Electrophysiological correlates of visual backward masking in patients with bipolar disorder

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ABSTRACT

In visual backward masking (VBM), a target is followed by a mask that decreases target discriminability. Schizophrenia patients (SZ) show strong and reproducible masking impairments, which are associated with reduced EEG amplitudes. Patients with bipolar disorder (BP) show masking deficits, too. Here, we investigated the neural EEG correlates of VBM in BP. 122 SZ, 94 unaffected controls, and 38 BP joined a standard VBM experiment. 123 SZ, 94 unaffected controls and 16 BP joined a corresponding EEG experiment, analyzed in terms of global field power. As in previous studies, SZ and BP show strong masking deficits. Importantly and similarly to SZ, BP show decreased global field power amplitudes at approximately 200 ms after the target onset, compared to controls. These results suggest that VBM deficits are not specific for schizophrenia but for a broader range of functional psychoses. Potentially, both SZ and BP show deficient target enhancement.

1. Introduction

Psychiatric disorders are heterogeneous and there is a considerable overlap between diseases (Craddock and Owen, 2010). For instance, both patients with bipolar disorder (BP) and schizophrenia patients (SZ) show similar cognitive and visual deficits (Sheffield et al., 2018; Trillenberg et al., 2016) as well as shared psychopathological features and genetic and psychosocial risk factors (Lichtenstein et al., 2009; Maciukiewicz et al., 2016). Therefore, these two disorders, which have been traditionally considered to be distinct from each other (American Psychiatric Association and others, 2013; Kraepelin, 1899), might belong to the same spectrum (Craddock and Owen, 2010; Linscott and van Os, 2010; Smoller et al., 2019).

Both schizophrenia and bipolar disorder are strongly influenced by genetics. However, single-nucleotide polymorphisms (SNP) explain only a small variance of the risk for the disorders (Farrell et al., 2015; Örrù and Carta, 2018; Prata et al., 2019). It is therefore of great interest to find endophenotypes, which are located between the genetic and the symptomatic levels, to identify risk factors and thus improve diagnosis (Glahn et al., 2014; Gottesman and Gould, 2003).

Several candidate endophenotypes have been proposed for both schizophrenia and bipolar disorder (Allen et al., 2009; Pearlson, 2015). Endophenotypes based on visual processing are of particular relevance because of their excellent reproducibility, etiology-independence, and their contributions to higher cognitive impairments such as object recognition (Calderone et al., 2013; Herzog and Brand, 2015; Silverstein, 2016; Silverstein and Keane, 2011). Visual backward masking (VBM) is such a candidate endophenotype for schizophrenia (Green et al., 2011; Rund et al., 1993), especially the shine-through paradigm, which has a much higher sensitivity and specificity than most other perceptual and cognitive tasks (Chkonia et al., 2010b). In backward masking, a target is followed by a mask that deteriorates performance on the target (Breitmeyer and Ogmen, 2006). In the shine-through paradigm, the target is a vertical vernier, i.e., two vertical bars slightly offset in the horizontal direction, and the mask consists of a grating of aligned verniers (see Figure 1A). Evidence for an endophenotype for schizophrenia comes from a series of studies showing that, first, SZ and schizoaffective patients have strong and reproducible performance...
deficits (Chkonia et al., 2012; Herzog et al., 2004). Second, masking deficits are already present in adolescents with psychosis (Holzer et al., 2014, 2009) and with first-episode psychosis (Favrod et al., 2018). Third, masking deficits are state-independent (Chkonia et al., 2010b). Fourth, healthy students scoring high in schizotypal traits also show masking deficits albeit they are highly functioning (Cappe et al., 2012; Favrod et al., 2017). Fifth and most importantly, unaffected siblings of SZ show masking deficits (Chkonia et al., 2010b; da Cruz et al., 2020b). Interestingly, siblings, adolescents with psychosis, and students scoring high in schizotypal traits are not medicated, adding further evidence that visual masking deficits are trait rather than state markers.

