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Psychophysical assessment of koniocellular pathway in patients with schizophrenia versus healthy controls

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ABSTRACT

This study was designed to perform psychophysical assessment of koniocellular pathway in patients with schizophrenia versus healthy controls. A total of 26 patients diagnosed with schizophrenia and 15 healthy controls were included. Snellen Visual Acuity Chart scores and Short Wavelength Automated Perimetry (SWAP) visual field testing including global visual field indices [mean deviation (MD), pattern standard deviation (PSD), test time (min)], reliability parameters [false negative responses (%), false positive responses (%) and fixed losses (%)] and average threshold sensitivity [central (parafovea), peripheral area, and four quadrants] were recorded in both groups. Significantly lower MD scores, higher PSD scores and lower average threshold sensitivity at each location across the visual field were noted in schizophrenia relative to control group. In conclusion, our findings revealed a deficit in koniocellular pathway with impaired SWAP global indices and lower threshold sensitivity at each location across the visual field among chronic schizophrenic patients as compared with control subjects. Our findings emphasize potential application of SWAP outside its original intended purpose as a glaucoma test, to provide deeper understanding of the specific contribution of lateral geniculate nucleus to the visual and cognitive disturbances of schizophrenia.

1. Introduction

Deficits in early visual information processing and visual perceptual abnormalities have been frequently documented in schizophrenia, while post-mortem data revealed visual defects to occur secondary to neuropathological abnormalities in visual cortex (Butler et al., 2001; Rund et al., 2004; Glantz and Lewis, 2000; Dorph-Petersen et al., 2007; Yoon et al., 2013; Jahshan et al., 2014). Visual deficits in schizophrenia are particularly important given their association with impaired higher-level cognition, negative symptoms, and functional impairment (Brittain et al., 2010; Green et al., 2012; Rassovsky et al., 2011; Phillips and Silverstein, 2003; Uhlhaas et al., 2005).

Accordingly, along with advanced state of scientific knowledge and availability of improved investigative methods in vision science, visual system has increasingly been recognized in investigating neural mechanisms of the schizophrenia (Yoon et al., 2013; Silverstein and Keane, 2011; Butler et al., 2008).

The magnocellular, parvocellular and the koniocellular systems are the three parallel streams that stretch from the retina, through the lateral geniculate nucleus (LGN) to the input layers of the primary visual cortex (Skottun and Skoyles, 2009; Merigan and Maunsell, 1993; Hendry and Reid, 2000). The parvocellular and koniocellular systems mainly provide the substrate for color vision, but also capable of responding to luminance stimuli, whereas the magnocellular system is mainly involved in the perception of luminance (Skottun and Skoyles, 2009). While the magnocellular pathway is responsible for vision in low light and seeing moving objects, parvocellular pathway is responsible for detailed vision and seeing static objects, and koniocellular pathway for transferring short or blue wavelength (Skottun and Skoyles, 2007; Mashayekhy et al., 2008; Khosravani and Goodarzi, 2013 and Yoonessi and Yoonessi, 2011).

Given their distinctive structural, morphological and physiological features, assessment of three different ganglion cell pathways via selective stimulation has been associated with specific deficits in various disorders (Yoonessi and Yoonessi, 2011).

Schizophrenia is considered to affect retinal ganglionic pathways in

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a similar way with neurological disorders such as multiple sclerosis, Alzheimer's disease, and Parkinson's disease (Yoonessi and Yoonessi, 2011).

Early visual processing dysfunction with preferential deficits in the magnocellular on/off (Butler et al., 2001; Khosravani and Goodarzi, 2013; Yoonessi and Yoonessi, 2011; Butler and Javitt, 2005; Martinez et al., 2008; Schechter et al., 2003, Kéri et al., 2004; Kim et al., 2005) and parvocellular chromatic red/green and achromatic (Skottun and Skoyles, 2007; Delord et al. 2006; Slaghuis, 1998) pathways were documented in schizophrenia, while koniocellular blue/yellow pathway has not been studied to date among schizophrenic patients.

Psychophysical methods, by allowing quantification and control of the deficit on visual task performance, are considered to offer better understanding of physiological and computational mechanisms underlying visual information processing in schizophrenia (Yoon et al., 2013; Silverstein, 2008; Knight and Silverstein, 2001).

Short Wavelength Automated Perimetry (SWAP) is a psychophysical visual field test based on a two-color increment threshold procedure (blue-on-yellow), and designed to assess the functional status of short-wavelength-sensitive color system by isolating the blue-yellow pathway (Demirel and Johnson, 1996; Racette and Sample, 2003). It utilizes a bright yellow background with superimposed blue stimuli that specifically evaluates the function of S cones, and hence konio-cells (Yoonessi and Yoonessi, 2011).

SWAP has been shown to reveal a greater spatial extent of visual field damage and thus earlier detection of visual field abnormalities in patients with glaucoma when compared to standard automated perimetry (white-on-white), and progression of visual field defects up to 3 years earlier (Demirel and Johnson, 1996; Racette and Sample, 2003). Although originally developed to detect visual loss in glaucoma patients, particularly for those at higher risk for glaucoma, it has also been considered useful in detection of vision loss associated with diabetic retinopathy and maculopathy, optic neuropathies, HIV, migraine, and multiple sclerosis (Racette and Sample, 2003; Wild, 2001).

