Published in final edited form as:

Neuropsychology. 2014 May ; 28(3): 366–372. doi:10.1037/neu0000033.

Binocular Depth Perception in Individuals at Clinical High Risk for Psychosis: no evidence of dysfunction

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Abstract

Objective—In the last decade the interest in the role of the visual system in schizophrenia has grown, with evidence pointing to dysfunction in bottom-up visual processing that leads to early visual processing deficits. A fundamental component of visual perception is binocular depth perception (BDP), i.e. depth perception derived by the difference between the images impressed upon the left and right retina. Two studies reported impaired BDP in schizophrenia and suggested a possible developmental deficit of brain structures involved in early visual processing. The aim of this study was to examine BDP in a young population at clinical high risk (CHR) of developing psychosis to determine if this dysfunction is present in this potentially pre-psychotic period.

Methods—Forty-two CHR participants and 44 healthy controls were assessed using a computerized test of depth perception; a subsample completed a test of stereopsis. The computerized test was comprised of two trial blocks, with four conditions at increasing level of difficulty, where participants were asked to discriminate the relative depth of two stimuli simultaneously presented on the screen.

Results—BDP was not impaired in the CHR group, whose performance was similar to that of the control group on both measures. For the CHR group performance in both tests was not correlated to positive symptoms.

Conclusions—These results indicate that BDP is preserved in individuals at CHR for psychosis and impaired BDP should not be considered a vulnerability marker for schizophrenia. Nevertheless future studies should verify BDP's potential power in predicting schizophrenia.

Keywords

stereopsis; depth perception; schizophrenia; clinical high risk; psychosis

1. Introduction

Visual perception is the result of complex mechanisms of integration of visual information coming from multiple sources. It is through these integrative mechanisms that a 3D spatial representation is created from the flat image impressed upon the retina. To achieve depth perception, our visual system elaborates information coming from both monocular (e.g.

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linear perspective, relative size, texture, gradient) and binocular depth cues (e.g. binocular disparity). Due to the horizontal separation between the eyes (approx. 6 cm), the images seen by the left and right eyes are slightly different. Using this difference, which is known as binocular disparity, the visual system is able to infer the distance of all objects in the visual field from our perspective. Binocular depth perception (BDP) is the perception of depth derived from binocular disparity. The “stereo pairs” of the visual scene are then combined to form one 3D percept through a mechanism known as *stereopsis*, which literally means *solid vision*. Although the cerebral mechanisms involved in stereopsis are still not fully understood, impaired BDP can be interpreted as evidence of a deficit in early visual processing, due to either damaged input coming from magnocellular and/or parvocellular visual pathways, or to impaired cortical integrative mechanisms of sensory information with top-down signals (Schechter et al., 2006; Parker, 2007).

Deficits in both early visual processing, as shown by studies using contrast sensitivity or transient event-related potentials (Javitt, 2009), and integrative visual processes, documented using tasks such as perceptual closure or contour integration (Silverstein & Keane, 2011), represent a core feature of schizophrenia. Although numerous visual and perceptual deficits have been consistently observed in individuals with schizophrenia, their first-degree relatives and individuals with schizotypy (e.g. Green, Lee, Wynn, & Mathis, 2011), other deficits seem to be associated with disorganized symptoms (Keane, Joseph, & Silverstein, 2013a; Silverstein, & Keane, 2011) and are particularly pronounced during the acute phase of the illness (Keane, Silverstein, Wang, & Papathomas, 2013b).

Most studies in the field of visual processing in schizophrenia have focused on bidimensional visual processing, with far less attention given to depth perception. Only two studies directly assessed binocular depth perception in this population (Schechter et al., 2006; Kantrowitz, Butler, Schechter, Silipo, & Javitt, 2009). These two studies assessed stereopsis illusion using tests of stereoacuity that are commonly used in routine visual examinations. Schechter and colleagues (2006) used the Graded Circle test (derived from the Wirt stereo test; Emmes, 1961), which has nine arrays of four circles, one of which appears as three-dimensional when seen through polarized glasses. Kantrowitz and colleagues (2009) also used the Graded Circle test along with the Frisby Stereo Test (Frisby, 1980) and random dot stereograms (Julesz, 1971). In both studies, although a deficit in BDP was observed in patients with schizophrenia and schizoaffective disorder, it was unrelated to positive and/or negative symptoms or anti-psychotic medications. Recommendations of both studies included the need to assess BDP at earlier stages of the illness. Since BDP starts developing in newborns and reaches adult level by the age of nine (Aslin, & Dumais, 1980; Atkinson, 1984), Schechter et al. (2006) suggest that a BDP deficit in schizophrenia could reflect a failure of plasticity occurring during childhood and thus could be already present before the onset of schizophrenia.

