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Impaired conscious access and abnormal attentional amplification in schizophrenia

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Abstract

Previous research suggested that the conscious perception of masked stimuli is impaired in schizophrenia, while unconscious bottom-up processing of the same stimuli, as assessed by subliminal priming, can be preserved. Here, we test this postulated dissociation between intact bottom-up and impaired top-down processing and evaluate its brain mechanisms using high-density recordings of event-related-potentials. Sixteen patients with schizophrenia and sixteen normal controls were exposed to peripheral digits at various degrees of masking, under conditions of either focused attention or distraction by another task. In the distraction condition, the brain activity evoked by masked digits was drastically reduced in both groups, but early bottom-up visual activation could still be detected and did not differ between patients and controls. By contrast, under focused top-down attention, a major impairment was observed: in patients, contrary to controls, the N1 component was insufficiently amplified by attention, and the late non-linear ignition associated with the P3 component was drastically reduced. Interestingly, the patients showed an essentially normal attentional amplification of the P1 and N2 components. These results suggest that some but not all top-down attentional amplification processes are impaired in schizophrenia, while bottom-up processing seems to be preserved.

Keywords

Attention – Psychosis – Visual awareness – Masking – Top-down – Bottom-up

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Introduction

Experimental studies of visual masking have reproducibly revealed an elevated threshold for the perception of masked visual stimuli in schizophrenia (Butler et al., 2003; Charles et al., 2017; Dehaene et al., 2003a; Del Cul et al., 2006; Green et al., 1999, 2011; Herzog et al., 2004; Herzog and Brand, 2015; Plomp et al., 2013). This finding was initially interpreted as indicating a low-level visual deficit (Butler et al., 2003; Cadenhead et al., 1998; Green et al., 2011). However, theoretical models of conscious processing suggest that the conscious perception of a masked stimulus involves not only a bottom-up propagation of sensory signals through the visual hierarchy, but also a top-down amplification by late and higher-level integrative processes (Dehaene et al., 2003b; Dehaene and Changeux, 2011). Whether sensory dysfunction in schizophrenia is associated with impairments of bottom-up processing or of top-down attention thus remains debated. The goal of the present work is to clarify this issue through recordings of event-related potentials (ERPs) under conditions of attention and inattention.

Previous ERP studies have revealed impairments of early event-related potentials in schizophrenia, and interpreted those findings as indicative of a dysfunction in bottom-up sensory processing. Indeed, schizophrenic patients exhibit classical deficits in prepulse inhibition of startle responses, a paradigm in which a weak sensory stimulus (the prepulse) inhibits the elicitation of the startle response caused by a sudden intense stimulus (Bolino et al., 1994; Braff et al., 1992). They also exhibit deficits in the auditory P50, which is normally decreased for the second paired stimuli compared to the first, but is insufficiently reduced in patients (Javitt and Freedman, 2015). Moreover, they are impaired in the detection of a deviant within a sequence of otherwise regular stimuli eliciting the cortical mismatch negativity potential (Shelley et al., 1991; Umbricht and Krljes, 2005). Finally, an impaired generation of the early visual P1 to low spatial frequency stimuli was repeatedly observed in schizophrenic patients and attributed to a specific magnocellular visual pathway dysfunction (Butler et al., 2005, 2007; Javitt, 2009a; Kim et al., 2006; Martínez et al., 2012). The increased sensitivity to visual masking in schizophrenia has been hypothesized to stem from this magnocellular dysfunction through low-level and bottom-up deficits (Butler et al., 2005, 2007; Javitt, 2009a; Kim et al., 2006; Martínez et al., 2012).

However, these findings do not allow to conclude in favour of a purely bottom-up impairment in schizophrenia, because the reduced activity of early ERP components might also stem from impaired top-down attentional processes (for a review, see: Berkovitch et al., 2017). Indeed, attention has a well-known modulatory effect on early brain activation including the mismatch negativity (Kasai et al., 1999; Oades et al., 1997; Sauer et al., 2017), the P1 (Feng et al., 2012; Hillyard and Anllo-Vento, 1998; Luck and Ford, 1998; Wyart et al., 2012), and probably the P50 in healthy controls (Guterman et al., 1992) and schizophrenic patients (Yee et al., 2010). Furthermore, previous research has repeatedly reported evidence in line with top-down impairments in schizophrenic patients (Dima et al., 2010; Fuller et al., 2006; Gold et al., 2007; Luck et al., 2006; Plomp et al., 2013). An additional argument suggesting that bottom-up processing may not be the origins of the patients' masking impairments comes from the observation that subliminal processing can be fully preserved in schizophrenia patients, as reported in a variety of paradigms with masked words (Dehaene et al., 2003a) or digits (Del Cul et al., 2006), subliminal error detection (Charles et al., 2017) and

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response inhibition (Huddy et al., 2009). This argument rests upon the idea that subliminal priming reflects a feed-forward propagation of sensory activation (Fahrenfort et al., 2008; Lamme and Roelfsema, 2000).

In summary, evidence for early visual-processing deficits in schizophrenia is inconclusive and could be due either to an impairment of bottom-up processing, or to a lack of appropriate top-down attentional modulation. Importantly, resolving this issue may also provide a test of theories of dysfunctional N-methyl-D-aspartate (NMDA) transmission in schizophrenia (Berkovitch et al., 2017; Coyle, 2006; Jentsch and Roth, 1999; Olney and Farber, 1995; Stephan et al., 2009). Early computer simulations of masking and access of consciousness postulated that bottom-up propagation of information is primarily supported by fast glutamatergic amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid (AMPA) receptors, whereas top-down amplification is primarily supported by slower glutamatergic NMDA receptors (Dehaene et al., 2003b; Dehaene and Changeux, 2005). Such a selective role for NMDA receptors in top-down processing was confirmed by electrophysiological studies using NMDA receptor antagonists (Herrero et al., 2013; Moran et al., 2015; Self et al., 2012; van Loon et al., 2016) Consequently, the hypothesis of an NMDA receptor dysfunction in schizophrenia (Coyle, 2006; Jentsch and Roth, 1999; Olney and Farber, 1995; Stephan et al., 2009) would predict the presence of impairments in conscious access and conscious processing, due to inefficient top-down amplification, but a preservation of unconscious bottom-up information processing.

Here we tested the hypothesis that bottom-up information processing is intact while top-down attentional amplification is deficient in schizophrenia by recording high-density electroencephalography (EEG) in a visual masking paradigm. We systematically and orthogonally manipulated a bottom-up factor (the delay between the mask and the target) and a top-down factor (whether the stimuli were attended or unattended). Our goal was two-fold. First, we probed the brain mechanisms by which attention amplifies the processing of masked stimuli in healthy controls, therefore lowering down their threshold for access to conscious report. Second, we evaluated which of these mechanisms are impaired in schizophrenic patients. The hypothesis of intact bottom-up processing predicts that, once attention is withdrawn, the evoked related potentials' (ERP) components should be equally reduced in both patients and controls, without any difference between these two groups. On the other hand, the difference between attended and unattended conditions, which provides a measure of attentional amplification, should reveal a deficiency of top-down amplification in schizophrenia, eventually resulting in a reduction or suppression of the global cortical ignition typically associated with conscious perception in normal subjects (Del Cul et al., 2007; Sergent et al., 2005).

