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Electrophysiological correlates of visual backward masking in patients with major depressive disorder

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A B S T R A C T

Depression and schizophrenia are two psychiatric diseases with high co-morbidity. For this reason, it is important to find sensitive endophenotypes, which may disentangle the two disorders. The Shine-Through paradigm, a visual backward masking task, is a potential endophenotype for schizophrenia. Masking is strongly deteriorated in schizophrenia patients, which is reflected in reduced EEG amplitudes. Here, we tested whether masking deficits and associated EEG changes are also found in patients with major depressive disorder. First, we replicated previous findings showing that depressive patients exhibit, at most, only weak masking deficits. Second, we found that the EEG amplitudes of depressive patients were reduced compared to controls and slightly increased compared to schizophrenia patients. As a secondary analysis, we compared the performance in the masking paradigm with three cognitive tasks, namely: the Wisconsin card sorting test, a verbal fluency test and a degraded continuous performance test. Performance in all but the verbal fluency test could discriminate schizophrenia from depression.

1. Introduction

Depression and schizophrenia are two major psychiatric diseases, which exhibit a considerable overlap in terms of their psychopathology (schizoaffective disorders) and their symptoms (negative symptoms: Andreasen and Olsen, 1982; Dai et al., 2018; delusions: Sax et al., 1996). There is also a strong genetic overlap between the two disorders (Lee et al., 2013; Smoller et al., 2019; Postolache et al., 2019). It is therefore of great interest to disentangle the neural underpinnings of the two diseases. For this purpose, endophenotypes are of crucial importance. An endophenotype must be: associated with the disease, inheritable, present at a higher rate within relatives, and state-independent (Gottesman and Gould, 2003).

Deficits in visual backward masking tasks, in particular the Shine-Through paradigm, have been proposed as potential endophenotypes of schizophrenia (Chkonia et al., 2010a). In the Shine-Through paradigm,

a target vernier is followed by a grating mask. A vernier is composed of two vertical bars separated by a small horizontal gap, and the task is to report whether the lower bar is offset to the left or to the right. The mask deteriorates the visibility of the target vernier. We measured the stimulus onset asynchrony (SOA) between the onset of the venier and the onset of the mask in an adaptive manner for each individual, such that 75% of correct responses were achieved. Schizophrenia patients needed SOAs of about 5 times longer than controls (Herzog et al., 2004), and healthy siblings of patients needed SOAs of about 2.5 longer than controls (Chkonia et al., 2010a). Masking was, not only impaired in schizophrenia patients, but also in schizoaffective and bipolar patients. On the other hand, patients with depression showed no deficit in visual masking (Chkonia et al., 2012). For this reason, the Shine-Through paradigm was considered to be an endophenotype of the schizophrenia spectrum (or psychosis spectrum).

Masking deficits of schizophrenia patients were reflected in the

electroencephalogram (EEG), being strongly associated with a reduced N1 component of event-related potentials (ERPs) as measured by the global field power (GFP; Plomp et al., 2012; da Cruz et al., 2020). For patients with first-episode psychosis, the neural correlates were at an intermediate level: GFP N1 traces were similar to those of controls when the task was easy, and similar to chronic schizophrenia patients when the task was challenging (Favrod et al., 2018). Comparably to controls, observers with high scores of schizotypy showed reduced GFP N1 amplitudes (Favrod et al., 2017). Surprisingly, siblings of schizophrenia patients showed higher GFP N1 amplitudes than controls, suggesting a compensation mechanism (da Cruz et al., 2020).

As mentioned, schizophrenia patients were impaired in the Shine-Through paradigm whereas depressive patients were not (Chkonia et al., 2012). The aim of the present study was to investigate the electrophysiological correlates of masking in major depressive disorder. Although the electrophysiological correlates are not the endophenotype themselves, they help to understand its underlying mechanisms. We also compared the Shine-Through paradigm to other cognitive tasks that often show impairments in schizophrenia patients, namely: the degraded continuous performance test (CPT), the Wisconsin card sorting test (WCST), and a verbal fluency test (VFT).

2. Methods

2.1. Visual backward masking

Stimuli were displayed on a Siemens Fujitsu P796-1 monitor with a refresh rate of 100 Hz. The screen resolution was 1024×768 pixels. Patients sat in a dimly illuminated room, at a distance of 3.5 m away from the monitor. The vernier and mask stimuli were presented in white (with a luminance of 100 cd/m^2) on a black background (<1 cd/m^2).

The vernier stimuli consisted of two vertical bars separated by a vertical gap of 1′ (arc min). The lower bar was slightly offset either to the left or to the right compared to the upper one. The horizontal vernier offset was 1.2′. Following the vernier, a mask was presented which consisted of two rows of either five or twenty-five aligned bars. The horizontal spacing between mask elements was 3.33′. An illustration of the stimuli display can be found in the supplementary material (Figure S1). Observers reported the offset direction of the lower bar by pushing one of the two hand-held buttons.

