



Increased psychophysiological parameters of attention in non-psychotic individuals with auditory verbal hallucinations

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ABSTRACT

Objective: Schizophrenia is associated with aberrant event-related potentials (ERPs) such as reductions in P300, processing negativity and mismatch negativity amplitudes. These deficits may be related to the propensity of schizophrenia patients to experience auditory verbal hallucinations (AVH). However, AVH are part of extensive and variable symptomatology in schizophrenia. For this reason non-psychotic individuals with AVH as an isolated symptom provide an excellent opportunity to investigate this relationship.

Methods: P300 waveforms, processing negativity and mismatch negativity were examined with an auditory oddball paradigm in 18 non-psychotic individuals with AVH and 18 controls.

Results: P300 amplitude was increased in the AVH group as compared to controls, reflecting superior effortful attention. A trend in the same direction was found for processing negativity. No significant differences were found for mismatch negativity.

Conclusion: Contrary to our expectations, non-psychotic individuals with AVH show *increased* rather than *decreased* psychophysiological measures of effortful attention compared to healthy controls, refuting a pivotal role of decreased effortful attention in the pathophysiology of AVH.

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1. Introduction

Decreased electrophysiological measures of attention, such as reduced P300 amplitude, are among the most consistently reported neurobiological abnormalities in schizophrenia (for an overview see Jeon and Polich, 2003). The P300 event-related potential (ERP) is a positive deflection of the electroencephalogram (EEG), occurring approximately 300 ms after the presentation of infrequent (deviant) stimuli. Since the P300 amplitude is largest when subjects are

requested to respond to the deviant stimulus, P300 waveforms are usually assessed in an oddball paradigm, in which the participant actively discriminates presented deviant stimuli from standard stimuli (Sutton et al., 1965). The P300 amplitude is thought to reflect aspects of further (conscious) processing of relevant stimuli (Näätänen, 1990), and is proportional to the amount of attentional resources that are allocated to the processing of a stimulus (Grillon et al., 1991; Kramer and Strayer, 1988; Sutton et al., 1965). The P300 amplitude has been proposed as a potential endophenotype for schizophrenia (Bramon et al., 2004), i.e. a biological marker that is meaningfully associated with the disease.

Another electrophysiological measure of attention associated with schizophrenia is processing negativity (PN). Processing negativity is elicited whenever a participant is

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requested to selectively attend to a certain stream of information, while having to ignore another (e.g. listen to a male voice, while ignoring a female voice or attend to stimuli to the left ear, while ignoring stimuli to the right ear). This negative deflection is thought to represent a mechanism by which the brain selectively attends to relevant stimuli (Näätänen, 1990). Reduced PN has been reported in medicated (Baribeau-Braun et al., 1983; Iwanami et al., 1998) as well as unmedicated schizophrenia patients (Michie et al., 1990; Ward et al., 1991).

In contrast to P300 and PN waveforms, mismatch negativity (MMN) is best elicited by an oddball paradigm in the absence of attention. This negative deflection to deviant stimuli is thought to reflect the automatic, pre-attentive detection of auditory changes (Näätänen et al., 1978; Näätänen, 1990). Reduced MMN amplitude in schizophrenia patients is a robust finding (Näätänen and Kahkonen, 2009; Umbricht and Krljes, 2005).