The present research capitalizes upon a previous study in which we demonstrated that event-related potentials could be used to monitor the successive stages of processing of a masked stimulus (Del Cul et al., 2007). In this seminal work, a digit target was presented for a brief fixed duration (14 ms), and was followed – after a variable stimulus-onset-asynchrony (SOA) – by a mask consisting of surrounding letters. In this experimental design, a fixed amount of sensory evidence was therefore initially injected, and a variable amount of time was available to accumulate this evidence before the processing of the mask disrupted it. ERPs were used to monitor the successive stages of visual information processing associated with

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unconscious processing and conscious vision. Following the subtraction of mask-evoked brain activity, a series of distinct stages were observed. First, the P1 and the N1 components were shown to very little vary with SOA, reflecting the unconscious processing of the incoming digits. Second, an intermediate negative waveform component (N2) linearly increased with SOA but stopped at a fixed latency with respect to the mask, suggesting evidence accumulation (Ratcliff, 1978) in occipito-temporal cortical areas and interruption by the mask. Finally, the late P3 component showed a sigmoidal variation with SOA, tightly parallel to subjective reports of target visibility, thus suggesting that the P3 indexes an all-or-none stage of conscious access to perceptual information.

In this study, we aimed at replicating those findings as well as probing which of these stages persist when the very same stimulus (a masked digit) is presented under conditions of severe inattention. To our knowledge, this study is the first to explore the interaction between the amount of masking (as modulated by target-mask SOA) and the availability of attentional resources, and to manipulate those variables while comparing schizophrenic patients and controls. Our design involved four SOAs and two conditions of attention (see Figure 1). In the focused attention condition, subjects were asked to focus their attention to the peripheral masked digits and to report their visibility. In the inattention condition, we maximized the withdrawal of attention from our masked stimuli through the use of a highly demanding concurrent task: the same masked digits were presented in the periphery of the visual field while subjects were asked to focus on small colour changes presented at fixation and to report which colour was predominant. Because the digits were entirely task-irrelevant, presented at a parafoveal location, and asynchronous with the colour changes, spatial, temporal and executive attention were all withdrawn.

Based on our hypothesis of preserved feedforward and impaired top-down processing in schizophrenia, we predicted that, under inattention, the early sensory components indexed by P1, N1 and even N2 would remain present (though reduced by inattention) and identical in patients and controls. We also expected that attention would amplify these sensory components in order to facilitate the accumulation of sensory evidence from the masked stimulus, and that this amplification would be drastically impaired in schizophrenia patients.

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Materials and methods

Participants

Sixteen patients with schizophrenia (mean age 37 years, range 25-51; 5 women) participated to the study. All were native French speakers. Patients met DSM-IV criteria for schizophrenia or schizo-affective disorders and were recruited from the psychiatric department of Creteil University Hospital (Assistance Publique, Hôpitaux de Paris). They had a chronic course and were stable at the time of the experiment. A French translation of the Signs and Symptoms of Psychotic Illness Scale (Liddle et al., 2002) was used to evaluate their symptomatology, and chlorpromazine equivalents were calculated to assess whether there was significant correlations between symptoms, treatment and behavioural results.

The comparison group consisted of sixteen control subjects (mean age 35.5 years, range 21-51, 4 women). Comparison subjects were excluded for history of any psychotic disorder, bipolar disorder, recurrent depression, schizotypal or paranoid personality disorder. Patients and controls with a history of brain injury, epilepsy, alcohol or substance abuse, or any other neurological or ophthalmologic disorders were also excluded. Patients and controls did not differ significantly in sex, age and level of education (see Table 1). All experiments were approved by the French regional ethical committee for biomedical research (Hôpital de la Pitié Salpêtrière), and subjects gave written informed consent.

Table 1 – Characteristics of participants

Characteristics	***Schizophrenic*** *mean (± s.d.)*	***Control*** *mean (± s.d.)*	**Statistical test** (test value, *p-value)*
Sample size	16	16	–
Age (y.o.)	37.44 (±7.4)	35.5 (±10.5)	$t_{26.999} = 0.60$, $p = 0.55$
Gender (M/F)	11/5	12/4	$\chi_1 = 0.16$, $p = 0.69$
Years of education (from first year of high school)	7.9 (±2)	8.9(±3.3)	$t_{24.90} = -1.04$, $p = 0.31$
SSPI* scale total score	12.2 (±6.8)	–	–
Antipsychotic equivalence dose (CPZ-Eq., in mg)	650.2 (±376.3)	–	–

* Sign and Symptom of Psychotic Illness.

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Design and procedure

The experimental paradigm is summarized in Figure 1. We used a variant of the masking paradigm designed in our previous studies in normal and clinical populations (Charles et al., 2017; Del Cul et al., 2007, 2006). A target digit (1, 4, 6 or 9) was presented for a fixed duration of ~14 ms at a random position among four (1.4 degrees above or below and 1.4 degrees right or left of the fixation cross). After a variable delay (stimulus onset asynchrony or SOA) a mask appeared at the target location for 250 ms. The mask was composed of four letters (two horizontally aligned M and two vertically aligned E) surrounding the target stimulus location without superimposing or touching it. Four levels of masking (SOAs 27, 54, 80 and 160 ms) and a mask-only condition were randomly intermixed across trials. In the mask-only condition, the target number was replaced by a blank screen with the same duration (i.e. 14 ms). The fixation cross was surrounded by 5, 6 or 7 successive coloured circles which could be blue or yellow. The presentation duration of these circles was 100 ms each, and the inter-stimulus interval between them was 413 ms (SOA = 513 ms).

The same exact sequence of stimuli was presented under two distinct conditions, which differed only in the requested task. Under the attention condition, subjects were asked to pay attention to the masked digits and give two behavioural responses: (1) decide whether the digit was larger or smaller than 5 (which provided an objective measure of target perception) and (2) report the digit visibility using a categorical response “seen” or “not seen” (which provided a subjective measure of conscious access). Under the inattention condition, participants had to estimate the predominant colour of the rapid sequence of coloured circles surrounding the fixation cross. Note that the peripheral stimuli always appeared between the 2nd and the 3rd coloured circles, while participants were still forced to pay attention to the central task because not enough evidence was yet delivered in order to accurately decide which of the 2 colours was the most frequent (given that the number of circles varied between five and seven). On each trial, feedback informed the subjects whether their answer was correct or not, in order to reinforce their motivation and help them to maintain attention. At the end of the unattended blocks, participants were asked whether they noticed anything in their peripheral visual field.

Instructions for both attended and unattended tasks were given at the beginning of the experiment. Then, subjects completed four blocks of trials: two “attended” blocks (A) and two “unattended” blocks (U), in A-U-U-A order for half of the subjects and in U-A-A-U order for the other half. There were 640 trials in total (320 unattended and 320 attended), i.e. 64 trials in each combination of attention (2 levels) and masking (5 levels, i.e. SOA = 27, 54, 80, or 160 ms, plus the mask-only condition).

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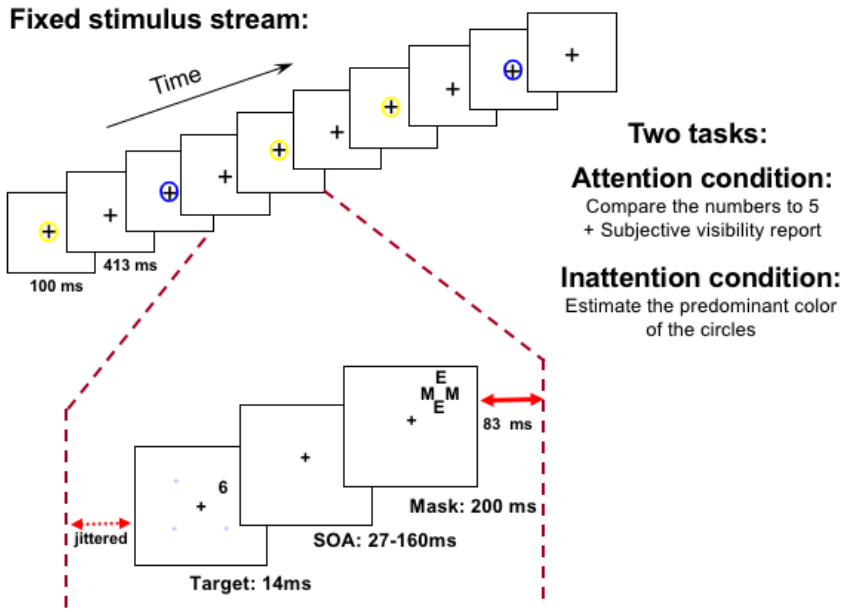

Figure 1 – Experimental design

On each trial, subjects viewed a stream of small circles presented at fixation, with a brief presentation of a masked digit at one of four possible locations in the periphery of the visual field. The same exact stimuli were presented under two experimental conditions. In the attention condition, subjects were asked to compare the target digit to a fixed reference of 5 (forced-choice objective task), then report whether they could see it or not (subjective visibility task). The delay between the target and the mask (SOA) varied between 27 and 160 ms in order to systematically modulate the amount of masking. In the inattention condition, subjects had to estimate the predominant colour of small circles surrounding the fixation cross, thus withdrawing attention from the irrelevant peripheral digit.

