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ORIGINAL PAPER

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Binocular depth inversion as a paradigm of reduced visual information processing in prodromal state, antipsychotic-naïve and treated schizophrenia

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Abstract The binocular depth inversion illusion test (BDII) represents a sensitive measure of impaired visual information processing that manifests in various experimental and naturally occurring psychotic states. This study explores impairment of visual processing in different major psychiatric diseases investigating 313 subjects, suffering of either an initial prodromal state of psychosis (IPS) or a first-episode, antipsychotic-naïve paranoid schizophrenia (SZ-N) as well as short-term antipsychotically treated schizophrenia (SZ-T), major depression (MDD), bipolar disorder (BD), dementia (D), and healthy controls (HC). Patients suffering from either IPS, SZ-N or a SZ-T showed significantly higher scores of BDII compared to HC, indicating that visual processing is already disturbed at an early state of the disease. For MDD, BD and D no statistically significant difference was found compared to HC. As the identification of individuals at high risk for developing schizophrenia relies on rating scales assessing subtle, pre-psychotic psychopathology, it would be of interest to have more diagnostic criteria available, testing, e.g. cognitive and perceptual impairment. We therefore analysed the receiver operating characteristic (ROC) curve, testing prodromal cases versus a clinically relevant sample of non-psychotic patients and controls, which included HC as well as the groups of patients suffering from MDD, BD or D revealing a AUC of 0.70. Thus, the BDII may be useful as an additional neuropsychological test for assessment of patients at high risk for developing schizophrenia.

Key words Binocular Depth Inversion Illusion (BDII) · schizophrenia · prodromal · depression · bipolar

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Introduction

Regular visual perception results from an interaction of exogenous (e.g. stimulus-driven) and endogenous (e.g. prior knowledge and attention) processes. At least two systems involved in visual processing need to be differentiated: brain areas primarily involved in "bottom-up" stimulus processing (e.g. striate and extra-striate cortex, temporal cortex), and brain areas primarily involved in "adaptive" or "top–down" modulation and stimulus processing (e.g. prefrontal cortex and posterior parietal cortex). Manipulations of exogenous factors like stimulus category or spatial frequency and endogenous factors like globally or locally directed attention or space-based attentions could be used to study the interaction of "top down" and "bottom up" processes [10]. Impairment of such adaptive systems for internal correction has been suggested to explain the disintegrative and reality-impairing properties of psychotic disorders and was tested by various paradigms that manipulate either the external or internal process: one such paradigm is the binocular depth inversion illusion (BDII) [4, 7–9, 20, 27, 30].

BDII describes an optical illusion that occurs when a three-dimensional object is presented pseudoscopically (i.e. visual information intended for the left eye is presented to the right eye and vice versa), thereby

giving rise to an inverted percept of the object; e.g. a face, which is normally convex, should be perceived as concave. Yet, under regular conditions, the face will continue to be experienced as convex which, though objectively wrong, is a well-known and more plausible percept. This internal correction of implausible sensory data is hypothesized to result from "adaptive" or "top-down" processes within perceptual networks, which adjust rather impossible or implausible contents of perception so that they become consistent with the current context and past experiences [reviewed in 10].

It has been shown that patients suffering from schizophrenia show a marked impairment in BDII, most likely reflecting an impairment of adaptive top-down processes of internal correction [3, 26, 27]. Schneider et al. [26] suggested that BDII impairments in psychotic disorders could be regarded as a state-marker, being most pronounced in severe acute states of the illness and returning to normal perception in remission. They investigated BDII in a group of acutely psychotic patients before and after treatment with antipsychotic medication and found a widely restored perception. An effect of gender or rescue medication, e.g. benzodiazepines, could not be observed. BDII impairments do occur in acute cannabis- or cannabinoid-induced altered states of consciousness [5, 18, 19]. Ha et al. [11] reported that dysfunction in perceptual processing in schizophrenic patients is seen in terms of configuration, but not feature, using a paradigm of depth inversion.