2.2. Adaptive experiment

For each observer, we found the vernier duration (VD) for which the threshold of offset discrimination was below 0.6′. Afterwards, we used the individual VD with a fixed vernier offset of 1.2′, and determined the stimulus onset asynchrony (SOA) threshold for each participant using an adaptive strategy (Parametric Estimation by Sequential Testing; Taylor and Creelman, 1967) such that 75% correct responses were achieved. The procedure was described in detail in (Cappe et al., 2012; Herzog et al., 2004; Shaqiri et al., 2015; Favrod et al., 2018).

2.3. EEG experiment

For the EEG experiment, we used only the 25-element mask. As in previous EEG studies (Favrod et al., 2017, 2018; Plomp et al., 2012), we tested four conditions: Vernier Only, Long SOA, Short SOA, and Mask Only. In the Vernier Only condition, the vernier was presented alone for 30 ms, which corresponded to the mean VD of schizophrenia patients in previous studies. In the Short and Long SOA conditions, the vernier was presented for 30 ms followed by a mask for 300 ms with an SOA of either 30 or 150 ms, which were the average SOAs for controls and schizophrenia patients, respectively. In the Mask Only condition, the mask was presented for 300 ms; no vernier was presented.

For each observer, 8 blocks of 80 trials (20 trials/condition) were

presented. The conditions order was pseudo-randomized within each block. In total, there were 160 trials per condition.

2.4. EEG recordings and pre-processing

We used the EEG BioSemi Active Two system with 64 Ag-AgCl sintered active electrodes distributed across the scalp according to the 10/20 layout system. The sampling frequency was 2048 Hz. EEG data were pre-processed offline in Matlab (R2012a, The MathWorks Inc., Natick, MA) with EEGLAB (Delorme and Makeig, 2004) and using an automated pre-processing pipeline (APP; da Cruz et al., 2018). The signal was down-sampled to 512 Hz, band-passed filtered from 1 to 40 Hz, and the 50 Hz line noise was removed using CleanLine (Mullen, 2012). Signal was re-referenced to the biweight estimate of the mean of all electrode-channels (Hoaglin and Mosteller, 1985; Hoaglin et al., 2000). Unstable and noisy channels were removed and interpolated with a 3D spline function. Eye blink artifacts were removed through an independent component analysis (ICA) approach. EEG epochs were extracted from a time interval comprising 100 ms before the stimulus onset (baseline) to 400 ms after the stimulus onset, i.e. [−100; +400] ms relative to stimulus onset, and then re-referenced to the common average. Reaction times outside the interval [300; 3000] ms were excluded. The EEG epochs corresponding to hits and missed trials were averaged together and baseline corrected, for each condition and each participant.

2.5. EEG analysis

The individual visual evoked potentials (VEP) were analyzed in MATLAB (R2018b, The MathWorks Inc., Natick, MA). Signal from two occipital electrodes (PO7 and PO8) were extracted to visualize the positive and negative components of the VEPs (supplementary material Figure S2). The global field power (GFP) was computed as the standard deviation across all electrodes at each time point, for each participant and each condition separately (Lehmann and Skrandies, 1980). We selected this measure to avoid the problem of selecting an electrode arbitrarily and also potential reference problems. Grand averages of GFPs were computed for each condition, and each group of participants.

2.6. CPT, WCST, and VFT

We administered a computerized version of the Nelson Test (Nelson, 1976), which is a modified Wisconsin card sorting test (WCST, Berg, 1948) with 48 cards. We recorded the number of categories that participants went through, as well as the numbers of correct responses, errors and preservative errors. We also administered a degraded continuous performance test (CPT, Rosvold et al., 1956). We reported d' values. Methodological details can be found in Chkonia et al., 2010a. The verbal fluency test (VFT) was derived from the Benton controlled oral word association Test (COWAT, Ruff et al., 1996). We asked the participants to report as many words as they could, belonging to either the animal or fruit/vegetable category. The number of words for each category was reported.

2.7. Statistical analysis

Repeated measures ANOVAs were performed using JASP (https://jasp-stats.org/, version 0.9.1.0). Statistical tests were Greenhouse–Geisser corrected for lack of sphericity when necessary, and were Bonferroni-Holm corrected for multiple comparisons.

2.8. Participants

All participants had normal or corrected-to-normal vision; with a visual acuity superior or equal to 0.8 determined for both eyes with

FrAct (Bach, 1996). All participants signed an informed consent and were informed that they could quit the experiments at any time. All procedures complied with the Declaration of Helsinki and were approved by the local ethics committee.

General exclusion criteria were: drug or alcohol abuse, and neurological or other somatic illnesses influencing the subjects' mental state.

