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Reduced P300 and P600 amplitude in the hollow-mask illusion in patients with schizophrenia

Danai Dima[a,b,*], Wolfgang Dillo[a], Catharina Bonnemann[a], Hinderk M. Emrich[a,b], Detlef E. Dietrich[a,b]

[a]Clinic for Psychiatry, Social Psychiatry and Psychotherapy, Medical School Hannover, Hannover, Germany
[b]Center for Systems Neuroscience (ZSN), Hannover, Germany

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ABSTRACT

Illusions provide a useful tool to study the mechanisms by which top-down and bottom-up processes interact in perception. Patients suffering from schizophrenia are not as subject to the hollow-mask illusion as healthy controls, since studies have shown that controls perceive a hollow mask as a normal face, while patients with schizophrenia do not. This insusceptibility to the illusion is indicating a weakened top-down processing in schizophrenia and little is understood about the neurobiology of this phenomenon. We used event-related potentials to investigate the hollow-mask illusion in patients with schizophrenia and healthy controls. We hypothesized that there would be a visible reduction of top-down processing in the patients' group and that this reduction would occur in the late stages of processing. We found significantly decreased amplitudes in the P300 and P600 components in the patients' group, indicating that visual information does not benefit from frontal, parietal or temporal activity for perceiving incoming stimuli. We propose that a deficit in functional connectivity may be responsible for impaired top-down visual processing in schizophrenia. These data further the understanding of the time course of top-down processing in patients with schizophrenia.

1. Introduction

Visual illusions can reveal the mechanisms of perception which attach meaning to the world around us. In order to perceive the environment around us as meaningful, the interaction between bottom-up and top-down processing has to be intact (Wallbott and Ricci-Bitti, 1993; Cauller, 1995). There are two kinds of visual illusion: physiological illusions that occur naturally (such as afterimages), and cognitive illusions that demonstrate how human perceptual systems work (Gregory, 1997). Cognitive visual illusions occur because the brain interprets any incoming sensory information on the basis of knowledge and tries to add sense to the stimulus. It has been shown that patients with schizophrenia show increased susceptibility to some visual illusions and some ... susceptibility to other illusions compared with healthy controls. Specifically, patients are more susceptible to the Muller-Lyer illusion (Weckowicz and Witney, 1960; Pessoa et al., 2008), but less susceptible to the Ponzo illusion and the Hermann grid. It has been suggested that this relative susceptibility may be related to impaired sensitivity to stimulus contrast and that deficits in early sensory gain affect subsequent integrative processes (Kantrowitz et al., 2009). Another visual illusion that has been studied in schizophrenia is motion-induced blindness which occurs when target stimuli are presented together with a moving distractor pattern and has been proved to originate from brain areas higher than those responsible for visual afterimages (Hofstoetter et al., 2004). A study by Tschacher et al. (2006) showed that positive symptoms and excitement enhanced the motion-induced blindness, whereas depression and negative symptoms attenuated the illusion.

In this study we use the principles of the 'hollow-mask illusion' or binocular depth inversion (Gregory, 1973). The hollow-mask illusion occurs when a hollow mask is perceived (incorrectly) as a normal face. It is thought to be a process that involves the generation of hypotheses about the three-dimensional shape of faces by interpreting bottom-up signals received from the eyes using conceptual and perceptual knowledge (top-down processing), as well as general rules of perception, such as Gestalt laws of organisation and perspective (Yellott, 1981; Ramachandran, 1988; Hill and Bruce, 1993; Gregory, 1998).

Emrich (1989) proposed that the pathogenesis of schizophrenia can be described as a functional dysequilibrium within the human brain, and that an impairment of the top-down processes may be a plausible explanation for the disintegrative and reality-impairing properties of psychotic disorders. Using the hollow-mask illusion, various studies have shown that patients suffering from schizophrenia are not subject to the illusion experienced by normal controls, meaning that they perceived the 'hollow' face as being hollow (Schneider et al., 1996a; Emrich et al., 1997; Schneider et al., 2002). These results indicate that weakened top-down processing in

* Corresponding author. Department of Psychosis Studies, Section of Neurobiology of Psychosis PO Box 66, Institute of Psychiatry, King's Health Partners, King's College London, De Crespigny Park, London, SE5 8AF, UK. Tel.: +44 20 7848 0425; fax: +44 20 7848 0983.
E-mail address: danai.dima@kcl.ac.uk (D. Dima).

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schizophrenia prevents the 'correction' of incoming sensory data. Frith and Done (1988, 1989) and Malenka et al. (1982) also suggested that internal correcting systems may be deficient in psychotic states and that an imbalance occurs in systems responsible for conceptual formation. Therefore, it has been proposed that patients with schizophrenia are forced to rely on stimulus-driven processing, wherein fragments of the stimulus are pieced together without reference to an expected or stored model (Hemsley, 1987, 2005). Similar results in regards to the hollow-mask illusion have also been found in other 'pro-psychotic' conditions such as cannabinoid-intoxicated states (Emrich et al., 1991, 1997; Leweke et al., 1999, 2000; Semple et al., 2003), alcohol withdrawal (Schneider et al., 1996b, 1998) and sleep deprivation (Sternemann et al., 1997).

We used three kinds of stimuli in our experiment — faces, objects and a mask — and each stimulus was presented in a 3D normal and a 3D inverted (hollow) way. We have previously used effective connectivity measures in functional magnetic resonance imaging (fMRI) data to demonstrate that in schizophrenic patients weakened top-down processing is accompanied by strengthened bottom-up processes when viewing 3D inverted faces compared to 3D normal ones (Dima, et al., 2009). Our previous study employed fMRI data providing an excellent spatial resolution, but did not specify the temporal course of these findings. The electroencephalogram provides a direct and 'real-time' index of neuronal activities at a millisecond scale of resolution and is ideally suited to examine the rapidly changing patterns of brain activities that underlie human cognitive function and dysfunction. In this study we used event-related potentials (ERPs) to explore the time-line of the 3D inversion factor (3D normal vs. 3D inverted stimuli) that has been associated with top-down processes.

