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Preserved emotional memory modulation in first episode psychosis

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ABSTRACT

Although patients with schizophrenia have severe memory impairments and emotional deficits, studies investigating emotional memory modulation (EMM) in schizophrenia show contradictory results, possibly due to methodological differences and small group size. We investigated whether impaired EMM is already present in First Episode Psychosis (FEP) and whether impairments in EMM are task or stimulus dependent. Forty-five FEP and thirty-seven Healthy Control (HC) male participants matched for age performed visual and verbal short-term (immediate recall) and long-term (after 24 h recognition) memory tasks with neutral, negative and positive stimuli. On all tasks overall memory performance for FEP was significantly below that of HC. Although EMM varied by task and type of stimulus, none of the tasks showed a difference in EMM between FEP and HC. There were no differences between FEP and HC in the way emotion modulates different memory domains. This could mean that EMM is spared in the early course of schizophrenia.

1. Introduction

Memory deterioration and emotional disturbances have been recognized as core features of schizophrenia since the early descriptions of the disease (Bleuler, 1916). More recent meta-analyses confirmed these impairments in both overall memory (Aleman et al., 1999; Mesholam-Gately et al., 2009) and emotional domains (Marwick and Hall, 2008) in patients with schizophrenia. In Healthy Controls (HC) memory is facilitated by emotional compared to neutral stimuli when using words, pictures or faces as stimuli (Kensinger and Corkin, 2003; LaBar and Cabeza, 2006; Kohler et al., 2010). It has been suggested that in schizophrenia there are disturbances in the effective integration of emotion and cognition (Herbener et al., 2008; Becerril and Barch, 2011). Anticevic and Corlett (2012) argue that cognitive and emotional impairments not only interact, but at the neural level share important pathophysiological features, such that disruptions caused by schizophrenia can affect both processes and the interaction between these processes (Anticevic and Corlett, 2012).

Consolidation is a key mechanism for memory formation. It entails the transformation of the initially fragile state of memories into stable, retrievable memory traces (McGaugh, 2000). On the psychological level the formation of memory can be described as the sequence of an event, the encoding of the event, the consolidation of the encoded event and by that the fixation of a memory which can be retrieved later on (Nadel et al., 2012). On the cellular level the process of consolidation seems to be based on long-term potentiation in the hippocampus and the subsequent induction of protein synthesis (McGaugh, 2000). Consolidation is a time-dependent process and the results of many different experiments suggest that sleep has an important role in successful memory consolidation (Mednick et al., 2011). Animal and human research indicates that emotionally significant experiences activate hormonal and brain systems that regulate the consolidation of newly acquired memories (Roozendaal and McGaugh, 2011; McReynolds and McIntyre, 2012). Anatomical research has detected that the amygdala, a key structure of emotional processing, influences the hippocampus, a key structure of memory formation through efferent projections deriving from the basolateral amygdala to the dentate gyrus of the hippocampus. Excitatory activity of these projection increase the amount and duration of long-term potentiation (Frey and Morris, 1997) and dendritic

Abbreviations: FEP, First Episode Psychosis patients; HC, Healthy Controls; STM, Short-Term Memory; LTM, Long-Term Memory; EMM, Emotional Memory Modulation

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protein synthesis (Lee et al., 2009). On the psychological level this process may cause information which would normally be forgotten to be stored in LTM when associated with emotional arousal (Bergado et al., 2011). There is a growing body of the literature on disturbances in the effect emotion has on memory in patients with schizophrenia. Emotional memory modulation is usually operationalized as the difference between the number of emotional stimuli (negative or positive) that are remembered in a memory task, compared to the number of remembered neutral stimuli (Dieleman and Roder, 2013).

Several studies have investigated emotional memory modulation (EMM) in patients with schizophrenia. Although two thirds of studies investigating EMM found no differences in EMM between patients with schizophrenia and HC, the remaining studies provide clues that EMM in schizophrenia is affected differently in short (STM) and long-term memory (LTM) (Dieleman and Roder, 2013). In patients with schizophrenia disturbances in EMM are found three times more often in tasks investigating LTM (Calev and Edelist, 1993; Hall et al., 2007; Herbener et al., 2007) than in tasks examining STM (Koh et al., 1976, 1981; Neumann et al., 2007; Lakis et al., 2011). Since consolidation is the main difference between short and long-term memory tasks , this suggests that an important problem with EMM in schizophrenia lies at the level of consolidation, similar to the disturbances in non-emotional memory found in schizophrenia (Manoach and Stickgold, 2009).

Studies investigating EMM in schizophrenia mostly consist of chronic patients of both genders. However, it has been shown that memory for emotional stimuli differs between men and women (Glaser et al., 2012) and this is accompanied by differences in brain processes as revealed by event-related potentials (Glaser et al., 2012). Several studies have shown that memory for emotional stimuli is influenced by the menstrual cycle (Nielsen et al., 2013) or the use of oral contraceptives (Nielsen et al., 2011). Neuroimaging findings have elucidated that during encoding of emotionally charged stimuli men have a stronger activation of the right and women of the left amygdala (Canli et al., 2002; Cahill et al., 2004). Age at onset in schizophrenia is usually later in women than in men (van der Werf et al., 2012) and both age (Addis et al., 2010) and gender (Tsai et al., 2012) influence memory performance. To reduce confounding influences we decided to investigate only male First Episode Psychosis patients (FEP).

