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Do deficits in the magnocellular priming underlie visual derealization phenomena? Preliminary neurophysiological and self-report results in first-episode schizophrenia patients

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ABSTRACT

Background: Early visual impairments probably partially caused by impaired interactions between magnocellular (M) and parvocellular (P) pathways (M priming deficit), and disturbances of basic self-awareness or self-disorders (SDs) are core features of schizophrenia. The relationships between these features have not yet been studied. We hypothesized that the M priming was impaired in first-episode patients and that this deficit was associated with visual aspects of SDs.
Aim: To investigate early visual processing in a sample of first-episode schizophrenia patients and to explore the relationships between M and P functioning and visual aspects of SDs addressed by the Examination of Anomalous Self-Experience (EASE) interview.
Method: Nine stimulating conditions were used to investigate M and P pathways and their interaction in a pattern reversal visually evoked potential (VEP) paradigm. N80 at mixed M- and P-conditions was used to investigate magnocellular priming. Generators were analyzed using source localization (Brain Electrical Source Analysis software: BESA). VEPs of nineteen first-episode schizophrenia patients were compared to those of twenty matched healthy controls by a bootstrap resample procedure. Visual aspects of SDs were analyzed through a factor analysis to separate symptom clusters of derealization phenomena. Thereafter, the associations between the main factors and the N80 component were explored using linear mixed models.
Results: Factor analyses separated two EASE factors ("distance to the world", and "intrusive world"). The N80 component was represented by a single dipole located in the occipital visual cortex. The bootstrap analysis yielded significant amplitude reductions and prolonged latencies in first-episode patients relative to controls in response to mixed M–P conditions, and normal amplitudes and latencies in response to isolated P- and M-biased stimulation. Exploratory analyses showed significant negative correlations between the N80 amplitude values at mixed M–P conditions and the EASE factor "distance to the world", i.e. relatively higher amplitudes in the patient group were associated with higher subjective perceived derealization ("distance to the world").
Conclusions: The early VEP component N80 evoked by mixed M–P conditions is assumed to be a correlate of M priming, and showed reduced amplitudes and longer latencies in first-episode patients. It probably reflects a hypoactivation of the M-pathway. The negative association between visual SDs (derealization phenomena characterized by visual experiences of being more distant to the world), and the M priming deficit was counterintuitive. It might indicate a dysregulated activity of the M-pathway in patients with SDs. Further research is needed to better understand this preliminary finding.

1. Introduction

The visual magnocellular (M) system transmits rapid and low-resolution information critical for orienting attention in space preferentially to parieto-occipital visual areas. The parvocellular (P) system conducts slow and high-resolution information critical for object recognition to temporal–occipital cortex (Butler et al.,

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2005). Visual schizophrenia impairments, a core feature of the illness (Javitt, 2009), are suggested to be partly caused by early processing deficits of the M pathway. This might include disturbed interactions between both visual systems (Butler et al., 2007; Laycock et al., 2007), which would affect the organizing function that the M system normally exerts on the P system (M priming).

The visual object recognition at least involves: a rapid activation of parietal attentional mechanisms (Cheng et al., 2004), and an initial object representation in frontal areas (Bar et al., 2006) by inputs from the M pathway (Laykock et al., 2007); lateral projections from the M pathway to the ventral stream (Doniger et al., 2002; Chen et al., 2007); and feedback projections from higher-level to lower-level areas (Kveraga et al., 2007). The brain network associated with this process (Sehatpour et al., 2008) originates from the dorsal (M) stream visual cortex, which provides low template resolution and informational inputs to both ventral stream and frontal brain areas for a more detailed exploration of visual stimuli (Sehatpour et al., 2006). This function is impaired in schizophrenia, leading to deficits at an intermediate level of visual processing, like the disruption observed in perceptual closure process. This impairment is regarded as the result of disturbed modulation of ventral stream visual areas (Lateral Occipital Complex; LOC) via impaired lateral M inputs (Donniger et al., 2002), and not as a consequence of intrinsic LOC dysfunctions (Sehatpour et al., 2010). It fits in with a recent electrophysiological evidence revealing that during a perceptual closure task, the processing of patients is altered from early to late event related potentials (ERP) (P100 and Ncl respectively), but not at the intermediate ERP (N180) representing the initial stages of object recognition (Azadmehr et al., 2013).