Behavioural data analysis

For each subject and each SOA, several behavioural parameters were measured. In the attended condition, we measured the performance in comparing the target against 5 (objective measure of conscious access) and the rate of seen trials (subjective measure of conscious access). In the unattended condition, we measured the performance in estimating which colour was more frequent. Analyses of variance (ANOVAs) were conducted on each of those behavioural measures, with SOA as a within-subject factor and group (patients/controls) as a between-subject factor. Within the patients group, Pearson correlation coefficients were computed between behavioural measures and variables such as the clinical scale (SSPI scale) and antipsychotic treatment posology (chlorpromazine equivalent).

ERP methods

ERPs were sampled at 250 Hz with a 128-electrode geodesic sensor net referenced to the vertex. We rejected voltage exceeding $\pm 200\ \mu V$, transients exceeding $\pm 100\ \mu V$, or electro-

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oculogram activity exceeding ± 70 μV. The remaining trials were averaged in synchrony with mask onset, digitally transformed to an average reference, band-pass filtered (0.5-20 Hz) and corrected for baseline over a 250 ms window during fixation at the beginning of the trial. Contralateral activity is represented conventionally on the left hemisphere and ipsilateral activity on the right one.

The activity observed on mask-only trials was subtracted from that on trials in which the target was effectively presented, thus isolating the target-evoked activity. The same procedure used in our previous study (Del Cul et al., 2007) was applied in order to differentiate ipsilateral and contralateral ERP components.

Linear regression models were fitted at the subject-level on the trial-averaged EEG signals, separately at each electrode and each time-point using the values of SOA as a parametric modulator (combined with an offset variable) of the EEG response. Grand averaged regression coefficients (beta) corresponding to SOA were estimated. R^2 values (i.e. proportion of explained variance) are also reported as an unbiased and normalized measure of the quality of fit.

ERP components were identified based on latencies, topographical responses (contralateral P1 and N1, bilateral N2 and P3) and previous work (Del Cul et al., 2007). For each subject, under each SOA and attention condition and for each digit-evoked ERP component, the EEG signals were averaged over corresponding clusters of electrodes and time windows (P1: 65-110 ms over parieto-temporal electrodes; N1: 125-200 ms over parieto-temporal electrodes; N2: 200-300 ms over fronto-central electrodes; P3: 300-500 ms over fronto-central electrodes; see Del Cul et al., 2007).

For each of these ERP components, we conducted analyses of variance (ANOVAs) on the corresponding averaged amplitude (over electrodes and time points) with SOA, attention condition (attended or not) and group (patients/controls) as categorical factors. We also compared the amplitude of each component against zero using a *t*-test in order to identify which of these components significantly persisted in the unattended condition.

Source localization

Cortical current density mapping was obtained using a distributed model consisting of 10.000 current dipoles. Dipole locations and orientations were constrained to the cortical mantle of a generic brain model built from the standard brain of the Montreal Neurological Institute, and warped to the standard geometry of the EEG sensor net. The warping procedure and all subsequent source analysis and surface visualization were performed using BrainStorm software (http://neuroimage.usc.edu/brainstorm) (Tadel et al., 2011). EEG forward modelling was computed with an extension of the overlapping-spheres analytical model (Huang et al., 1999). Cortical current maps were computed from the EEG time series using a linear inverse estimator (weighted minimum-norm current estimate or wMNE; see Baillet et al., 2001, for a review). We localized the sources separately for each subject and computed a group average

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that was then smoothed at 3 mm FWHM (corresponding to 2.104 edges on average), and thresholded at 40% of the maximum amplitude (cortex smoothed at 30%).

Statistical comparisons

For most of the statistical comparisons, frequentist statistics were adopted (values of the statistic, e.g. *t*s or *F*s, as well as *p*-values are reported). However, because many of the hypotheses at stake lie on an absence of difference (e.g. preserved feedforward processing in schizophrenic patients), we also conducted Bayesian statistics whenever required. Contrary to frequentist statistics, Bayesian statistics symmetrically quantify the evidence in favour of the null (H_0) and the alternative (H_1) hypotheses (Wagenmakers et al., 2010). To do so, the *BayesFactor* package (http://bayesfactorpcl.r-forge.r-project.org) implemented in R (https://www.r-project.org) was used. For each Bayesian statistical test, the corresponding Bayes factor ($BF_{10} = p(data|H_1)/p(data|H_0)$) is reported. Even though threshold values of Bayes factors have been proposed (e.g. a BF larger than 3 is usually taken has providing substantial evidence), a BF value of *x* can directly be interpreted as the observed data being approximately *x* times more probable under the alternative compared to the null hypothesis. When BFs favored the null hypotheses (i.e. $BF_{10} < 1$), we directly reported the inverse Bayes factor (i.e. $BF_{01} = 1/BF_{10}$) quantifying the evidence in favor of the null compared to the alternative hypothesis.

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Results

Behaviour

Behavioural results appear in Figure 2. Under the attended condition, a main effect of SOA was observed on both objective performance ($F_{1,30}$ = 184.02, p < 0.001) and subjective visibility ($F_{1,30}$ = 287.17, p < 0.001). Objective performance was significantly lower for patients compared to controls (73.7% vs. 80.7% group effect $F_{1,30}$ = 7.437, p = 0.011), but a significant group × SOA interaction ($F_{3,90}$ = 3.137, p = 0.029) reflected the fact that this difference was significant only at the longest SOAs 80 and 160 ms ($F_{1,30}$ = 11.21, p = 0.0022), not at the shortest SOAs 27 and 54 ms ($F_{1,30}$ = 2.781, p = 0.11, 1/BF = 1.8), although performance was higher than chance in both groups (controls: 66.2%, t_{31} = 6.192, p < 0.001, patients: 61.7%, t_{31} = 5.624, p < 0.001). Subjective visibility was also affected by a group × SOA interaction ($F_{3,90}$ = 5.825, p = 0.001), indicating that patients were significantly impaired only at SOAs 80 ms and 160 ms (81.1% vs. 91.3%; $F_{1,30}$ = 4.525, p =0.0417), but not at the shortest SOAs 27 and 54 ms ($F_{1,30}$ = 1.638, p = 0.21, 1/BF = 2.3).

Importantly, the patients' objective performance was neither significantly correlated with the treatment (Pearson r = 0.095, t_{14} = 0.358, p = 0.725, 1/BF = 5.0), nor with the clinical score (Pearson r = -0.275, t_{14} = -1.068, p = 0.304, 1/BF = 3.1). Subjective performance showed a weak trend towards a negative correlation with treatment (across all SOAs: Pearson r = -0.504, t_{14} = -2.184, p = 0.046, BF = 1.4, for SOAs = 80 or 160 ms: Pearson r = -0.470, t_{14} = -1.993, p = 0.066, BF = 1.0), but this correlation was strongly driven by one participant's results (chlorpromazine equivalent: 1550 mg per day, subjective visibility across all SOAs: 16.0%, correlation while excluding this participant: Pearson r = -0.1607, t_{13} = -0.587, p = 0.567, 1/BF = 4.4). Finally, the clinical score was not correlated with subjective visibility (all SOAs: Pearson r = 0.001, t_{14} = -0.004, p = 0.997, 1/BF = 5.3; for SOAs = 80 or 160 ms: Pearson r = -0.144, t_{14} = -0.543, p = 0.596, 1/BF = 4.6). Moreover, objective and subjective visibility were strongly correlated within subjects in both groups, and the strength of this correlation did not significantly differ between the two groups (mean of Pearson r for controls: 0.967 vs. 0.963 for patients, $t_{29.85}$ = 0.303, p = 0.764, 1/BF = 2.9).