With recent progress in risk identification methodology, it is now possible to identify individuals who appear to be putatively prodromal for psychosis, that is at clinical high risk (CHR) (Addington, & Heinssen, 2012) of developing a psychotic disorder, 36% of whom will develop psychosis within 3 years (Fusar-Poli et al., 2012). With respect to visual processing, there is already evidence suggesting alterations in visual contrast sensitivity

(Keri, & Benedek, 2007), visual form perception (Kimhy et al., 2007), and late stage visual processing (Oribe et al., 2013) in the CHR population. There is also evidence of an abnormal sensitivity to depth-inversion illusions (i.e. visual illusions where concave objects appear convex) in both patients with schizophrenia and CHR individuals (Koethe et al., 2006; Koethe et al. 2009) using the Binocular Depth Inversion Illusion test (BDII; Emrich, 1989). However, the lack of sensitivity to these illusions is based on the hypothesis that individuals would have a poor top-down processing that is unable to contrast misleading sensory (stereoscopic) information and therefore depth-inversion illusions do not aim to assess binocular depth perception directly. Interestingly, abnormal sensitivity to depth-inversion illusions was not observed in a recent study including a large sample of CHR individuals and healthy controls, using the BDII (Lee, Rapisarda, Kraus, Chong, & Keefe, 2012). However, in this study stereoacuity, as assessed by the Randot Stereotest (Stereo Optical and Co.), was found to be significantly lower in the CHR group compared to healthy controls.

Based on this preliminary evidence and on prospective longitudinal studies of children at family high risk for schizophrenia showing that visual dysfunction is already present during early childhood and predicts schizophrenia spectrum disorders in adulthood (Schiffman et al., 2006; Schubert, Henriksson, & McNeil, 2005), the aim of this study was to directly examine BDP in those who are at CHR of developing schizophrenia to assess if this dysfunction is present in this potentially pre-psychotic period. Since a deficit in BDP can be easily diagnosed during early childhood, an in-depth examination of binocular vision could potentially become part of risk identification techniques.

2. Methods and Materials

2.1 Participants

The sample consisted of 42 CHR participants (17 male, 25 female) and 44 age-matched healthy controls (14 male, 30 female). Participants in the CHR group were recruited at the Calgary site as part of the multi-site North American Prodrome Longitudinal Study 2 (NAPLS 2) (Addington et al., 2012) which was established to investigate predictors and mechanisms of conversion to psychosis. All CHR participants were required to meet the Criteria of Prodromal Syndromes (COPS) using the Structured Interview for Prodromal Syndromes (SIPS) (McGlashan, Walsh, & Woods, 2010). Participants were excluded if they met criteria for any current or lifetime axis I psychotic disorder, IQ < 70, past or current history of a clinically significant central nervous system disorder or strabismus. A more detailed description of ascertainment, inclusion and exclusion criteria, and participant details is provided elsewhere (Addington et al., 2012). Healthy controls were recruited through the research participation pool system of the Department of Psychology at the University of Calgary. They were excluded if they had had any psychotic-like experiences, if they had a first degree relative with a current or past psychotic disorder, or if they had strabismus in the past or at the time of the study.

2.2 Measures

Basic demographic information such as age, gender and handedness, were collected. Symptoms were assessed with the Scale of Prodromal Symptoms (SOPS), which consists of 19 items in 4 symptom domains: positive, negative, general, and disorganized. IQ was assessed using the Vocabulary and Block Design of the Wechsler Abbreviated Scale of Intelligence (WASI; Wechsler, 1999).