In SZ and in patients with first-episode psychosis, masking deficits are associated with decreased neural amplitudes of the N1 component at around 200 ms, as determined by the global field power (GFP) (Favrod et al., 2018; Plomp et al., 2013). Similar results were found in healthy students scoring high in schizotypal traits (Favrod et al., 2017).

Since BP have similar masking deficit as SZ (Chkonia et al., 2012), we hypothesized that they show also similar neural correlates.

### 2. Methods

#### 2.1. Participants

123 SZ, 46 BP, and 94 unaffected controls participated in the experiment. Patients were recruited from the Tbilisi Mental Health Hospital. Controls were recruited from the general population in Tbilisi, aiming to match patients’ characteristics as close as possible. Participants’ age ranged from 18 to 58 years. Behavioral data of 22 out of the

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**Table 1**

<table>
<thead>
<tr>
<th></th>
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<th>SZ (EEG)</th>
<th>ctrl</th>
<th>BP (adaptive)</th>
<th>BP (EEG)</th>
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<tbody>
<tr>
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<td>111</td>
<td>121</td>
<td>94</td>
<td>38</td>
<td>16</td>
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<tr>
<td>Gender (F/M)</td>
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<td>18/103</td>
<td>47/47</td>
<td>24/14</td>
<td>11/5</td>
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<td>Age</td>
<td>35.9 ± 0.8</td>
<td>36.1 ± 0.8</td>
<td>35.2 ± 0.9</td>
<td>34.4 ± 1.5</td>
<td>35.0 ± 2.2</td>
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<tr>
<td>Education (years)</td>
<td>13.3 ± 0.3</td>
<td>13.3 ± 0.2</td>
<td>15.2 ± 0.3</td>
<td>14.4 ± 0.4</td>
<td>14.7 ± 0.5</td>
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<tr>
<td>Handedness (L/R)</td>
<td>5/106</td>
<td>6/115</td>
<td>6/88</td>
<td>0/36</td>
<td>0/13</td>
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<tr>
<td>Visual acuity</td>
<td>1.4 ± 0.0</td>
<td>1.4 ± 0.0</td>
<td>1.6 ± 0.0</td>
<td>1.4 ± 0.1</td>
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<tr>
<td>Illness duration (years)</td>
<td>11.9 ± 0.8</td>
<td>12.1 ± 0.7</td>
<td>10.7 ± 1.2</td>
<td>11.5 ± 2.1</td>
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<tr>
<td>SANS</td>
<td>10.4 ± 0.5</td>
<td>10.5 ± 0.5</td>
<td>31.3 ± 1.1</td>
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<td>SAPS</td>
<td>9.8 ± 0.7</td>
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<td>BPRS</td>
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<td>32.6 ± 0.4</td>
<td>31.3 ± 1.1</td>
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<td>CPZ equivalent</td>
<td>563.7 ± 37.3</td>
<td>586.7 ± 36.8</td>
<td>409.1 ± 62.7</td>
<td>241.3 ± 24.7</td>
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</table>

**Figure 1.** Adaptive procedure. (A) Stimulus display: The vernier duration (VD) was determined for each observer individually. Then, a mask with variable inter-stimulus interval (ISI) followed the vernier. The mask was composed of either 5- or 25-elements. The mask duration (MD) was 300 ms. (B) Behavioral results: VDs and stimulus onset asynchrony (SOA) for the two types of masks. (Note: SOA = VD + ISI, longer SOAs = stronger deficits). Mean VDs and mean SOAs of SZ (red) and BP (cyan) are higher as compared to controls (black). Error bars represent the standard error of the mean.
3

