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Neural mechanisms of mood-induced modulation of reality monitoring in schizophrenia

Karuna Subramaniam [a,*], Kamalini G. Ranasinghe [b], Daniel Mathalon [a], Srikantan Nagarajan [c] and Sophia Vinogradov [a]

[a] Department of Psychiatry, University of California, San Francisco, CA, USA
[b] Department of Neurology, University of California, San Francisco, CA, USA
[c] Department of Radiology and Biomedical Imaging, University of California, San Francisco, CA, USA

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ABSTRACT

Reality monitoring is the ability to accurately distinguish the source of self-generated information from externally-presented information. Although people with schizophrenia (SZ) show impaired reality monitoring, nothing is known about how mood state influences this higher-order cognitive process. Accordingly, we induced positive, neutral and negative mood states to test how different mood states modulate subsequent reality monitoring performance. Our findings indicate that mood affected reality monitoring performance in HC and SZ participants in both similar and dissociable ways. Only a positive mood facilitated task performance in Healthy Control (HC) subjects, whereas a negative mood facilitated task performance in SZ subjects. Yet, when both HC and SZ participants were in a positive mood, they recruited medial prefrontal cortex (mPFC) to bias better subsequent self-generated item identification, despite the fact that mPFC signal was reduced in SZ participants. Additionally, in SZ subjects, negative mood states also modulated left and right dorsal mPFC signal to bias better externally-presented item identification. Together our findings reveal that although the mPFC is hypoactive in SZ participants, mPFC signal plays a functional role in mood–cognition interactions during both positive and negative mood states to facilitate subsequent reality monitoring decision-making.

1. Introduction

It is well recognized that patients with schizophrenia (SZ) have deficits in cognitive, social and emotional processes (Barch & Dowd, 2010; Mandal, Pandey, & Prasad, 1998; Penn et al., 2000). Indeed, a range of social and emotional deficits, along with impaired reality-monitoring (defined as the ability to distinguish self-generated from externally-derived information), are core features of the disorder (Bentall, Baker, & Havers, 1991; Johnson, Hashtroudi, & Lindsay, 1993; Keefe, Arnold, Bayen, & Harvey, 1999; Morrison & Haddock, 1997; Subramaniam, Luks, et al., 2012; Vinogradov et al., 1997;

* *Corresponding author*. Department of Psychiatry, University of California, San Francisco, 513 Parnassus Avenue, HSE604, San Francisco, CA, 94143, USA.
E-mail address: karuna.subramaniam@ucsf.edu (K. Subramaniam).
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Vinogradov, Luks, Schulman, & Simpson, 2008). However, nothing is known about how changes in mood states may affect such cognitive processes in SZ, even though such interactions are well-studied in healthy individuals, and even though it has consistently been shown that SZ participants have an intact ability to experience “in-the-moment” positive affect (Gard, Kring, Gard, Horan, & Green, 2007; Herbener, Song, Khine, & Sweeney, 2008; Kring & Moran, 2008; Kring & Neale, 1996). Based on these prior findings, here we investigate whether it is possible to recruit an intact neurobehavioral process in SZ (the hedonic experience of a positive mood) to improve impaired processing during reality-monitoring goal-directed functions.

Reality-monitoring requires working memory and cognitive control processes, which are multifaceted processes, involving the recruitment of frontal regions – including medial prefrontal cortex/anterior cingulate cortex (mPFC/ACC) as well as bilateral prefrontal cortices, implicated in controlling attention, encoding of relevant information from environmental stimuli into working memory and switching attention to select the correct response (Hedden & Gabrieli, 2006; Kondo, Osaka, & Osaka, 2004). A plethora of behavioral evidence reveals that when healthy participants are in positive mood state, they show broader attention, broader thought-action repertoires, better working memory and greater cognitive flexibility (Ashby, Isen, & Turken, 1999; Ashby, Maddox, & Bohil, 2002; Estrada, Young, & Isen, 1994; Fredrickson, 2004; Isen, Johnson, Mertz, & Robinson, 1985; Isen, Daubman, & Nowicki, 1987; Isen, Rosenzweig, & Young, 1991; Isen, 1999, pp. 521–539). Additional studies reveal that prefrontal regions mediating different aspects of source memory encoding and retrieval processes (Mitchell & Johnson, 2009), and which are also activated during positive mood states may also help to predispose and facilitate overall memory recognition processes (Adcock, Thangavel, Whitfield-Gabrieli, Knutson, & Gabrieli, 2006; Elward, Vilberg, & Rugg, 2015). Thus, we hypothesized that people in a positive mood may show enhanced reality monitoring abilities mediated via prefrontal signal supporting enhanced attention and long term potentiation of relevant information from environmental stimuli into working memory processes; and/or enhanced switching of attention to enable better selection of the correct response.

