Neural activity during object perception in schizophrenia patients is associated with illness duration and affective symptoms

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ARTICLE INFO

ABSTRACT

Background: Abnormalities in visual processes have been observed in schizophrenia patients and have been associated with alteration of the lateral occipital complex and visual cortex. However, the relationship of these abnormalities with clinical symptomatology is largely unknown.

Methods: We investigated the brain activity associated with object perception in schizophrenia. Pictures of common objects were presented to 26 healthy participants (age = 36.9; 11 females) and 20 schizophrenia patients (age = 39.9; 8 females) in an fMRI study.

Results: In the healthy sample the presentation of pictures yielded significant activation (p_{FWE} (cluster) < 0.001) of the bilateral fusiform gyrus, bilateral lingual gyrus, and bilateral middle occipital gyrus. In patients, the bilateral fusiform gyrus and bilateral lingual gyrus were significantly activated (p_{FWE} (cluster) < 0.001), but not so the middle occipital gyrus. However, significant bilateral activation of the middle occipital gyrus (p_{FWE} (cluster) < 0.05) was revealed when illness duration was controlled for. Depression was significantly associated with increased activation, and anxiety with decreased activation, of the right middle occipital gyrus and several other brain areas in the patient group. No association with positive or negative symptoms was revealed.

Conclusions: Illness duration accounts for the weak activation of the middle occipital gyrus in patients during picture presentation. Affective symptoms, but not positive or negative symptoms, influence the activation of the right middle occipital gyrus and other brain areas.

1. Introduction

Visual perception abnormalities have been observed in patients with schizophrenia and, notably, have been found to be associated with under-activation and impaired coupling of the lateral occipital complex (Green et al., 2009; Harvey et al., 2011). This area is involved in object perception and recognition (Cichy et al., 2012; Grill-Spector et al., 2001; Macevoy, 2013). Alterations were also observed in various areas of the visual cortex (Schultz et al., 2013; Sehatpour et al., 2010; Silverstein et al., 2009). At the clinical level, visual abnormalities in patients with schizophrenia have been related to negative symptomatology (Bedwell et al., 2011; Green et al., 2011; Lee et al., 2010; Perez et al.,

2012; Slaghuis and Curran, 1999). A study with evoked potentials recently reported that negative symptoms were related to perceptual processing dysfunction in these patients (González-Hernández et al., 2014). Whether negative symptoms are related to cerebral under-activation during visual perception has not been clearly established.

Although affective symptoms are not routinely assessed in patients with schizophrenia, several groups have reported them to play a significant role in memory (Lysaker et al., 2000; Möser et al., 2006; Sanfilipo et al., 2002) and attention (Möser et al., 2006) in this population. Our previous work suggested that depression and/or anxiety affected verbal (Brébion et al., 2001, 2009, 2013) as well as visual (Brébion et al., 2015) memory, while potential associations between memory and negative symptoms were mostly an artifact of the overlap between affective and negative symptoms. Depression and anxiety, rather than negative symptoms, might similarly have some effect on visual perception. Indeed, basic visual perceptual deficits have been reported in depressed patients (Clark et al., 2014).

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The brain areas involved in visual perception have been clearly established in healthy participants. A recent meta-analysis of functional magnetic resonance imaging (fMRI) studies revealed that viewing of pictures of art was associated with activation of vision-related as well as emotion-related brain areas (Vartanian and Skov, 2014). The identified visual brain areas included the lingual gyrus, the middle occipital gyrus, and the fusiform gyrus. The precuneus, allegedly involved in visuo-spatial exploration of visual stimuli, was also identified, as were the inferior temporal gyrus, involved in visual representation of forms and colours, the parahippocampal gyrus, involved in the perception and recognition of scenes, and the superior temporal gyrus, which might be related to the semantic processing of objects within the pictures. The additional activation of emotional areas was attributed to the aesthetic component of the paintings. These areas included the putamen, presumably associated with the anticipation of rewards, as well as the anterior insula. A recent review showed the critical role of the insula in emotion (Gasquoine, 2014).

In this study we attempted to identify some of the brain structures involved in impaired visual perception in schizophrenia, and the clinical factors that may be related to abnormal activation of these structures. The brain areas associated with the viewing of pictures of common objects were investigated in healthy participants and patients with schizophrenia. It was expected that, in healthy individuals, visual, but not emotional, brain areas would be activated. Patients were expected to demonstrate under-activation of the same brain areas. Further, we hypothesized that these brain abnormalities were associated with negative, but not positive, symptomatology. We sought to determine whether affective symptoms (depression and anxiety), allegedly related to negative symptoms, presented similar associations with brain activation as they did, and might even account for the associations with negative symptoms. Potential associations between brain abnormalities and illness duration were explored.

