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Emotional memory in schizophrenia

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Abstract

Emotionally arousing scenes are better remembered than neutral ones. The biological basis of this emotional memory effect has been studied in lesion and neuro-imaging studies and depends upon an interaction between the amygdala and medial temporal lobe memory systems including the hippocampus. This study sought to investigate whether patients with schizophrenia had performance deficits on emotional memory tasks consistent with abnormal amygdala function. Patients with schizophrenia and matched control subjects were shown scenes with negative, positive and neutral emotional content. Subjects rated the slides according to how emotionally arousing they found them and then performed surprise memory tests at 10 min (recall) and 3 weeks (recall and recognition). Subjects with schizophrenia did not differ from control subjects in their ratings of the slides. However, patients showed a significant loss of the emotional enhancement of recognition memory for both negative and positive scenes. In addition, patients showed an overall deficit in recall memory, with a selective impairment in recall of the most arousing negative slides. These findings are consistent with the view that medial temporal lobe and in particular amygdala function is abnormal in schizophrenia.

Keywords: Emotion; Memory; Schizophrenia; Amygdala; Hippocampus; Scenes

1. Introduction

Emotionally arousing events are better remembered than neutral events (Bradley, Greenwald, Petry, & Lang, 1992). This ability to enhance episodic memory for events of emotional significance is clearly of adaptive value. The memory modulation hypothesis proposes that the substrate for this emotional memory effect is an interaction between the amygdala and memory systems in the medial temporal lobe including the hippocampal complex, resulting in increased memory consolidation (McGaugh, 2004; Phelps, 2004). Support for this hypothesis comes from animal studies which show that lesions of the amygdala or post-training intra-amygdala infusions of β-adrenaline-receptor antagonists block the enhancement of memory consolidation by stress hormones (McGaugh, 2000; McGaugh & Roozendaal, 2002; Roozendaal & McGaugh, 1996; Roozendaal, Portillo-Marquez, & McGaugh, 1996). In addition, electrophysiological studies have shown that stimulation of the amygdala increases induction of long-term potentiation (LTP) in the hippocampus, whilst amygdala lesions or intra-amygdala infusions of β-adrenaline-receptor antagonists block the induction of LTP (Akirav & Richter-Levin, 1999; Frey, Bergado-Rosado, Seidenbecher, Pape, & Frey, 2001; Ikegaya, Saito, & Abe, 1994, 1995a,b; Ikegaya, Saito, Abe, & Nakanishi, 1997).

Human studies have provided further evidence for the memory-modulation hypothesis (LaBar & Cabeza, 2006; Phelps, 2004). Subjects with bilateral amygdala damage show a selective loss of the enhancement of memory for emotional events (Adolphs, Cahill, Schul, & Babinsky, 1997; Cahill, Babinsky, Markowitsch, & McGaugh, 1995). In addition, neuroimaging studies have demonstrated that increased amygdala activation during the viewing of emotional scenes is correlated with enhanced hippocampal activation and subsequent memory (Canli, Zhao, Brewer, Gabrieli, & Cahill, 2000; Dolcos, LaBar, & Cabeza, 2004a,b; Hamann, Ely, Grafton, & Kilts, 1999). Activation of the amygdala is correlated with subsequent memory for emotionally arousing stimuli, independent of their valence (positive or negative) (Kensinger & Corkin, 2004). The involvement of the medial temporal lobe in emotional memory is not restricted to encoding, as studies have also shown amygdala and hippocampus activation during delayed recognition of emotional

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scenes (Dolcos, LaBar, & Cabeza, 2005). Evidence regarding the involvement of brain regions outside the medial temporal lobe in emotional memory is scarce, but functional neuroimaging studies have shown that activation of the lateral prefrontal cortex accompanies memory enhancement for affectively valenced stimuli even if these are of low arousal (Kensinger & Corkin, 2004), an effect that may be enhanced for emotionally arousing stimuli (Dolcos et al., 2004a).

Abnormalities in medial temporal lobe structure, and in particular decreased volumes of the amygdala and hippocampus, are one of the most replicated findings in magnetic resonance imaging (MRI) studies of patients with schizophrenia (Lawrie & Abukmeil, 1998; Wright et al., 2000). Medial temporal lobe volume reductions are also seen in the relatives of patients with schizophrenia and have been considered to be a heritable vulnerability state for the disorder (van Rijn, Aleman, Swaab, & Kahn, 2005). Functional imaging studies of patients with schizophrenia have demonstrated reduced amygdala activation during the viewing of emotional faces or mood induction, and reduced hippocampal activation in episodic memory tasks (Achim & Lepage, 2005; Gur et al., 2002; Schneider et al., 1998). Subjects with schizophrenia also have decreased amygdala activation when viewing scenes (Takahashi et al., 2004; Taylor, Liberzon, Decker, & Koeppe, 2002), although this has not been investigated in relation to subsequent memory. On the basis of these findings amygdala abnormalities have been argued to represent an intermediate phenotype in schizophrenia that may be related to the development of both positive and negative symptoms of the disorder (Aleman & Kahn, 2005; Shayegan & Stahl, 2005; van Rijn et al., 2005).