A very recent study of our own group showed a disturbance of BDII already in patients meeting the criteria for an initial prodromal state of psychosis (IPS) [15]. These patients showed BDII scores, which appeared at an intermediate level between healthy controls and patients with schizophrenia (SZ). However, while this was statistically significant when compared to healthy controls, there was no such significant difference from patients experiencing their first schizophrenic episode. BDII impairments at an early, prodromal state of the illness suggest that the impairment in visual information processing precedes the first manifestation of acute psychosis rather than reflects its psychopathological features [1, 25].

Semple et al. [30] found that regular cannabis users have significantly higher BDII scores for inverted images of human faces. This was not due to disturbances in the primary processing of visual information, as there was no significant difference between the groups of depth perception of normal images. They concluded that, compared to other neuropsychological tests used, BDII appears to be a more sensitive tool for the detection of subtle impairments of visual information processing.

However, most of these studies were done with small samples and examined patients already under antipsychotic medication. Additionally, a comparison of these findings to different psychiatric diseases is still lacking. Therefore, we investigated the hypothesis that visual information processing is impaired particularly in schizophrenia and already in prodromal states and first-episode, antipsychotic-naïve schizophrenic patients but not in other relevant psychiatric diseases like major depression, bipolar disorders, and dementia, when compared to healthy controls. We designed this study as a naturalistic and clinically driven approach to the value of the BDII as a diagnostic tool.

Experimental procedure

The study was carried out in accordance with the Declaration of Helsinki. The study was performed at the University of Cologne and the local Ethics Committee approved the study protocol. All patients and volunteers gave written informed consent.

Subjects

A total of 313 patients and volunteers participated in the study and were investigated between 1999 and 2006.

Eighty-one healthy controls (HC) were recruited by word of mouth and participated in the study. They were carefully screened for medical disorders and for current or previous psychiatric illnesses using the SCID for DSM-IV. They were paid to compensate for their expenses. Those with a history of a manifest psychiatric disorder (according to DSM-IV) or a serious medical illness were excluded from the study. History of drug use was taken from all participants. No previous or current cannabis abuse or dependence and no cannabis use within the last six months prior to entering the study was allowed for HC. All volunteers showed a negative urine drug screening [17].

The six patient samples consisted of 75 antipsychotic-naïve (i.e. never treated with antipsychotics) first-episode acute paranoid schizophrenic patients (SZ-N) and 74 shortly (for an average of 9 days) antipsychotically treated acute paranoid schizophrenic patients (SZ-T) and 22 patients suffering from an initial prodromal state of psychosis (IPS), who had been referred to the Department of Psychiatry and Psychotherapy of the University of Cologne. Further 35 patients were suffering from major depression (MDD), 20 were suffering from bipolar disorder (BD), and six patients suffered dementia of Alzheimer's type. All patients fulfilled pertinent DSM-IV diagnostic criteria [2] for the respective disease (DSM-IV: 295.4 or 295.30; 296.2; 296.4/5; 290.10).

The respective psychopathology was documented using the appropriate established rating scales, as the Positive and Negative Symptom Scale (PANSS) [13], the Hamilton Depression Rating Scale (HAMD) [12],

Table 1 Basic demographic data

		IPS	SZ-N	SZ-T	MDD	BD	D	HC
	n	22	75	74	35	20	6	81
Age in years	Mean	26.0	28.7	30.9	42.9	37.0	65.5	27.3
	SD	5.1	8.3	11.4	16.1	11.5	12.9	5.8
	P value*	0.631	0.603	0.346	0.000001	0.0004	0.00005	–
Gender	Male	18	51	54	20	9	1	43
	Female	4	24	20	15	11	5	38
	p value†	0.016	0.072	0.013	0.839	0.620	0.110	–
Cannabis use	Low	16	49	55	33	17	6	80
	High	6	26	19	2	3	0	1
	P value†	0.0003	<0.0001	<0.0001	0.497	0.024	1.000	–

HC healthy controls, *IPS* initial prodromal state of psychosis, *SZ-N* antipsychotic-naïve, first-break paranoid schizophrenia, *SZ-T* antipsychotically treated paranoid schizophrenia, MDD: major depressive disorder, *BD* bipolar affective disorder, *D* dementia, *SD* standard deviation
*Mann Whitney test, HC versus IPS, SZ-N, SZ-T, MDD, BD, and D
†Fisher's exact test, HC versus IPS, SZ-N, SZ-T, MDD, BD, and D

the Young Mania Rating Scale (YMRS) [32] and the Mini Mental State Examination (MMSE) [6].

