Psychiatry Research 229 (2015) 708–714

Contents lists available at ScienceDirect

Psychiatry Research

journal homepage: www.elsevier.com/locate/psychres

High estradiol levels improve false memory rates and meta-memory in highly schizotypal women

Sophie Hodgetts*, Markus Hausmann, Susanne Weis

Department of Psychology, Durham University, South Road, Durham DH1 3LE, United Kingdom

ARTICLE INFO

Article history:
Received 3 February 2015
Received in revised form
1 July 2015
Accepted 10 August 2015
Available online 10 August 2015

Keywords:
Oestrogen
Cognitive disorganisation
Knowledge corruption
False recognition

ABSTRACT

Overconfidence in false memories is often found in patients with schizophrenia and healthy participants with high levels of schizotypy, indicating an impairment of meta-cognition within the memory domain. In general, cognitive control is suggested to be modulated by natural fluctuations in oestrogen. However, whether oestrogen exerts beneficial effects on meta-memory has not yet been investigated. The present study sought to provide evidence that high levels of schizotypy are associated with increased false memory rates and overconfidence in false memories, and that these processes may be modulated by natural differences in estradiol levels. Using the Deese–Roediger–McDermott paradigm, it was found that highly schizotypal participants with high estradiol produced significantly fewer false memories than those with low estradiol. No such difference was found within the low schizotypy participants. Highly schizotypal participants with high estradiol were also less confident in their false memories than those with low estradiol; low schizotypy participants with high estradiol were more confident. However, these differences only approached significance. These findings suggest that the beneficial effect of estradiol on memory and meta-memory observed in healthy participants is specific to highly schizotypal individuals and might be related to individual differences in baseline dopaminergic activity.

1. Introduction

Schizophrenia is a severe psychiatric disorder characterised by positive symptoms (e.g. hallucinations, delusions), negative symptoms (e.g. blunted affect, anhedonia) and cognitive deficits (e.g. cognitive disorganisation). While many aspects of cognition are impaired (Green, 1996; Lesh et al., 2011), it has been purported that memory processes in particular are severely affected (e.g. verbal memory: Toulopoulou and Murray, 2004; working memory: Manoach et al., 2000; see Aleman et al. (1999), for a meta-analysis).

Memory impairments in schizophrenia have been linked to delusions (Moritz and Woodward, 2006), that is, false beliefs characterised by implausibility, which are fixed in spite of evidence to the contrary and asserted with a high degree of confidence (e.g., grandiose delusions, persecutory delusions, paranoid delusions). While delusions are a hallmark of the diagnosis of schizophrenia, an understanding of their neurocognitive basis is still lacking (Gilleen and David, 2005). It has been suggested, though, that delusions are underpinned, at least in part, by a general susceptibility to forming false beliefs/memories with a high level of confidence (Laws and Bhatt, 2005; Moritz and Woodward, 2006). Therefore, investigating the factors influencing confidence in false memories could be of high clinical relevance by improving an understanding of the development and maintenance of delusions, and by potentially influencing individual treatment options for schizophrenia (Favrod et al., 2014; for a review, see Moritz et al. (2014)).

To date, false memories in schizophrenia have received comparatively little attention, which might primarily be due to methodological problems. For example, most neurocognitive memory assessments measure recall and recognition accuracy by assessing hit rates, but neglect false recall and recognition, which can be assessed via false positive error rates (Moritz and Woodward, 2006). Those studies that have investigated false memories in schizophrenia have mainly used the Deese–Roediger–McDermott (DRM) paradigm. In this paradigm, participants study a series of words (e.g. piano, sound, note, sing, melody, band, concert and instrument) that are semantically associated to a non-presented target word (e.g. “music”, the “critical lure”, Roediger and McDermott, 1995). Participants are then required to freely recall as many words from the list as possible (recall phase), before being asked to complete a forced choice recognition test on a list comprised of previously seen words. The recognition list is comprised of the critical lure (strongest association to the study list), new words that are related to the study list (strongly associated, but

* Corresponding author.
E-mail address: s.l.hodgetts@dur.ac.uk (S. Hodgetts).

http://dx.doi.org/10.1016/j.psychres.2015.08.016
0165-1781/

less so than the critical lure), and new words that are unrelated to the study list). Typically, healthy participants falsely remember seeing the critical lure and/or new-related items ("false-positive response"; Roediger et al., 2001), during both the recall and the recognition test. Using this paradigm, it has been shown that while patients have poor recall abilities compared to healthy controls (increased forgetting, Elvevåg et al., 2004), they do not demonstrate increased false recognition (Elvevåg et al., 2004; Moritz et al., 2004). Using the same paradigm, Bhatt et al. (2010) found that patients, both with and without delusions, made more false positive responses during recognition, compared to controls. Moreover, during free recall, patients with delusions produced significantly more false positives than patients without delusions, and healthy controls (see also Brébion et al. (1999) and Stirling et al. (1997)). Thus, the proneness to false memories seems to be strongly related to the presence of delusions and a possible reason for the inconsistencies in present studies may be that some studies (e.g. Elvevåg et al., 2004; Moritz et al., 2004) did not differentiate between patients with and without delusions.