Hence, two ERP-components were of special interest regarding our experiment. The P300 component of the ERP is a late positive wave that peaks approximately 300–600 ms after the presentation of an informative task-relevant stimulus and reflects higher-level information processing functions (Duncan-Johnson and Donchin, 1983; Verleger, 1988). It most likely reflects brain processes functionally linked to attention allocation and memory updating operations in the brain (Polish and Kok, 1995). It has been shown that the P300 is impaired in schizophrenia and more specifically the P300 amplitude is smaller overall in patients with schizophrenia compared to control participants, with the strongest effect across the midline and temporal electrode sites (Jeon and Polich, 2001, 2003). The P600 component of the ERPs is also a late positive wave that usually peaks between 600 and 800 ms and that has been shown to be a distinct component from the P300 (Friederici, 2002; Frisch et al., 2003). P600 generators have been identified in several regions considered (i.e., hippocampus, entorhinal, cingulate, and ventral prefrontal cortex) important for episodic/declarative memory (Halgren et al., 1994; Fernandez et al., 1999; Guillem et al., 1999). Furthermore, psychophysiological research suggested that the P600 component indexes the completion of any synchronized operation immediately following target detection, in other words, signals the second pass paring processes of information processing and is impaired in schizophrenia (Papageorgiou et al., 2001; Ruchsow et al., 2003).

The stimuli (faces, objects and a mask) presented in our study differed in their everyday familiarity (Hill and Bruce, 1994). Previous studies have shown that objects with a higher degree of everyday familiarity, i.e. faces, tend to evoke a more pronounced binocular depth inversion (Yellott, 1981; van den Enden and Spekreijse, 1989; Hill and Bruce, 1994). Thus, we hypothesized the illusion to be stronger in the face and mask condition for the controls compared to the patients and that in the object condition there would be n difference between the two groups in terms of susceptibility to the illusion. In connection to this we expected to find disrupted top-down cognitive processes in the face and mask condition in schizophrenia, as reflected by a reduction of the amplitudes of the P300 and P600 components in regards to the 3D inversion factor and no differences in the object condition.

2. Methods

2.1. Subjects

Participants comprised 20 patients (16 men, 4 women) suffering from schizophrenia and 20 age-matched healthy subjects (16 men, 4 women) (see Table 1). All patients fulfilled DSM-IV and ICD-10 criteria for schizophrenia and received antipsychotic medication which was stable for at least 10 days (15 patients were taking older and 5 patients second generation antipsychotic medication). Schizophrenic patients with other psychiatric disorders, including, e.g. personality disorders, drug or alcohol abuse, and neurological disorders, were excluded. The Positive and Negative Syndrome Scale (PANSS) was used to evaluate the current symptomatology of the patients. The level of education was quantified using a scale from 1 to 5 coding different levels from high school to graduate university studies, according to the German educational system. All subjects underwent an ophthalmological examination before the study. Subjects were included in the study only if their vision was normal or corrected to normal, and all had normal color vision. Stereoscopic vision was tested using the Netherlands Organisation for Applied Scientific Research TNO test (Lameris, Utrecht, Netherlands). We included this vision test because recent studies have shown that patients suffering from schizophrenia are less susceptible to stereopsis (Schechter et al., 2006). Thus, all participants included in this study had normal stereoscopic vision. All participants were right-handed as assessed with the Edinburgh Handedness Inventory (Oldfield, 1971). Subjects provided written informed consent prior to their inclusion in the study, and the study was approved by the local ethics committee.

2.2. Stimuli and design

In order to test binocular depth inversion, stereoscopic pictures were taken (at a slightly different angle towards the displayed object) from three groups of different natural objects: ordinary objects (e.g. a chair), a mask (see Fig. 1), and faces of men and women. Faces were photographed at frontal views. The pictures of the mask were taken from the rear, looking into the concavity of the shape (primary concave view, Fig. 1), and also from the frontal view (convex view). The stereoscopic pictures were presented on a computer monitor with high resolution (overall stimulus size 800×600 points, 30.0×22.5 cm) and color depth (16 bits) for a maximum of 5 s. A Wheatstone mirror stereoscope (Wheatstone, 1838) was used to achieve stereoscopic vision. Under laboratory conditions, it is possible to create a strong impression of three-dimensionality by presenting each eye with the corresponding stereoscopic image of the same face or object. The mirror stereoscope used four semi-silvered trapezoid mirrors with two central right and left eye display mirrors (25 cm^2), and two larger lateral right and left mirrors (160 cm^2), each with a vertical axis of rotation. The distance between the presentation unit and the mirror stereoscope in front of it was 80 cm. The lateral mirrors

Table 1
Demographic and psychopathological data: Mean (S.D.).

	Control group	Schizophrenia group	Statistic
N (male)	20 (16)	20 (16)	Fisher's exact test, $P=1$
Age	33.25 (12.5)	33.45 (10.2)	$t(40)=-0.055$, $P=0.956$
Educational level	3.5 (0.8)	3.1 (0.7)	$t(40)=1.71$, $P=0.095$
Negative PANSS	—	18.6 (6.2)	—
Positive PANSS	—	20.2 (7.6)	—
Total PANSS	—	80 (22.4)	—
Medication (mg/day, chlorpromazine equivalent)	—	3.2 (1.9)	