



Cognitive disorganisation in schizotypy is associated with deterioration in visual backward masking

Céline Cappe^{a,*}, Michael H. Herzog^a, Daniela A. Herzig^{b,c}, Andreas Brand^d, Christine Mohr^b

^a *Laboratory of Psychophysics, Brain Mind Institute, School of Life Sciences, Ecole Polytechnique Fédérale de Lausanne (EPFL), Station 19, CH-1015, Lausanne, Switzerland*

^b *Faculté des sciences sociales et politiques, Institut de Psychologie, Bâtiment Anthropole, 1015 Lausanne, Switzerland*

^c *Groupe de Recherche sur la Santé des Adolescents, Institut Universitaire de Médecine Sociale et Préventive, Route de la Corniche 2, 1066 Epalinges, Lausanne, Switzerland*

^d *Klinikum Bremen-Ost, Center for Psychiatry and Psychotherapy, Bremen, Germany*

ARTICLE INFO

Article history:

Received 21 February 2012

Received in revised form

28 June 2012

Accepted 2 July 2012

Keywords:

Low-level visual perception

High risk studies

Endophenotype

Dimensional and categorical models of

schizotypy

WCST

ABSTRACT

To understand the causes of schizophrenia, a search for stable markers (endophenotypes) is ongoing. In previous years, we have shown that the shine-through visual backward masking paradigm meets the most important characteristics of an endophenotype. Here, we tested masking performance differences between healthy students with low and high schizotypy scores as determined by the self-report O-Life questionnaire assessing schizotypy along three dimensions, i.e. positive schizotypy (unusual experiences), cognitive disorganisation, and negative schizotypy (introverted anhedonia). Forty participants performed the shine-through backward masking task and a classical cognitive test, the Wisconsin Card Sorting Task (WCST). We found that visual backward masking was impaired for students scoring high as compared to low on the cognitive disorganisation dimension, whereas the positive and negative schizotypy dimensions showed no link to masking performance. We also found group differences for students scoring high and low on the cognitive disorganisation factor for the WCST. These findings indicate that the shine-through paradigm is sensitive to differences in schizotypy which are closely linked with the pathological expression in schizophrenia.

© 2012 Elsevier Ireland Ltd. All rights reserved.

1. Introduction

Psychosis is a severe mental disorder affecting individuals usually during late adolescence to early adulthood causing severe personal, familial, and societal harm (see Ernst and Cacioppo, 1999 for overview; Patel et al., 2006; Salize et al., 2009). Representative examples of harm include that many patients show difficulties establishing close personal relationships, withdraw socially even from family members, have drug problems, depict cognitive impairments, and depend on public support such as regular health service and financial support, because patients are commonly unable to hold a job. Patients with psychosis face unfavourable prognosis (Bottlender et al., 2003). Despite immense scientific progress, full etiological understanding and successful treatments are still desperately missing (Levine et al., 2012; Tandon et al., 2008). Given that earlier detection of the disease generally results in better prognosis (Bird et al., 2010; Larsen et al., 2011; Marshall and Rathbone, 2006), factors predicting vulnerability to the illness are warranted. Genetic analysis has determined a plethora of candidate genes. However, each gene

explains only a small share of the genetic risk to suffer from psychosis (Sanders et al., 2008). For this reason, there is an ongoing search for stable tests, so-called “endophenotypes” which are thought to reflect certain gene combinations underlying the disease. According to Gottesman and Gould (2003), an endophenotype needs to: (i) be associated with the illness in the population, (ii) be state independent, (iii) show a familial association, (iv) co-segregate within families, and (v) be heritable.

We have established a potential endophenotype with a high sensitivity and specificity based on visual backward masking (Chkonia et al., 2010a; Herzog et al., 2004). We used the shine-through masking paradigm in which a target vernier was presented. A vernier comprises two horizontally offset vertical lines and observers indicate whether the lower line is offset to the left or right relative to the upper line (Fig. 1; see also Herzog and Koch, 2001; Herzog et al., 2001). Patients with schizophrenia as compared to controls are only slightly impaired in this task (Herzog et al., 2004). However, when a masking grating follows the vernier, offset discrimination is dramatically deteriorated in patients as compared to controls (Herzog et al., 2004). As required for an endophenotype (Gottesman et al., 2003), firstly, unaffected relatives of patients with schizophrenia showed stronger masking deficits than healthy controls (Chkonia et al., 2010a). Secondly, masking deficits in patients did not significantly change within

* Corresponding author. Tel.: +41 21 693 1741; fax: +41 21 693 1749.

E-mail address: celine.cappe@epfl.ch (C. Cappe).

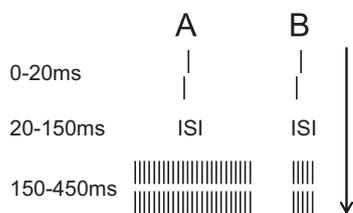


Fig. 1. A vernier (duration adapted for each participant individually; 0–20ms is shown as an example) was followed by a grating comprising 25 lines (A). We determined the SOA (VD+ISI) between vernier and grating onset yielding a predefined performance level (with VD for vernier duration). We also used a grating comprising 5 lines (B).

a year indicating state independency (Chkonia et al., 2010a,b). Thirdly, masking deficits were specific to psychosis (schizophrenia, bipolar disorder, schizoaffective disorder) and were absent in non-psychotic diseases such as depression (Chkonia et al., in press). Fourthly, the test is very sensitive and specific in distinguishing patients with schizophrenia from unaffected controls as determined with Receiver Operating Characteristics (ROC) analysis (sensitivity: 87%; specificity: 89%, Chkonia et al., 2010a). Further evidence for an endophenotype would be demonstrated if patients with milder forms of psychosis (e.g. schizotypal personality disorder, Reichenberg and Harvey, 2007 for a review) or unaffected people with psychotic-like (i.e. schizotypal) features show also deficient backward masking performance.

The schizotypy concept was originally introduced as a genetic diathesis-stress model for schizophrenia (Meehl, 1962). This concept is based on the assumption that symptoms of schizophrenia exist on a spectrum. Patients with schizophrenia show the most severe expression of these symptoms whereas schizotypal individuals in the general healthy population show mildest expression. This dimensional approach is supported by studies reporting that *preselected, highly* schizotypal subjects show cognitive (Gooding et al., 1999; Kim et al., 2011; Park et al., 1995), attentional (Gooding et al., 2006; Sarkin et al., 1998), behavioural (Kelley and Coursey, 1992) and physiological (Klein et al., 1999; Pizzagalli et al., 2000) deficits similar to those of patients with schizophrenia. Such behavioural similarities between schizotypy and schizophrenia were also observed in *randomly selected* individuals from the general population for whom schizotypal features are quantitatively less prominent yet qualitatively equivalent (Barnett and Corballis, 2002; Brugger and Graves, 1997; Ettinger et al., 2005; Kalaycioglu et al., 2000; Mohr et al., 2001; Stefanis et al., 2006). Because of these behavioural similarities along the spectrum, the respective tests were considered endophenotypes (e.g. Ettinger et al., 2005; Gooding et al., 2006). However, it is currently hard to determine whether the deficits of high schizotypes in these tests lie in between the ones of patients and controls, because the task difficulty in these paradigms often differs between clinical and schizotypy studies (Barch et al., 2003; Kerns and Becker, 2008; Koychev et al., 2012) or even different paradigms are used across studies to test for the same functions (for visual backward masking, e.g. see Butler et al., 2002; Merritt and Balogh, 1989). When the same paradigm was applied, performance was best for controls (low in schizotypy), relatively deficient in schizotypal individuals (Kim et al., 2011; Lenzenweger and Korfine, 1994), and worst in patients with schizophrenia (Gold et al., 1997; Laurent et al., 2000).