2.9. Depressive patients

Patients were recruited either from the Tbilisi Mental Health Hospital or from the Acute Psychiatric Departments of Multiprofile Clinics. Patients were diagnosed with major depressive affective disorder in a recurrent episode according to the Diagnostic and Statistical Manual of Mental Disorders IV/V, by means of an interview based on the Structured Clinical Interview, information of the staff, and the study of the records (ICD-9; mild: 296.31, $n = 14$; moderate: 296.32, $n = 18$; severe: 296.33, $n = 7$). Psychopathology was assessed by an experienced psychiatrist (EC) through the Brief Psychiatric Rating Scale (BPRS; Overall and Gorham, 2004) and the Hamilton scale (Hamilton, 1960). No depressive patient had an additional axis I disorder.

In total, 39 depressive patients were recruited. Not all of them participated in each task for various reasons. Thirty-eight performed the WCST. Thirty-seven performed the CPT degraded test. Thirty-six performed the VFT. Thirty-four performed the masking task. Finally, twenty-six of them performed the masking paradigm with EEG. Group characteristics were depicted in Table 1 for the two masking experiments (behavioral/adaptive and EEG/fixed SOA) and in Table S1 in the supplementary material for the other data subset (CPT, WCST, and VFT). Out of the 34 patients that performed the masking task, 30 patients took antidepressants (fluoxetine, fluvoxamine, clomipramine, venlafaxine, escitalopram) and 24 patients were receiving neuroleptic medication. Out of the 26 patients who performed the EEG, 24 patients received antidepressants and 19 were receiving neuroleptic medication. The depressive patients were recovering from depression and were tested when stabilized. At the time of testing, patients had Hamilton scores not higher than 28. The majority of the depressive patients were taking neuroleptic medication as an adjunctive treatment either as maintenance dose or as sedation. Patients not receiving traditional antidepressants were treated with quetiapine or aripiprazole as neuroleptics for antidepressant effects.

2.10. Controls and schizophrenia patients

The results obtained for the schizophrenia patients and controls are also reported in da Cruz et al., 2020. We used them here for comparison with the depressive group and re-plotted them. The EEG data for the three groups were collected and analyzed using the same experimental setup and pre-processing pipeline, as described in a previous section (APP; da Cruz et al., 2018). Psychopathology was assessed by the Scales for the assessment of negative and positive symptoms (SANS, Andreasen, 1984a; SAPS, Andreasen, 1984b). Out of the 76 controls, 75 performed the CPT, 74 the WCST and 48 the VFT. Out of the 90 patients, 89 of them did the WCST, 88 the CPT and 23 the VFT. All of them were considered for the masking experiments (adaptive and EEG).

3. Results

3.1. Visual backward masking

The VD was significantly lower for controls compared to both groups of patients, as can be seen in Fig. 1a and Table 2.

Schizophrenia patients performed significantly worse (longer SOAs) than both depressive patients and controls (Fig. 1a, Table 2). There was no significant difference in SOAs between controls and depressive patients when both masks were combined (main effect, Table 2), replicating previous findings from Chkonia et al., 2012. When considering the interaction between the 5- and 25-element masks, one comparison turned out to be significant: depressive patients performed significantly ($p_{holm} = 0.045$) worse than controls with the 25-element mask (Table S3 of the supplementary material). This result contradicted previous findings. In the EEG experiment (25-element mask), we found no significant difference in performance between controls and depressive patients. Consistently, we did find significant differences between controls and schizophrenia patients and between depressive and schizophrenia patients (Table 2, Fig. 1b). In summary, depressive patients performed better than schizophrenia patients and similarly to controls in most masking conditions (the 25-element mask of the adaptive procedure being the only exception).

3.2. Visual backward masking: global field power

We performed the repeated measures ANOVA for the peak of the GFP grand average (N1 component), for each group and each condition, as shown in Fig. 2 (peaks and latencies were shown in Table S2, in the supplementary material).

We found a strong and significant difference between controls and schizophrenia patients, a significant difference between controls and depressive patients and no significant difference between depressive and schizophrenia patients. In particular, compared to schizophrenia patients, patients with depression showed a significantly greater GFP N1 amplitude in the Long SOA condition and a marginally greater GFP N1 amplitude in the Vernier Only condition. Statistical tests were reported in Table 3.

For comparative analysis with previous studies (Favrod et al., 2017; 2018; da Cruz et al., 2020), statistics across the whole epoch (i.e.,

Table 1

Demographics for the controls, the depressive patients (two groups: the adaptive experiment and the EEG experiment subgroup) and schizophrenia patients.