Under the unattended condition, performance in the central colour task was lower for patients compared to controls (81.9 % vs 90.9 %, $F_{1,30}$ = 11.48, p = 0.002). There was no main effect of SOA ($F_{4,120}$ = 0.388, p > 0.5) nor a group × SOA interaction ($F_{4,120}$ = 1.162, p = 0.331). Within the patients group, performance was neither significantly correlated with treatment (Pearson r = 0.432, t_{14} = 1.791, p = 0.095, 1/BF = 1.3) nor with clinical score (Pearson r = -0.454, t_{14} = -1.906, p = 0.077, BF = 1.1) but Bayes factors were inconclusive.

After the experiment, all subjects reported that they noticed the masked stimuli in the unattended condition but that these stimuli could not be precisely identified and did not prevent them from estimating the dominant colour of the central circles.

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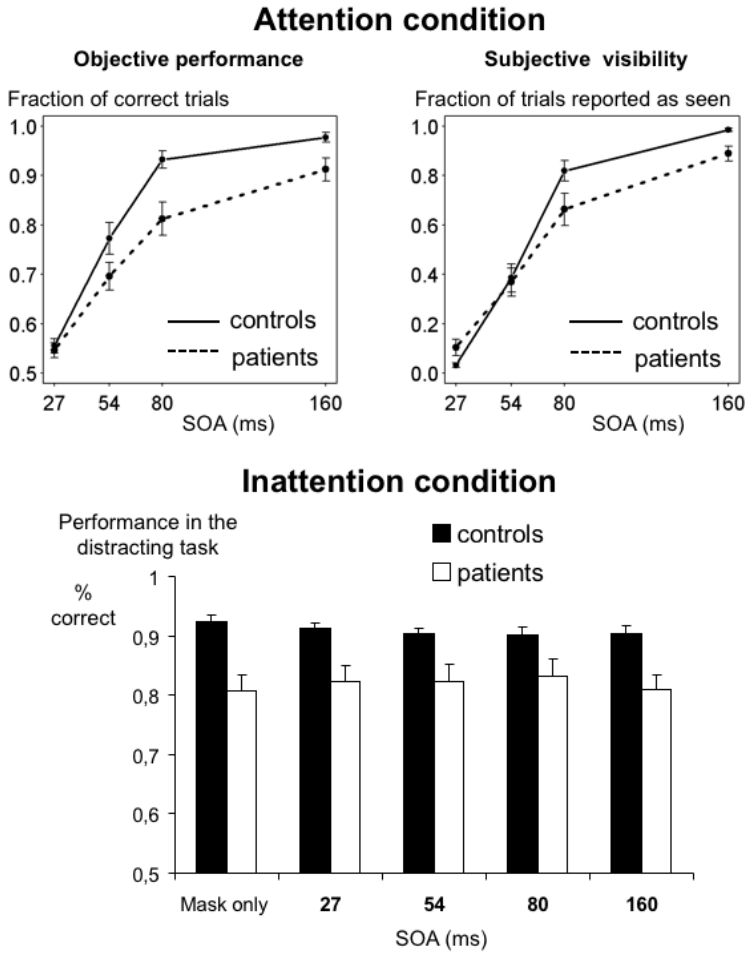

Figure 2 – Behavioural results

Top, processing of the masked digits in the attention condition as a function of SOA. Controls (solid lines) performed better and reported better visibility than patients (dashed lines) in the number comparison task (objective performance). Bottom, performance in the distracting colour task in the inattention condition. Patients performed consistently worse than controls, but there was no effect of SOA.

EEG activity evoked by the target

Target-evoked brain activity is displayed in Figure 3A in the case of the longest SOA (i.e. 160 ms) in the attended condition for both groups. Scalp topographies and corresponding sources reconstruction are shown at specific time points (0, 88, 160, 252, 324, 392 and 600 ms post-target). At least five different components specific to conscious EEG visual responses could be identified: contralateral P1 (peaking at 88 ms) and N1 (160 ms) followed by bilateral N2 (252 ms), P3a (324 ms) and P3b (392 ms). First, at 88 ms and 160 ms (corresponding to P1 and N1 components), brain activity elicited by the target was restricted to contralateral occipito-temporal regions (conventionally presented in the left hemisphere) in both groups, reflecting the activation of early visual areas. The activity was slightly more diffuse in the

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patients group at 160 ms. At 252 ms (with a topography corresponding to the N2/P3a component), the activity spread to the ipsilateral hemisphere and moved forward in the postero-lateral part of the inferior temporal gyrus, including the visual number form area (Shum et al., 2013), and anterior prefrontal activity was detected. Then, at 324 ms, as a posterior P3b began to emerge in the scalp topography, the source activity spread bilaterally into the ventral stream, though more pronounced in the contralateral hemisphere, as well as in the inferior prefrontal and parietal cortices. Finally, at 392 ms (corresponding to the full-blown P3b component), activity became intense and fully bilateral in both groups, reaching ventral and dorsolateral prefrontal as well as parietal regions, especially in the controls group. At 600 ms, in both groups, activity strongly decreased in the occipital lobes while remaining sustained in anterior frontal and temporal regions. The parametric modulation of SOA on the topographical responses recorded in the attended condition are summarized using linear regression (see Methods). Resulting coefficients (beta) and R^2 values (i.e. proportion of explained variance) are reported in Figure 3B.

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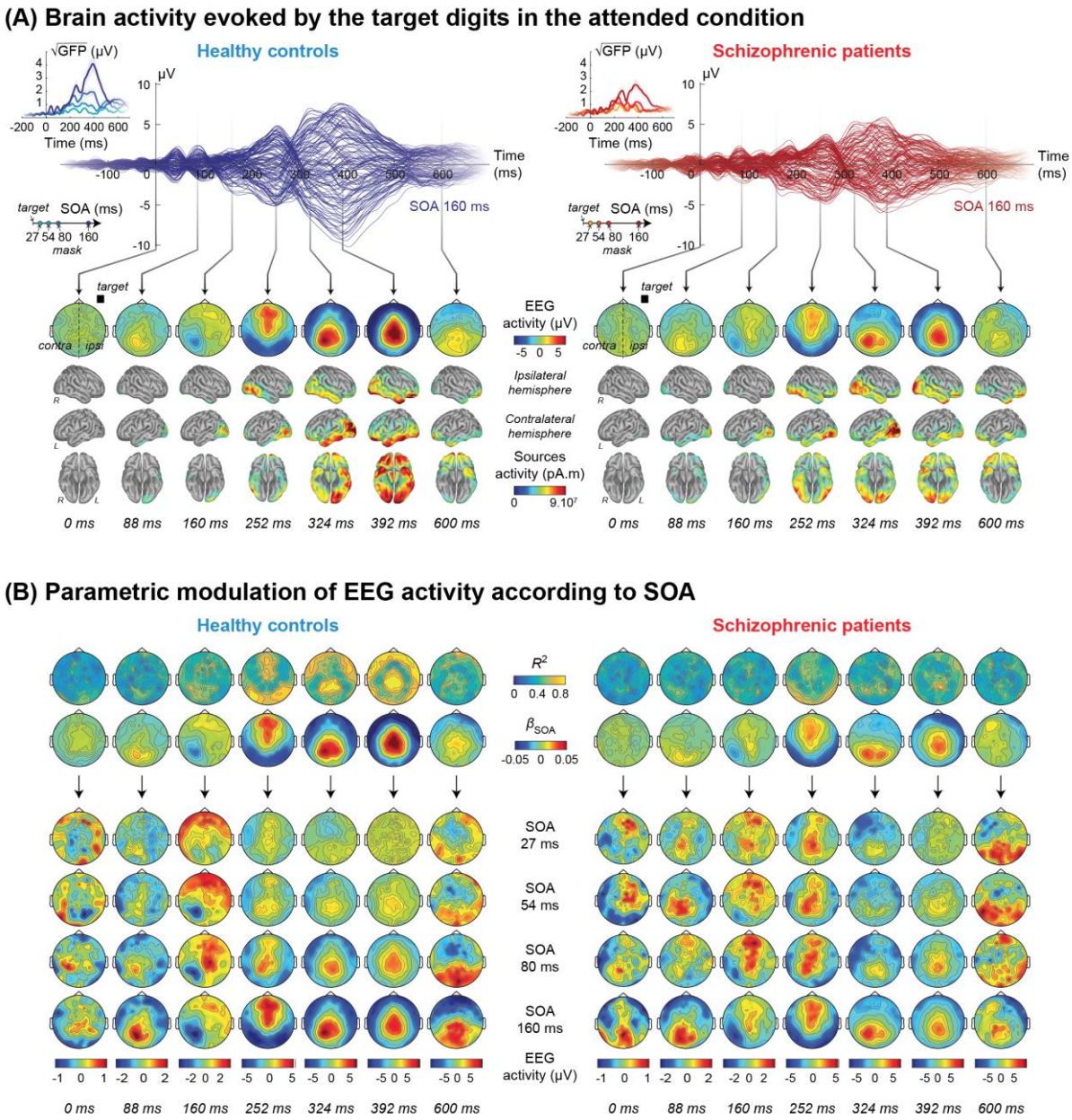