Conventionally, in the search for endophenotypes of schizophrenia, most research has focused on cognitive markers such as deficits in sustained attention (Cornblatt and Erlenmeyer-Kimling, 1985; Cornblatt and Malhotra, 2001), working memory (Barrantes-Vidal et al., 2007; Glahn et al., 2003), cognitive flexibility (Wobrock et al., 2009), and verbal fluency (Lin et al., 2011; Wobrock et al., 2009). Cognitive tasks such as the Wisconsin Card

Sorting Task (WCST) have been shown to reveal deficits not only in patients, but along the schizophrenia spectrum (Kim et al., 2011; Rajji et al., 2009; Suhr, 1997; Szöke et al., 2005). Performance in the WCST relies on a variety of (cognitive) sub-functions such as mental flexibility, executive functioning, and working memory (Eling et al., 2008; Hartman et al., 2003). This variety may impede the understanding of the underlying brain mechanisms. Moreover, various studies reported no WCST deficits along the schizophrenia spectrum (Jahshan and Sergi, 2007; Stratta et al., 1997) as well as diminished WCST performance in other psychiatric (Martin et al., 1991; Wafar and Lewine, 2010) and neurological (Paolo et al., 1996) conditions. For these reasons, simpler tests and tests with a high sensitivity to distinguish between different populations are of interest, such as the visual backward masking paradigm (Chkonia et al., 2010a; Herzog et al., 2004).

Here, we tested performance in 40 undergraduate students with the same visual backward masking paradigm and the same version of the WCST we used in our study on schizophrenia previously (Chkonia et al., 2010a). In addition, we used the O-Life schizotypy scale assessing positive symptoms, negative symptoms, and cognitive disorganisation, i.e. the same dimensions usually described for schizophrenia (Liddle, 1987b; Mason et al., 1995, 2005). As mentioned, if visual backward masking is a reliable endophenotype, we expect deteriorated masking performance for individuals with high scores on schizotypy, particularly, for the positive and the cognitive disorganisation dimension in accordance with previous schizotypy studies (e.g. Ettinger et al., 2005; Herzig et al., 2010; Lenzenweger and Korfine, 1994; Schofield and Claridge, 2007; Stefanis et al., 2006).

2. Methods

2.1. Participants

Thirty eight undergraduate psychology students from the University of Lausanne (eight males) and two students from the Ecole Polytechnique Fédérale de Lausanne volunteered. Participants were naïve to the study question, fluent French speakers, and had a mean age of 21.1 years (S.D. 2.0 years, range 19–27 years). Participants had normal or corrected to normal vision as determined with the Freiburg visual acuity test (Bach, 1996), i.e. all participants reached a value of > 0.8 for at least one eye. Most ($n=37$) were right-handed according to a standardized handedness questionnaire (Oldfield, 1971). Participants took part to obtain course credit or a financial compensation for their time. The study was conducted in accordance with the guidelines of the declaration of Helsinki. All participants provided written informed consent prior participation after having received detailed written study information. As indicated by self-report, none of the participants reported a current or previous history of psychiatric or neurological illness (Mohr et al., 2006).

2.2. Self-report questionnaire—short O-Life

The short O-Life questionnaire (Mason et al., 2005) is a validated 43-item self-report questionnaire assessing schizotypy in terms of four dimensions. Positive schizotypy is assessed by 12 items pertaining to Unusual Experiences (UnEx, maximum score 12, including items such as ‘Are your thoughts sometimes so strong that you can almost hear them?’), negative schizotypy is assessed by 10 items pertaining to Introverted Anhedonia (IntAn, maximum score 10, including items such as ‘Do you prefer watching television to going out with people?’), and Cognitive Disorganisation is assessed by 11 items (CogDis, maximum score 11, including items such as ‘Are you easily confused if too much happens at the same time?’). Finally, 10 items assess Impulsive Nonconformity (maximum score 10), which does not represent a schizotypy dimension (Mason et al., 1995). For each item, participants have to indicate whether the statement is true or false. The number of positive responses (some items are reversely formulated) is summed so that higher scores indicate higher schizotypy. Normative English values can be found in Mason et al. (2005) and the scale has shown good internal consistency as well as high correlations with the original O-Life questionnaire (Mason et al., 1995, 2005). Here, we used a French version of the O-Life questionnaire that has been translated and back-translated (normative values on the French version of the O-Life questionnaire are to be presented elsewhere).

2.3. Low-level and high-level function tasks

2.3.1. Shine-through backward masking test paradigm

Stimuli were presented from a distance of 3 m in a dimly illuminated room. A pixel of the screen comprised about 18" (arcsec) at this distance. The stimuli were white (100 cd/m²) on a black background. In a first step, we presented vernier stimuli which consisted of two vertical bars of 10' (arc min) length which were offset in the horizontal direction. In each trial, the vernier offset direction was chosen randomly. Participants indicated the offset direction of the lower bar compared to the upper bar (binary task). Errors were indicated by an auditory signal. For each observer, we determined the individual vernier duration (VD) to reach 75% correct responses using a staircase procedure (Fig. 1; for details, see Herzog et al., 2004). In the second step, we used a vernier offset size of 1.15' for all observers and individual VD as defined in the first step. The vernier was followed by a variable inter-stimulus interval (ISI), i.e. a blank screen, and then a grating was displayed for 300 ms (Fig. 1). The grating consisted of either 5 or 25 verniers without offset of the same length as the target vernier (referred to as BM5 or BM25 respectively, BM for backward masking).

The 5 element grating leads to stronger masking than the 25 element grating even though the 5 element grating is contained in the 25 element grating (Herzog and Koch, 2001). This difference in masking strength indicates that a substantial part of the masking power is not of retinal origin because retinal processing is mainly determined by the sheer amount of light, e.g., the number of grating elements presented. In addition, we used both the 5 and 25 element gratings to cover the different ranges of sensitivity of patients and controls. Patients with schizophrenia showed strong deficits with the 25 element grating whereas controls performed in the ceiling regime. In the current study, we again expect ceiling performance with the 25 element grating in the high and low schizotypy populations, but expect the 5 element grating to be more sensitive to reveal differences between the schizotypy populations.

The horizontal distance between grating elements was about 3.33'. We varied the ISI adaptively using a staircase procedure (PEST; Taylor and Creelman, 1967). We assessed the ISI target which yields a performance level of 75% correct responses (in the figures, we plot Stimulus-Onset Asynchrony (SOA)=VD+ISI, rather than ISI). The starting value of the SOA was 200. Conditions were presented in blocks of 80 trials.

2.3.2. Wisconsin Card Sorting Test (WCST)

We administered a computerised version of the WCST (Berg, 1948; used from the PEBL Psychological Test Battery: <http://pebl.sourceforge.net/battery.html>) in which four cards were displayed at the top of the computer screen. Each card showed items that differed from the other three cards in three dimensions, namely, in shape (crosses, triangles, circles or stars), number (1–4 items) and colour (red, blue, yellow, and green). A fifth card was then presented on the bottom of the screen, and participants needed to match the fifth card according to either the shape, number of items or colour by clicking on one of the four cards displayed at the top of the screen.

Participants were not told according to which dimension they were supposed to match the cards. After 10 correct trials, the matching criterion changed. The maximum number of trials was 128. The experiment always ended as soon as participants had completed nine categories (three times for each rule). Feedback about whether or not cards were successfully matched was given after each response.

From the WCST, various measures can be extracted (Gooding et al., 1999; Wagman and Wagman, 1992). Here, we used the total number of errors (sum of total errors, perseverative errors, and non-perseverative errors) as the dependent variable, in line with our previous study (Chkonia et al., 2010a).