	Controls	Depression (adaptive)	Depression (EEG)	Schizophrenia
n	76	34	26	90
Gender (F/M)	34/42	22/12	16/10	15/75
Age (years) ± SD	34.9 ± 8.1	32.6 ± 10.0	32.3 ± 9.6	35.8 ± 8.8
Education (years) ± SD	15.0 ± 2.8	14.8 ± 2.6	14.8 ± 2.6	13.2 ± 2.7
Illness Duration (months) ± SD		5.9 ± 5.2	6.2 ± 5.5	11.3 ± 8.0
SANS ± SD				10.7 ± 5.3
SAPS ± SD				10.0 ± 8.1
BPRS		31.4 ± 6.9	30.4 ± 5.0	
Hamilton		15.8 ± 5.6	14.9 ± 5.4	
CPZ equivalent ± SD		236 ± 246.4	215 ± 182.3	549.3 ± 398.5
Handedness (L/R)	5/71	1/33	1/25	4/86
Visual Acuity ± SD	1.6 ± 0.4	1.4 ± 0.4	1.4 ± 0.4	1.5 ± 0.4

Note: Only 29 of the 34 depressive patients were assessed with the Hamilton scale (and 22 for the EEG dataset). 72 of the 90 schizophrenic patients received neuroleptic medication.
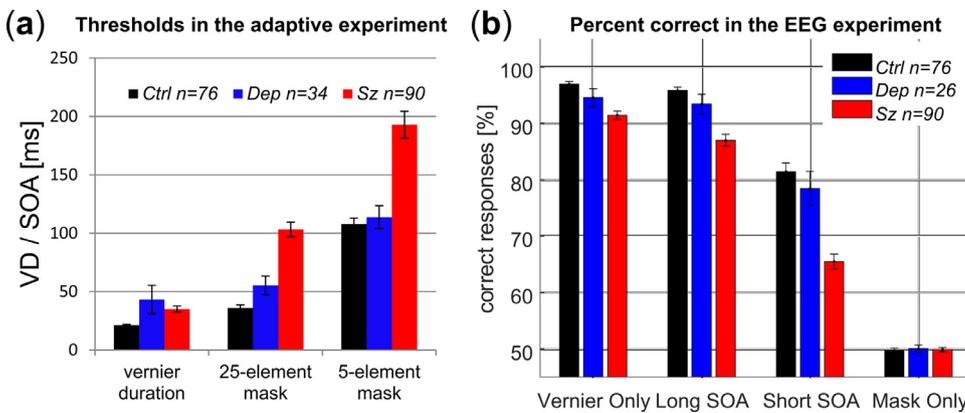
Fig. 1. Behavioral performance (**a**) Thresholds obtained with the adaptive procedure, for controls (Ctrl), depressive patients (Dep) and schizophrenia patients (Sz): vernier duration (VD) for the vernier condition and the stimulus onset asynchronies (SOA) for the two masking conditions with the 5- and 25-element masks (**b**) Percentage of correct responses in each condition of the EEG experiment (25-element mask) for the Ctrl, Dep, and Sz groups. Depressive patients were almost at the same level than controls.

Table 2

Statistical analysis for the visual backward masking performance: adaptive masking experiment (Vernier, 5- and 25-element masks) and EEG experiment.

Vernier Duration			Comments
group	$F(2,197) = 6.08$, $p = 0.003$, $\eta^2 = 0.058$		
post-hoc	**Ctrl vs Dep**	**Ctrl vs Sz**	**Dep vs Sz**
	$t(108) = -3.161$, $d = -0.553$, $p_{holm} = 0.005$	$t(164) = -2.635$, $d = -0.753$, $p_{holm} = 0.018$	$t(122) = -1.201$, $d = =0.191$, $p_{holm} = 0.231$

5-element and 25-element masks (SOA)			
mask	$F(1,197) = 230.420$, $p < 0.001$, $\eta^2 = 0.530$		
post-hoc	**SOA5 vs SOA25**		
	$t(197) = 17.32$, $d = 1.225$, $p_{holm} < 0.001$		
mask*group	$F(2,197) = 3.570$, $p = 0.030$, $\eta^2 = 0.016$		simple main effects and post-hoc tests were reported in the supplementary material (Table S3)
group	$F(2,197) = 38.39$, $p < 0.001$, $\eta^2 = 0.280$		
post-hoc	**Ctrl vs Dep**	**Ctrl vs Sz**	**Dep vs Sz**
	$t(218) = -1.045$, $d = -0.074$, $p_{holm} = 0.297$	$t(330) = -8.366$, $d = -0.592$, $p_{holm} < 0.001$	$t(246) = -5.403$, $d = -0.382$, $p_{holm} < 0.001$

Percent correct in the EEG experiment			
condition	$F(1.788,338.005) = 1285.76$, $p < 0.001$, $\eta^2 = 0.847$		simple main effects and post-hoc tests were reported in the supplementary material (Table S3)
condition*group	$F(3.577, 338.005) = 21.40$, $p < 0.001$, $\eta^2 = 0.028$		
group	$F(2,189) = 31.71$, $p < 0.001$, $\eta^2 = 0.251$		
post-hoc	**Ctrl vs Dep**	**Ctrl vs Sz**	**Dep vs Sz**
	$t(406) = 1.334$, $d = =0.096$, $p_{holm} = 0.184$	$t(662) = 7.785$, $d = =0.562$, $p_{holm} < 0.001$	$t(462) = 4.085$, $d = =0.295$, $p_{holm} < 0.001$

computed at each time frame) are shown in the supplementary material (Figure S3).