IPS inpatients were examined for prodromal and psychotic symptoms at the Cologne Early Recognition and Intervention Centre for mental crises (FETZ) using the Schizophrenia Prediction Instrument—Adult version (SPI-A) [28], the Scale of Prodromal Symptoms (SOPS) [22] and the PANSS. An initial prodromal state was assumed if any of ten cognitive-perceptive basic symptoms, which were found to be highly predictive of schizophrenia in an earlier prospective study [14], or, in line with the 'ultra-high risk' (UHR) criteria [24], any attenuated (APS) or any transient psychotic symptom (BLIPS) was present. The UHR criteria have shown an average 12-month conversion rate of 38.2% in unspecifically or untreated prodromal subjects predominantly with APS [21]. Exclusion criteria for IPS were: (1) present or past psychotic episode; (2) current substance abuse or dependence; (3) neurological, cerebral or other somatic illness that may account for the symptoms; (4) mental retardation, and (5) age below 18 or above 40 years. Eight of the IPS (36.4%) inpatients have developed manifest psychosis since the date of the examination. The mean time from baseline assessment to transition was 54.7 (standard error 9.4) months. Patients not yet converted were followed up from 19 to 93 months.

IPS, SZ-N, SZ-T, and HC were classified according to lifetime cannabis use (low cannabis use, less than twenty times/lifetime; moderate cannabis use, more than 20 times/ lifetime).

Stereoscopic vision was tested using the TNO test (Lameris, Utrecht, Netherlands) in all subjects. Details of sample characteristics are given in Table 1. Experienced psychiatrists, required for giving correct psychopathological assessments, performed all investigations and were not blinded. To avoid a rater's influence in BDII, the BDII rating scale comprises a falsehood score, and participants exceeding the cut-off value were excluded from the study.

Binocular depth inversion illusion test (BDII)

A detailed description of the BDII is given elsewhere [19]. Stereoscopic pictures were taken from two different groups of natural objects: ordinary objects with a high degree of familiarity (e.g. a chair) and human faces of middle-age males. BDII total score (BDII-Total) is defined as the average value of the sum of all measures. The group score for faces (BDII-Faces) was most affected in previous studies [15, 19, 30] and will therefore be expressed separately.

Faces were photographed as frontal views. Nineteen stereoscopic pictures were scanned and presented on a computer screen (overall stimulus size 1024×768 pixels) for a maximum of 60 sec. each. Stimuli were presented twice, either in regular or psychoscopic view. Depth inversion was achieved by swapping the images such that the original left-eye image was delivered to the right eye and vice versa.

A mirror stereoscope slightly modified from the original described by Wheatstone [31] was used to achieve stereoscopic vision (Fig. 1). The distance between the computer screen and the mirror stereoscope in front was approximately 40 cm. The ability to rotate the lateral mirrors enabled the adjustment of the stereoscope to the individual interocular distance of each participant. The subjects were told that the objects presented would be either convex or concave, and they were asked to describe each image in terms of depth of the nose and overall impression using the terms 'clearly concave', 'concave', 'flat', 'convex' or 'clearly convex'. A score between zero and four was awarded for each description, on a five-point rating scale. For each feature a maximum score of four could be achieved; for clearly identifying the true depth, whereas zero points were assigned for complete perceived inversion. BDII-total for each group of pictures was expressed as the sum of the BDII scores of each inverted object, divided by the maximum possible score, thus covering a range from 0 = 'total BDII' or

