



## Review

# Psychobiology of threat appraisal in the context of psychotic experiences: A selective review



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## ABSTRACT

A key factor in the transition to psychosis is the appraisal of anomalous experiences as threatening. Cognitive models of psychosis have identified attentional and interpretative biases underlying threat-based appraisals. While much research has been conducted into these biases within the clinical and cognitive literature, little examination has occurred at the neural level. However, neurobiological research in social cognition employing threatening stimuli mirror cognitive accounts of maladaptive appraisal in psychosis. This review attempted to integrate neuroimaging data regarding social cognition in psychosis with the concepts of attentional and interpretative threat biases. Systematic review methodology was used to identify relevant articles from Medline, PsycINFO and EMBASE, and PubMed databases. The selective review showed that attentional and interpretative threat biases relate to abnormal activation of a range of subcortical and prefrontal structures, including the amygdala, insula, hippocampus, anterior cingulate, and prefrontal cortex, as well as disrupted connectivity between these regions, when processing threatening and neutral or ambiguous stimuli. Notably, neural findings regarding the misattribution of threat to neutral or ambiguous stimuli presented a more consistent picture. Overall, however, the findings for any specific emotion were mixed, both in terms of the specific brain areas involved and the direction of effects (increased/decreased activity), possibly owing to confounds including small sample sizes, varying experimental paradigms, medication, and heterogeneous, in some cases poorly characterised, patient groups. Further neuroimaging research examining these biases by employing experimentally induced anomalous perceptual experiences and well-characterised large samples is needed for greater aetiological specificity.

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## 1. Introduction

Cognitive models state that a key factor in the transition to psychotic symptoms is the negative interpretation or 'appraisal' of anomalous perceptual experiences [26,25,55,3,4]. Maladaptive appraisals endorsed by patients typically represent perceptions of externalised, personalised threat [8,48,78]. Attentional and interpretative cognitive biases are considered to underlie these threat-based appraisals [25]. An attentional bias would relate to threatening perceptual cues taking on excessive salience, while an interpretative bias would refer to the misinterpretation of neutral or positive stimuli as

threatening. These cognitive biases are considered to be transdiagnostic, helping to explain maladaptive cognition in anxiety and depression, as well as psychosis [69]. Additionally, while these biases may help give rise to paranoid delusions, they are not specific to any sub-type of psychosis, instead thought to primarily contribute to the distress associated with positive symptoms [55,83].

These biases are well-established within the clinical literature, with a growing body of research in which tasks designed to mimic anomalous perceptions have been used to investigate appraisals experimentally [46,75,79]. Although attentional and interpretative biases have not been incorporated into the neurobiological literature [26], there are substantial experimental and neuroimaging data on threat processing in anxiety and psychosis [29]. Findings in social cognition and the neuroscience of threat echo cognitive accounts of appraisal in clinical research, even employing analogous terminology [76].

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Within the social cognitive literature, appraisal is taken to mean the classification of stimuli with regards to their emotional-motivational significance, an important determinant of emotional response [65,53]. In essence, appraisal establishes the personal relevance of environmental stimuli according to the individual's concern for well-being, based on needs, goals, and beliefs [53,20].

'Threat appraisal' therefore denotes classifying a stimulus based on its capacity for harming the organism [9]. A possible negative outcome of this adaptive mechanism, having evolved to assist effective threat detection [29], is that threat cues can take on excessive salience, creating a hyper-vigilance or attentional bias towards threat [28,2]. This attentional bias has been observed behaviourally in delusion-prone individuals [30] and psychosis patients, in studies where participants evaluate positive and negative facial emotions [29,54].

Furthermore, evidence suggests that psychosis patients experience strong aversive emotion when processing neutral stimuli [60,12]. Instead of an impairment for neutral valence recognition, this aversive response may reveal an interpretative bias where neutral/ambiguous stimuli are processed as negative. Taken together, these findings suggest that at the core of threat appraisals are two cognitive biases, namely an attentional bias and an interpretative bias towards threat.

Despite this apparent overlap between clinical and social cognitive conceptions of threat appraisal and its underlying biases, little neuroimaging research has directly examined attentional and interpretative biases, beyond cohorts of anxiety patients [27]. Nonetheless, an acceptable proxy may be to survey existing neuroimaging studies of emotion perception in psychosis [76,18,44], and interpret their findings within the context of attentional and interpretative biases. Facilitating this interpretation is a model of aberrant emotion perception in schizophrenia [59]. Derived from structural and functional neuroimaging studies, it outlines two negatively correlated networks, the ventral and dorsal systems. The ventral system links the ventrolateral prefrontal cortex (PFC), orbitofrontal cortex, ventral anterior cingulate (AC), amygdala, insula, ventral striatum, and the brainstem nuclei, is considered to process identification of the emotional significance of a stimulus, and is largely automatic. Concomitantly, the dorsal system, comprised of the dorsolateral and dorsomedial PFC, dorsal AC, and the hippocampus, is implicated in the effortful regulation of resultant affective states. Utilising this model, this review evaluated the current evidence for the neural underpinnings of attentional and interpretative biases in psychosis.