Figure 3 – EEG activity evoked by target digits in the attention condition

(A) Time course of brain activity at the longest SOA (i.e. 160 ms) for controls (blue curves on the left) and patients (red curves on the right). Specific moments were selected and the corresponding topographies and source reconstructions are presented below, providing an overview of brain activity evoked by the target as a function of time. Global field potentials are shown in inset as a function of time and SOA. (B) Topographies of R^2 and β from a linear regression of EEG signals on SOA, performed on each electrode and time point. Below, classical EEG voltage topographies are shown for each time point (horizontally) and for each SOA (vertically).

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ANOVAs were conducted on each target-evoked EEG component with factors of SOA, attention (attended or unattended) and group (patients/controls) and their interactions. The results are summarized in table 2.

We first report the effects obtained when averaging across SOAs. In the controls group, under the attended condition, the amplitude of all ERP components was significantly different from zero (P1: $t_{15} = 3.71$, $p = 0.002$; N1: $t_{15} = -5.07$, $p < 0.001$; N2: $t_{15} = -4.88$, $p < 0.001$; P3: $t_{15} = 7.50$, $p < 0.001$), while under unattended conditions, only the amplitude of the N1 and N2 components was significantly different from zero (N1: $t_{15} = -3.09$, $p = 0.008$, N2:$t_{15} = -3.72$, $p = 0.002$). Similar results were observed in the patients group under attended condition (P1: $t_{15} = 2.63$, $p = 0.019$; N1: $t_{15} = -3.01$, $p = 0.009$; N2: $t_{15} = -2.56$, $p = 0.022$; P3: $t_{15} = 5.79$, $p < 0.001$) but only the N2 amplitude was significantly different from zero under unattended condition ($t_{15} = -2.41$, $p = 0.029$). In both groups, the P3 component totally vanished under unattended conditions (controls: $t_{15} = -0.484$, $p = 0.636$, patients: $t_{15} = -0.835$, $p = 0.417$). The results therefore indicate that unattended stimuli can trigger ERPs up to ~270 ms after they were presented, but fail to induce a detectable P3 component.

Crucially, amplitude differences between schizophrenic patients and healthy controls were only observed under the attended condition (Figure 4). Attended ERP amplitude was lower in patients compared to controls for the N1 (group effect: $F_{1,105} = 8.76$, $p = 0.004$) and the P3 (group effect: $F_{1,105} = 5.64$, $p = 0.019$) but not for P1 and N2 ($p > 0.5$, P1: 1/BF = 4.5, N2: 1/BF = 4.8). Under the unattended condition, no significant differences were observed between the two groups ($p > 0.1$; also confirmed by Bayesian statistics: 1/BFs for P1: 5.3, N1: 3.1, N2: 3.8, P3: 4.3)

We now turn to the effects of SOA, starting with the attended condition. The modulation of ERP amplitude by SOA under attended condition is shown in Figure 3B. Target-evoked EEG activity was parametrically modulated by SOA, with the longest SOA inducing the strongest EEG signals. This modulation was particularly pronounced at the time of the N2 and P3a/b components (R^2 larger than 0.4). Those results replicate previous findings in normal subjects (Del Cul et al., 2007). In detail, the P1 was not significantly affected by masking (SOA effect: $F_{3,45} = 2.26$, $p = 0.0941$, 1/BF = 1.6) and the SOA effect on the N1 was primarily driven by a reduced amplitude at the shortest SOA (across all SOAs, $F_{3,45} = 12.74$, $p < 0.001$; but the effect ceased to be significant when excluding SOA = 27 ms: $F_{2,30} = 2.41$, $p = 0.107$, 1/BF = 4.3). On the contrary, N2 and P3 amplitudes significantly increased with SOA (N2: $F_{3,45} = 29.49$, P3: $F_{3,45} = 69.58$, $p < 0.001$). In the patients group, N2 and P3 significantly increased with SOA (N2: $F_{3,45} = 13.42$, P3: $F_{3,45} = 16.82$, $p < 0.001$). A significant effect of SOA on P1 amplitude was driven by the longest SOA (across all SOAs $F_{3,45} = 2.86$, $p = 0.047$) but vanished when excluding SOA = 160 ms ($F_{2,30} = 1.47$, $p = 0.247$, 1/BF = 3.1). No significant group x SOA interaction was observed for P1 and N2 ($p > 0.5$, P1: 1/BF = 6.8, N2: 1/BF = 8.8). Contrary to the control group, the patients' N1 was found to significantly increase with SOA ($F_{3,45} = 6.60$, $p < 0.001$), and this effect was also observed while excluding the shortest SOA, i.e. 27 ms ($F_{2,30} = 3.49$, $p = 0.043$), but this group difference was again non-significant, as no group x SOA interaction was observed (across all SOAs: $F_{3,105} = 0.550$, $p = 0.650$, 1/BF = 7.8; while excluding SOA = 27 ms: $F_{2,75} = 0.221$, $p = 0.803$, 1/BF = 5.7). A significant interaction was only observed at the level of the P3, reflecting a much reduced effect of SOA on P3 amplitude in patients compared to controls ($F_{1,105} = 6.33$, $p < 0.001$), and a triple interaction of group, SOA and attention ($F_{3,225} =$

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2.98, p = 0.032) indicated that this impairment was unique to the attended condition (see Table 2 for statistics). Interestingly, in the patients group, the SOA effect on the P3 was mainly driven by the longest SOA ($F_{2,30}$ = 0.92, p = 0.41 when excluding SOA = 160 ms) and was significantly lower than in the control group (group effect × SOA: $F_{1,105}$ = 6.33, p < 0.001). Such a reduced modulation of P3 by SOA in patients may underpin their lower objective and subjective behavioural performances compared to controls in the attended task (see Discussion).