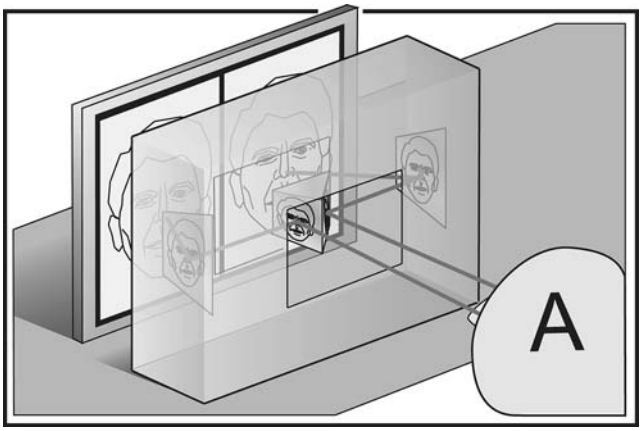

Fig. 1 Schematic drawing of BDII test condition. A stereoscopically taken picture of an object is presented on a computer monitor and mirrored to a viewing area where both halves of the stereoscopic picture are presented to the respective eye of an observer. Exchanging the *left* and the *right* half of the stereoscopic picture when presented to the observer reveals pseudoscopic vision

'internally adjusted depth perception' to 1 = 'no BDII' or 'correct, unadjusted depth perception'.

Statistical analysis

Statistical analyses were performed using SPSS software (SPSS Inc., Chicago, IL). BDII score data (total scores, image group 'faces') were analyzed for group differences in location by means of the Kruskal-Wallis test (more than two groups) and the Mann–Whitney test (two groups) corrected for ties. Supplementary, in order to adjust for a possible confounding by age, gender and cannabis use, results from one-way analysis of variance with covariates are presented (score data are only approximately normally distributed). Only raw *P* values are presented. However, to guard against the pitfalls of multiple testing, comparisons of patient groups with healthy volunteers remaining significant after a Bonferroni correction (i.e. $P < 0.05/12 = 0.0042$) were highlighted. Correlation between psychopathological tests (HAMD, YMRS, PANSS, MMSE) and BDII total scores was assessed by calculation of Spearman's rank correlation coefficient (with two-sided *P* value). Finally, ROC analyses were performed (curves and areas underneath).

Results

Binocular depth inversion

The overall group comparison revealed significant differences for BDII 'total' scores (Table 2) between schizophrenic patients, antipsychotic-naïve and the healthy controls (HC) as well as in all other groups (IPS, SZ-T, MDD, BD, D), and a more prominent difference in the BDII scores 'faces', showing significant differences between the group of psychotic patients including initial prodromal patients (SZ-N, SZ-T and IPS) and HC, MDD, BD and D (both Kruskal–Wallis tests: $P \leq 0.004$).

For BDII 'total', in SZ-N the score was significantly elevated compared to HC (P = 0.001), a trend was seen in the antipsychotics-treated group SZ-T ($P = 0.008$) and in IPS ($P = 0.037$).

The BDII 'faces' scores were significantly elevated in IPS ($P = 0.002$), SZ-N and SZ-T (both $P < 0.001$), when compared to healthy controls, as shown in the figures for BDII 'total' (Fig. 2a) and BDII 'faces' (Fig. 2b).

Regarding prognosis we did not find any association between BDII scores and time to transition into frank psychosis ($P = 0.24$, log rank test at median split of BDII scores).

The BDII scores for the other groups of patients did not differ from HC, patients suffering MDD showed slightly higher scores than HC ('faces': $P = 0.171$, 'total': $P = 0.331$), in bipolar disorder the score was lower ('faces': $P = 0.973$, 'total': $P = 0.959$),

Table 2 Binocular depth inversion scores 'total' and 'faces' compared to healthy volunteers

