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The neural basis of a deficit in abstract thinking in patients with schizophrenia

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ABSTRACT

Abnormal abstract thinking is a major cause of social dysfunction in patients with schizophrenia, but little is known about its neural basis. In this study, we aimed to determine the characteristic abstract thinking-related brain responses in patients using a task reflecting social situations. We conducted functional magnetic resonance imaging while 16 patients with schizophrenia and 16 healthy controls performed a theme-identification task, in which various emotional pictures depicting social situations were presented. Compared with healthy controls, the patients showed significantly decreased activity in the left frontopolar and right orbitofrontal cortices during theme identification. Activity in these two regions correlated well in the controls, but not in patients. Instead, the patients exhibited a close correlation between activity in both sides of the frontopolar cortex, and a positive correlation between the right orbitofrontal cortex activity and degrees of theme identification. Reduced activity in the left frontopolar and right orbitofrontal cortices and the underlying aberrant connectivity may be implicated in the patients' deficits in abstract thinking. These newly identified features of the neural basis of abnormal abstract thinking are important as they have implications for the impaired social behavior of patients with schizophrenia during real-life situations.

1. Introduction

"Abstract thinking" is the ability to consider beyond an immediate and specific stimulus situation and to think about circumstances in general and symbolic ways (Harrow et al., 1974). The opposite of abstract thinking, referred to as "concrete thinking," includes thinking about objects or ideas about specific items. While concrete thinking is acquired relatively early during human development and is less influenced by aging or brain injury (Kroll and Merves, 1986; Wang et al., 2013), the ability for abstract thinking develops later and usually decreases with aging (Albert et al., 1990; Kiang et al., 2007).

Although definite evidence is insufficient, the lateral prefrontal cortex has been focused on as the neural correlate of abstract thinking because this region is important for attention, cognitive control, and maintaining relevant information (Miller and Cohen, 2001; Everling et al., 2002). Many scientists have agreed that in terms of abstract and concrete concepts, there are at least three levels of hierarchical organization within the lateral prefrontal cortex: the anterior, ventrolateral, and dorsolateral regions (Badre and D'Esposito, 2007; Christoff et al., 2009). The broad consensus is that the anterior part is pertinent to highly abstract representations, whereas the ventrolateral part is pertinent to concrete concepts (Azuar et al., 2014; Badre and D'Esposito, 2007, 2009; Botvinick, 2008; Christoff et al., 2009). In light of this, the frontopolar cortex (FPC), the most anterior part of the prefrontal cortex, may be responsible for abstract thinking. This role of the FPC is thought to develop during childhood and adolescence (Dumontheil, 2014).

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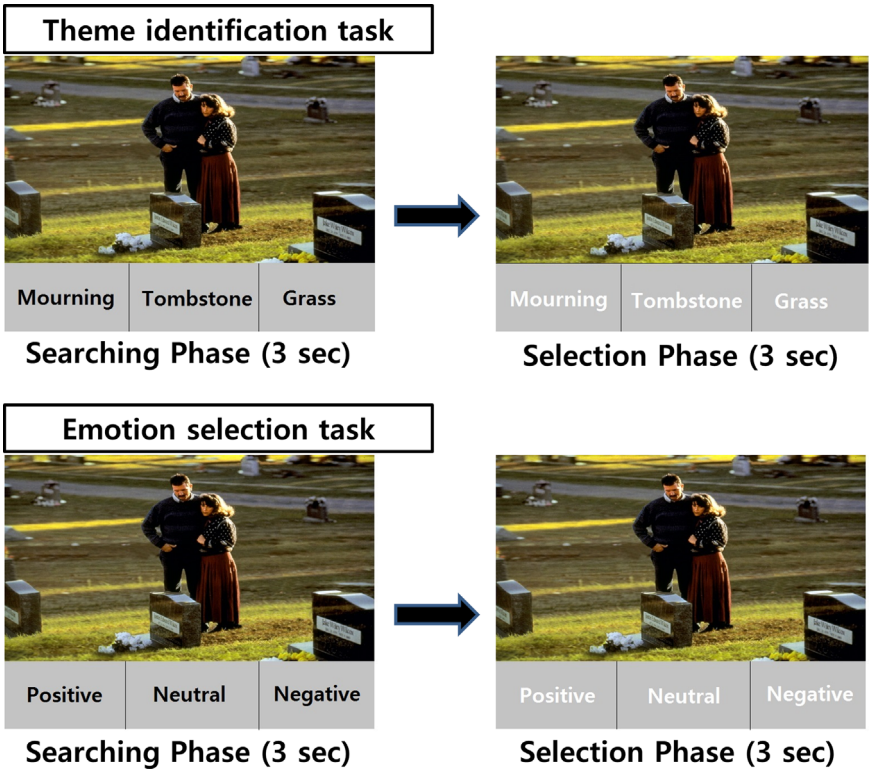