2.4. Overall procedure

The tests were administered in the following order: shine-through backward masking paradigm, WCST, and O-LIFE questionnaire. The procedure took about 90 min to complete. Additional visual tests were conducted to assess effects of broader visual perception. These tests were conducted at the end of all other tests and are not reported here.

2.5. Data analysis

To best compare our current findings with previous clinical studies (Chkonia et al., 2010a; Herzog et al., 2004), we split our population into high and low groups at the median scale scores (Table 1) for each subscale separately resulting in a high ($n=21$) and low ($n=19$) UnEx group, a high ($n=22$) and low ($n=18$) CogDis group, and a high ($n=22$) and low ($n=18$) IntAn group. It is important to note that a participant can belong to the high group in one dimension and to the low group in another dimension. A further consequence of this approach is that the number of participants differs between the high and low schizotypy groups. Because of that, we computed statistics for each schizotypy dimension separately.

Table 1
Schizotypy subscores.

	Current sample			Mason et al. (2005)	
	Mean \pm S.D.	Range	Median	Mean \pm S.D.	Cohen's <i>d</i>
UnEx	3.5 \pm 2.9	0–9	3	3.4 \pm 2.9	0.05
CogDis	4.8 \pm 2.7	0–10	5	4.4 \pm 2.9	0.14
IntAn	1.9 \pm 1.6	0–6	2	2.5 \pm 2.0	–0.28

Schizotypy subscores of the present sample together with normative values from a previous sample (Mason et al., 2005). The means of the present sample are compared with the normative sample using Cohen's *D*. (SD: Standard Deviation, UnEx: Unusual Experiences, CogDis: Cognitive Disorganisation, IntAn: Introverted Anhedonia).

In the case of the shine-through masking task, to test whether performance differed between the respective schizotypy groups, we performed separate repeated measures ANOVAs for each schizotypy dimension with performances (SOA) in the two masking conditions (BM5, BM25) as repeated measure and schizotypy group (high, low) as between-subject factor. To investigate whether significant differences between schizotypy groups for the shine-through masking task are also observed for the higher cognitive task (total number of errors in the WCST), we compared this measure between the high and low schizotypy subscale groups in three independent samples *t*-tests.

Kolmogorov–Smirnov tests revealed normal distribution for all behavioural measures and questionnaire scores. All *p*-values were two-tailed and the α -level was 0.05.

3. Results

3.1. Participants' schizotypy scores

Schizotypy subscores can be found in Table 1 including means (\pm S.D.) and ranges. Spearman's correlations between schizotypy subscores show similar values as in previous reports (Herzig et al., 2010; Mason et al., 1995; Tsakanikos and Reed, 2003) showing positive correlations between UnEx scores and CogDis scores and between UnEx and IntAn scores (Table 2). There was no significant correlations between CogDis and IntAn scores (Table 2). Self-report measures were compared to a previously published normative English sample (Mason et al., 2005) via calculations of Cohen's *d*. In accordance with Cohen (1992), values of $\pm 0.2/\pm 0.5/\pm 0.8$ are indicative of a small/ medium/ large effect size, respectively, meaning the higher the value, the greater the difference between groups. The present sample was comparable with the normative sample (normative O-LIFE values for the total sample were obtained on request from Oliver Mason, UCL, see Table 1), as all effect sizes were small.

3.2. Visual backward masking and WCST

The mean (\pm s.e.m.) shine-through backward masking threshold (SOA) was 27.9 ms (± 2.6 ms) for the 25 element grating and 68.3 ms (± 4.4 ms) for the 5 element grating. In the WCST, participants made on average 17.1 (± 0.9) total errors. Spearman correlations between the number of total errors in the WCST and thresholds in the visual backward masking task were not significant for the 25 element grating and the 5 element grating (Table 2). Thresholds for the 25 and 5 elements grating were positively and significantly correlated (Table 2). This result is not unexpected because the two measurements differ only in the number of mask elements, and thus tap into potentially similar mechanisms.

3.3. Visual backward masking, WCST, and schizotypy groups

For the shine-through backward masking task, the ANOVA on UnEx group revealed a significant main effect of task ($F_{(1,38)}=118.06$; $p < 0.001$, BM5 > BM25 (see previous paragraph)), but no main effect of UnEx group ($F_{(1,38)}=1.04$;

Table 2
Spearman correlation results.

	Unusual experiences	Cognitive disorganisation	Introvertive Anhedonia	BM25	BM5	WCST_total errors
Unusual experiences	1	$r=0.450$ $p=0.004$	$r=0.314$ $p=0.049$	$r=-0.049$ $p=0.764$	$r=-0.002$ $p=0.992$	$r=0.214$ $p=0.186$
Cognitive disorganisation	$r=0.450$ $p=0.004$	1	$r=0.162$ $p=0.317$	$r=0.109$ $p=0.504$	$r=0.190$ $p=0.240$	$r=0.220$ $p=0.172$
Introvertive Anhedonia	$r=0.314$ $p=0.049$	$r=0.162$ $p=0.317$	1	$r=-0.025$ $p=0.876$	$r=-0.297$ $p=0.063$	$r=0.069$ $p=0.671$
BM25	$r=-0.049$ $p=0.764$	$r=0.109$ $p=0.504$	$r=-0.025$ $p=0.876$	1	$r=0.528$ $p<0.001$	$r=0.056$ $p=0.730$
BM5	$r=-0.002$ $p=0.992$	$r=0.190$ $p=0.240$	$r=-0.297$ $p=0.063$	$r=0.528$ $p<0.001$	1	$r=0.161$ $p=0.321$
WCST_total errors	$r=0.214$ $p=0.186$	$r=0.220$ $p=0.172$	$r=0.069$ $p=0.671$	$r=0.056$ $p=0.730$	$r=0.161$ $p=0.321$	1

BM 25 and BM 5: Backward Masking with 25 or 5 elements; WCST_Total errors: total number of errors in the Wisconsin Card Sorting Test. Results with p -values < 0.05 are highlighted in bold.

Table 3
Mean values (\pm standard error of the mean) for different tasks.

	Unusual experiences			Cognitive disorganisation			Introvertive Anhedonia		
	High ($n=21$)	Low ($n=19$)	p -values	High ($n=22$)	Low ($n=18$)	p -values	High ($n=22$)	Low ($n=18$)	p -values
BM 25	25.4 (± 3.8)	30.8 (± 3.4)	0.298	30.6 (± 3.9)	24.7 (± 3.1)	0.257	28.8 (± 3.9)	26.9 (± 3.2)	0.714
BM 5	64.8 (± 5.8)	72.0 (± 6.7)	0.420	77.0 (± 6.8)	57.6 (± 4.1)	0.026	64 (± 5)	74 (± 7)	0.252
WCST	17.8 (± 1.4)	16.2 (± 1.1)	0.395	18.6 (± 1.4)	15.1 (± 0.7)	0.045	17.5 (± 1.1)	16.4 (± 1.5)	0.533
Total errors	(± 1.4)	(± 1.1)		(± 1.4)	(± 0.7)		(± 1.1)	(± 1.5)	

Mean values for backward masking threshold (in ms) with 25 (BM 25) or 5 (BM 5) elements, total number of errors in the Wisconsin Card Sorting Test (WCST Total errors) regarding the different schizotypy dimensions categorized according to a median split into a high and low scoring group for each dimension into high and low scores in each dimension. We compared the groups' performances using independent t -tests; results are indicated as p -values. Results with p -values < 0.05 are highlighted in bold.