BDII scores		IPS	SZ-N	SZ-T	MDD	BD	D	HC
	n	22	75	74	35	20	6	81
'Total'	Mean value	0.42	0.43	0.41	0.39	0.34	0.25	0.35
	Standard deviation	0.16	0.16	0.16	0.19	0.18	0.15	0.16
	Non-parametric *P* value*	0.037	0.001†	0.008	0.331	0.959	0.115	–
	Parametric *P* value‡	0.096	0.008(†)	0.029	0.093	0.998	0.589	–
'Faces'	Mean	0.42	0.42	0.39	0.36	0.31	0.22	0.30
	Standard deviation	0.17	0.18	0.18	0.21	0.21	0.14	0.15
	Non-parametric *P* value*	0.002†	0.00002†	0.0004†	0.171	0.973	0.247	–
	Parametric *P* value‡	0.011(†)	0.0002†	0.002†	0.019	0.571	0.910	–

HC healthy controls, *IPS* initial prodromal state of psychosis, *SZ-N* antipsychotic-naïve, first-break paranoid schizophrenia, *SZ-T* antipsychotically treated paranoid schizophrenia, MDD: major depressive disorder, BD: bipolar affective disorder, *D* dementia

*Mann–Whitney test, HC versus IPS, SZ-N, SZ-T, MDD, BD, and D

‡One-way ANOVA with diagnosis (Total [Faces] $P = 0.069$ [0.004]), adjusted for age ($P = 0.111$ [0.043]), sex ($P = 0.975$ [0.528]) and cannabis use ($P = 0.391$ [0.569]), HC versus IPS, SZ-N, SZ-T, MDD, BD, and D

†Still significant at (multiple) level 0.05 when accounting for multiple testing, i.e. $P \leq 0.05/12 \approx 0.0042$ (Bonferroni correction) (†)*P* values 0.008 (total, SZ-N vs. HC) and 0.011 (faces, IPS vs. HC) are not statistically significant anymore when accounting for multiple testing (Bonferroni bound 0.05/12 = 0.0042)