P300, PN and MMN waveform abnormalities may be related to the neuropathology of schizophrenia, or to specific parts of the disorder. Information about associations between attention and specific symptoms of schizophrenia could increase understanding of the role attention may play in the pathophysiology of schizophrenia. However, in schizophrenia patients it is difficult to disentangle specific associations with symptom clusters, as the presence and severity of many symptoms are usually correlated. One of the characteristic symptoms of schizophrenia is auditory verbal hallucinations (AVH), occurring in at least 70% of the patients (Sartorius et al., 1986; Slade, 1988). Previous studies have found an association between P300 amplitude and AVH in schizophrenia patients. Havermans et al. (1999) reported a reduction in P300 amplitude in schizophrenia patients with chronic auditory hallucinations compared to patients without auditory hallucinations, and Turetsky et al. (1998) found an inverse correlation between the severity of auditory hallucinations and a frontal P300 subcomponent. It could therefore be hypothesized that the liability of schizophrenia patients to experience AVH may be associated to their decreased attentional capacity. However, most schizophrenia patients with AVH also experience delusions, some degree of disorganisation, and negative symptoms. In addition, patients who do not experience AVH may still be predisposed to hallucinate and develop AVH in another stage of their illness. Interestingly, 10–15% of healthy individuals also experience AVH (Tien, 1991). In this population, AVH occur in the absence of delusions and negative or cognitive symptoms, although the tendency for schizotypal behavior and delusional beliefs is higher than in healthy individuals without AVH (Sommer et al., 2008). Moreover, these non-psychotic individuals with AVH are not using antipsychotic medication, nor do they have a history of hospitalization. Therefore, non-psychotic individuals with AVH provide an opportunity to study whether the deficits of attention associated with schizophrenia are specifically related to AVH, or rather to other aspects of the disease such as negative symptoms or cognitive dysfunction.

Because non-psychotic individuals with AVH and schizophrenia patients share a single isolated symptom, we hypothesize that abnormalities in P300, MMN, and PN amplitudes are similar to those found in schizophrenia patients and will be reduced compared to control subjects without AVH.

2. Methods

2.1. Subjects

Eighteen non-psychotic individuals with AVH and 18 controls were recruited via a website: www.verkenuwgeest.nl (“explore your mind”), see Sommer et al. (2008) for an extended description of the recruitment and selection procedure. All non-psychotic individuals with AVH participated in a previous study by our group, which had the following inclusion criteria (Sommer et al., 2008): (1) Voices were distinct from thoughts and had a “hearing” quality, (2) voices were experienced at least once a month, (3) absence of psychiatric disorders other than anxiety or depressive disorder in full remission as assessed in a psychiatric examination using the Comprehensive Assessment of Symptoms and History interview (CASH) (Andreasen et al., 1992) and the structured clinical interview for personality disorder (SCID-II) (First et al., 1995), (4) absence of alcohol or drug abuse for at least 3 months prior to the assessments, (5) no chronic somatic disorder.

Non-psychotic subjects with AVH and controls without AVH did not meet criteria for a DSM-IV diagnosis, as measured with the CASH and SCID-II interviews. Depressive disorder in complete remission was not an exclusionary criterion. Although the healthy subjects with hallucinations did not have clinical delusions, they did have an elevated schizotypal as shown on the Schizotypal Personality Questionnaire (SPQ) (Raine, 1991). The scores on the Peters et al. Delusions Inventory (PDI) (Peters and Garety, 1996) also showed an elevated paranoid tendency. The combination of hallucinations (perceptual aberrations) and magical ideation present in most non-psychotic individuals with AVH made them score on at least three items on the DSM-IVR criteria for schizotypal personality disorder. However, there was no lack in social capacity nor did the subjects have inadequate or constrained affect. Other important arguments why the subjects did not meet criteria for schizotypy were that their magical beliefs were largely socially accepted (mainly spiritual ideas) and that they were functioning well.

Individuals in the hallucinating group experienced AVH for a mean period of 31 years (s.d.: 15). Neither the non-psychotic individuals with AVH nor the healthy controls had ever participated in psychophysiological research before. To confirm the absence of drug abuse, urine samples were collected and tested for opiates, amphetamines/XTC, cocaine and cannabis. Subjects were tested at 500, 1000, and 6000 Hz (40 dB) to screen for hearing deficits. Smoking and intake of caffeine was not allowed from 1 h prior to testing. Mean age of the AVH group (3 males, 15 females) was 42.8 years (s.d. 11.7), while mean age of the healthy age and gender matched control group (3 males, 15 females) was 43.8 years (s.d. 13.1). The study was approved by the local ethics committees of the University Medical Center of Utrecht. All participants gave their written informed consent before participation in the study.

2.2. Stimulus presentation

All auditory stimuli were presented by a computer using Presentation® (Neurobehavioral systems Inc, Albany, CA, USA) software (soundcard: Creative soundblaster®, 5.1) and

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