$p=0.32$) and no significant interaction between task and UnEx group ($F_{(1,38)}=0.06$; $p=0.81$). The analogue ANOVA on CogDis group showed again the significant main effect of task ($F_{(1,38)}=128.97$; $p<0.001$), and a significant main effect of CogDis groups ($F_{(1,38)}=4.52$; $p=0.04$: high CogDis group $>$ low CogDis group, Fig. 2), and a statistical trend for the interaction between task and CogDis groups ($F_{(1,38)}=3.58$; $p=0.07$) (see also Table 3). Post-hoc Tukey HSD test comparisons (controlling for multiple testing) showed that thresholds were higher for the five than 25 element gratings in both groups (p -values < 0.001), but that the high CogDis group showed higher threshold than the low CogDis group for the 5 elements grating ($p=0.04$) while no such difference was observed for the 25 elements grating ($p=0.83$; Fig. 2). Finally, the analogue ANOVA for the IntAn group showed only the significant main effect of task ($F_{(1,38)}=126.67$; $p<0.001$); main effect of IntAn group: $F_{(1,38)}=0.44$; $p=0.51$; interaction between task and IntAn group: $F_{(1,38)}=2.83$; $p=0.10$).

The independent t -tests on the total number of errors in the WCST were not significant for the UnEx groups and IntAn groups, but showed that the high CogDis group performed more errors than the low CogDis group (Fig. 3, Table 3).

4. Discussion

Stable markers of schizophrenia (endophenotypes) are of theoretical and clinical relevance (Allen et al., 2009; Keri and Janka, 2004; Wickham and Murray, 1997). A wide range of endophenotypes was proposed including structural brain abnormalities such as ventricle volume (Chua et al., 2007), physiologic abnormalities such as niacin flushing (Lin et al., 2007) and neuromotor abnormalities such as smooth pursuit eye movement (Holahan and O'Driscoll, 2005). In the

cognitive domain, research on endophenotypes has mostly focused on higher cognitive functions (e.g. WCST) (Allen et al., 2009), which often depend on a variety of sub-functions, in the case of the WCST on mental flexibility, executive functioning, and working memory (Eling et al., 2008; Hartman et al., 2003). This variety in sub-functions might: (i) complicate the understanding of underlying brain mechanisms, (ii) result in heterogeneous findings along the schizophrenia spectrum (Jahshan and Sergi, 2007; Stratta et al., 1997; Thurston-Snoha and Lewine, 2007), and (iii) may explain why WCST deficits might also be found in other psychiatric (Martin et al., 1991; Waford and Lewine, 2010), and neurological (Paolo et al., 1996) conditions. We suggest that visual tasks tap into fewer and simpler mechanisms yielding better signal to noise ratios and, hence, less performance variability. In previous studies, we found reliable masking deficits in patients with schizophrenia and their unaffected relatives when compared to controls (Chkonia et al., 2010a,b). In addition, masking deficits were specific for psychotic patients (schizophrenia, bipolar, and schizoaffective) compared to both healthy controls and non-psychotic patients (depression, abstinent alcoholics'; Chkonia et al., in press).

If visual backward masking is sensitive to trait variations along the schizophrenia spectrum, we expected stronger visual backward masking in individuals with high as compared to low schizotypy scores, in particular for UnEx and/ or CogDis. Results show indeed that high as compared to low scoring individuals on CogDis revealed significant visual backward masking deficits, which were most evident for the 5 element masking grating. However, we found no significant group differences for the UnEx or IntAn groups.

The three symptom dimensions of schizotypy, also described for schizophrenia, are thought to differently relate to the pathological condition. In the case of negative symptoms, these were found to precede acute psychotic symptoms (Cornblatt et al.,

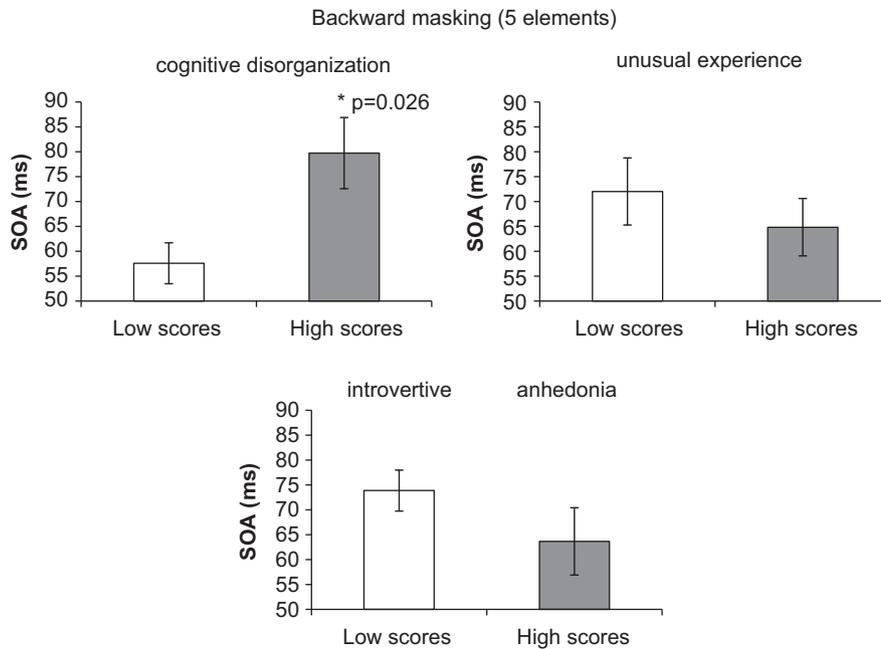


Fig. 2. Mean visual backward masking threshold with 5 elements for low and high scores in CogDis dimension (s.e.m. are indicated).

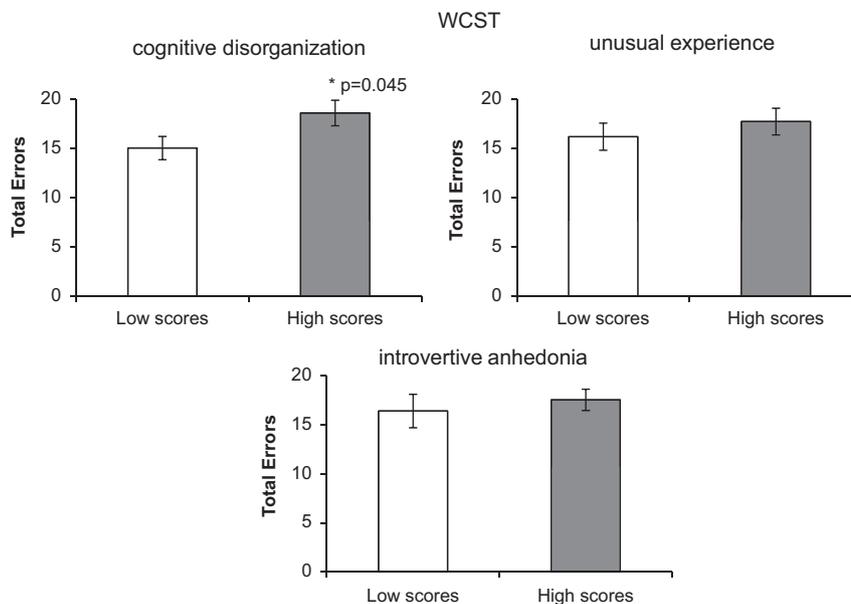


Fig. 3. Mean total number of errors in the the WCST for low and high scores in CogDis dimension (s.e.m. are indicated).

