Available online at www.sciencedirect.com
ScienceDirect
Psychiatry Research: Neuroimaging 155 (2007) 29–44
PSYCHIATRY RESEARCH NEUROIMAGING
www.elsevier.com/locate/psychresns

Fronto-limbic and autonomic disjunctions to negative emotion distinguish schizophrenia subtypes

Leanne (Lea) M. Williams[a,b,*], Pritha Das[a,c], Belinda J. Liddell[a,b], Gloria Olivieri[a,d], Anthony S. Peduto[a,d], Anthony S. David[e], Evian Gordon[a,b], Anthony W.F. Harris[a,b]

[a]*Brain Dynamics Centre, Westmead Hospital, NSW, 2145, Australia*
[b]*Psychological Medicine, University of Sydney, Australia*
[c]*Neuroscience Institute of Schizophrenia and Allied Disorders (NISAD), Sydney, Australia*
[d]*MRI Unit, Westmead Hospital, NSW, 2145, Australia*
[e]*Institute of Psychiatry, Kings College London, SE5 8AF, UK*

Received 25 May 2006; received in revised form 8 November 2006; accepted 25 December 2006

Abstract

Schizophrenia patients show a disconnection in amygdala-medial prefrontal cortex and autonomic arousal systems for processing fear. Concurrent functional magnetic resonance imaging [fMRI] and skin conductance recording were used to determine whether these disturbances are specific to fear, or present in response to other signals of danger. We also examined whether these disturbances distinguish a specific symptom profile. During scanning, 27 schizophrenia (13 paranoid, 14 nonparanoid) and 22 matched healthy control subjects viewed standardized facial expressions of fear, anger and disgust (versus neutral). Skin conductance responses [SCRs]were acquired simultaneously to assess phasic increases in arousal. 'With-arousal' versus 'without-arousal' responses were analysed using non-parametric methods. For controls, 'with-arousal' responses were associated with emotion-specific activity for fear (amygdala), disgust (insula) and anger (anterior cingulate), together with common medial prefrontal cortex [MPFC] engagement, as predicted. Schizophrenia patients displayed abnormally *increased* phasic arousal, with concomitant reductions in emotion-specific regions and MPFC. These findings may reflect a general disconnection between central and autonomic systems for processing signals of danger. This disjunction was most apparent in patients with a profile of paranoia, coupled with poor social function and insight. Heightened autonomic sensitivity to signals of fear, threat or contamination, without effective neural mechanisms for appraisal, may underlie paranoid delusions which concern threat and contamination, and associated social and interpersonal difficulties.
© 2007 Elsevier Ireland Ltd. All rights reserved.

Keywords: Schizophrenia; fMRI; Skin conductance responses [SCRs]; Negative emotion; Fear anger and disgust; Amygdala; Medial prefrontal cortex

1. Introduction

Individuals with schizophrenia show impairments in processing facial expressions of emotion in both behavioral and neurocognitive tasks, which are particularly marked for threat-related expressions such as fear (Streit et al., 1997; Mandal et al., 1998; Edwards et al.,

* Corresponding author. Brain Dynamics Centre, Acacia House, Westmead Hospital, Westmead NSW, 2145, Australia.
E-mail address: lea@psych.usyd.edu.au (L.(L.)M. Williams).

0925-4927/$ - see front matter © 2007 Elsevier Ireland Ltd. All rights reserved.
doi:10.1016/j.pscychresns.2006.12.018

2002; Loughland et al., 2002). The amygdala and medial prefrontal cortex [MPFC] networks have a central role in processing fear (Williams et al., 2001, 2004a), and functional neuroimaging studies have also revealed pronounced disturbances in these networks in schizophrenia (Phillips et al., 1999; Gur et al., 2002; Williams et al., 2004b; Das et al., in press).

Perception of fearful face stimuli, presented as briefly as 500 ms, can produce a subjective experience of fear (Wild et al., 2001), consistent with the notion that these evolutionary-determined expressions signal biological responses to potential threat. It has been proposed that amygdala-MPFC networks are modulated by reciprocal connections to autonomic arousal systems, creating a feedback loop between the internal representation of emotionally salient stimuli and somatic emotional states (Damasio, 1996). In support of this mechanism, we have observed increases in skin conductance arousal with activation of amygdala-MPFC activation in healthy subjects (Williams et al., 2001, 2004a, 2005a).