In summary, the GFP N1 amplitudes of depressive patients were reduced compared to controls and increased compared to schizophrenia patients (in particular for the Long SOA condition and only slightly for the Vernier Only condition).

3.3. CPT, VFT, and WCST

For the CPT, we found that controls performed better than schizophrenia patients as shown by the post-hoc tests (Table 4). Depressive patients were also significantly better than schizophrenia patients (Fig. 3a).

In the VFT, we found a group effect, with controls performing better than schizophrenia patients and also better than depressive patients (Table 4). No significant differences were found between depressive and schizophrenia patients (Fig. 3b), which spoke against VFT as an endophenotype for schizophrenia because of the lack of specificity.

For the WCST, we found a significant interaction between measure and group, showing that schizophrenia patients made more mistakes, were less accurate and were going through fewer categories compared to controls and depressive patients (Fig. 3c). We did not find any significant differences between controls and depressive patients for either measure. Statistical tests are reported in Table 4.

In summary, we found significant differences between controls and schizophrenia patients for all tasks. We found a significant difference between controls and depressive patients for VD, the GFP N1 amplitude and the VFT. Finally, we found significant differences between depressive and schizophrenia patients for the SOAs (adaptive masking), the CPT and the WCST.

4. Discussion

In a series of previous publications, we showed that the Shine-through masking paradigm is a potential endophenotype of schizophrenia. Differences were rather small for the unmasked vernier performance; however, patients needed much longer SOAs than healthy controls when the mask was presented, which made the paradigm both spatially and temporally challenging. In the masking conditions, SOAs were 5 and 2 times longer in the 25- and 5-element mask conditions, respectively. Similar results were found for bipolar and schizoaffective patients (Chkonia et al., 2012). An important criterion for an endophenotype is that unaffected siblings of schizophrenia patients show deficits compared to controls. Indeed, we found that unaffected siblings show masking deficits compared to healthy controls (factor 2.5). The same was true for first episode psychosis patients and adolescents with psychosis (Favrod et al., 2018; Holzer et al., 2009). We did not find masking differences in depressive patients and abstinent alcoholics
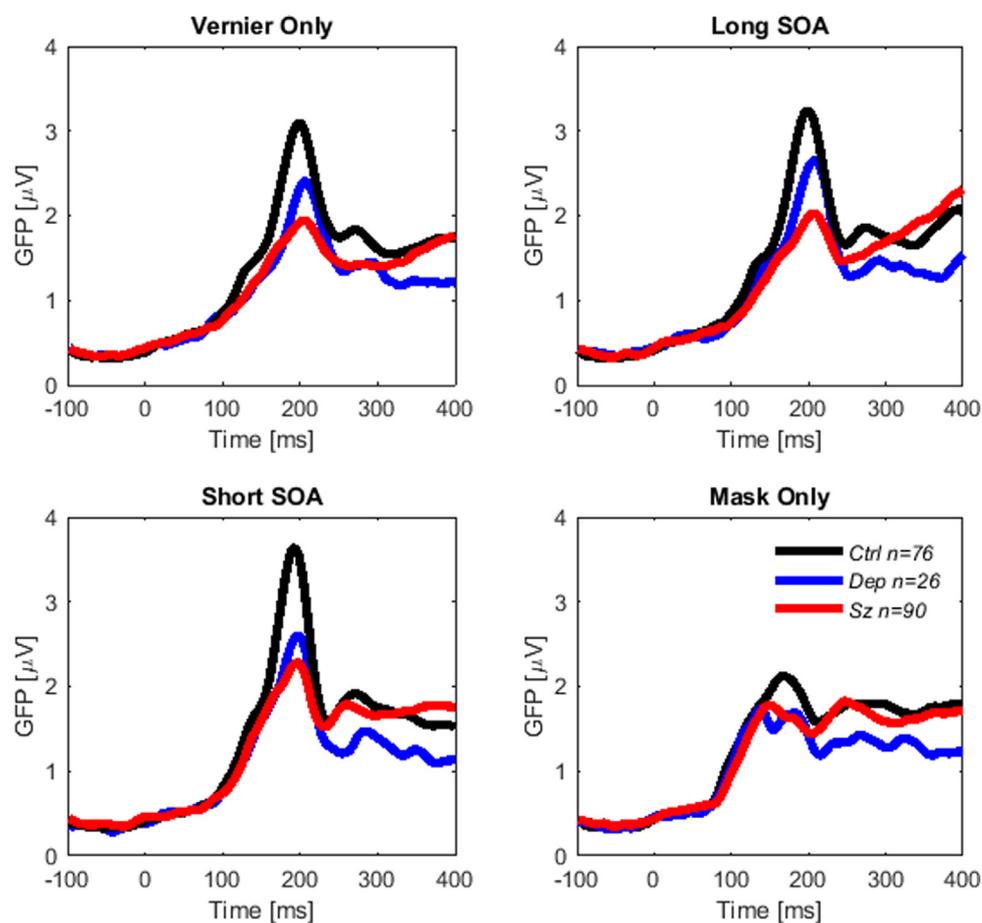
Fig. 2. Global Field Power (GFP) for the four EEG conditions with the 25-element mask. Black: controls (Ctrl); Blue: depressive patients (Dep), and Red: schizophrenia patients (Sz). In all four conditions with a vernier, the N1 component peaks around 200 ms.