2003) and to predict an unfavourable outcome (Brill et al., 2009; Ventura et al., 2009). Positive symptoms, on the other hand, are most responsive to antipsychotic treatment (Walker et al., 2009), and are those that fluctuate most over the course of the illness (Cornblatt et al., 2003). Disorganisation symptoms seem relevant to cognitive functioning deficits, e.g. performance in the WCST (Nieuwenstein et al., 2001), or other tests of concentration and memory (Liddle, 1987a; Walter and Wolf, 2008). In the case of schizotypy, it has been argued that positive schizotypy is of minor clinical relevance (McCreery and Claridge, 2002; Schofield and Claridge, 2007), and might associate with enhanced creative potential (Gianotti et al., 2001; O'Reilly et al., 2001). High cognitive disorganisation, on the other hand, might lack this experiential advantage (Schofield and Claridge, 2007) and is also

associated with cognitive attenuations in schizotypal populations (Kerns and Becker, 2008). Our present findings support a particular role of CogDis to relative impaired visual backward masking performance, suggesting that this dimension might be more clinically relevant than UnEx and IntAn.

We additionally found that high as compared to low scoring individuals on CogDis made more total errors in the WCST. The same WCST was used in our previous study on visual backward masking in patients with schizophrenia (Chkonia et al., 2010a). In this previous study, the WCST showed also a good sensitivity and specificity for schizophrenia when compared to controls, but the sensitivity and specificity was higher for the visual backward masking paradigm. Interestingly, in this former clinical study, total errors in the WCST did not correlate with the shine-through masking performance, as it was

also the case in the present study. As described earlier, we proposed that both tests tap into different underlying mechanisms (Chkonia et al., 2010a), a proposition supported by our present findings. For example, visual load is minor in the WCST because stimuli are clearly visible and presented for a long duration. In the shine-through task, the opposite is true: stimuli differ on a very fine spatial scale, are presented shortly and masked. Possibly, the visual task needs good iconic memory and efficient target processing whereas this is not necessary in the WCST. On the other hand, the task requirements are extremely simple in the shine-through paradigm (binary forced choice task), but depend on flexible executive functions and good working memory in the WCST (adapting to new response strategies).

We found stronger performance differences for the 5 element grating compared to the 25 element grating, possibly because of a ceiling effect (see also Section 2.3.1). All students, independent of their schizotypy scores, performed close to optimal with the 25 element grating because of its weak masking power. Variance was much larger for the more potent 5 element grating. In our previous study, patients, to the contrary, were also strongly affected by the 25 element grating in comparison to healthy participants (Chkonia et al., 2010a). As a comparison, mean SOAs of students with high CogDis scores were 77 ms and 30.6 ms for the 5 and 25 grating respectively and 57.6 ms and 24.7 ms for students with low CogDis scores (current study). For patients with schizophrenia these values were 235 ms and 143 ms (Chkonia et al., 2010a).

Our results are well in line with previous studies showing increased visual masking deficits in individuals scoring high in schizotypy (Merritt and Balogh, 1989) as well as in those with a schizotypal personality disorder (Braff, 1981; Saccuzzo and Schubert, 1981) in particular with increasing symptomatology (Cadenhead et al., 1996). In the case of the schizotypy studies, the Minnesota Multiphasic Personality Inventory (MMPI) (Merritt and Balogh, 1985), a combined measure of positive schizotypal features (perceptual aberration and magical ideation) (Balogh and Merritt, 1985; Merritt and Balogh, 1989), or a total schizotypy score (Bedwell and Orem, 2008) were used. None of these measures distinguishes between positive schizotypy and disorganisation though.

For many years, masking deficits were attributed exclusively to dysfunctions of the magnocellular system sensitive to low spatial frequencies. The parvocellular system is assumed to be intact. In this line, Merritt and Balogh (1989) found no masking deficits in high scoring positive schizotypal students when using a spatial high frequency mask, assumed to trigger the parvocellular system, but performance deficits with a low spatial frequency mask, assumed to trigger the magnocellular system. However, the shine-through masking paradigm uses a high spatial frequency mask which may be processed rather by the parvocellular system than the magnocellular one. For this it remains an open question how much dysfunctions of either system contribute to masking deficits in schizophrenia and elevated schizotypy (see also Skottun and Skoyles, 2011; Plomp et al., in press).

The masking deficits in high as compared to low scoring CogDis individuals support the notion of a dimensional model of schizophrenia. According to this model, symptoms of patients with schizophrenia are also observable, although quantitatively less severe, in the general population. Dimensional models of psychopathology have been debated by personality researchers for decades (Meehl, 1962; Rado, 1953), and, more recently, received increasing attention from the clinical community (van Os et al., 2009, for a recent review). Within this tradition, the specificity of our findings to CogDis raises the question of pathologically relevant and irrelevant symptom dimensions (Chapman et al., 1994; Cornblatt et al., 2003; Kerns and Becker, 2008; Schofield and Claridge, 2007) triggering future studies in which high scoring individuals could be preselected (e.g. Gooding et al., 1999; Kim et al., 2011), or even high and low scorers on

different symptom dimensions could be contrasted in their performance (Laws et al., 2011; Leonards and Mohr, 2009). It might be that scoring high on positive schizotypy only relates to a well-adapted cognitive profile, while high scores in CogDis alone and/or in combination with high scores in positive schizotypy might yield the most disadvantageous cognitive profile.

Admittedly, the present study suffers from various limitations. One common limitation in the field is the question whether our sample was sufficiently large. If sample sizes of previous studies are representative, our own sample size falls within the common range of the field (Bedwell and Orem, 2008; Herzog et al., 2010; Merritt and Balogh, 1989; Mohr et al., 2003). In addition, our sex distribution favoured female over male participants as common in studies performed in undergraduate populations (e.g. Barnett and Corballis, 2002; Ettinger et al., 2005; Gooding et al., 1999) contrary to sex proportions in clinical studies where the sex ratio is frequently reversed (e.g. Barch et al., 2003; Bottlender et al., 2003; Chkonia et al., 2010a). Accordingly, future studies should balance or even reverse the sex composition (men > women) which may result in even stronger masking differences between groups. Another limitation is the median-split analysis. We used this approach because of its previous use in schizotypy research (e.g. Laws et al., 2011; Mohr et al., 2003) and to compare our findings with previous studies using the shine-through backward masking paradigm in which also group comparisons, schizophrenic patients versus healthy controls, were performed (Chkonia et al., 2010a,b; Herzog et al., 2004). No significant findings were observed for correlations ($r = -0.049$, $r = 0.109$ and $r = -0.025$ for BM25 vs. UnEx, CogDis, and IntAn, $p > 0.5$ for all three comparisons; $r = -0.002$, $r = 0.190$, and $r = -0.297$ for BM 5 vs. UnEx, CogDis, and IntAn, $p > 0.07$ for all three comparisons, see also Table 2). The potential relevance of our findings to the CogDis dimension is new, and could be clinically relevant as well as important for personality studies.

In summary, we observed visual backward masking deficits as a function of high CogDis, but not as a function of UnEx or IntAn scores in a healthy undergraduate sample. Future studies will have to investigate whether this specificity to CogDis could be clinically relevant. Our findings add further evidence to the dimensional approach to schizophrenia showing that masking deficits can be found along the schizophrenia spectrum with masking deficits becoming stronger the more severe schizophrenia symptoms are expressed. In this respect, these findings add further evidence to the shine-through masking paradigm as a sensitive endophenotype potentially detecting dysfunctions which may contribute to schizophrenia.

Acknowledgements

This work was supported by the National Center of Competence in Research (NCCR) SYNAPSY of the Swiss National Science Foundation (SNF). We thank Guillaume Sierro and Kevin Richards for the French version of the O-LIFE questionnaire.