## 2. Methods

Systematic review methodology was used to identify relevant articles [52]. A search strategy combining subject headings and text words relating to psychosis, schizophrenia, paranoid, persecutory, cognitive models, appraisal, attention, referential, threat, need for care, bias, and neuro\$ (truncated), was devised and adapted for the electronic databases Medline, PsycINFO and EMBASE (1806 to May 2015), as well as on PubMed. See flowchart (Fig. 1) for a detailed description of the selection process.

Neuroimaging of attentional and interpretative biases towards threat is yet to be conducted in psychosis populations. Neuroimaging studies of emotion perception in psychosis provide the nearest analogue, but are varied in their design, making it difficult to outline a typical study design for inclusion in this review. Of those included, the majority of studies asked participants to evaluate different facial emotions in a variety of paradigms, either explicitly or implicitly, comparing brain activation of patients and controls in between-participants or mixed designs. Typically, explicit evaluation of facial emotions referred to tasks in which

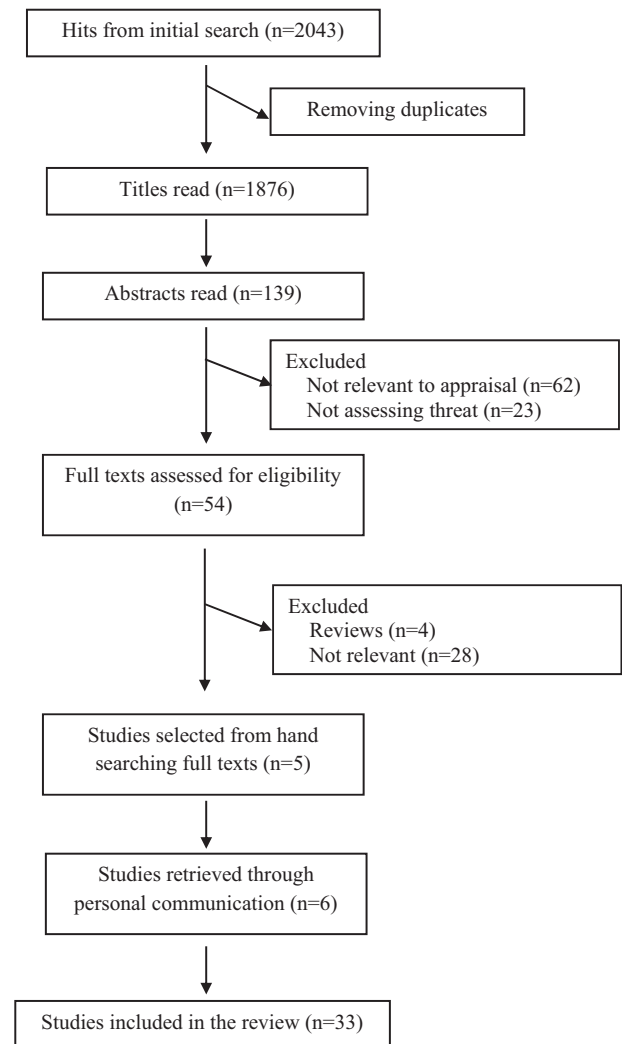


Fig. 1. Flowchart of study selection.

participants labelled or evaluated the emotions as positive or negative, while implicit paradigms equated to passive viewing of facial emotions, or to their exposure while performing a task, such as labelling gender. Only studies using images of direct and indirect social threat, namely angry and fearful faces, were considered. Although the International Affective Picture System [IAPS; 31] images are often employed to study emotion, such studies were excluded due to their lack of specificity to social threat.

Studies were divided into two categories: those relevant to an attentional bias towards threat, and those potentially revealing an interpretative bias. Assigning studies to one category over another was occasionally a compromise, since there is no perfect theoretical overlap between cognitive models of psychosis, and social cognitive research into threat processing. Nonetheless, studies were considered relevant to elucidating the neural correlates of an attentional bias if activity was recorded in the dorsal and ventral systems while patients were exposed to angry or fearful faces, and of an interpretative bias towards threat if exposed to neutral or happy faces.

Specifically, a desirable outcome was a group  $\times$  stimulus interaction wherein patients showed patterns of activity different from controls when processing neutral or threatening stimuli, although studies finding no differences were also included. Behavioural or self-report data corroborating these findings, such as patients mislabelling neutral faces as angry or fearful, were considered.

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