46 BP were already published in a previous study (Chkonia et al., 2012). Also, EEG data of 110 SZ and 83 controls were published in previous work (da Cruz et al., 2020b, 2020a; Favrod et al., 2019). Patients were diagnosed according to the Diagnostic and Statistical Manual of Mental Disorders, (DSM-IV/V) based on the Structured Clinical Interview for DSM-IV-V (Clinician Version) by an experienced psychiatrist (EC). Psychopathology of SZ was assessed by the Brief Psychiatric Rating Scale (BPRS; Overall and Gorham, 2004). Psychopathology of all BP was out of the 123 SZ were assessed by the Brief Psychiatric Rating Scale (BPRS). 52 SZ, 24 BP and 66 controls performed the verbal fluency task (CPT). 52 SZ, 24 BP and 66 controls performed the verbal fluency task (CPT). 52 SZ, 24 BP and 66 controls performed the verbal fluency task (CPT).

ANOVA and post-hoc Welch’s t-tests were performed for both analyses. Chi-square tests were performed with categorical variables. P-values Bonferroni-Holm corrected for multiple comparisons for each pairwise group comparisons within each variable of interest. The three groups differed in terms of gender, education, and visual acuity.

2.2. Stimuli and apparatus

Stimuli were displayed on a Siemens Fujitsu P796-1 monitor (31.0 cm (H) x 23.3 cm (V)) with a refresh rate of 100 Hz. Screen resolution was 1024 × 768 pixels. Participants sat in a dimly illuminated room at 3.5 m away from the monitor. At this distance, a pixel comprised about 18° (arc seconds).

The vernier stimuli were composed of two vertical bars, each 10' (arc min) long, separated by a vertical gap of 1°. The two bars were offset in the horizontal direction of 1.2°. In each trial, the vernier offset direction was randomly chosen. The mask elements were aligned verniers, i.e., without the horizontal offset, separated horizontally by 3.3°. The vernier and the central element of the masking grating always appeared in the middle of the screen. The vernier and the two mask stimuli were presented in white (with light intensity of 100 cd/m²) on a black background (<1 cd/m²).

Participants reported the perceived offset direction of the lower bar compared to the upper bar of the vernier stimuli by hand-held button presses (left vs. right). When uncertain, participants guessed the direction. Accuracy was emphasized over speed.

2.3. Adaptive experiment

The detailed procedure can be found in Herzog and colleagues (Herzog et al., 2004). Masking parameters were determined individually for each participant. First, an adaptive staircase procedure (PEST; Taylor and Creelman, 1967) was used to determine the vernier duration (VD) necessary to reach 75% of correct responses for a vernier offset below 0.6°. Participants had to reach a VD shorter than 100 ms. 90 SZ and 3 BP were excluded at this stage. Second, the vernier offset was fixed to 1.2°, and individual VDs were used in the VBM task. The vernier stimulus was followed by a grating mask (lasting for 300 ms), with variable inter-stimulus interval (ISI). For each participant, the stimulus onset...
asynchrony ($\text{SOA} = \text{VD} + \text{ISI}$) to reach 75% correct responses was determined by the adaptive PEST (Taylor and Creelman, 1967). Two types of masks of either 5- or 25-elements were used (Figure 1A). Each participant performed twice; for each type of mask, the two runs were averaged and then submitted to statistical analysis. Participants with mean SOAs longer than 300 ms for the 25-elements mask and longer than 450 ms for the 5-elements mask, i.e., twice the mean SOAs of SZ in previous works (Chkonia et al., 2010b; Favrod et al., 2018; Herzog et al., 2004), were excluded at this stage (2 SZ and 2 BP).

2.4. EEG experiment

To keep stimuli constant as required for EEG experiments, we used the same VD and SOAs for all participants. Only the 25-elements mask was used in the EEG experiment. VD was fixed to 30 ms, i.e., the average VD for SZ according to previous studies (Chkonia et al., 2010b; Herzog et al., 2004). Two SOA durations corresponding to the mean performance level of controls (30 ms) and of SZ (150 ms) were used (Chkonia et al., 2010b; Favrod et al., 2018; Herzog et al., 2004).