In schizophrenia, by contrast, reductions in amygdala-MPFC responses to fear have been associated with excessive arousal, particularly in patients with paranoid symptomatology, suggesting a disconnection in the central-autonomic systems for processing signals of potential threat (Williams et al., 2004b). Here, we tested the prediction that this disjunction is associated with poor functional outcome, in terms of social functioning and insight, given evidence for a link between poor outcome and heightened arousal. We also investigated whether the arousal/amygdala-MPFC disjunction is present in response to other signals of negative emotion which relate to the content of paranoid delusions.

An extensive body of electrodermal research has identified two types of abnormality in schizophrenia: hyper- and hypo-responsivity (Bernstein et al., 1982; Gruzelier and Venables, 1972). Hyper-responsive schizophrenia patients show heightened skin conductance orienting to innocuous stimuli, along with an elevated skin conductance level and frequent non-specific skin conductance responses [SCRs] (Dawson and Schell, 2002). Notably, patients who show heightened orienting to innocuous stimuli have also been found to show heightened skin conductance responses to emotional film clip stimuli (Kring and Neale, 1996; Kring et al., 1999). Electrodermal hyper-responsivity is most often associated with poor symptomatic, social and functional outcome (Dawson and Schell, 2002). Hyper-responsivity is also an episode indicator, particularly in recent-onset schizophrenia (Dawson et al., 1994), and predicts schizophrenia-like features in longitudinal studies (e.g., Raine et al., 2002), suggesting its potential value as a marker of prognosis. On the other hand, electrodermal non-responding has been associated with better outcome in schizophrenia (Schell et al., 2002), although contrary reports exist (Öhman et al., 1989). It is also present in both first-degree relatives and remitted schizophrenia, pointing to its potential as a vulnerability marker (Schell et al., 2002).

Evidence that heightened skin conductance reactivity to emotional stimuli may be confined to a particular subgroup of schizophrenia patients (Kring and Neale, 1996; Kring et al., 1999) accords with the heterogenous presentation of this condition. In the previous study of functional magnetic resonance imaging [fMRI] with concurrent skin conductance recording, the disjunction of arousal and amygdala-MPFC activity distinguished schizophrenia patients with paranoid symptomatology (Williams et al., 2004b). The separation into paranoid versus nonparanoid subtypes has revealed comparatively consistent differences in neurocognitive profile (Zalewski et al., 1998; Zureick and Meltzer, 1988), relative to other clinical groupings. Consistent with the association of electrodermal hyper-responsivity with poor outcome in schizophrenia, paranoid schizophrenia has been associated specifically with poor adulthood adjustment (Karakula and Grzywa, 1999). Since emotional expressions are so central to social interaction and forming and maintaining social relationships (Keltner and Kring, 1998), we might expect these patients to be defined by poor social functioning in particular. Paranoid delusions have also been highly related to poor insight, an important factor in functional outcome (McEvoy et al., 1989).

The presence of fear-related deficits accords with the paranoid symptomatology of this subtype. However, paranoid delusions encompass fears of other sources of potential danger, including poisons and contaminants and aggression from others (Kim et al., 1993). Facial signals of disgust and anger are universally recognized social signals which communicate the potential presence of these dangers (Ekman et al., 1972). Fear, anger and disgust have been found to elicit common activity in the MPFC, consistent with a general role in the cognitive aspects of emotion processing, including attention to internal emotional state and emotion regulation (Phan et al., 2002; Williams et al., 2005a). While anger and disgust have been associated with amygdala activity, fear elicits the most robust amygdala response. Anger has most consistently been associated with activity in the anterior cingulate and orbitofrontal cortex, and disgust with the anterior insula and basal ganglia (Blair et al., 1999; Phan et al., 2002; Phillips et al., 1997, 1998). We have shown that the MPFC and these emotion-specific regions are engaged with increased

دریافت فوری ← متن کامل مقاله

ISIArticles
مرجع مقالات تخصصی ایران

✓ امکان دانلود نسخه تمام متن مقالات انگلیسی
✓ امکان دانلود نسخه ترجمه شده مقالات
✓ پذیرش سفارش ترجمه تخصصی
✓ امکان جستجو در آرشیو جامعی از صدها موضوع و هزاران مقاله
✓ امکان دانلود رایگان ۲ صفحه اول هر مقاله
✓ امکان پرداخت اینترنتی با کلیه کارت های عضو شتاب
✓ دانلود فوری مقاله پس از پرداخت آنلاین
✓ پشتیبانی کامل خرید با بهره مندی از سیستم هوشمند رهگیری سفارشات