References

- Allen, A.J., Griss, M.E., Folley, B.S., Hawkins, K.A., Pearlson, G.D., 2009. Endophenotypes in schizophrenia: a selective review. *Schizophrenia Research* 109, 24–37.
- Bach, M., 1996. The Freiburg visual acuity test—automatic measurement of visual acuity. *Optometry and Vision Science* 73, 49–53.
- Balogh, D.W., Merritt, R.D., 1985. Susceptibility to Type A backward pattern masking among hypothetically psychosis-prone college students. *Journal of Abnormal Psychology* 94, 377–383.
- Barch, D.M., Sheline, Y.I., Csernansky, J.G., Snyder, A.Z., 2003. Working memory and prefrontal cortex dysfunction: specificity to schizophrenia compared with major depression. *Biological Psychiatry* 53, 376–384.

- Barnett, K.J., Corballis, M.C., 2002. Ambidexterity and magical ideation. *Laterality: Asymmetries of Body, Brain and Cognition* 7, 75–84.
- Barrantes-Vidal, N., Aguilera, M., Campanera, S., Fatjo-Vilas, M., Guitart, M., Miret, S., Valero, S., Fananas, L., 2007. Working memory in siblings of schizophrenia patients. *Schizophrenia Research* 95, 70–75.
- Bedwell, J.S., Orem, D.M., 2008. The effect of red light on backward masking in individuals with psychometrically defined schizotypy. *Cognitive Neuropsychiatry* 13, 491–504.
- Berg, E.A., 1948. A simple objective technique for measuring flexibility in thinking. *The Journal of General Psychology* 39, 15–22.
- Bird, V., Premkumar, P., Kendall, T., Whittington, C., Mitchell, J., Kuipers, E., 2010. Early intervention services, cognitive-behavioural therapy and family intervention in early psychosis: systematic review. *The British Journal of Psychiatry* 197, 350–356.
- Bottlender, R., Sato, T., Jäger, M., Wegener, U., Wittmann, J., Strauß, A., Möller, H.-J., 2003. The impact of the duration of untreated psychosis prior to first psychiatric admission on the 15-year outcome in schizophrenia. *Schizophrenia Research* 62, 37–44.
- Braff, D.L., 1981. Impaired speed of information processing in nonmedicated schizotypal patients. *Schizophrenia Bulletin* 7, 499–508.
- Brill, N., Levine, S.Z., Reichenberg, A., Lubin, G., Weiser, M., Rabinowitz, J., 2009. Pathways to functional outcomes in schizophrenia: the role of premorbid functioning, negative symptoms and intelligence. *Schizophrenia Research* 110, 40–46.
- Brugger, P., Graves, R., 1997. Right hemispatial inattention and magical ideation. *European Archives of Psychiatry and Clinical Neuroscience* 247, 55–57.
- Butler, P.D., DeSanti, L.A., Maddox, J., Harkavy-Friedman, J.M., Amador, X.F., Goetz, R.R., Javitt, D.C., Gorman, J.M., 2002. Visual backward-masking deficits in schizophrenia: relationship to visual pathway function and symptomatology. *Schizophrenia Research* 59, 199–209.
- Cadenhead, K.S., Perry, W., Braff, D.L., 1996. The relationship of information-processing deficits and clinical symptoms in schizotypal personality disorder. *Biological Psychiatry* 40, 853–858.
- Chapman, L.J., Chapman, J.P., Kwapil, T.R., Eckblad, M., Zinser, M.C., 1994. Putatively psychosis-prone subjects 10 years later. *Journal of Abnormal Psychology* 103, 171–183.
- Chkonia, E., Roinishvili, M., Makhatazde, N., Tsverava, L., Stroux, A., Neumann, K., Herzog, M.H., Brand, A., 2010a. The shine-through masking paradigm is a potential endophenotype of schizophrenia. *Plos One* 5.
- Chkonia, E., Roinishvili, M., Herzog, M.H., Brand, A., 2010b. First-order relatives of schizophrenic patients are not impaired in the Continuous Performance Test. *Journal of Clinical and Experimental Neuropsychology* 32, 481–486.
- Chkonia, E., Roinishvili, M., Reichard, L., Wurch, W., Puhlmann, H., Grimsen, C., Herzog, M.H., Brand, A. Patients with functional psychoses show similar visual backward masking deficits. *Psychiatry Research*, in press, <http://dx.doi.org/10.1016/j.psychres.2012.02.020>.
- Chua, S.E., Cheung, C., Cheung, V., Tsang, J.T., Chen, E.Y., Wong, J.C., Cheung, J.P., Yip, L., Tai, K.S., Suckling, J., McAlonan, G.M., 2007. Cerebral grey, white matter and CSF in never-medicated, first-episode schizophrenia. *Schizophrenia Research* 89, 12–21.
- Cohen, J., 1992. A power primer. *Psychological Bulletin* 112, 155–159.
- Cornblatt, B.A., Erlenmeyer-Kimling, L., 1985. Global attentional deviance as a marker of risk for schizophrenia: specificity and predictive validity. *Journal of Abnormal Psychology* 94, 470–486.
- Cornblatt, B.A., Malhotra, A.K., 2001. Impaired attention as an endophenotype for molecular genetic studies of schizophrenia. *American Journal of Medical Genetics* 105, 11–15.
- Cornblatt, B.A., Lencz, T., Smith, C.W., Correll, C.U., Auther, A.M., Nakayama, E., 2003. The schizophrenia prodrome revisited: a neurodevelopmental perspective. *Schizophrenia Bulletin* 29, 633–651.
- Eling, P., Derckx, K., Maes, R., 2008. On the historical and conceptual background of the Wisconsin Card Sorting Test. *Brain and Cognition* 67, 247–253.
- Ernst, J.M., Cacioppo, J.T., 1999. Lonely hearts: psychological perspectives on loneliness. *Applied and Preventive Psychology* 8, 1–22.
- Ettinger, U., Kumari, V., Crawford, T.J., Flak, V., Sharma, T., Davis, R.E., Corr, P.J., 2005. Saccadic eye movements, schizotypy, and the role of neuroticism. *Biological Psychology* 68, 61–78.
- Gianotti, L.R.R., Mohr, C., Pizzagalli, D., Lehmann, D., Brugger, P., 2001. Associative processing and paranoid belief. *Psychiatry and Clinical Neuroscience* 55, 595–603.
- Glahn, D.C., Therman, S., Manninen, M., Huttunen, M., Kaprio, J., Lönnqvist, J., Cannon, T.D., 2003. Spatial working memory as an endophenotype for schizophrenia. *Biological Psychiatry* 53, 624–626.
- Gold, J.M., Carpenter, C., Randolph, C., Goldberg, T.E., Weinberger, D.R., 1997. Auditory working memory and Wisconsin Card Sorting Test performance in schizophrenia. *Archives of General Psychiatry* 54, 159–165.
- Gooding, D.C., Kwapil, T.R., Tallent, K.A., 1999. Wisconsin Card Sorting Test deficits in schizotypic individuals. *Schizophrenia Research* 40, 201–209.