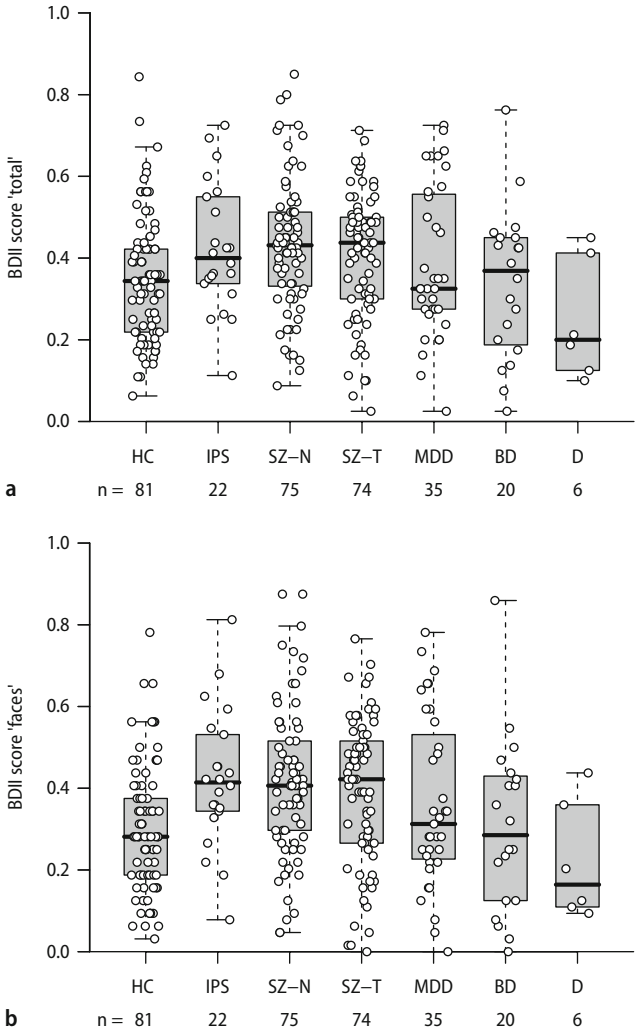

Fig. 2 **a** Binocular depth inversion illusion (BDII) score for all stimuli ('total'). Patients at their initial prodromal state (*IPS*; $P = 0.037$), antipsychotic-naïve first episode schizophrenia patients (*SZ-N*; $P = 0.001$) and treated schizophrenia patients (*SZ-T*; $P = 0.008$) differed significantly from healthy controls (*HC*). No significant difference could be observed for patients suffering major depression (*MDD*; $P = 0.331$), bipolar disorder (*BD*; $P = 0.959$) or dementia (*D*; $P = 0.115$). **b** Binocular depth inversion illusion (BDII) score for 'faces'. Patients at their initial prodromal state (*IPS*; $P = 0.002$), antipsychotic-naïve first episode schizophrenia patients (*SZ-N*; $P < 0.001$) and treated schizophrenia patients (*SZ-T*; $P < 0.001$) differed significantly from healthy controls (*HC*). No significant difference could be observed for patients suffering major depression (*MDD*; $P = 0.171$), bipolar disorder (*BD*; $P = 0.973$) or dementia (*D*; $P = 0.247$)

while lowest BDII scores were observed in dementia ('faces': $P = 0.247$, 'total': $P = 0.115$).

Two patients of the group of bipolar disorder were suffering mania, but higher scores in the YMRS were not associated with higher BDII scores (first patient: YMRS score: 30, BDII-scores 'total': 0.350 and 'faces': 0.250; second patient YMRS score: 15, BDII-scores 'total': 0.175 and 'faces': 0.125).

Investigating the influence of age, gender, and lifetime cannabis use by applying an additional one-way analysis of variance with covariates (see above), we found that none of these factors affected our results essentially (Table 2) though *P* values from the parametric approach (adjusted for age, gender and lifetime cannabis use) tend to be larger than those from the non-parametric approach. Specifically, the *P* values 0.011 ('faces', IPS vs. HC) and 0.008 ('total', SZ-N vs. HC) did not remain statistically significant when accounting for multiplicity (Bonferroni bound 0.05/12 = 0.0042). This may in part be a consequence of adjustment for confounding and/or due to greater complexity of the applied parametric method (i.e. addressing more hypotheses, making more assumptions which may only hold approximately, using only complete observations). As the Bonferroni method is conservative (i.e. more stringent than necessary) we thus argue in favor of statistically significant differences between IPS and HC ('faces') and between SZ-N and HC ('total').

Psychopathology

There was no significant correlation between BDII scores ('total', 'faces') and psychopathology in any group (PANSS for IPS, SZ-N, SZ-T; SOPS, SPI-A for IPS; HAMD for MDD, BD; YMRS for BD; MMSE in D), except in the group of first-onset; antipsychotic-naïve psychosis a weak correlation was shown for the PANSS subscore for negative symptoms (Spearman's rho correlation coefficient: 'total' 0.233, $P = 0.048$; 'faces' 0.259, $P = 0.028$).

ROC analyses

The discriminatory value of BDII 'faces' was evaluated by ROC (receiver operating characteristics) analysis (Fig. 3). A ROC curve depicts the trade-off between sensitivity and 1—specificity with varying threshold value (positivity criterion). The area under the ROC curve (AUC) is a popular summary measure of the discriminatory capacity of a marker where a value of 0.5 means random classification and of 1.0 perfect discrimination.

To test the diagnostic value of BDII 'faces' we compared a mixed group of 81 healthy controls and 61 non-psychotic patients (MDD, BD, and D) to two samples from schizophrenia spectrum:

First, we compared to 75 SZ-N and an area under the curve (AUC) of 0.67 (Fig. 3a) was revealed (standard error 0.038; asymptotic significance <0.001).

Second, we compared to 22 IPS and an area under the curve (AUC) of 0.69 was revealed (standard error 0.056; asymptotic significance 0.004). Choosing a cut-off value of 0.26 yields a sensitivity of 0.86 and a 1-specificity of 0.56 (Fig. 3b).