2. Method

2.1. Participants

Forty-eight participants were tested, but data from the functional series were disregarded for one healthy participant and one patient due to machine errors. After removing these two participants, the following participant samples were obtained:

Twenty-six healthy participants (11 females) with normal or corrected-to-normal vision were recruited from the general population by means of announcements displayed in the public access areas of the hospital campus: age: m = 36.9, sd = 9.3; education level: m = 6.1[1]; estimated verbal IQ: m = 104.[2] The inclusion criteria were age between 18 and 60 years, and fluency in Spanish. The exclusion criteria were neurological or mental disease, intellectual disability, head injury, alcohol or drug abuse in the past six months, and current severe physical disease, as well as the standard exclusion criteria for participation in fMRI procedures, namely claustrophobia, and metallic implants including fitted pacemaker or cochlea implants.

Twenty patients with schizophrenia (DSM-IV criteria, 8 females) were recruited from the Parc Sanitari Sant Joan de Déu network of mental health services in Barcelona, Spain: age: m = 39.9, sd = 11.5; education level: m = 4.8[1]; verbal IQ: m = 98[2]. Illness duration[3]: m = 12.8, sd = 9.9. The inclusion criteria were the same as for healthy participants

with the additional criterion of being able to provide informed consent. The exclusion criteria were also the same except that the exclusion of mental disease only applied to organic mental disorders and dementia.

The two groups were equivalent for age and sex distribution. However, the healthy controls presented significantly higher educational level (t(44) = 2.9, p < 0.01) and verbal IQ (t(44) = 2.1, p < 0.05) than did the patients. All of the procedures were approved by the Parc Sanitari Sant Joan de Déu ethics committee, and all participants provided informed consent before taking part in the study.

2.2. Clinical rating scales

Positive and negative symptoms were assessed in patients using the Spanish version of the Scale for the Assessment of Positive Symptoms (SAPS) and the Scale for the Assessment of Negative Symptoms (SANS) (Peralta and Cuesta, 1999). The scores tallied for positive symptoms were hallucinations, delusions, thought disorganisation, and total SAPS scores. The scores tallied for negative symptoms were flat affect, alogia, avolition, anhedonia, attention disorder, and total SANS scores. Affective symptoms were assessed by means of the Calgary Depression Scale and the Hamilton Anxiety Rating Scale. Clinical assessment was conducted shortly after the completion of the task by a trained clinical psychologist who was blind to the experimental hypotheses. The main scores obtained were: SAPS: m = 14.9, sd = 16.6, range [0–51]; SANS: m = 4.7, sd = 6.0, range [0–18]; Calgary Depression Scale: m = 2.7, sd = 3.8, range [0–14]; Hamilton Anxiety Rating Scale: m = 6.2, sd = 4.4, range [0–17].

2.3. Material and procedure

All procedures reported here form part of a task designed to examine reality-monitoring deficits in schizophrenia. Participants were first presented with a mixture of target words and pictures (encoding phase). Then, in the recall phase, they were presented with the labels of the target items and required to remember whether a picture of the item had been presented at encoding. This current report focuses on the perceptual aspects of the task, and therefore only the encoding phase (presentation of words and pictures) will be described (see Fig. 1).

Ninety items were selected, including 72 common objects (e.g., *saw, apron, envelope*) and 18 vegetables (e.g., *carrot, cauliflower, onion*). Participants were presented with either the verbal label of the item alone or the picture of the item along with its verbal label. Half of the items were presented as word only and the other half were presented as word/picture pairs. Two versions of the stimuli were prepared; the 45 stimuli that were presented as words in one version were presented as word/
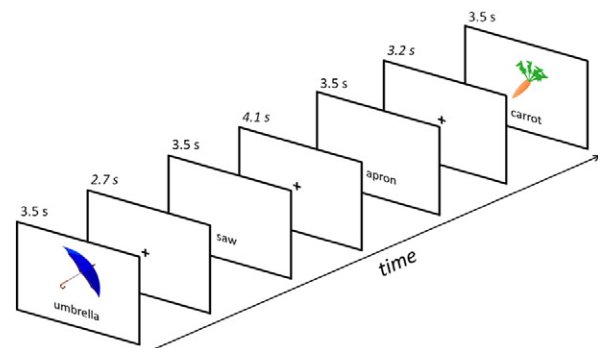

Fig. 1. Schematic representation of the encoding phase of the fMRI task. The target items (45 words and 45 word/picture pairs) were presented one by one in pseudo-random order. Each stimulus slide was presented for 3.5 s. Fixation-crosses (duration between 2 and 5.5 s according to an exponential distribution) separated the stimuli. Participants were asked to indicate whether the presented items were vegetables or not, and to give their response by pressing one of two buttons ('vegetable' or 'other'). Responses were considered valid if they were provided during the presentation of the stimulus or the presentation of the subsequent fixation-cross. The total duration of the task was 10 min.

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[1] The scale used was: 1 = no studies; 2 = uncompleted primary studies; 3 = completed primary studies; 4 = high school uncompleted; 5 = high school completed; 6 = uncompleted undergraduate studies; 7 = bachelor's or master's degree; 8 = doctorate.

[2] Verbal IQ was assessed by means of the Acentuación de Palabras test (TAP). Equivalence with standard verbal IQ was estimated according to norms (IQ = 104 for TAP = 24.3, and IQ = 98 for TAP = 21.1) (Gomar et al., 2011).

[3] Illness duration was calculated as the number of years elapsed since the first psychiatric hospitalization.