2.2.1 The BDP test—Tests of stereopsis, such as the Graded Circles test or the random dot stereograms, can be very informative as they show the participant's stereoacuity threshold, i.e. the smallest binocular disparity that can be reliably discriminated. However, 3D perception in the real world is never exclusively dependent on binocular disparity, but rather it is enhanced by other binocular and monocular cues of depth. Consequently, even in presence of dysfunctional BDP, depth perception can be preserved. For this reason, the BDP test was developed to assess BDP with and without the influence of monocular depth cues and at different levels of difficulty (Barbato, Collinson, & Casagrande, 2011). The BDP test is a behavioral computerized procedure with stereoscopic images viewed by means of 3D shutter glasses. This test consists of two different trial blocks. In the first trial block (BD+), images containing binocular disparity within a depth context with monocular cues are presented; in the second trial block (BD) images with binocular disparity as the only depth cue are presented. In the BD+ block stimuli are presented on a complex background representing the interior of a room, while in the BD block stimuli are presented on a simple grey background (Figure 1).

Participants are asked to look at the relative position in depth of two target stimuli, compare their position, and judge whether they are standing at the same depth or not. Target stimuli are black spheres occupying a $2^\circ \times 2^\circ$ area on the computer screen when located close to the observer and a $1^\circ \times 1^\circ$ area when presented in the far position. They are presented at 5° of visual angle, at both right and left sides with respect to the fixation point, which is placed centrally in the visual scene. Stereo pairs of the same visual scene are presented. One image corresponds to the right-eye view and the other to the left-eye view. Binocular fusion is guaranteed by synchronizing the alternated frame rate (60 Hz per eye) of shutter glasses (NuVision, Mc) to the monitor refresh rate (120 Hz). When creating the stimuli, the targets' size and their position in depth were manipulated in a way that determined four conditions with different difficulty level: different depth-different size (DDDS), different depth-same size (DDSS), same depth-different size (SDDS), and same depth-same size (SDSS). By manipulating the size and the depth of the stimuli independently, we obtained that the size was acting as a distractor in 50% of the trials (conditions DDSS and SDDS) thus determining an increasing level of difficulty from SDSS (lowest difficulty) to DDSS to DDSS to SDDS (highest difficulty). When target stimuli were at the same depth, they could be located both close to the observer or both far from him; at different depth levels they could be presented with the right stimulus near to the observer and the left one far from him or vice versa. An example of the four conditions is shown in Figure 2.

Each experimental trial block was preceded by a practice block. A trial block consisted of 128 trials, 32 trials for each of the four conditions. Participants were asked to attend to the

task for 20 minutes, with a short rest at the end of each block. An initial background showing an empty room (or a grey background in the BD block) was presented for about 1s, followed by the target stimuli, which lasted for 3s. The initial background was presented again for 500 ms, before the next trial began. Participants were asked to press different keys on a standard keyboard: “S” for objects located at the same depth, “D” for objects located at different depth. They were explicitly asked to ignore the targets’ size and to judge only according to the stereoscopic 3-D effect. They were sitting in a darkened room in front of a computer display at 56 cm distance. A more detailed description of the BDP test can be found elsewhere (Barbato, Collinson, & Casagrande, 2011).

Stimuli were presented on a high definition CRT 21-inch monitor. E-Prime software controlled stimuli presentation, timing operations, and data collection. Responses were gathered with a standard keyboard. Stimuli have been created using a commercial 3-D rendering package (Cinema 4D). Stereopsis was achieved by means of liquid crystal shutter glasses (NuVision shutter glasses, MacNaughton and Co.).

2.2.2 The Stereo Butterfly Test—Since the BDP test had only been used in one previous study (Barbato, Collinson, & Casagrande, 2011), a subsample of our participants (CHR=14; Controls=14) was administered the Stereo Butterfly Test (Stereo Optical and Co.) which includes sub tests that were used in previous studies with individuals with schizophrenia (Schechter et al., 2006; Kantrowitz, Butler, Schecter, Silipo, & Javitt, 2009). The Stereo Butterfly Test consists of the Graded Circle Stereotest (GCS), the Animals Stereotest and the Random Dot Stereogram (RDS). Since the Animals test is a test to assess stereopsis in young children, it was not used in this study. The GCS consists of nine items of graded difficulty, measuring sensitivity to binocular disparities from 800 to 40s of arc. Each item contains four circles. One of these circles (target) appears to stand out from the background when viewed through polarized glasses if stereopsis is adequate at the given disparity level. Participants were requested to indicate the target. In the RDS participants were requested to recognize the body of a butterfly hidden in a pattern of random dots, measuring sensitivity to binocular disparities of 2000 to 700s of arc.