There is some evidence that memory impairments are related to psychopathology (Lysaker et al., 2000), but numerous studies found no relation between disturbances in EMM and psychopathology of patients (Dieleman and Roder, 2013). Impairments in EMM in both the visual (Hall et al., 2007; Herbener et al., 2007; Neumann et al., 2007; Lakis et al., 2011) and verbal (Koh et al., 1976, 1981; Calev and Edelist, 1993) domains are reported, however there are no studies comparing these two types of stimuli for both STM and LTM within the same sample.

The aim of our study was to investigate three different aspects of EMM in patients with schizophrenia, 1) whether impairments in EMM are present in FEP, 2) are possible impairments differently present in long or short-term memory, 3) are possible impairments differently present in the verbal or visual domain. To answer these questions, we tested long and short-term visual and verbal memory in a group of male FEP and compared their performance to age and gender matched HC.

2. Methods

2.1. Participants

Forty-nine male patients were recruited at the Department of Psychiatry of the Erasmus Medical Center in Rotterdam, The Netherlands (see also Table 1). All patients met criteria for schizophrenia (either at time of testing or after 6 months of follow-up). Diagnoses were based on clinical consensus by expert clinicians (CR and NvB) and confirmed using the Structured Clinical Interview for DSM-IV Axis I (SCID-I) (First et al., 2002). Inclusion criteria were normal or corrected vision and age between 18 and 30. Because we only wanted to include recent-onset schizophrenia patients, we excluded patients with illness duration of more than 5 years counting from the occurrence of either positive symptoms or clear limitations in social or occupational functioning. This method yields a relatively long duration of illness when compared with assessing only positive symptoms. Mean duration of illness was 14.8 months (S.D. 16.9 months). Four patients were excluded for not performing all tasks. Mean age in years was 23.3 (S.D. 4.0 years). 34 out of 45 FEP were using anti-psychotic drugs at the time of testing (see also Table 1). Other exclusion criteria for patients were: any co-morbid psychiatric or neurologic disorder including substance related disorders, use of more than one anti-psychotic drug and IQ below 75. To asses current psychopathology, we used the Positive and Negative Syndrome Scale (PANSS, Kay et al., 1987) as a general psychopathology indicator. We used the Scale for the Assessment of Negative Symptoms (SANS, Andreasen, 1983) and the Scale for the Assessment of Positive Symptoms (SAPS, Andreasen, 1984) to measure current negative and positive psychopathology more specifically (see Table 1 for psychopathology ratings). SCID, SANS, SAPS and PANSS assessments were performed by S.D. who received yearly training. The Dutch 20-item version Subjective Well-being under Neuroleptics scale (SWN, Haan de et al., 2002) was used to evaluate well-being. The Dutch Adult Reading Test (DART) (Schmand et al., 1991) was used to estimate premorbid verbal intelligence and the Raven Progressive Matrices (Raven, 2006) was used for non-verbal intelligence.

Male HC were recruited through advertisements on internet and word-of-mouth referrals. Mean age was 23.1 years (S.D. 4.3 years). Additional exclusion criteria for HC were: presence of any psychiatric disorder including substance abuse disorders or presence of a first or second generation family member with a past or present psychotic disorder.

Because of methodological problems when trying to match patients with schizophrenia with HC on variables such as education and intelligence (Meehl, 1970), we decided not to try to match HC with patients on level of education. Due to the high percentage of second-generation immigrants in our patient population, measures of socio-economic status or education of parents would not correctly represent possible differences in intelligence.

This study was part of a larger project investigating the interaction between emotion and cognition in FEP over two consecutive days. On both days all participants first performed the verbal memory task, second the visual memory task and finally an attention task, assessments and interviews. All participants gave informed consent and the study was conducted in compliance with the Helsinki Declaration and the regulations regarding Good Clinical Practice in the European Community (GCP) and in concordance with the current National Regulations. The protocol was reviewed and approved by the Medical Ethical Committee of Erasmus MC.

2.2. Materials and procedure

Visual emotional memory was tested using pictures from the International Affective Picture System (IAPS) (Lang et al., 2005). Two sets of 60 pictures each (20 neutral, 20 negative and 20 positive) were selected. The two sets were matched for valence and for content (same number of pictures featuring humans, animals, objects, etc.) (see Supplementary Materials: list S1 for the stimuli). The IAPS provides normative scores based on the Self-Assessment Manikin (SAM), ranging from 1 (very negative) to 9 (very positive) (Lang et al., 2005). Mean male normative

Table 1
Demographic and clinical data of participants.

	First Episode Psychosis patients (S.D.)	Healthy Controls (S.D.)
N	45	37
Age (years)$^{n.s.}$	23.3 (4.0)	23.1(4.3)
Education (years) ***	7.3(1.6)	8.7(1.6)
DART IQ***	93.44(8.6)	101.8(8.5)
Raven IQ**	102.1(17.2)	115.1(18.9)
SWN***	83.3(15.7)	96.5(10.1)
PANSS total	58.5(15.0)	
SANS	39.2(21.8)	
SAPS	18.2(15.5)	
Chlorpromazine equivalents ($n=34$)	263(168)	
Duration off illness (months)	14.8 (16.9)	

Differences were calculated using independent sample *t*-tests: n.s. not significant.
** $p < 0.01$.
*** $p < 0.001$.