As in previous work (da Cruz et al., 2020b; Favrod et al., 2019, 2018, 2017; Plomp et al., 2013), the following four conditions were tested (Figure 2A): (1) Vernier Only, i.e., the vernier was presented alone for 30 ms; (2) Long SOA, i.e., the vernier was followed by the mask with an SOA of 150 ms; (3) Short SOA, i.e., the vernier was followed immediately by the mask with an SOA of 30 ms; and (4) Mask Only, i.e., the mask was presented for 300 ms (control condition). For each observer, eight blocks of 80 trials (20 trials/condition in pseudo-random order) were presented. For each recording, 160 trials per condition were computed. In the Mask Only condition, the left/right offset responses were compared to a randomly chosen notional offset.

2.5. EEG recording and pre-processing

EEG was recorded using a 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. Offline data were pre-processed in MATLAB (R2012a, The MathWorks Inc., Natick, MA) using an automated pre-processing pipeline (da Cruz et al., 2018) (see supplemental information for details). For the EEG analysis, we excluded 1 BP due to incomplete EEG data and 2 SZ due to excessive muscular artifacts or noisy electrodes.
GFP amplitude group differences appear around the peak latencies of the points), for each of the conditions separately. This analysis indicates that groups for each time point between 0 and 400 ms (205 consecutive time amplitudes of the individual evoked-related potentials (ERPs) between 2.7. CPT, VFT, WCST occipital electrodes (PO7 and PO8). Additionally, the positive and negative components of the group latencies (i.e., the N1 component) across participants and conditions. Thus, in the second analysis we compared the GFP amplitudes at peak GFP for each condition, and the peak latencies differ for each condition. The GFP traces were analyzed in two ways. First, we compared GFP-dependent measure and avoids the arbitrary selection of electrodes. There is a significant difference around 200 ms in all conditions. Shaded areas indicate SEM.

![Figure 3](image)

**Figure 3.** GFP analysis. (A) Group grand-average ERPs for the PO7 and PO8 electrodes. Participants showed negative deflections peaking around 200 ms, resembling a N1 component. (B) Group average global field power (GFP) time series in each condition. The bottom lines show the significant results of the timewise statistics. There is a significant difference around 200 ms in all conditions. Shaded areas indicate SEM.

### 2.6. GFP analysis

The GFP was computed for each participant and each condition. The GFP is the standard deviation of potentials of all electrodes at each time point (Lehmann and Skrandies, 1980). The GFP is a reference-in-dependent measure and avoid the arbitrary selection of electrodes. The GFP traces were analyzed in two ways. First, we compared GFP amplitudes of the individual evoked-related potentials (ERPs) between groups for each time point between 0 and 400 ms (205 consecutive time points), for each of the conditions separately. This analysis indicates that GFP amplitude group differences appear around the peak latencies of the GFP for each condition, and the peak latencies differ for each condition. Thus, in the second analysis we compared the GFP amplitudes at peak latencies (i.e., the N1 component) across participants and conditions. Additionally, the positive and negative components of the group grand-average ERPs were visualized by extracting the signal from two occipital electrodes (PO7 and PO8).

### 2.7. CPT, VFT, WCST

Three cognitive tests were administered: (1) The degraded continuous performance test (CPT; Rosvold et al., 1956) with three blocks (720 digits, 10% targets, degradation 40%), for a total duration of 12 minutes (methodological details in Chkonia and colleagues; Chkonia et al., 2010a). We computed $d'$, which is $z$(hit rate)–$z$(false alarm rate). (2) The verbal fluency test (VFT), which was derived from the Benton controlled oral word association test (Ruff et al., 1996). Participants had to report as many words as possible belonging to either the animal or fruit/vegetable category. For each category, participants had one minute to reply. The numbers of words were reported. (3) A computerized version of the Nelson test (Nelson, 1976), which was a modified version of the Wisconsin card sorting test (WCST; Berg, 1948) with 48 cards. Four measures are reported (i.e., the number of categories that subjects went through, the number of correct responses, the number of errors, and the number of perseverative errors).