Visual evoked potentials (VEPs), one of the most commonly used paradigms to address mechanisms underlying visual information processing, consistently elicit a three-phasic pattern with three major components (Barnikol et al., 2006). Amplitude reductions and delayed latencies have been reported for the earliest component (N80), a negative deflection with onset latency between 40–70 ms, peaking around 70–90 ms after stimulus onset (Schechter et al., 2005; Butler et al., 2007), and mainly driven by parvocellular inputs (Foxe et al., 2008). Significant N80 amplitude reductions in response to mixed M–P conditions, regarded as an electrophysiological correlate of the M priming, were observed in early onset schizophrenia patients many years after first-episode, but not in adult onset patients (Núñez et al., 2013). This finding points toward an M priming deficit in early onset patients and is compatible with the neurodevelopmental hypothesis of schizophrenia, probably reflecting brain maturational abnormalities of visual area V1/V2 (Henze et al., 2010; Schultz et al., 2011) and parietal lobes (Kumra et al., 2004) which play an important role in visual information processing. Evidence coming from behavioral studies indicates that M impairments are linked to visual symptoms in the early stages of the illness (Kéri and Benedek, 2007), probably leading to both disturbed highlighting of relevant information and slower visual information processing (Kiss et al., 2010). Kéri et al. (2005) reported significant relationships with abnormal subjective perceptual experiences, which include unclear seeing, partial sight, photopsia, micro-macropsia, changes in perception of others' faces and figures, skewed sight/disturbed perspective, and disturbed sense of distance, among others (Kéri, 2008). These anomalous visual experiences seem to be more pronounced in the early stages of the illness (Klosterkötter et al., 2001). Moreover, significant associations with M impairments were found in high-risk psychosis subjects and never-medicated first-episode schizophrenia patients (Kéri et al., 2005; Kéri and Benedek, 2007; Kiss et al., 2010; Akroyd, 2013). Electrophysiological evidence for the M impairment in first episode schizophrenia is scant. Katsanis et al. (1996) did not find significant differences in amplitude and latencies between patients and controls. In contrast, Yeap et al. (2008) reported reduced P100 amplitudes in patients, suggesting that early visual impairments might be present before the illness onset. To our knowledge, the associations between M impairments and perceptual subjective anomalies in first-episode schizophrenia patients have not been investigated using electrophysiological data.

A particular kind of subjective anomalies, probably manifested at the beginning of the illness, gravitating around a basic disturbance of self-awareness, is currently being investigated, mainly as a consequence of the increasing interest in both early detection and prevention of psychosis (Raballo et al., 2011; Nelson et al., 2012). These anomalies, termed self-disorders (SDs) (Møller et al., 2011), involve a wide range of changes concerning the experience of self, identity and intersubjectivity. They express real complaints of patients and might be considered as a potential trait phenotype for the clinical characterization of the schizophrenia spectrum disorders (Parnas et al., 2011; Raballo et al., 2011). One available scale for addressing self-disorders is the Examination of Anomalous Self-Experience (EASE, Parnas et al., 2005), reported as a reliable and internally consistent tool to evaluate the subjective experience in first-episode schizophrenia patients (Møller et al., 2011).

The present study analyzed both source waveforms derived from the EEG signals elicited by pattern-reversal visual evoked potentials and anomalous self-experiences using the EASE interview in first-episode schizophrenia patients and their matched controls. The main focus was the first VEP component (N80) at mixed M–P conditions as a correlate for magnocellular priming of the parvocellular system (Núñez et al., 2013). Two hypotheses were assessed: (1) The M priming is impaired in first-episode patients with schizophrenia. It is reflected either in reduced amplitudes and/or prolonged latencies of the N80 component in patients relative to controls in conditions addressing M-priming, i.e. combined conditions (M- and P-stimulation). For isolated M- and P-conditions, intact responses were expected. (2) The M priming deficit is associated with a specific pattern of anomalous self-experience (Parnas et al., 2005), especially with anomalous experiences of the visual channel which result in derealization experiences such as a diminished sense of presence and feeling distant from the world.

2. Material and methods

2.1. Subjects

Nineteen first-episode schizophrenia patients (ICD-10: F2; FEP) treated in the Psychiatric Hospital of the University of Heidelberg between 2008 and 2011 were recruited and compared to twenty matched controls (CG) recruited during the same period (Table 1). Patients exhibiting either neurological co-morbidity or other psychiatric diseases were not included in the study. Control subjects without exhibiting neurological or psychiatric disorders and without any first-

Table 1
Demographic characteristics of patient (FEP) and control groups (CG)—mean (standard deviation).

N	CG	FEP	*p*
	20	19	
Gender (m = male, f = female)	11 m, 9 f	13 m, 6 f	
Age at testing (years)	23.3 (3.7) Range [16.4–29.9]	23.22 (2.8) Range [18.5–27.1]	ns
Education			
≤12 years of education	5	6	ns
≥13 years of education	15	14	ns
Premorbid-verbal IQ	27.0 (6.7)	26.2 (5.0)	ns
PANSS positive		11.1 (3.5)	
PANSS negative		17.0 (4.6)	
PANSS general		31.6 (6.0)	
Visual acuity (right)	.93 (.13)	.85 (.12)	ns
Visual acuity (left)	.93 (.14)	.85 (.11)	ns
Antipsychotic medication			
Chlorpromazine equivalent + SD (mg)		349.6 (+335.5)	