compared to controls (Chkonia et al., 2012). Hence, the Shine-through paradigm was specific for the psychosis spectrum. These results were surprising since depression is also a severe brain disease with often heavy medication. In addition, there is a substantial overlap between depression and schizophrenia in terms of both symptoms and genetics.

Here, we tested a new cohort of depressive patients and replicated previous masking behavioral results. In the adaptive condition (5-element mask) and the fixed SOA condition (EEG experiment) with the 25-element mask, depressive patients performed approximately at the level of controls. In the adaptive condition with the 25-element mask, we found a significant difference in patients, contrary to previous results. One reason for this difference might be due to under-sampling. Potentially, there was a very small difference between controls and depressive patients, which sometimes lead to significant results but mostly did not. Another plausible explanation emerged from a post-hoc analysis. We found that the difference between controls and depressive patients in the 25-element mask disappeared when we controlled for gender (supplementary material Table S4-S7). There were more female participants in the depressive group than the schizophrenia group, and female participants performed slightly worse than male participants (Shaqiri et al., 2018). Hence, the small significant difference might be explained by a gender unbalance between the two samples.

Moreover, we also analyzed EEG data from the new cohort of depressive patients. In the Mask Only condition (when there was no task relevance), only a small N1 amplitude was elicited at around 200 ms after stimulus onset. Controls and schizophrenia patients showed no significant group differences. Hence, in schizophrenia patients, processing was mainly intact when no task-relevant stimulus (target) was presented. However, when the target vernier was presented (Vernier

Only, Long SOA, and Short SOA conditions), controls showed strongly increased N1 amplitudes, while these remained almost similar to the ones of schizophrenia patients in the Mask Only condition. We suggested that schizophrenia patients could not enhance the neural responses to the target vernier, making it more prone to masking (target enhancement deficit; Herzog and Brand, 2015). Importantly, the N1 amplitudes, even though moderately correlated with performance, did not reflect performance *per se*. In fact, in the Vernier Only condition, performance was similar between schizophrenia patients and controls (>90%), but the ERP responses were different. We proposed then that the N1 amplitudes reflected, among other things, the amplification of the target (Herzog et al., 2013). Under normal everyday conditions, vernier-like differences go unnoticed. Only when the vernier is important, e.g. task-relevant, does the human brain enhance vernier-related information by attention and neuromodulation. The cholinergic system might play an important role in this process (Bakanidze et al., 2013). We proposed that such target enhancement was deficient in schizophrenia patients, which was mainly evident in the demanding masking conditions. In support of this hypothesis, we found that, if healthy observers passively attended to task-irrelevant verniers, the verniers elicited only low N1 amplitudes, similar to those of schizophrenia patients (da Cruz, 2019; da Cruz et al., 2019). Interestingly, unaffected siblings of schizophrenia patients showed moderate performance deficits but increased N1 amplitudes compared to controls (da Cruz et al., 2020). We interpreted this increased N1 amplitudes in siblings as a compensatory mechanism, which would over-activate a network of brain regions. This over-activation, reflected in the N1 amplitudes, suggested that siblings engaged more *effort* in order to be able to perform better than patients.

Table 3
Statistical analysis for the GFP N1 peak measured in the EEG experiment.