### 2.8. Statistical analysis

In the GFP timewise analysis (2.6), the GFP traces amplitudes were compared between groups for each time point trough a one-way ANOVA, and for each condition separately. The longest significant difference in the baseline (i.e., before the stimulus onset) was used as a threshold for multiple comparisons correction. Here, an effect was considered significant ($\alpha < .05$) when at least 14 consecutive time points
investigate non-significant group comparisons. Bayesian independent samples t-tests with Cauchy priors (Rouder et al., 2009) were used, when opportune, to used for group comparisons. Welch’s t-tests were Bonferroni-Holm corrected for multiple comparisons using RStu.

This approach has been shown to partially control for multiple comparisons in the baseline or unrealistic effects (too early) were removed. -

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Statistical analysis for the three cognitive tasks

| Table 5 | Statistical analysis for the three cognitive tasks |
|-----------------|--------------------------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|
| **Group**       | **ANOVAs**                         | **Post-hoc t-tests** | **Control vs. SZ** | **BP vs. Controls** | **SZ vs. Controls** | **Error correction** | **P-values** |
|                 |                                |                  |                  |                  |                  |                               |                |
| **VFT**         | **2 (categories) x 3 (groups)**   |                  |                  |                  |                  |                               |                |
|                 | t(201.835)                        | t(69.850)         | (80.372)         |                  |                  |                               |                |
|                 | 6.628,                            | 3.835             | .926,            |                  |                  |                               |                |
|                 | d=—9.99,                         | d=—7.27,          | 161,            |                  |                  |                               | .001           |
|                 | P<0.001                          | P<0.001           | P<0.001         |                |                |                               |                |
| **Wisconsin card sorting test** | **Greenhouse-Geisser as assumption of sphericity is violated** |                                |                  |                  |                  |                               |                |
| **Measure**     | **F(2,670) = 12.928, ηp² = 0.19, P<0.001** |                  |                  |                  |                  |                               |                |
| **Post-hoc**    | **t(197.932)**                   | **t(74.357)**     | **t(66.830)**   | **t(22.58)**    | **t(69.023)**    | **t(69.783)**               | **t(48.110)** |
|                 | 3.891,                           | 3.521             | 1.967,          | 3.647,          | 1.479,           | 1.421,                       |                |
|                 | d=—7.14,                         | d=—4.47,          | 1.219,          | 1.421,          | 1.421,           |                               |                |
|                 | P<0.001                          | P<0.001           | P<0.001         |                |                |                               |                |
| **Error**       | **t(198.578)**                   | **t(69.147)**     | **t(69.023)**   | **t(22.58)**    | **t(69.783)**    | **t(48.110)**               | **t(48.110)** |
|                 | 5.332,                           | 2.815             | .967,           | 2.897,          | 2.897,           | 2.897,                       |                |
|                 | d=—7.26,                         | d=—5.34,          | 1.21,           | 1.21,           | 1.21,            |                               | .001           |
|                 | P<0.001                          | P<0.001           | P=0.001         |                |                |                               |                |
| **Pervasive**   | **t(212.329)**                   | **t(58.093)**     | **t(59.563)**   | **t(22.58)**    | **t(48.110)**    | **t(48.110)**               | **t(48.110)** |
|                 | 3.891,                           | 3.521             | 1.967,          | 3.647,          | 1.479,           | 1.421,                       |                |
|                 | d=—7.14,                         | d=—4.47,          | 1.219,          | 1.421,          | 1.421,           |                               |                |
|                 | P<0.001                          | P<0.001           | P<0.001         |                |                |                               |                |
| **Group**       | **t(22.58)=1.481, ηp²=0.111, P=0.229** |                  |                  |                  |                  |                               |                |

The following statistical tests were conducted: for VFT: 1 (d) x 3 (groups) ANOVA, for VFT: 2 (categories) x 3 (groups) rm-ANOVA, and for WCST: 4 (measures) x 3 (groups) rm-ANOVA. P-values Bonferroni-Holm corrected for multiple comparisons.