Discussion

We investigated the hypothesis that binocular depth inversion illusion (BDII), a visual, 'top–down' driven

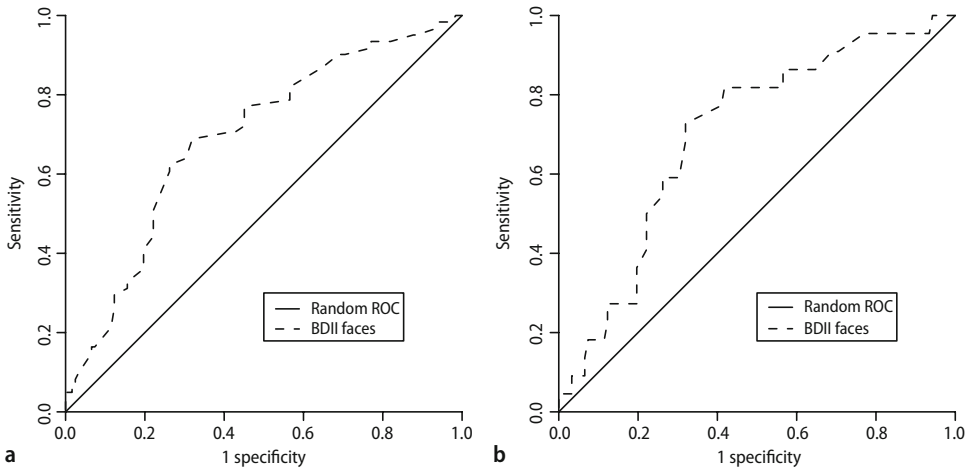

Fig. 3 **a** ROC analysis of BDII score 'faces' for antipsychotic-naïve patients (n = 71; SZ-N) versus the group of healthy controls and subjects suffering depressive or bipolar disorder or dementia (n = 142; AUC: 0.69). **b** ROC analysis of BDII score 'faces' for initial prodromal patients (n = 22; IPS) versus the same group of healthy controls and subjects suffering depressive or bipolar disorder or dementia (AUC: 0.70)

information process [10], is impaired in schizophrenia and particularly in its early stages, but neither in healthy controls nor in other major psychiatric illnesses.

In accordance with our hypothesis, patients suffering from either an initial prodromal state of psychosis (IPS) or from first-episode, antipsychotic-naïve schizophrenia (SZ-N) showed significantly higher scores of the BDII score 'faces' compared to healthy controls (HC), indicating that visual processing is already disturbed at this early state of the disease [15]. In accordance with previous studies, BDII scores in short-term antipsychotically treated schizophrenic patients (SZ-T) were significantly higher than in HC [26]. A larger sample of antipsychotic-naïve schizophrenic and initial prodromal patients was not systematically investigated before. Our group reported elevated BDII scores in initial prodromal states of psychosis and patients suffering first episode of psychosis in a smaller sample, which was investigated in an experimental model psychosis [15]. This study revealed significantly elevated BDII scores for IPS patients when compared to healthy controls. However, BDII scores of these patients did not differ significantly from first episode schizophrenia patients.

Interestingly, differences between the groups IPS, SZ-N and SZ-T were not statistically different in our study. In this much larger collection of patients, IPS showed an impairment of BDII well comparable to SZ-N. This may represent an early perceptual disturbance reported by other groups, which was found most predicting for the transition into frank psychosis [14].

Schneider et al. [26] reported an improvement of disturbed BDII during antipsychotic treatment. The inversed faces were perceived more illusionary, driven by a suggested increase in top-down processing during recovery. By the time of discharge from hospital, there was no significant difference between the group of clinically remitted schizophrenic patients and healthy controls in BDII. In our study, the group of already treated patients was taking antipsychotic medication for a short period of time only. One may speculate that this short-time treatment was not sufficient to affect the highly elevated scores of BDII significantly. Nevertheless, the extent of BDII impairment in initial prodromal states of psychosis would argue for BDII being either a very early, preceding state marker or a trait marker of schizophrenia. The latter is further supported by own unpublished data of a double-blind, controlled clinical trial in acute schizophrenic patients treated with two different antipsychotic drugs for four weeks, where no differences of BDII scores were found. Therefore, the finding of Schneider et al. [26] may be considered a false positive result.