Additionally, ours and several other prior neuroimaging studies have shown that the mPFC/ACC is a key region that supports reality monitoring and self-referential processing (Frith & Frith, 1999; Cabeza et al., 2004; Gilbert et al., 2007; Northoff et al., 2006; Vinogradov et al., 2006, 2008; Mitchell & Johnson., 2009, for review; Subramaniam, Luks, et al., 2012). The mPFC/ACC is also a region that is also modulated by positive mood states and positive rewarding stimuli in Healthy Control (HC) participants to facilitate cognitive outcomes (Knutson & Cooper, 2005; Subramaniam, Kounios, Parrish, & Jung-Beeman, 2009; Subramaniam, Faust, Beeman, & Mashal, 2012; 2016). In our previous functional Magnetic Resonance Imaging (fMRI) studies of mood–cognition interactions in HC participants, we found two additional regions within posterior cingulate cortex (PCC) and putamen that showed positive mood-sensitive signals, which also modulated upcoming cognitive performance (Subramaniam et al., 2009; Subramaniam & Vinogradov, 2013; 2016). In general, we expected a positive mood state to modulate a network of regions in HC participants, including prefrontal cortices, PCC, parahippocampal cortices, and basal ganglia, consistent with previous research which has shown recruitment of these regions during positive mood states, and during overall episodic source memory retrieval (Elward et al., 2015).

It must also be noted that we have shown that aberrant hypoactive mPFC signal in SZ is amenable to the effects of intensive computerized cognitive training (Subramaniam, Luks, et al., 2012). Specifically, we have demonstrated that after 16 weeks of intensive computerized cognitive training when compared to baseline, SZ participants showed increased activation in the mPFC during reality-monitoring (Subramaniam, Luks, et al., 2012). When HC participants perform the reality-monitoring task, they show increased activation in mPFC, which correlated with identification of self-generated information. However, at baseline, prior to cognitive training, SZ participants revealed hypoactivation within mPFC, and performed significantly worse than HC participants when identifying themselves as the source of self-generated information (Subramaniam, Luks, et al., 2012). Together, our prior findings indicate that cognitive training induced improvements in SZ participants whereby behavioral performance is improved after training and becomes correlated with increased mPFC signal change. In light of these findings, the objectives of the present study were to: 1) Examine whether the specific cognitive-enhancing effects of a positive mood observed in HC participants can be observed in SZ; 2) Examine whether and how mood may be able to have similar cognitive-enhancing effects to that of cognitive training (via modulation of mPFC activity) on reality-monitoring performance in SZ participants.

Additionally, we sought to investigate how a negative mood state may modulate cognition in HC and SZ participants, as compared to a positive mood state. Negative mood states have also been associated with increased activity within the subgenual mPFC/ACC and amygdala, but little is known about how this influences cognition (Mayberg et al., 1999; Murphy, Nimmo-Smith, & Lawrence, 2003; Ochsner, Bunge, Gross, & Gabrieli, 2002). We, therefore, predicted that when participants were in a negative mood as compared to a neutral mood, they would activate mPFC and parahippocampal/amygdala cortices. Less is known about the neural mechanisms of how a negative mood impacts cognition; in particular, the interaction between mood induced activity in mPFC and its role in reality monitoring has never been investigated to date. However, previous research has shown that in contrast to certain cognitive-enhancing effects of a positive mood (in terms of broadening attention, memory and cognitive control), behaviorally, negative mood states such as anxiety and depression have been associated with deficits in attentional and cognitive control mechanisms (Bishop, Duncan, Brett, & Lawrence, 2004; Mayberg et al., 1999). Reality-monitoring is a multifaceted process which requires components of attention, memory and cognitive control; consequently, when HC participants were in a negative mood state, we expected to find somewhat opposite effects (or null effects) of negative mood states on reality-monitoring, as compared to a positive mood. By contrast, prior research has shown that SZ participants demonstrate enhanced attention