Our hypothesis was that the demonstration of a koniocellular deficit argues against the specificity of a magnocellular deficit in schizophrenia and favours the idea of a global visual deficit in the all early channels in line with already documented parvocellular deficits (Delord et al. 2006; Slaghuis, 1998).

The present study was therefore designed to perform SWAP-based psychophysical assessment of koniocellular pathway for the first time in patients with schizophrenia as compared with healthy controls.

2. Methods

2.1. Participants

A total of 26 patients diagnosed with schizophrenia (mean(SD) age: 36.0(7.2) years, 7.7% were females)and 15 healthy controls (mean(SD) age: 33.9(8.8) years, 33.3% were females) were included in this study conducted at departments of Psychiatry and Ophthalmology in Van Training and Research Hospital, Van. Diagnosis of schizophrenia was made by psychiatrists based on Structured Clinical Interview for DSM-IV (SCID1) criteria for schizophrenia. The control group was randomly selected from patients admitted to our ophthalmology clinic for refraction problems who had no abnormal findings on psychiatric interview considering the Mini International Neuropsychiatric Interview to exclude possible Axis I psychiatric diagnoses and SCID II modules to exclude schizoid, paranoid and schizotypal personality disorders.

All subjects underwent complete ophthalmic examination including slit lamp biomicroscopy, intraocular pressure (IOP) measurement, dilated stereoscopic fundus examination and color vision assessment via the Ishihara test, the Farnsworth Panel D-15 test. Subjects with history of acute angle closure, congenital glaucoma, secondary glaucoma, ocular trauma, ocular infection or inflammatory disease (within the past 6 months), narrow angles or other angle abnormalities, intraocular surgery and severe retinal disease, use of systemic medications that may affect intraocular pressure or visual field sensitivity, co-morbid diseases affecting the visual field (e.g., pituitary lesions, demyelinating diseases, HIV+ or AIDS, or diabetic retinopathy), first-episode schizophrenia, any neurological disorder that might affect performance, psychiatric disorder or substance abuse, as assessed by the SCID, strabismus, best-corrected distance visual acuity worse than 16/20, refractive error greater than ± 5.00 diopters spherical equivalent or greater than ± 2.50 diopters cylinder, lens opacity, cataract, suspected or pathological optic discs and any deficits of color vision (red-green or blue-yellow) were excluded from the study.

Written informed consent was obtained from each subject following a detailed explanation of the objectives and protocol of the study which was conducted in accordance with the ethical principles stated in the “Declaration of Helsinki” and approved by the Van Training and Research Hospital Ethics Committee.

2.2. Procedure

Data on demographic characteristics (age, gender), Snellen Visual Acuity Chart scores and SWAP visual field testing including global visual field indices [mean deviation (MD), pattern standard deviation (PSD), test time (min)], reliability parameters [false negative responses (%), false positive responses (%) and fixed losses (%)] and average threshold sensitivity [dB; central (parafovea), peripheral area, superior nasal quadrant, inferior nasal quadrant, superior temporal quadrant, inferior temporal quadrant] were recorded in both groups. Data on treatment (atypical antipsychotics, typical antipsychotics) and positive (SAPS) and negative (SANS) syndrome scale scores were also recorded in patients with schizophrenia.

In accordance with difference in the monocular nasal and temporal projection toward the colliculus leading to different information representation, entire visual field was assessed to identify the potential differences between crossing and non-crossing ganglion axons as well as between six koniocellular layers in LGN (Nicholls et al., 2001).

2.2.1. Visual acuity

Visual acuity was evaluated via Snellen Visual Acuity Chart scores with higher scores indicating better visual acuity. For analysis purposes, scores obtained on the chart were converted to numerical data (e.g., 20/40 was converted to 0.50).

2.2.2. SWAP visual field testing

SWAP is used to assess the blue-yellow (Short Wavelength Sensitive, SWS) chromatic channel. A blue stimulus, with a peak wavelength that approximates to that of the peak response of the blue cones (also known as S-cones), is presented on a high luminance yellow background. The high luminance yellow background helps to saturate (i.e. reduce the response of) the green, or Medium Wavelength Sensitive (MWS) cones (M-cones), and the red, or Long Wavelength Sensitive (LWS) cones (L-cones) and to suppress, simultaneously, rod activity whilst leaving the S-cones largely unaffected. As a consequence, a degree of ‘pure’ SWS pathway response can be isolated which is not mediated by either the MWS or the LWS pathways (Wild, 2001).

Prior to study enrollment, all subjects had SWAP visual field testing (one in each eye) to limit the likelihood of a residual learning curve effect on the long-term variability. This was considered as the training testing, and only data from the second visual field testing were used in the statistical analysis.

SWAP test was applied at two sessions with 15-min interval and each session included 24-2 SITA SWAP test and 24-2 Full Threshold SWAP test. Overall, three tests including two SITA SWAP tests (training testing and measurement testing) and 1 Full Threshold SWAP test were applied to each eye. For each subject, only one eye with visual field parameters considered reliable was included. Criteria of reliability