2.3 Procedure

The study was approved by the Calgary Institutional Review Board. Demographics for the CHR group were part of NAPLS 2 and the controls were asked brief details on age, gender and race. For the CHR participants depth perception was assessed during one of their bi-annual visits for NAPLS 2. For the control group, the BDP test, the Stereo Butterfly Test and the WASI were administered on the same day.

2.4 Data analysis

T-test and Chi-square test were used to compare groups on demographics and IQ. Repeated measures ANOVA, with Group as the independent factor and Block and Condition as within factors, was used to analyze the results of the BDP test, with two separate ANOVAs performed one for accuracy (i.e. percentage of correct responses) and one for response times (RTs). Results of the GCS and RDS were log transformed for normality and analyzed with a

MANOVA between groups. Pearson's and Spearman's correlations were used to determine the association between symptoms and depth perception.

3. Results

3.1 Demographics and IQ

No significant differences between groups were observed in age (CHR: mean=19 years, SD=4.6); Controls: mean=20 years, SD =2.2), gender (CHR: M=17, F=25; Controls: M=14, F=30), or handedness (CHR: R=39, L=3; Controls: R=43, L=1). The IQ was lower in the CHR group (mean IQ 106) as compared to healthy controls (mean IQ=115; $t=-2.66$; $p<0.05$).

3.2 BDP test – Accuracy

Performance of both groups was heterogeneous. The mean accuracy for the CHR group was 79% and the mean accuracy for the control group was 81%. A few participants in each groups performed at such a low level that it was below chance (50%). All the analyses were performed with and without those individuals and the results did not change. See Figure 3.

The ANOVA revealed a main effect for the *Condition* [$F(3,252)=42.46$; $p<0.0001$], with lower accuracy (mean accuracy= 65.76%) in SDDS (highest difficulty), as compared to the other three conditions (DDDS=85.32%; DDSS=82.55%; SDSS=87.82%). See Figure 4. The interaction *Block* by *Condition* [$F(3,252)=7.718$; $p<0.0001$] showed in the SDDS condition lower accuracy in the BD+ trial block (mean accuracy= 61.88%) as compared to BD (mean accuracy=69.63%). The *Group* and *Block* and all other interactions were not significant. See Figure 5.

3.3 BDP test –Response times

The ANOVA revealed a main effect for the *Block* [$F(1,84)=4.079$; $p<0.05$], with longer RTs in the BD+ block (mean RT=1340 ms) compared to BD (mean RT=1299 ms). A main effect for the *Condition* [$F(3,252)=75.10$; $p<0.0001$] showed longer RTs in SDDS condition (mean RT=1493 ms) as compared to the other conditions (DDDS=1243 ms; DDSS=1255 ms; SDSS=1287 ms). The *Group* and all interactions were not significant.

3.4 The Stereo Butterfly Test

In both groups there were only two participants who performed poorly at this test, probably showing that they did not understand the instructions or simply were not motivated to perform the task. The remaining 12 participants in each group performed very well, showing a stereoacuity between 40 and 80 arcseconds for local stereopsis and of 700 arcseconds for global stereopsis. Results of the MANOVA showed that the groups did not differ on the GCS [$F(1,24)=0.023$; $p=0.88$] or on the RDS [$F(1,24)=1.846$; $p=0.19$].

3.5 Relationships with symptoms

There were no significant correlations between positive, negative, disorganized or general symptoms and depth perception (mean accuracy at the BDP test and stereoacuity at the Stereo Butterfly Test) (all $p>0.05$).

