders and schizophrenia: meta-analysis of the neural correlates of social cognition. PLoS ONE 6 (10), e25322.
Suri, R., Burt, V.K., Altshuler, L.L., Zuckerbrow-Miller, J., Fairbanks, L., 2001. Fluvoxamine for postpartum depression. Am. J. Psychiatry 158 (10), 1739–1740.
Taylor, G.J., Bagby, M.R., Parker, J.D.A., 1999. Disorders of Affect Regulation: Alexithymia in Medical and Psychiatric Illness. Cambridge University Press, Cambridge.
Taylor, S.F., Kang, J., Brege, I.S., Tso, I.F., Hosanagar, A., Johnson, T.D., 2012. Meta-analysis of functional neuroimaging studies of emotion perception and experience in schizophrenia. Biol. Psychiatry 71 (2), 136–145.
Teasdale, J.D., 1988. Cognitive vulnerability to persistent depression. Cognit. Emot. 2, 247–274.
Torrisi, S., Moody, T.D., Vizueta, N., Thomason, M.E., Monti, M.M., Townsend, J.D., Bookheimer, S.Y., Altshuler, L.L., 2013. Differences in resting corticolimbic functional connectivity in bipolar I euthymia. Bipolar Disord. 15 (2), 156–166.
Trull, T.J., Useda, D., Conforti, K., Doan, B., 1997. Borderlinepersonality disorder features in nonclinical young adults: 2. Two-year outcome. J. Abnorm. Psychol. 106, 307–314.
Townsend, J., Altshuler, L.L., 2012. Emotion processing and regulation in bipolar disorder: a review. Bipolar Disord. 14 (4), 326–339.
Unoka, Z., Fogd, D., Füzy, M., Csukly, G., 2011. Misreading the facial signs: specific impairments and error patterns in recognition of facial emotions with negative valence in borderline personality disorder. Psychiatry Res. 189 (3), 419–425, http://dx.doi.org/10.1016/j.psychres.2011.02.010.
Van der Velde, J., Servaas, M.N., Goerlich, K.S., Bruggeman, R., Horton, P., Costafreda, S.G., et al., 2013. Neural correlates of alexithymia: a meta-analysis of emotion processing studies. Neurosci. Biobehav. Rev. 37 (8), 1774–1785.
Vanheule, S., Desmet, M., Meganck, R., Bogaerts, S., 2007. Alexithymia and interpersonal problems. J. Clin. Psychol. 63 (1), 109–117.
Van Os, J., Kapur, S., 2009. Schizophrenia. Lancet 374 (9690), 635–645.
Van Steensel, F.J.A., Bogels, S.M., Perrin, S., 2011. Anxiety disorders in children and adolescents with autistic spectrum disorders: a meta-analysis. Clin. Child Fam. Psychol. Rev. 14 (3), 302–317.

Van't Wout, M., Aleman, A., Bermond, B., Kahn, R.S., 2007. No words for feelings: alexithymia in schizophrenia patients and first-degree relatives. Compr. Psychiatry 48 (1), 27–33.

Vaskinn, A., Sundet, K., Friis, S., Simonsen, C., Birkenaes, A.B., Engh, J.A., et al., 2007. The effect of gender on emotion perception in schizophrenia and bipolar disorder. Acta Psychiatr. Scand. 116 (4), 263–270.

Vizueta, N., Rudie, J.D., Townsend, J.D., Torrisi, S., Moody, T.D., Bookheimer, S.Y., et al., 2012. Regional fMRI hypoactivation and altered functional connectivity during emotion processing in nonmedicated depressed patients with bipolar II disorder. Am. J. Psychiatry 169 (8), 831–840.

Vocks, S., Busch, M., Gronemeyer, D., Schulte, D., Herpertz, S., Suchan, B., 2010. Neural correlates of viewing photographs of one's own body and another woman's body in anorexia and bulimia nervosa: an fMRI study. J. Psychiatr. Neurosci. 35 (3), 163–176.

Vuilleumier, P., Pourtois, G., 2007. Distributed and interactive brain mechanisms during emotion face perception: evidence from functional neuroimaging. Neuropsychologia 45, 174–194.

Wiens, S., Peira, N., Golkar, A., Ohman, A., 2008. Recognizing masked threat: fear betrays, but disgust you can trust. Emotion 8 (6), 810–819.

Williams, L.M., Gatt, J.M., Schofield, P.R., Olivieri, G., Peduto, A., Gordon, E., 2009. 'Negativity bias' in risk for depression and anxiety: brain–body fear circuitry correlates, 5-HTT-LPR and early life stress. Neuroimage 47 (3), 804–814.

Whittaker, J.F., Deakin, J.F., Tomenson, B., 2001. Face processing in schizophrenia: defining the deficit. Psychol. Med. 31 (3), 499–507.

Young, K.D., Zotev, V., Phillips, R., Misaki, M., Yuan, H., Drevets, W.C., Bodurka, J., 2014. Real-time fMRI neurofeedback training of amygdala activity in patients with major depressive disorder. PLoS ONE 9 (2), e88785.

Zahradnik, M., Stewart, H.S., Marshall, G.N., Schell, T.L., Jaycox, L.H., 2009. Anxiety sensitivity and aspects of alexithymia are independently and uniquely associated with posttraumatic distress. J. Trauma Stress 22 (2), 131–138.

Zeitlin, S.B., McNally, R.J., 1993. Alexithymia and anxiety sensitivity in panic disorder and obsessive-compulsive disorder. Am. J. Psychiatry 150 (4), 658–660.

Zhang, W.N., Chang, S.H., Guo, L.Y., Zhang, K.L., Wang, J., 2013. The neural correlates of reward-related processing in major depressive disorder: a meta-analysis of functional magnetic resonance imaging studies. J. Affect. Disord. 151 (2), 531–539.

Zhu, Y., Hu, X., Wang, J., Chen, J., Guo, Q., Li, C., et al., 2012. Processing of food, body and emotional stimuli in anorexia nervosa: a systematic review and meta-analysis of functional magnetic resonance imaging studies. Eur. Eat. Disord. Rev. 20 (6), 439–450.

Ziv, M., Goldin, P.R., Jazaieri, H., Hahan, K.S., Gross, J.J., 2013. Emotion regulation in social anxiety disorder: behavioral and neural responses to three socio-emotional tasks. Biol. Mood Anxiety Disord. 3, 20.

Zotev, V., Phillips, R., Young, K.D., Drevets, W.C., Bodurka, J., 2013. Prefrontral control of the amygdala during real-time fMRI neurofeedback training of emotion regulation. PLoS ONE 8 (11), e79184.