- Gooding, D.C., Matts, C.W., Rollmann, E.A., 2006. Sustained attention deficits in relation to psychometrically identified schizotypy: evaluating a potential endophenotypic marker. *Schizophrenia Research* 82, 27–37.
- Gottesman, I.I., Gould, T.D., 2003. The endophenotype concept in psychiatry: etymology and strategic intentions. *American Journal of Psychiatry* 160, 636–645.
- Hartman, M., Steketee, M.C., Silva, S., Lanning, K., Andersson, C., 2003. Wisconsin Card Sorting Test performance in schizophrenia: the role of working memory. *Schizophrenia Research* 63, 201–217.
- Herzig, D.A., Tracy, J., Munafò, M., Mohr, C., 2010. The influence of tobacco consumption on the relationship between schizotypy and hemispheric asymmetry. *Journal of Behavior Therapy and Experimental Psychiatry* 41, 397–408.
- Herzog, M.H., Koch, C., 2001. Seeing properties of an invisible object: feature inheritance and shine-through. *Proceedings of the National Academy of Sciences of the United States of America* 98, 4271–4275.
- Herzog, M.H., Koch, C., Fahle, M., 2001. Shine-through: temporal aspects. *Vision Research* 41, 2337–2346.
- Herzog, M.H., Kopmann, S., Brand, A., 2004. Intact figure-ground segmentation in schizophrenia. *Psychiatry Research* 129, 55–63.
- Holahan, A.L., O'Driscoll, G.A., 2005. Antisaccade and smooth pursuit performance in positive- and negative-symptom schizotypy. *Schizophrenia Research* 76, 43–54.
- Jahshan, C.S., Sergi, M.J., 2007. Theory of mind, neurocognition, and functional status in schizotypy. *Schizophrenia Research* 89, 278–286.
- Kalacyioglu, C., Nalacci, E., Budanur, O.E., Genc, Y., Cicek, M., 2000. The effect of familial sinistrality on the relation between schizophrenia like thinking and pseudoneglect. *Brain and Cognition* 44, 564–576.
- Kelley, M.P., Coursey, R.D., 1992. Lateral preference and neuropsychological correlates of schizotypy. *Psychiatry Research* 41, 115–135.
- Keri, S., Janka, Z., 2004. Critical evaluation of cognitive dysfunctions as endophenotypes of schizophrenia. *Acta Psychiatrica Scandinavica* 110, 83–91.
- Kerns, J.G., Becker, T.M., 2008. Communication disturbances, working memory, and emotion in people with elevated disorganized schizotypy. *Schizophrenia Research* 100, 172–180.
- Kim, M.-S., Oh, S.H., Hong, M.-H., Choi, D.B., 2011. Neuropsychologic profile of college students with schizotypal traits. *Comprehensive Psychiatry* 52, 511–516.
- Klein, C., Berg, P., Rockstroh, B., Andresen, B., 1999. Topography of the auditory P300 in schizotypal personality. *Biological Psychiatry* 45, 1612–1621.
- Koychev, I., McMullen, K., Lees, J., Dadhiwala, R., Grayson, L., Perry, C., Schmechtig, A., Walters, J., Craig, K.J., Dawson, G.R., Dourish, C.T., Ettinger, U., Wilkinson, L., Williams, S., Deakin, J.F.W., Barkus, E., 2012. A validation of cognitive biomarkers for the early identification of cognitive enhancing agents in schizotypy: a three-center double-blind placebo-controlled study. *European Neuropsychopharmacology* 22, 469–481.
- Larsen, T.K., Melle, I., Auestad, B., Haahr, U., Joa, I., Johannessen, J.O., Opjordsmoen, S., Rund, B.R., Rossberg, J.I., Simonsen, E., Vaglum, P., Friis, S., McGlashan, T., 2011. Early detection of psychosis: positive effects on 5-year outcome. *Psychological Medicine* 41, 1461–1469.
- Laurent, A., Biloa-Tang, M., Bougerol, T., Duly, D., Anchisi, A.-M., Bosson, J.-L., Pellat, J., d'Amato, T., Dalery, J., 2000. Executive/attentional performance and measures of schizotypy in patients with schizophrenia and in their nonpsychotic first-degree relatives. *Schizophrenia Research* 46, 269–283.
- Laws, K.R., Kondel, T.K., Clarke, R., Nillo, A.-M., 2011. Delusion-prone individuals: stuck in their ways? *Psychiatry Research* 186, 219–224.
- Lenzenweger, M.F., Korfne, L., 1994. Perceptual aberrations, schizotypy, and the Wisconsin Card Sorting Test. *Schizophrenia Bulletin* 20, 345–357.
- Leonards, U., Mohr, C., 2009. Schizotypal personality traits influence idiosyncratic initiation of saccadic face exploration. *Vision Research* 49, 2404–2413.
- Levine, S.Z., Rabinowitz, J., Faries, D., Lawson, A.H., Ascher-Svanum, H., 2012. Treatment response trajectories and antipsychotic medications: examination of up to 18 months of treatment in the CATIE chronic schizophrenia trial. *Schizophrenia Research* 137, 141–146.
- Liddle, P.F., 1987a. Schizophrenic syndromes, cognitive performance and neurological dysfunction. *Psychological Medicine* 17, 49–57.
- Liddle, P.F., 1987b. The symptoms of chronic schizophrenia: a re-examination of the positive-negative dichotomy. *The British Journal of Psychiatry* 151, 145–151.
- Lin, S., Liu, C., Chang, S., Hwu, H., Liu, S.K., Hwang, T.J., Hsieh, M.H., Guo, S.C., Chen, W.J., 2007. Familial aggregation in skin flush response to niacin patch among schizophrenic patients and their nonpsychotic relatives. *Schizophrenia Bulletin* 33, 174–182.
- Lin, A., Wood, S.J., Nelson, B., Brewer, W.J., Spiliotacopoulos, D., Bruxner, A., Broussard, C., Pantelis, C., Yung, A.R., 2011. Neurocognitive predictors of functional outcome two to 13 years after identification as ultra-high risk for psychosis. *Schizophrenia Research* 132, 1–7.
- Marshall, M., Rathbone, J., 2006. Early intervention for psychosis. *Cochrane Database of Systematic Reviews*.
- Martin, D.J., Oren, Z., Boone, K., 1991. Major depressives' and dysthymics' performance on the wisconsin card sorting test. *Journal of Clinical Psychology* 47, 684–690.
- Mason, O., Claridge, G., Jackson, M., 1995. New scales for the assessment of schizotypy. *Personality and Individual Differences* 18, 7–13.
- Mason, O., Linney, Y., Claridge, G., 2005. Short scales for measuring schizotypy. *Schizophrenia Research* 78, 293–296.
- McCreery, C., Claridge, G., 2002. Healthy schizotypy: the case of out-of-the-body experiences. *Personality and Individual Differences* 32, 141–154.
- Meehl, P.E., 1962. Schizotaxia, schizotypy, schizophrenia. *American Psychologist* 17, 827–838.
- Merritt, R.D., Balogh, D.W., 1985. Critical stimulus duration: schizophrenic trait or state? *Schizophrenia Bulletin* 11, 341–343.