Controls ≠ N1 peak BP rather than for the null hypothesis H0 (i.e., N1 peak controls = N1 peak BP), because BF_{p10}=1 (i.e., Vernier Only: BF_{p10}=2.060; Long SOA: BF_{p10}=1.797). In the Mask Only condition, GFP peak amplitudes of the three groups are comparable.

3.3. CPT, VFT, and WCST

Overall, controls perform better than patients in all three cognitive tasks (Figure 4, Table 5). We find a significant difference between BP and controls for 5 out of 7 test variables. No significant differences were found between SZ and BP for any of the test variables. Overall, Bayesian independent samples t-tests give more evidence for H0 than H1 (i.e., SZ tests variables = BP tests variables): CPT: d: BF_{p1}=3.647; VFT, cat I: BF_{p1}=2.125, cat II: BF_{p1}=3.732; WCST, cat: BF_{p1}=3.213, corr: BF_{p1}=4.228, err: BF_{p1}=1.421, pers: BF_{p1}=5.360.

4. Discussion

Backward masking performance in SZ is impaired compared to unaffected controls (Braff and Saccuzzo, 1981; Bredgaard and Gletsjoj, 2000; Butler et al., 2007; Green et al., 2011; Herzog et al., 2004). In BP, results are mixed. Some studies found impaired VBM performance of BP compared to controls (Chkonia et al., 2012; Macqueen et al., 2001; McClure, 1999), while two studies found unaffected performance of BP (Goghari and Sponheim, 2008; Jahshan et al., 2014). However, sample sizes and hence statistical power are not large, ranging from 22 to 43 participants, which may explain the heterogeneous results. We tested 43 BP with the adaptive procedure and found that the performance of both groups of patients was strongly and similarly deteriorated compared to controls (SZ vs. controls: d=−.871, BP vs. controls: d=−.794). Masking deficits for BP compared to controls were also found in the EEG experiment. Our results replicate previous findings (Chkonia et al., 2012; Macqueen et al., 2001; McClure, 1999) and thus support the notion that schizophrenia and bipolar disorder belong to one spectrum (Cradick and Owen, 2010).

Neurophysiologically, SZ showed strongly reduced GFP amplitudes at approximately 200 ms after the target onset compared to controls in the shine through paradigm (Plomp et al., 2013). Similar results were also found in patients with first episode psychosis and students with high schizotypal traits (Favrod et al., 2018, 2017). Here, we investigated whether the behavioral deficits found in BP are reflected neurophysiologically in a similar manner as in SZ. Qualitatively, the GFP curves of BP resembled the ones of SZ. We found significant GFP reductions of N1 peaks amplitudes in SZ and BP relative to controls in the three conditions with the target vernier. Differences between BP and controls survived the correction for multiple comparisons for the Short SOA condition (P_{null}=0.003), whereas they did not for the Vernier Only (P<0.01, P_{null}=0.055) and the Long SOA conditions (P<0.01, P_{null}=0.076). A sensitivity analysis (two-tails independent sample t-tests, alpha = 0.05, power = 0.80, size BP group = 16, size control group = 94) showed that, between BP and controls, we had a sensitivity to detect an effect size of 0.76, which is a large effect size according to Cohen (Cohen, 1988). Following Bayesian analysis, we found weak evidence for a difference between BP and controls also for the Vernier Only and the Long SOA conditions. Therefore, the decreased GFP amplitudes of BP compared to controls is similar to the difference between SZ and controls and a lack of statistical power may explain why we did not find a significant difference in the Vernier Only and in the Long SOA conditions between controls and BP. No difference was found in the Mask Only condition, indicating that these deficits are specific to the target vernier and are not caused by the sheer presentation of stimuli, which may be expected by low level deficits such as generally diminished excitation.