Our study investigated for the first time disturbances in visual information processing using the BDII not only in schizophrenia spectrum disorders but also in distinct groups of patients suffering depression, bipolar disorder or dementia. For these groups of patients we found no statistically significant difference compared to healthy controls.

In the longitudinal study of Schneider et al. [26] impaired BDII in schizophrenia was compared to samples of healthy volunteers and depressive patients. In the small group (n = 10) of depressive patients BDII scores were elevated but differed significantly from both schizophrenic patients and healthy controls. Limitations of this study are the small sample sizes and the lack of correction for multiple testing.

In line with these results, our study shows a slightly altered visual information processing in a larger sample of patients acutely suffering from major depression, extending this research to bipolar disorders as well. Recent research on mood disorders has given us an increasingly detailed picture of the emotion processing abnormalities in these disorders as well as of the underlying cognitive and neural mechanisms. In sum, the data indicate that MDD is associated with more attention and memory bias toward negative cues and may be linked to with abnormalities in the excitability of the brain emotion-related circuits

as well as disruption of the cortico-limbic connections which are important for the regulation of emotional responses [16]. However, also of potential neurobiological interest, our findings gained no statistical significance.

Our results suggest that visual information processing is disturbed to a far lesser extend in other major groups of psychiatric patients. This leads to the question of the clinical usefulness of BDII as a diagnostic tool.

Schizophrenia is associated with an immense burden for patients, relatives and the society. Thus it is of utmost interest and importance to detect persons clinically at risk for psychosis as early as possible in their initial prodromal states. As the rationale for prevention relies on the validity of prediction, it always implies limitations [29]. In terms of prediction, the criteria currently used for risk assessment are almost exclusively based on psychiatric interviews. As to cognitive basic symptoms, examinations of accuracy regarding onset of psychosis within 12 months after index-assessment revealed that presentation with at least two out of nine symptoms of the "cognitive disturbances"-cluster resulted in a transition rate to psychosis of 23.9% within 12 months. The sensitivity of this predictive basic symptom syndrome for transition from initial prodromal states to psychosis within 12 months was 0.67, the specificity 0.83 and the positive predictive value 0.79 [14]. As it would be interesting to have more diagnostic criteria available, the BDII offers the possibility to obtain information about cognitive impairments; the added neuropsychological information might be useful for the diagnosis an initial prodromal state of psychosis. Thus, we performed a receiver operating characteristic (ROC) curve, which is an effective method of evaluating the quality of performance of a diagnostic test, testing acutely schizophrenic and prodromal cases against a group of controls, which included healthy controls as well as the groups of patients suffering from depression, bipolar disorder or dementia. The mixed group was chosen to reflect a more clinical setting.

In our sample of IPS patients, the AUC will be 0.70 as a measure of overall diagnostic performance, combining sensitivity and 1-specificity for varying threshold value (Fig. 2b). In SZ-N patients, the AUC was slightly less 0.69. This is comparable to other neuropsychological test performance in psychiatry. Merely the numerical value of AUC is not helpful in specific diagnostic situations, e.g. during screening for a serious disease in a high risk group, thus, a cutoff range for a positive test should be chosen in a way as to provide good sensitivity, even if the false positive rate (FPR) is high [23]. For IPS patients, choosing a cut off value of the BDII score of 0.257 yields a sensitivity of 0.86 and a FPR (1-specificity) of 0.56. Given the convenience of the BDII, which is as a test accomplished in about 20 minutes and feasible by medical stuff, the BDII which is as a test accomplished in about 20 minutes and unproblematic to carry out, the BDII may be useful as an additional neuropsychological test. This could be of value for centers of early recognition of psychosis as well as hospitals specializing in the treatment of schizophrenic patients.

In conclusion, BDII represents a valid tool for the diagnostic of psychotic disorders and schizophrenia in particular. The most powerful part of the BDII is the sub-score "faces" and for diagnostic purposes it may well be sufficient to use this sub-score solely. Up to now, none of the studies investigating BDII used controlled or blinded designs. These studies are currently ongoing and may add to our understanding of the diagnostic value of BDII.

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