- Merritt, R.D., Balogh, D.W., 1989. Backward masking spatial frequency effects among hypothetically schizotypal individuals. *Schizophrenia Bulletin* 15, 573–583.
- Mohr, C., Rohrenbach, C.M., Laska, M., Brugger, P., 2001. Unilateral olfactory perception and magical ideation. *Schizophrenia Research* 47, 255–264.
- Mohr, C., Bracha, H.S., Brugger, P., 2003. Magical ideation modulates spatial behavior. *Journal of Neuropsychiatry and Clinical Neurosciences* 15, 168–174.
- Mohr, C., Landis, T., Brugger, P., 2006. Lateralized semantic priming: modulation by levodopa, semantic distance, and participants' magical beliefs. *Neuropsychiatric Disease and Treatment* 2, 71–84.
- Nieuwenstein, M.R., Aleman, A., de Haan, E.H.F., 2001. Relationship between symptom dimensions and neurocognitive functioning in schizophrenia: a meta-analysis of WCST and CPT studies. *Journal of Psychiatric Research* 35, 119–125.
- O'Reilly, T., Dunbar, R., Bentall, R., 2001. Schizotypy and creativity: an evolutionary connection? *Personality and Individual Differences* 31, 1067–1078.
- Oldfield, R.C., 1971. The assessment and analysis of handedness: the Edinburgh inventory. *Neuropsychologia* 9, 97–113.
- Paolo, A.M., Tröster, A.L., Blackwell, K.T., Koller, W.C., Axelrod, B.N., 1996. Utility of a Wisconsin card sorting test short form in persons with Alzheimer's and Parkinson's disease. *Journal of Clinical and Experimental Neuropsychology* 18, 892–897.
- Park, S., Holzman, P.S., Lenzenweger, M.F., 1995. Individual differences in spatial working memory in relation to schizotypy. *Journal of Abnormal Psychology* 104, 355–363.
- Patel, A., Everitt, B., Knapp, M., Reeder, C., Grant, D., Ecker, C., Wykes, T., 2006. Schizophrenia patients with cognitive deficits: factors associated with costs. *Schizophrenia Bulletin* 32, 776–785.
- Pizzagalli, D., Lehmann, D., Gianotti, L., Koenig, T., Tanaka, H., Wackermann, J., Brugger, P., 2000. Brain electric correlates of strong belief in paranormal phenomena: intracerebral EEG source and regional Omega complexity analyses. *Psychiatry Research—Neuroimaging* 100, 139–154.
- Plomp, G., Roinishvili, M., Chkonia, E., Kapanadze, G., Kereselidze, M., Brand, A., Herzog, M.H. Electrophysiological evidence for ventral stream deficits in schizophrenia patients. *Schizophrenia Bulletin*, in press, <http://dx.doi.org/10.1093/schbul/sbr175>.
- Rado, S., 1953. Dynamics and classification of disordered behaviour. *American Journal of Psychiatry* 110, 406–416.
- Rajji, T.K., Ismail, Z., Mulsant, B.H., 2009. Age at onset and cognition in schizophrenia: meta-analysis. *British Journal of Psychiatry* 195, 286–293.
- Reichenberg, A., Harvey, P.D., 2007. Neuropsychological impairments in schizophrenia: integration of performance-based and brain imaging findings. *Psychological Bulletin* 133, 833–858.
- Saccuzzo, D.P., Schubert, D.L., 1981. Backward masking as a measure of slow processing in schizophrenia spectrum disorders. *Journal of Abnormal Psychology* 90, 305–312.
- Salize, H.J., McCabe, R., Bullenkamp, J., Hansson, L., Lauber, C., Martinez-Leal, R., Reinhard, I., Rössler, W., Svensson, B., Torres-Gonzalez, F., van den Brink, R., Wiersma, D., Priebe, S., 2009. Cost of treatment of schizophrenia in six European countries. *Schizophrenia Research* 111, 70–77.
- Sanders, A.R., Duan, J., Levinson, D.F., Shi, J., He, D., Hou, C., Burrell, G.J., Rice, J.P., Nertney, D.A., Olincy, A., Rozić, P., Vinogradov, S., Buccola, N.G., Mowry, B.J., Freedman, R., Amin, F., Black, D.W., Silverman, J.M., Byerley, W.F., Crowe, R.R., Cloninger, C.R., Martinez, M., Gejman, P.V., 2008. No significant association of 14 candidate genes with schizophrenia in a large European ancestry sample: implications for psychiatric genetics. *American Journal of Psychiatry* 165, 497–506.
- Sarkin, A.J., Dionisio, D.P., Hillix, W.A., Granholm, E., 1998. Positive and negative schizotypal symptoms relate to different aspects of crossover reaction time task performance. *Psychiatry Research* 81, 241–249.
- Schofield, K., Claridge, G., 2007. Paranormal experiences and mental health: schizotypy as an underlying factor. *Personality and Individual Differences* 43, 1908–1916.
- Skottun, B.C., Skoyles, J.R., 2011. On identifying magnocellular and parvocellular responses on the basis of contrast-response functions. *Schizophrenia Bulletin* 37, 23–26.
- Stefanis, N.C., Vitoratou, S., Smyrnis, N., Constantinidis, T., Evdokimidis, I., Hatzimanolis, I., Ntzoufras, I., Stefanis, C.N., 2006. Mixed handedness is associated with the disorganization dimension of schizotypy in a young male population. *Schizophrenia Research* 87, 289–296.
- Stratta, P., Daneluzzo, E., Mattei, P., Bustini, M., Casacchia, M., Rossi, A., 1997. No deficit in Wisconsin Card Sorting Test performance of schizophrenic patients' first-degree relatives. *Schizophrenia Research* 26, 147–151.
- Suhr, J.A., 1997. Executive functioning deficits in hypothetically psychosis-prone. *Schizophrenia Research* 27, 29–35.
- Szöke, A., Schürhoff, F., Mathieu, F., Meary, A., Ionescu, S., Leboyer, M., 2005. Tests of executive functions in first-degree relatives of schizophrenic patients: a meta-analysis. *Psychological Medicine* 35, 771–782.
- Tandon, R., Keshavan, M.S., Nasrallah, H.A., 2008. Schizophrenia, "Just the facts" what we know in 2008. 2. Epidemiology and etiology. *Schizophrenia Research* 102, 1–18.
- Taylor, M.M., Creelman, C.D., 1967. PEST: efficient estimates on probability functions. *Journal of the Acoustical Society of America* 41, 782–787.
- Thurston-Snoha, B.-J., Lewine, R.R.J., 2007. Intact Wisconsin Card Sorting Test performance: implications for the role of executive function in schizophrenia. *British Journal of Clinical Psychology* 46, 361–369.
- Tsakanikos, E., Reed, P., 2003. Visuo-spatial processing and dimensions of schizotypy: figure-ground segregation as a function of psychotic-like features. *Personality and Individual Differences* 35, 703–712.
- van Os, J., Linscott, R.J., Myin-Germeys, I., Delespaul, P., Krabbendam, L., 2009. A systematic review and meta-analysis of the psychosis continuum: evidence for a psychosis proneness–persistence–impairment model of psychotic disorder. *Psychological Medicine* 39, 179–195.
- Ventura, J., Helleman, G.S., Thames, A.D., Koellner, V., Nuechterlein, K.H., 2009. Symptoms as mediators of the relationship between neurocognition and functional outcome in schizophrenia: a meta-analysis. *Schizophrenia Research* 113, 189–199.
- Waford, R.N., Lewine, R., 2010. Is perseveration uniquely characteristic of schizophrenia? *Schizophrenia Research* 118, 128–133.
- Wagman, A.M.I., Wagman, W., 1992. On the Wisconsin. In: Walker, E.F., Dworkin, R.H., Cornblatt, B.A. (Eds.), *Progress in Experimental Personality and Psychopathology Research*. Springer, New York, pp. 162–182.
- Walker, E.F., Cornblatt, B.A., Addington, J., Cadenhead, K.S., Cannon, T.D., McGlashan, T.H., Perkins, D.O., Seidman, L.J., Tsuang, M.T., Woods, S.W., Heinssen, R., 2009. The relation of antipsychotic and antidepressant medication with baseline symptoms and symptom progression: a naturalistic study of the North American Prodrome Longitudinal Sample. *Schizophrenia Research* 115, 50–57.
- Walter, H., Wolf, R.C., 2008. Arbeitsgedächtnis und Psychopathologie schizophrener Störungen. *Fortschritte der Neurologie-Psychiatrie* 76, S16–S23.
- Wickham, H., Murray, R.M., 1997. Can biological markers identify endophenotypes predisposing to schizophrenia? *International Review of Psychiatry* 9, 355–364.
- Wobrock, T., Ecker, U.K.H., Scherk, H., Schneider-Axmann, T., Falkai, P., Gruber, O., 2009. Cognitive impairment of executive function as a core symptom of schizophrenia. *World Journal of Biological Psychiatry* 10, 442–451.