Considering that generally poorer memory in patients as opposed to healthy controls might confound the formation of false memories (Laws and Bhatt, 2005), an alternative avenue for research employs a non-clinical model of schizophrenia by investigating healthy participants with varying degrees of certain schizotypal personality traits (Ettinger et al., 2014; Johns and van Os, 2001). Using the DRM paradigm, Laws and Bhatt (2005) investigated false memories in healthy participants, grouped according to their scores on the Peters et al. (2004) Delusional Inventory (PDI); during recall, high PDI scorers produced significantly more false positives compared to low PDI scorers. Saunders et al. (2012) extended these findings to determine which aspects of schizotypy are related to false memories by including a multidimensional schizotypy measure (The Oxford–Liverpool Inventory of Feelings and Experiences (O–LIFE), Mason et al., 2005). The O–LIFE comprises four subscales: Unusual Experiences (i.e. perceptual aberrations and odd beliefs), Cognitive Disorganisation (i.e. attentional difficulties and thought disorganisation), Introvertive Anhedonia (i.e. blunted affect), and Impulsive Non-Conformity (i.e. antisocial behaviour). Saunders et al. (2012) found that high scorers on Unusual Experiences and/or Cognitive Disorganisation produced more false positives during recall compared to low scorers. Consequently, the authors suggest that specific subtypes of schizotypy are more susceptible to false memories, and thus might also be more delusion-prone.

The investigation of memory processes in schizophrenia and schizotypy has recently extended to acknowledge meta-cognitive processes (Bhatt et al., 2010; Moritz and Woodward, 2002; Moritz et al., 2003; 2004; 2005; 2006). Meta-memory refers to an individual's knowledge and awareness of their memory capabilities, and the processes of memory self-monitoring (Nelson and Narens, 1990; Pannu and Kaszniak, 2005). While many measures of meta-memory have been developed (Pannu and Kaszniak, 2005), retrospective confidence ratings are most relevant in the context of false memories and delusions. Indeed, Moritz and Woodward (2006) have argued that high confidence in false belief is a "defining feature of delusions" (p.185), and that the level of confidence one has in a (false) memory determines its impact on overt behaviour. That is, one is unlikely to act upon a memory, if one is not confident that it is correct. However, high confidence in a false memory could elicit drastic behavioural consequences.

As a meta-cognitive measure of confidence in false memories, Moritz et al. (2004) introduced the knowledge corruption index (KCI) defined as the proportion of high confidence responses that are errors. Employing the DRM paradigm, these authors found that while patients with schizophrenia and controls did not differ in number of false memories per se, patients made more high confidence errors both when forgetting items that were presented ("misses") and during false positive recognition.

With respect to meta-memory processes in healthy participants with schizotypal traits, Laws and Bhatt (2005) reported higher KCI scores for false memories in high PDI scorers, suggesting they are more confident in their errors than low PDI participants are. Corlett et al. (2009) extended these findings by including multiple schizotypy measures. In line with the findings of Moritz et al. (2004, 2006), highly schizotypal participants did not produce more false positives during recognition than those with low schizotypy. However, a positive correlation was found between schizotypy scores and confidence in false positive responses, particularly for subscales analogous to positive schizophrenic symptoms (e.g. perceptual aberrations, magical ideation). These findings provide further evidence that schizotypy provides an appropriate non-clinical model by which to investigate meta-memory impairments in schizophrenia.

A separate stream of research has shown that oestrogen can act as a neuroleptic agent against the symptoms of schizophrenia (Seeman and Lang, 1990; Häfner, 2003; Riecher-Rössler et al., 1994; Kulkarni et al., 2013). Riecher-Rössler et al. (1994) directly investigated the possible neuroleptic properties of estradiol by assessing symptomology across the menstrual cycle. A significant association was found between levels of estradiol and clinical assessment scores; symptoms appeared to improve with increases in estradiol, and deteriorate when estradiol levels decreased. Further research has suggested that memory processes, including working memory (Hampson and Morley, 2013), verbal memory (Joffe et al., 2006), implicit memory (Maki et al., 2002), and discriminability (Keenan et al., 2001) can be enhanced with increased levels of oestrogen (for recent reviews see Duarte-Guterman et al., 2015; Frankfurt and Luine, 2015). However, it is currently unclear whether the effect of oestrogen on memory occurs because of direct effects of oestrogen on memory or rather via hormonal effects on memory control functions, such as meta-memory processes (Colzato et al., 2010). Indeed, it has been suggested that the enhancing effect of oestrogen is particularly evident during tasks that demand a high level of (meta-) cognitive control, (Hjelmervik et al., 2012; Jacobs and D'Esposito, 2011). Given that meta-memory processes are conceptually comparable to cognitive control processes, it follows that meta-memory abilities should be enhanced under high oestrogen conditions.

In summary, previous research has suggested that false memories and impaired meta-memory (indicated by overconfidence in errors) are found both in schizophrenia (potentially providing the basis for the experience of delusions in these patients) and in healthy participants scoring highly on certain schizotypy traits. Still, studies including measures of meta-memory are largely lacking. Another line of research suggests that within memory processes, especially meta-cognitive control functions in memory might be modulated by individual differences in oestrogen.

In light of these previous studies, the present study employed a verbal DRM paradigm to further investigate whether or not high levels of schizotypy are characterised by increased false memory rates (indicated by a high rate of false positive responses during recognition) and with impaired meta-memory (as evidenced by high confidence in false memories). In addition, we sought to investigate whether false positive recognition rates and meta-memory abilities are affected by naturally fluctuating estradiol levels.

It was expected that participants with high levels of schizotypy would make more false positive errors than low schizotypy scorers and show overconfidence in these false memories, especially when their estradiol levels were low. Further, it was hypothesised that high levels of estradiol should have a beneficial effect, especially with respect to meta-cognitive control of false memories.