In the unattended condition, in both groups, SOA had a significant effect only on N1 and N2 (controls: N1: $F_{3,45}$ = 4.43, p = 0.008, N2: $F_{3,45}$ = 4.05, p = 0.013; patients: N1: $F_{3,45}$ = 3.06, p = 0.038, N2: $F_{3,45}$ = 5.61, p = 0.002) suggesting that sensory information could still be processed as a function of SOA even when unattended (see Discussion). These SOA effects did not differ between patients and controls under unattended conditions (p > 0.3 for all interactions group x SOA under unattended condition; also confirmed by Bayesian statistics: 1/BFs for P1: 11.1, N1: 5.6, N2: 8.9, P3: 7.7).

We end by reporting the interactions involving the attentional manipulation. In the controls group, a significant attention effect was observed on N1 amplitude ($F_{1,15}$ = 17.70, p < 0.001) and P3 amplitude ($F_{1,15}$ = 34.43, p < 0.001) across all SOAs. There was no significant effect of attention on P1 and N2 across all SOAs ($F_{1,15}$ = 2.00, p = 0.181, BF = 1.0 and $F_{1,15}$ = 3.71, p = 0.0732, BF = 1.0 respectively), but an effect emerged on the N2 when restricting the analysis to the longest SOAs 80 and 160 ms ($F_{1,15}$ = 11.02, p = 0.005). In the patients group, no significant attentional effect was found on P1, N1 and N2 (all p > 0.1, 1/BF = 1.5, 1.5 and 1.8 respectively), but the effect was highly significant for the P3 ($F_{1,15}$ = 35.54, p < 0.001). No significant interaction between group and attention was observed using a frequentist ANOVA (all p > 0.1). The Bayesian ANOVA confirmed the absence of interaction group x attention for P1 (1/BF = 5.0), N2 (1/BF = 5.3) and P3 (1/BF = 3.3), but indicated an inconclusive interaction for N1 (1/BF = 2.6). There was a significant interaction SOA × attention for N2 and P3 components in the control group ($F_{3,105}$ = 6.32, p < 0.001 and $F_{3,105}$ = 28.23, p < 0.001 respectively) but only for P3 component in the patient group ($F_{3,105}$ = 8.47, p < 0.001, for N2: $F_{3,105}$ = 1.30, p = 0.278, 1/BF = 5.3), suggesting that attention modulates the rate of accumulation of sensory information per unit of time (see Discussion). The triple interaction between group, SOA and attention did not reach significance for the early components (all p > 0.1, 1/BFs for P1: 9.8, N1: 5.196, N2: 6.6), but did for the P3 ($F_{3,225}$ = 2.98, p = 0.032). Thus, at that stage, the attentional modulation effect was significantly lower in the patients compared to the controls.

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Table 2 – *p*-values from ANOVAs on ERP components (N.S. is non-significant)

ERP component	***P1***	***N1***	***N2***	***P3***
Group	N.S.	**0.0018**	N.S.	**0.029**
SOA	N.S.	**< 0.001**	**< 0.001**	**< 0.001**
Attention	**< 0.001**	**< 0.001**	**< 0.001**	**< 0.001**
Group x SOA	N.S.	N.S.	N.S.	**0.004**
SOA x attention	N.S.	N.S.	0.003	**< 0.001**
Group x attention	N.S.	N.S.	N.S.	N.S.
Group x SOA x attention	N.S.	N.S.	N.S.	**0.032**
Group effect (attended)	N.S.	**0.004**	N.S.	**0.019**
Group effect (unattended)	N.S.	N.S.	N.S.	N.S.
SOA effect (attended)	**0.019**	**< 0.001**	**< 0.001**	**< 0.001**
SOA effect (unattended)	N.S.	**0.008**	**< 0.001**	N.S.
Group x SOA (attended)	N.S.	N.S.	N.S.	**< 0.001**
Group x SOA (unattended)	N.S.	N.S.	N.S.	N.S.

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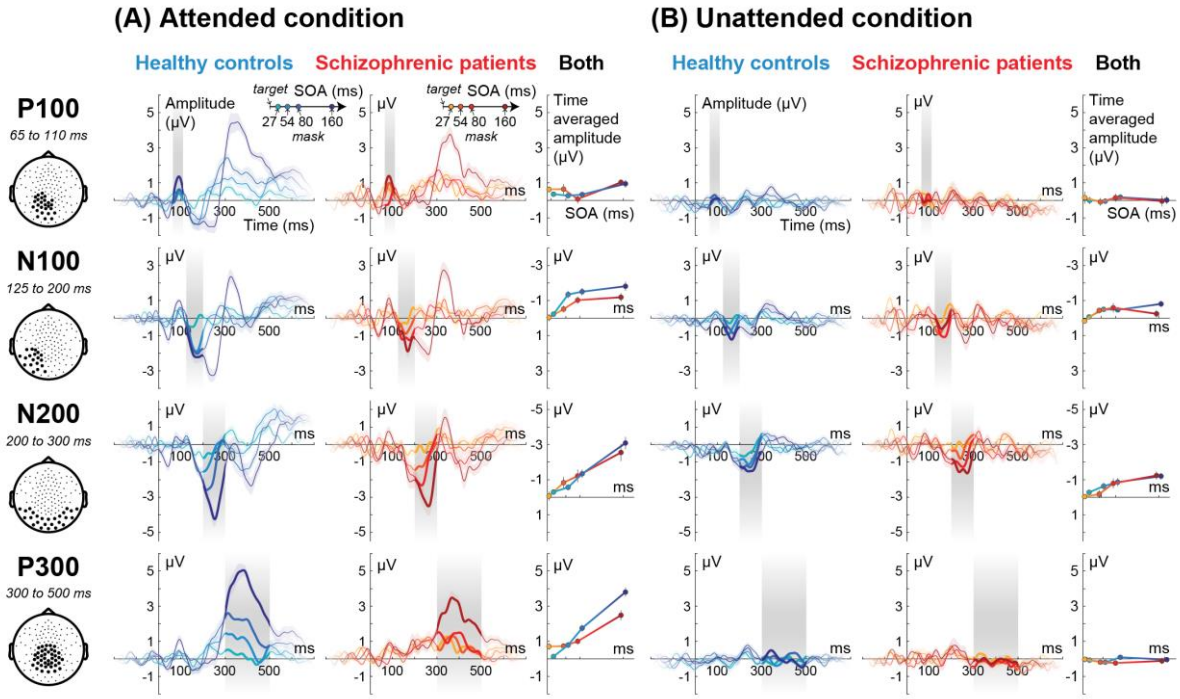

Figure 4 – Modulation of ERP components as a function of SOA

Each diagram shows the time course of ERPs as a function of SOA in the controls and the patients groups under attended and unattended conditions. For each component, the preselected cluster of electrodes is depicted by black dots in the topographies at left. Preselected time-windows of interest, used for statistical analysis, are shown by grey rectangles. The averaged amplitude of each component in this window is also plotted (column marked “both”).

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Discussion

Summary of the results

We measured the effect of top-down attention on visual stimuli whose degree of masking varied systematically by changing the target-mask SOA. Our main results can be summarized as follows.

In the healthy controls group, when subjects attended to the masked digits, we replicated our previous observations (Del Cul et al., 2007) of a monotonic increase in ERP amplitude (N1, N2, P3) as the target-mask interval increased. Inattention reduced the amplitude of all ERP components, decreased the slope with which the N1 and N2 varied as a function of SOA, and led to a complete disappearance of the P3 component. Thus, attention had a modulatory influence on early perceptual processing and an all-or-none effect on the late P3 component. As far as patients are concerned, no difference was observed between the schizophrenic patients and the healthy controls groups under inattention conditions. However, the patients' subjective and objective consciousness thresholds were abnormally elevated, and the patients' N1 and P3 components were strongly reduced relative to controls, in the attended condition only. This finding points to a disruption, in schizophrenia, of the attentional mechanisms that modulate the sensory gain in controls subjects.