Fig. 1. Examples of visual stimuli composing each trial during the theme-identification or emotion-selection tasks. During theme identification, participants were asked to select a theme word for the picture. In this example, "Mourning" was the theme word (the correct answer), "Tombstone" was the related word, and "Grass" was the unrelated word. During emotion selection, participants were asked to select the valence of the picture. In this example, "Negative" is the correct emotion of the picture. Subjects had to search for the correct answer during the first 3 s, and then had to select the answer during the remaining 3 s.

However, reports on the neural correlates of abstract thinking have not been restricted to the FPC. For example, some studies have shown that the dorsolateral prefrontal cortex (DLPFC) plays an important role in abstract thinking (Berman et al., 1988; Weinberger et al., 1988). Since another report indicates that the DLPFC also engages in concrete thinking (Binder et al., 2005), the role of this region has not yet been conclusively established. In addition, a meta-analysis showed that other brain regions, including the orbitofrontal cortex (OFC) and superior temporal gyrus (STG), are more active during abstract thinking (Wang et al., 2010). The involvement of multiple regions in abstract thinking may be attributed to the differences in tasks used in the studies. Indeed, elucidating the neural correlates of abstract thinking is challenging because task difficulty can affect the results. As a task becomes more difficult, more of the anterior part of the PFC is recruited (Christoff et al., 2009). Consequently, despite multiple studies on abstract thinking (Shallice and Cooper, 2013; Vigliocco et al., 2014), the actual neural mechanisms remain unclear because of the difficulty in comparing studies.

Cognitive deficits in patients with schizophrenia have long been investigated (Miller and Cohen, 2001; Sharma and Antonova, 2003; Lysaker et al., 2005), and an abnormality in abstract thinking is one of the established deficits (Flavell, 1956; Harrow et al., 1974). Abstract thinking is markedly impaired in schizophrenia, particularly when the patients show chronic or severe symptoms (Harrow et al., 1974), making it difficult for patients to behave appropriately during social interactions (Flavell, 1956). Furthermore, decreased cognitive speed during abstract thinking leads to poor performance during work or rehabilitation (Lysaker et al., 2005). Therefore, a deficit in abstract thinking may underlie the maladjustment of these patients in society.

Many neuroimaging studies have pointed to PFC dysfunctions as the neural basis of the cognitive deficit in schizophrenia (Hashimoto et al., 2014; Mothersill et al., 2014; Kauppi et al., 2015). For example, studies using tasks that test abstract thinking, such as rule-based categorization (Frascarelli et al., 2015) or finding similarities (Sanfilipo et al., 2002), have revealed that prefrontal dysfunctions may be responsible for impaired abstract thinking. These findings are not unexpected since the PFC is crucial for many cognitive functions such as working memory (Kaller et al., 2014; Subramaniam et al., 2014), theory of mind (ToM), (Dodell-Feder et al., 2013) and decision-making (Krug et al., 2014). It is unclear, however, whether these prefrontal dysfunctions are specific to a deficit in abstract thinking, because behavioral tasks used in previous studies test multiple cognitions besides abstract thinking. Moreover, tasks involving card sorting or similarity (Sanfilipo et al., 2002; Frascarelli et al., 2015) have limitations in evaluating abstract thinking in real-life situations. Accordingly, further investigation using a task that is more specific to abstract thinking and mimics real life situations is essential to elucidate the neural basis of impaired abstract thinking.

A previous behavioral study on schizophrenia used a newly developed task for exclusively evaluating abstract thinking, which was to identify a theme for situational pictures (Oh et al., 2014). Theme identification is the process of extracting key information from situations people confront. Indeed, patients with schizophrenia exhibited impaired ability for theme identification, which was closely related to social anhedonia (Oh et al., 2014). Since social anhedonia brings on social dysfunctions (Pandina et al., 2013), this cascade of deficits in patients with schizophrenia can cause enormous trouble to social adjustment.

Given this background, the present study was designed to elucidate the neural basis of deficits in abstract thinking in patients with schizophrenia using a theme-identification task. We predicted that theme identification would be a useful probe for finding dysfunctional correlates specific to impairment of abstract