4. Discussion

This study aimed at assessing whether a deficit in BDP can be observed in a sample of youth at clinical high risk of developing psychosis. Our results did not highlight any difference between groups in either the BDP test or the Stereo Butterfly Test. In particular, results of the BDP test suggested that the condition with targets of different sizes presented at the same depth (SDDS) was of equal difficulty for both groups. This increase in difficulty was specially impacting performance when monocular depth cues were added to the display, as shown by increase in response times and decrease in accuracy, a result that could be attributed to the use of more complex visual images, which may have increased the cognitive load (Casagrande et al., 2012). Alternatively, the decrease in accuracy observed when monocular cues were added to the display, as confirmed by the main effect for the Block, could have been determined by the lack of familiarity with the task, as the order of the two trial blocks was not randomized between participants. On average, the accuracy of both groups was high (CHR: 79%, Controls: 81%), and did not differ in any condition or trial block. A few participants performed poorly in both tests. However, this result was observed for both groups and possible could be interpreted as a lack of motivation or interest in the tests. Alternatively, although only participants whose vision was normal or corrected to normal were included in our study, it is still possible that some of them were affected by undiagnosed visual impairment (e.g. amblyopia) without being aware of it. At a group level, our results suggest that BDP is preserved in the CHR individuals. These results are in contrast with what has been observed for other aspects of visual processing (e.g. Keri, & Benedek, 2007; Oribe et al., 2013). However, there is also evidence suggesting that not all aspects of visual perception are impaired in this population (e.g. Silverstein et al., 2006; Uhlhaas, & Silverstein, 2005 for a review).

We examined potential relationships between attenuated positive symptoms and BDP and there were no significant correlations. In a recently published study Keane and colleagues (2013b) using depth-inversion illusions, showed a state-dependent effect in patients with schizophrenia as compared to healthy controls, with significantly reduced sensitivity to depth-inversion illusions as patients experienced more positive symptoms. Depth-inversion illusions have proven to be an interesting and useful measure of visual information processing, although they do not allow the direct assessment of monocular and binocular depth perception. We could speculate that these results support those of our study and it could be that an impairment of BDP can only be seen once positive symptoms reach psychotic level. However, the results of Keane and colleagues (2013b) vary somewhat from those of Koethe et al. (2006; 2009), who used a similar paradigm and observed that performance of patients with schizophrenia and individuals at risk for psychosis was equally impaired and significantly different than that of healthy controls. Regardless their paradigms are not a direct measure of BDP.

However, in contrast to our results Lee et al. (2012) used a measure of stereoacuity and a significant difference between at-risk individuals and healthy controls was observed in a large sample of 463 controls and 75 at-risk individuals. Unfortunately stereoacuity was measured only in a sub-sample of 14 of our participants within each group.

This study has several limitations. It is cross sectional, and as such we do not know the clinical outcome of these CHR individuals, i.e., we do not know how many of our CHR participants will convert to psychosis, and amongst potential converters we do not know how many will develop schizophrenia. Secondly, the sample size was very small for the assessment of stereoacuity. If a BDP deficit is the result of failure of plasticity occurring during childhood (Schechter et al., 2006), it should be possible to observe this deficit early on in those who later develop schizophrenia. Larger and longitudinal studies may answer this question by monitoring over time BDP in CHR individuals. Alternatively, the impaired BDP observed by previous studies could be the result of degenerative processes that take place after the first episode or even later on during the course of the illness. The strengths of this study are that it is the first to directly assess BDP in a sample of youth at CHR of developing psychosis using both a new and well established measure to assess depth perception. Relative to other cross sectional studies in this field, we had a reasonably sized sample for our BDP test.

In conclusion, it appears as if BDP may be preserved in individuals at CHR for psychosis; therefore a dysfunctional BDP may not be a vulnerability marker for schizophrenia. Future longitudinal studies may be able to verify the potential predictive power of BDP in helping predict the risk of developing schizophrenia.

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Figure 1.
Different backgrounds used in the two trial blocks

DDDS= different depth, different size; DDSS= different depth, same size; SDDS= same depth, different size; SDSS= same depth, same size.

Figure 2.
Four target conditions

*mean accuracy= 79%, **mean accuracy= 81%, CHR= Clinical high risk

Figure 3.
Performance of both groups on the BDP test.

DDDS= different depth, different size; DDSS= different depth, same size; SDDS= same depth, different size; SDSS= same depth, same size.

Figure 4.

Main effect of the Condition in the analysis performed on accuracy

* $p < 0.0001$

DDDS= different depth, different size; DDSS= different depth, same size; SDDS= same depth, different size; SDSS= same depth, same size; BD= binocular disparity; BD+= binocular disparity + monocular depth cues.

Figure 5.
Interaction Block by Condition in the analysis performed on accuracy