Persistence of bottom-up processing under inattention condition

One of the main goals of our experiment was to examine which of the activations evoked by a masked stimulus resist under a condition of severe inattention. Our inattention task, which involved continuous attention to the colour of the fixation point, was specifically designed to induce a complete withdrawal of spatial, temporal and executive attention resources to the peripheral masked stimulus. For several minutes, this peripheral stimulus was completely task-irrelevant and ignored. As a consequence, we could not record any behavioural or introspective measurements as to how this stimulus was processed. An indirect indication of strong inattention, however, was that target presence and target-mask SOA had no effect on the performance of the colour estimation task, although this performance was far from ceiling.

We predicted that, in spite of this strong inattention, peripheral stimuli should still elicit early visual ERP components, up to about 300 ms, but should no longer yield a P3 waveform. This pattern is exactly what was observed, thus further strengthening the hypothesis that attention was maximally distracted. Under the unattended condition, the P1 component was strongly attenuated and did not achieve significance. The N1 and N2 components, although also attenuated, were highly significant, and corresponded to a clear activation of occipito-temporal cortices after source reconstruction. Furthermore, the N1 and N2 components still increased with SOA, suggesting that the accumulation of evidence about the target continued to occur without attention. The situation was however very different for the P3, which collapsed to an undetectable and non-significant level. These results are compatible with our previous postulate that the P1, N1 and N2 events prior to 300 ms

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correspond to a series of largely automatic "pre-conscious" perceptual stages (Dehaene et al., 2006), while the P3 reflects an all-or-none stage of conscious access to the available perceptual information (Dehaene and Changeux, 2011; Del Cul et al., 2007). A relative preservation of early activations (P1, N1, N2) was also described in other inattention paradigms such as the attentional blink (Harris et al., 2013; Marti et al., 2012; Sergent et al., 2005; Vogel and Luck, 2002) or inattentional blindness (Pitts et al., 2011). It may explain that priming effects are preserved both in inattentional blindness and attentional blink conditions. Source reconstruction again suggests that the brain state underlying conscious access corresponds to a highly distributed joint activation of bilateral inferior frontal, anterior temporal and inferior parietal cortices. When attention is distracted during the inattention task, we observe that brain activity is spatially reduced and restricted to posterior visual and occipital areas.

Attention and the amplification of evidence accumulation

The original contribution of the present paradigm is to demonstrate, through the manipulation of SOA, that attention amplifies sensory evidence and its accumulation rate relative to a strong inattention condition. The literature on attention has primarily focused on the issues of whether attention modulates early as well as late processes. Our study confirms that attention can have a strong modulating influence on early components, although withdrawal of attention does not completely eradicate them (Feng et al., 2012; Hillyard and Anllo-Vento, 1998; Kastner and Ungerleider, 2000; Luck and Ford, 1998; Woodman and Luck, 2003; Zotto and Pegna, 2015). However, our study points to another way in which attention impacts on perceptual processing. By manipulating the SOA between the target and a subsequent mask, we found that many processing stages integrate stimulus information, in the sense that their activation increases monotonically with SOA. This point was clearest in the case of N2, which as noted earlier (Del Cul et al., 2007), starts at a fixed delay relative to target onset, ends at a fixed delay relative to mask onset, and appears to increase linearly in amplitude as a function of the interval elapsed between these two events. Those findings suggest an accumulation of sensory evidence which lasts until it is interrupted by the presentation of the mask. The present results now show that the slope of this SOA effect, i.e. the amount of integrated information per unit of time, can be modulated by attention. Under conditions of inattention, ERP amplitude either increased less as a function of SOA, or ceased to increase altogether, suggesting that attention modulates the temporal integration constant of perceptual networks. Crucially, the target was presented for the same duration in all conditions (14 ms). It therefore seems that the brain buffers the sensory information and is able to accumulate it through a series of processing stages, with a slope proportional to attention, until another concurrent information (i.e. the mask) interrupts this accumulation. Attention seems to enable a specific mode of amplification and integration in which a fixed quantity of sensory evidence provided at input is able to trigger a series of successive stages of increasingly amplified activation, and which ultimately translates into a global ignition.

The attentional modulation of information processing observed in our results is consistent with the predictive coding framework, which proposes that spatially selective attention reflects the precision (confidence or inverse uncertainty) of perceptual inference

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(Brown and Friston, 2013; Feldman and Friston, 2010; Vossel et al., 2014). According to this view, attentional selection serves to increase the precision of sensory channels, enabling faster responses to attended stimuli through an increase in the synaptic gain of neuronal populations encoding prediction error. In accordance with previous theoretical models, we propose that peripheral processors accumulate sensory information which will be consciously perceived if it crosses a threshold within a distributed *global workspace* able to integrate and broadcast back evidence from multiple brain processors (Baars, 1993; Dehaene, 2011; Dehaene and Changeux, 2011; Lafuente and Romo, 2006). Importantly, an accumulation of evidence has already been observed unconsciously (Vlassova et al., 2014; Vorberg et al., 2003) and seems to precede conscious access (Vorberg et al., 2003). Our results concur with this idea by showing a significant increase in ERP amplitude with SOA even under inattention conditions. However, they indicate that evidence accumulation is amplified by top-down attention and suggest that, at a late stage, the crossing of a threshold in evidence accumulation is associated with conscious perception (Dehaene, 2011; Kang et al., 2017; King and Dehaene, 2014; Ploran et al., 2007; Shadlen and Kiani, 2011).

P3 increases beyond the minimal consciousness threshold

In our previous work (Del Cul et al., 2007), SOA varied only in the range 16-100 ms. Over this range and under attention conditions we observed a sigmoidal variation of objective and subjective indices of target visibility, and we found that the P3 wave closely tracked this sigmoidal shape. Here, however, by extending the SOA to longer values (27-160 ms), we observed that the P3 amplitude continued to increase in the range 100-160 ms where subjective visibility reached a fixed ceiling. Still, P3 amplitude again closely tracked visibility in the sense that it was nil at SOA = 27 ms, precisely when subjects reported that stimuli were essentially invisible, and then increased for larger SOAs when the stimuli became visible. Thus, the P3 did show a threshold-like non-linearity at short SOAs (see Figure 3), unlike other waveforms such as the N2 which were already significantly positive for the invisible stimuli (i.e. SOA = 27 ms). These results are coherent with much prior research, using different criteria, which indicates that the P3 correlates tightly with conscious access (using a variety of paradigms with fixed stimuli and variable subjective experience: Babiloni et al., 2006; Del Cul et al., 2007; Fernandez-Duque et al., 2003; Lamy et al., 2008; Pins and Ffytche, 2003; Sergent et al., 2005).

However, the continued P3 increase at long SOAs was unexpected and indicates a departure for the close parallelism that we previously suggested between conscious reports and P3 size (Babiloni et al., 2006; Del Cul et al., 2007; Fernandez-Duque et al., 2003; Lamy et al., 2008; Pins and Ffytche, 2003; Sergent et al., 2005). This aspect of our results suggests that, like previous ERP stages, the P3 may reflect an evidence-accumulation process, but within a high-level cognitive route associated with subjective experience and reportability, above and beyond the mere sensori-motor mapping level (Dehaene, 2011; Del Cul et al., 2009; King and Dehaene, 2014; Shadlen and Kiani, 2011). Indeed, several other studies have shown how the P3 is associated with the formation of decisions and correlates with prior knowledge and evidence accumulation (Gold and Shadlen, 2007; O'Connell et al., 2012; Twomey et al., 2015) as well as with post-decision confidence (Boldt and Yeung, 2015; Murphy et al., 2015). Given

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those studies, it seems possible that the binary subjective measure that we used (seen/not seen) did not fully do justice to the rich introspection that subjects could have had about target visibility. Had we measured a more continuous parameter such as confidence or clarity, it seems possible that one or several such behavioural indices would have grown continuously with SOA, paralleling the observed increase in P3 size.