N1 peak (~200 ms)	Ctrl vs Dep	Ctrl vs Sz	Dep vs Sz	Comments
group	$F_{(2,189)} = 20.26$, $p < 0.001$, $\eta^2 = 0.177$			
post-hoc	**Ctrl vs Dep**	**Ctrl vs Sz**	**Dep vs Sz**	
	$t_{(406)} = 2.883$, $d = =0.208$, $p_{holm} = 0.009$	$t_{(662)} = 6.341$, $d = =0.458$, $p_{holm} < 0.001$	$t_{(462)} = 1.495$, $d = =0.108$, $p_{holm} = 0.137$	
condition	$F_{(2.108,398.337)} = 60.01$, $p < 0.001$, $\eta^2 = 0.221$			post-hoc tests were reported in the supplementary material (Table S3)
condition*group	$F_{(4.215, 398.337)} = 11.32$, $p < 0.001$, $\eta^2 = 0.083$			
post-hoc	**Ctrl vs Dep**	**Ctrl vs Sz**	**Dep vs Sz**	
Vernier Only	$t_{(100)} = 2.564$, $d = =0.539$, $p_{holm} = 0.022$	$t_{(164)} = 6.279$, $d = =0.951$, $p_{holm} < 0.001$	$t_{(114)} = 1.777$, $d = =0.451$, $p_{holm} = 0.077$	$F_{(2,189)} = 19.74$, $p < 0.001$, $\eta^2 = 0.173$
Long SOA	$t_{(100)} = 2.195$, $d = =0.457$, $p_{holm} = 0.037$	$t_{(164)} = 6.599$, $d = =1.011$, $p_{holm} < 0.001$	$t_{(114)} = 2.377$, $d = =0.598$, $p_{holm} = 0.037$	$F_{(2,189)} = 21.81$, $p < 0.001$, $\eta^2 = 0.188$
Short SOA	$t_{(100)} = 3.330$, $d = =0.685$, $p_{holm} = 0.002$	$t_{(164)} = 6.378$, $d = =0.967$, $p_{holm} < 0.001$	$t_{(114)} = 1.065$, $d = =0.278$, $p_{holm} = 0.288$	$F_{(2,189)} = 20.87$, $p < 0.001$, $\eta^2 = 0.181$
Mask Only	$t_{(100)} = 1.885$, $d = =0.416$, $p_{holm} = 0.122$	$t_{(164)} = 2.419$, $d = =0.367$, $p_{holm} = 0.050$	$t_{(114)} = -0.231$, $d = =-0.055$, $p_{holm} = 0.817$	$F_{(2,189)} = 3.489$, $p = 0.032$, $\eta^2 = 0.036$

Table 4
Statistical analysis for the three cognitive tasks: degraded continuous performance test (CPT), verbal fluency test (VFT), and Wisconsin card sorting test (WCST).