Here, we propose the following hypothesis. The N1 amplitudes reflect, among other things, an interaction between the amplification of the target (Herzog et al., 2013) and how much intrinsic effort is put in the task (Favrod et al., 2019). Under normal everyday conditions, vernier-like differences go unnoticed as only a weak neural response is elicited (da Cruz et al., 2019). Only when the vernier is task-relevant, the human brain enhances vernier-related information to avoid overwriting by subsequently presented stimuli. Attention, recurrent processing, and neuromodulation (e.g., the cholinergic nicotinic system) may play a role in target enhancement (Bakandite et al., 2013; Reynolds and Heeger, 2009; Lamme and Roelfsema, 2000; Picciotto, 2013). In SZ and BP, amplitudes are low in all target conditions. Thus, masking deficits might occur because SZ and BP cannot enhance the neural responses to the target vernier, making it more vulnerable to masking. Deficits in target enhancement happen not only in visible but also in other sensory modalities, as reflected in the mismatch negativity, auditory P3, and P50 suppression in both SZ and BP (Jahshan et al., 2012; Kaur et al., 2012; Sánchez-Morá et al., 2008). Siblings of SZ exhibited masking behavioral deficits but surprisingly higher GFP N1 peak amplitudes compared to controls, suggesting a compensation mechanism (da Cruz et al., 2020b). Siblings of SZ may engage more effort allowing them to recruit more neural resources to partially compensate for their behavioral deficits, if the task is not too challenging. Depressive patients showed no...
behavioral deficits but their N1 peaks amplitudes were reduced, though not at the level of SZ (Favrod et al., 2019). This suggests that depressive patients can stabilize the neural representation of the target, making it less prone to masking and that their low amplitudes might represent less intrinsic effort.

In DSM-IV and ICD-10 bipolar disorder and depression are thought to belong to the same family of affective disorders (Bell, 1994; World Health Organization, 2004). This has been changed in DSM-5 where bipolar disorder has an own chapter (American Psychiatric Association and others, 2013). Our results show that in terms of neurocognitive performance (VBM) and the underlying brain processes (EEG), bipolar disorder is more similar to schizophrenia than to depression.

Regarding the CPT, VFT, and WCST, controls performed better than patients in all tasks in agreement with previous studies (Sanchez-Morla et al., 2009; Zhu et al., 2019). We found a significant difference between BP and controls for 5 out of 7 output measures (Table 5). Following Bayesian analysis, we can conclude that SZ and BP performances were similar in the cognitive tasks.

Limitations. First, sample size of the BP group in the EEG experiment was small compared to the two other groups. Thus, the lack of a clear statistical difference of the N1 amplitude between BP and controls might be due to the small sample size of BP. Second, the three groups differed in terms of gender, education, and visual acuity. To control for these variables, which have inconsistently shown to play a role in VBM performance (Shaqiri et al., 2018), a supplementary statistical analysis including gender as a factor and visual acuity and education as covariates was conducted. The analysis showed that, overall, results were comparable to the ones obtained in the main analysis (results are shown and discussed in supplementary Tables S4, S5, and S6). Third, severity of the disorder and medications can introduce confounding factors (Butler et al., 1996; Fernandez et al., 2011; Slaghtuis and Curran, 1999). Generally, severity (BPRS) did not correlate with masking outcomes, in particular in BP (supplementary Table S7, left). Contrary to SZ (da Cruz et al., 2020b), in the bipolar group, there was no correlation of CPZ and performance (VBM) and the underlying brain processes (EEG), bipolar disorder was more similar to schizophrenia than depression.

In summary, we found that BP show similar masking and EEG abnormalities as SZ, suggesting that similar mechanisms are at work.

Declaration of Competing Interest

None.

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Supplementary materials


References