In order to investigate the performance of patients with schizophrenia on a cognitive task known to be sensitive to damage to the amygdala we have studied the performance of patients and matched control subjects on tests of emotional memory for scenes. Previous studies of the modulatory effect of emotion on memory have used word stimuli (Calev & Edelist, 1993; Danion, Kazes, Huron, & Karchouni, 2003; Koh, Kayton, & Peterson, 1976; Mathews & Barch, 2004). Some of these studies have shown a relative preservation of emotional memory effects in schizophrenia in terms of both recall (Calev & Edelist 1993; Koh et al., 1976; Mathews & Barch, 2004) and recognition (Mathews & Barch, 2004) whilst others have shown selective deficits in recognition memory (Danion et al., 2003). The use of word stimuli in these previous studies may however have limited the degree of emotional arousal elicited by the stimuli. In addition, some earlier studies have examined memory at short recall intervals (Danion et al., 2003; Koh et al., 1976; Mathews & Barch, 2004), although the effects of emotional arousal on memory consolidation are greatest after a delay (LaBar and Phelps, 1998). We, therefore, tested emotional memory using scenes from a well characterised battery that have been shown to include pictures that are highly emotionally arousing (Lang, Bradley, & Cuthbert, 1997; Lang, Greenwald, Bradley, & Hamm, 1993). Our primary outcome measure was delayed recognition memory, an objective measure which has previously been shown to be correlate with enhanced amygdala activation and amygdalo-hippocampal activation during the encoding of emotional scenes (Canli et al., 2000; Hamann et al., 1999). We hypothesised that patients with schizophrenia would show an impairment in the emotional enhancement of recognition memory for scenes, reflecting abnormal amygdala function.

2. Method

2.1. Participants

Twenty subjects with schizophrenia participated in the study, including both outpatients (13) and stable inpatients (7). Diagnosis was established on clinical consensus, based on DSM IV criteria (APA, 1994). Thirteen were men and seven were women; mean age was 34.5 years (S.D. 11.5); mean illness duration was 12.8 years (S.D. 8.8) and mean pre-morbid IQ assessed by the National Adult Reading Test (NART) (Nelson & Willison, 1991) was 110.9 (S.D. 8.8). All patients were treated with antipsychotic medication with a mean chlorpromazine equivalent dose of 597.5 mg (S.D. 456.0) per day (BMA, 2006; Woods, 2003). In total 10 subjects were receiving atypical antipsychotics, 7 subjects were receiving typical antipsychotics and 3 subjects were receiving both. In addition, 8 subjects were receiving antidepressants, 7 subjects were receiving anti-cholinergic mediation and 5 subjects were receiving benzodiazepines. Symptoms were rated prior to testing using the positive and negative syndrome scale (PANSS) (Kay, Fiszbein, & Opler, 1987) by a single clinician (JH) with established intra-rater reliability (intra-class correlation coefficient > 0.8) and the mean PANSS total score was 48.2 (S.D. 14.1). Paternal occupation was manual in 25% and non-manual in 75%. Exclusion criteria were age under 18 or over 65, co-morbid neurological conditions or brain injury, dependence on alcohol or non-prescribed drugs and major psychiatric disorder other than schizophrenia.

Matched healthy controls were recruited from hospital nursing and auxiliary staff, local industries and other volunteers. Thirteen were men and seven were women. They did not differ from patients in age (35.5 years, S.D. 11.1) or IQ (114.0, S.D. 6.5). Paternal occupation was manual in 25% of controls. Control subjects were screened for any family or personal history of psychotic illness and were additionally subject to the same exclusion criteria as the patients.

Ethical approval for the study was obtained from the Lothian Research Ethics Committee. Participants were given a complete description of the study, and their written consent was obtained.

2.2. Procedure

Emotional memory was tested using pictures from the International Affective Picture System (Lang et al., 1997). One hundred and twenty pictures were selected for the initial (encoding) phase of the study, of which 60 depicted emotionally neutral scenes, 30 depicted positive emotional scenes and 30 depicted negative emotional scenes. The mean normative control ratings for emotional valence (scored from 1 most negative to 9 most positive) and emotional arousal (scored from 1 minimum to 9 maximum) for these scenes was: neutral pictures valence 4.9 (S.D. 0.5), arousal 3.1 (S.D. 0.7); negative pictures valence 2.5 (S.D. 0.7), arousal 6.5 (S.D. 0.5) and positive pictures valence 7.1 (S.D. 0.6), arousal 5.7 (S.D. 0.8). A further group 120 matched pictures was selected as distractors for the recognition memory test (mean normative population ratings neutral pictures valence 5.0 (S.D. 0.6), arousal 3.4 (S.D. 0.7); negative pictures valence 2.4 (S.D. 0.6), arousal 6.2 (S.D. 0.6); positive pictures valence 7.1 (S.D. 0.7), arousal 5.6 (S.D. 0.8)). Pictures were the same for male and female subjects except for 4 positive pictures per set with erotic content. For these, individuals viewed images of people to whom they were presumed to have a sexual attraction (the participant's sexual orientation having been discussed in the screening interview). All slides were presented on a PC using E-Prime software (Psychology Software Tools).

Subjects performed an incidental encoding task in which they were told that they would view a series of slides on a computer screen and would be required to rate the pictures according to how emotionally arousing they found them at the time. Arousal ratings have previously been shown to predict both immediate and delayed recall (Bradley et al., 1992). Subjects were instructed in rating pictures for arousal using a semantic differential scale based on the Self-Assessment