| CPT	Ctrl vs Dep	Ctrl vs Sz	Dep vs Sz	Comments
group	$F_{(2,197)} = 13.32$, $p < 0.001$, $\eta^2 = 0.119$			
post-hoc	**Ctrl vs Dep**	**Ctrl vs Sz**	**Dep vs Sz**	
	$t_{(110)} = 1.499$, $d = =0.311$, $p_{holm} = 0.136$	$t_{(161)} = 5.109$, $d = =0.846$, $p_{holm} < 0.001$	$t_{(123)} = 2.561$, $d = =0.461$, $p_{holm} = 0.022$	
VFT				
group	$F_{(2,104)} = 10.48$, $p < 0.001$, $\eta^2 = 0.168$			
post-hoc	**Ctrl vs Dep**	**Ctrl vs Sz**	**Dep vs Sz**	
	$t_{(160)} = 3.213$, $d = =0.311$, $p_{holm} = 0.003$	$t_{(140)} = 4.223$, $d = =0.408$, $p_{holm} < 0.001$	$t_{(110)} = 1.358$, $d = =0.131$, $p_{holm} = 0.177$	
category	$F_{(1,104)} = 66.644$, $p < 0.001$, $\eta^2 = 0.374$			simple main effects and post-hoc tests were reported in the supplementary material (Table S3)
category*group	$F_{(2,104)} = 3.753$, $p = 0.027$, $\eta^2 = 0.042$			
WCST				
group	$F_{(2,198)} = 0.631$, $p = 0.533$, $\eta^2 = 0.015$			
measure	$F_{(1.304,258.141)} = 1156.75$, $p < 0.001$, $\eta^2 = 0.841$			
measure*group	$F_{(2.607, 258.141)} = 10.24$, $p < 0.001$, $\eta^2 = 0.015$			
post-hoc	**Ctrl vs Dep**	**Ctrl vs Sz**	**Dep vs Sz**	post-hoc tests were reported in the supplementary material (Table S3) all simple main effects were significant $p < 0.001$
category	$t_{(110)} = -0.023$, $d = =-0.004$, $p_{holm} = 0.982$	$t_{(161)} = 5.222$, $d = =0.839$, $p_{holm} < 0.001$	$t_{(125)} = 4.263$, $d = =0.828$ $p_{holm} < 0.001$	
correct response	$t_{(110)} = -0.627$, $d = =-0.125$, $p_{holm} = 0.531$	$t_{(161)} = 3.730$, $d = =0.597$, $p_{holm} < 0.001$	$t_{(125)} = 3.674$, $d = =0.699$, $p_{holm} < 0.001$	
error	$t_{(110)} = 0.699$, $d = =0.126$, $p_{holm} = 0.485$	$t_{(161)} = -3.314$, $d = =-0.544$, $p_{holm} = 0.002$	$t_{(125)} = -3.410$, $d = =-0.696$, $p_{holm} = 0.002$	
perseverative error	$t_{(110)} = 0.858$, $d = =0.180$ $p_{holm} = 0.392$	$t_{(161)} = -4.050$, $d = =-0.652$, $p_{holm} < 0.001$	$t_{(125)} = -4.172$, $d = =-0.757$, $p_{holm} < 0.001$	
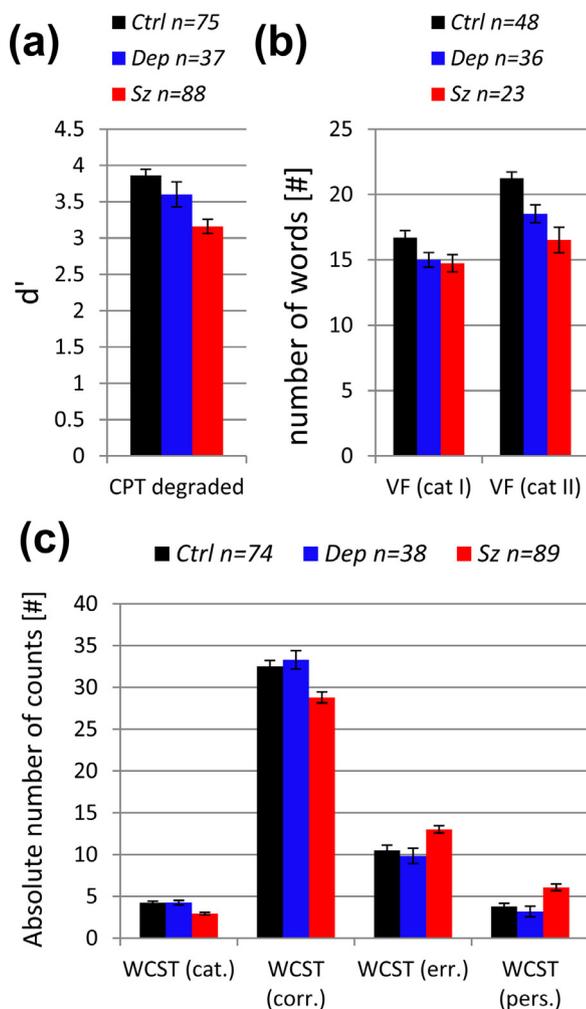
Fig. 3. Performance for the continuous performance test (CPT), the verbal fluency test (VFT) and the Wisconsin card sorting test (WCST), in the three groups (Ctrl, Dep and Sz). (**a**) d' for the CPT (**b**) number of words for the VFT - category I: animals, category II: vegetables/fruits (**c**) the four different measures for the WCST: the categories (cat.), the number of correct responses (corr.), the number of errors (err.) and the perseverative errors (pers.).

patients showed no deficits (Chkonia et al., 2010b).

In summary, schizophrenia patients had a low ability to enhance faint targets, such as briefly presented verniers, which made them more prone to masking effects. Similarly, siblings of schizophrenia patients had low target enhancement compared to control. However, by engaging more resources they could partially compensate for the deficits, which improved performance compared to schizophrenia patients. However, this compensation was not sufficient to achieve healthy controls-like performance. In contrast to schizophrenia patients, depressive patients enhanced targets similarly to controls, and their performance was comparable to that of controls. However, depressive patients tended to perceive any kind of task as more difficult (Brinkmann and Gendolla, 2008) and presumably disengaged from the task, which was reflected in their lower GFP N1 amplitudes compared to controls.

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Supplementary materials

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Here, we found that depressive patients had good behavioral performance but relatively low N1 amplitudes. We, therefore, speculated that the N1 amplitudes reflected an interaction between target enhancement effects and how much intrinsic *effort* was put in the task. Potentially, depressive patients had no impairments regarding the stability of the representation (target enhancement), but they were disengaged in general, which was reflected in the lower EEG amplitudes. The depressive patients, however, complied with the task explaining the good performance.

An alternative explanation for the reduced N1 amplitudes in depression is that the neural correlates of masking are state-dependent (at least for depression). For example, N1 amplitudes changed depending on whether the depressive patients were in remission or in relapse, as evident for the P300 component (see Bruder et al., 2012, for a review).

In all our studies on schizophrenia, we regularly conducted the CPT, VFT, and WCST. For this reason, we applied these tests also to depressive patients. For the VFT, depressive patients were impaired as much as schizophrenia patients. In contrast, in the CPT and WCST (number of errors), depressive patients performed better than schizophrenia patients, and were in fact almost at the level of controls. We would like to mention that the CPT was often proposed as an endophenotype for schizophrenia. However, results were mixed and evidence spoke rather against this claim because siblings of schizophrenia

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