Abnormal attentional amplification in schizophrenia

Behaviourally, we replicated the previous finding that schizophrenia patients have a higher subjective and objective threshold for conscious perception during masking (Butler et al., 2003; Charles et al., 2017; Dehaene et al., 2003a; Del Cul et al., 2006; Green et al., 2011, 1999; Herzog and Brand, 2015; Plomp et al., 2013). The main goal of our study was to evaluate whether this deficit was associated with impairments of bottom-up and/or top-down processing. The results were clear-cut: schizophrenic patients, compared to healthy controls, showed major anomalies in evoked brain activity only under attended conditions. Contrary to controls, the N1 component was not amplified by attention, and the late non-linear ignition component associated with the P3 component was drastically reduced. Crucially, no difference was found under inattention conditions. In particular, the SOA effect on N2 was preserved in the patient group. In other words, the processing of the target and the initial accumulation of evidence as a function of SOA took place normally when the stimulus was unattended.

We therefore conclude that the patient's deficit in perceiving masked stimuli is probably mainly due to a lack of appropriate top-down attentional modulation. At the level of the N1 waveform already, which showed little or no modulation by SOA beyond the shortest value, the difference between patients and controls groups was independent of SOA, i.e. was observed in both conscious and unconscious conditions. This difference between patients and controls is thus likely to reflect a pure attentional top-down impairment, stable regardless of the time available to amplify information before the mask appears. In accordance with this proposal, the patients' N1 profile, under attention instructions, was close to the one observed under inattention instructions in both patients and controls (see Figure 4). This observation suggests a severely reduced attentional amplification of that processing stage in patients.

At a later stage, the P3 difference between patients and controls was highly significant, but the patients still exhibited an easily detectable P3 in the attended compared to the unattended condition (see Figure 4). Furthermore, the patients' P3 amplitude increased with SOA, although at a slower rate than in the control subjects. Those findings suggest a partial P3 impairment in schizophrenia, as also observed in previous research (Charles et al., 2017; Jeon and Polich, 2003; Mathis et al., 2012; Oribe et al., 2015).

Interestingly, the patients also showed essentially normal attentional amplification of the P1 and N2 components in our study. The present study was not designed to disentangle the specific contributions of each of those ERP components. However, in the future, such work will be essential in order to better specify the exact nature of the deficit, for instance by

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varying the quality of sensory evidence at different hierarchical levels or by varying the type of attention deployed (spatial, temporal, executive),

As reviewed in the introduction, some authors proposed that the elevated threshold for conscious access in schizophrenia was due to a low-level visual deficit (Butler et al., 2003; Cadenhead et al., 1998; Green et al., 2011). Indeed, early sensory processing deficits have been repeatedly observed in schizophrenic patients (Bolino et al., 1994; Braff et al., 1992; Butler et al., 2007, 2005, Javitt, 2009b, 2009a; Javitt and Freedman, 2015; Kim et al., 2006; Martínez et al., 2012; Shelley et al., 1991; Umbricht and Krljes, 2005). In particular, a reduced N1 amplitude was repeatedly found in the auditory modality (Brockhaus-Dumke et al., 2008; Turetsky et al., 2008) and in several visual masking paradigms (Neuhaus et al., 2011; Wynn et al., 2013). To account for those results, a specific dysfunction of the magnocellular pathway was hypothesized, while the parvocellular visual pathway was thought to be preserved (Butler et al., 2007, 2005; Javitt, 2009a; Kim et al., 2006; Martínez et al., 2012). Tapia and Breitmeyer (2011), however, revisited this issue and proposed that magnocellular channels contribute to conscious object vision mainly through a top-down modulation of reentrant activity in the ventral object-recognition stream. The link between magnocellular circuits and visual masking in schizophrenia was also contested recently, as there seems to be no clear evidence of either hyper or hypo-activity of the magnocellular pathway in schizophrenia (Herzog and Brand, 2015).

Importantly, if the elevated threshold for conscious perception in schizophrenia was solely due to abnormal bottom-up sensory processing, one would expect non-conscious processing, such as unconscious number comparison, to be abnormal too – but, on the contrary, even subtle measures of subliminal priming has repeatedly been shown to be fully preserved in schizophrenia (Dehaene et al., 2003a; Del Cul et al., 2006; for a review, see: Berkovitch et al., 2017). The present results extend this logic by showing that, following the total withdrawal of spatial, temporal and executive attention, the remaining brain activity evoked by a flashed stimulus is indistinguishable between patients and controls. By hypothesis, this activity should provide a proper measure of bottom-up processing, which therefore appears to be essentially intact.

An alternative hypothesis should therefore be considered, according to which the elevated consciousness threshold in schizophrenia is due to an abnormal top-down amplification of sensory information. This hypothesis receives strong support from the present results: the amplification factor on attended compared to unattended trials was clearly reduced in patients, at least for the N1 and P3 components. Our results also corroborate other studies showing impairments in top-down processing (Dima et al., 2010; Plomp et al., 2013) and selective attention (Fuller et al., 2006; Luck et al., 2006) in schizophrenia patients. Several studies have reported that the difference in cerebral activity between attended and unattended conditions is reduced in schizophrenia (Force et al., 2008; Martínez et al., 2012; Michie et al., 1990). Moreover, schizophrenic patients are less likely to report that they perceived an unexpected event during inattentional blindness (Hanslmayr et al., 2013) and show an exaggerated attentional blink effect compared to controls, associated with a decreased P3 (Mathis et al., 2012). An abnormal P3 and ignition deficits have also been previously reported in schizophrenia (Charles et al., 2017; Jeon and Polich, 2003; Oribe et al., 2015). The present results refine those studies, however, by (1) clearly distinguishing bottom-

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up versus top-down processes; (2) showing that some top-down attentional amplification (underlying P1 and N2 components) can remain preserved in schizophrenia.

Overall, our results are fully compatible with previous observations that subliminal processing are preserved in schizophrenia (for a review, see: Berkovitch et al., 2017) and are not accounted for by pure bottom-up impairments in early perceptual stages or sensory processing. We suggest that the previous reports of elevated masking threshold and abnormal conscious processing in schizophrenia (Butler et al., 2003; Charles et al., 2017; Dehaene et al., 2003a; Del Cul et al., 2006; Green et al., 1999; Herzog et al., 2004; Plomp et al., 2013) are linked to the impairments in top-down attentional amplification of the N1 and P3 that we observed. Tentatively, one may also suggest that the activations that were found to be preserved in schizophrenic patients (i.e. P1 and N2) might account for the observed preservation of subliminal processing.

More broadly, the present results fit with several other physiopathological aspects of schizophrenia (Berkovitch et al., 2017). Schizophrenic patients exhibit anomalies in long-distance anatomical connectivity (Bassett et al., 2008; Benetti et al., 2015; Jones et al., 2006; Kubicki et al., 2005; Sigmundsson et al., 2001) and functional connectivity (Ford et al., 2002; Frith et al., 1995; Lawrie et al., 2002; Vinckier et al., 2014) in distributed networks that are thought to underlie the broadcasting of conscious information in the global workspace (Dehaene and Changeux, 2011). Moreover, the long-range synchrony of gamma and beta-band oscillations is disturbed in schizophrenic patients (Cho et al., 2006; Lee et al., 2003; Mulert et al., 2011; Spencer et al., 2004; Uhlhaas and Singer, 2010), while conscious perception in normal subjects is accompanied by late increases in gamma-band power (Doesburg et al., 2009; Gaillard et al., 2009; Melloni et al., 2007; Wyart and Tallon-Baudry, 2009) and beta band phase synchrony (Gaillard et al., 2009; Gross et al., 2004; King et al., 2013). Finally, abnormal regulation of NMDA receptors was suggested as a putative core pathology in schizophrenia (Coyle, 2006; Jentsch and Roth, 1999; Olney and Farber, 1995; Stephan et al., 2009). NMDA receptors are broadly involved in connectivity and synaptic plasticity (Stephan et al., 2009) as well as inter-areal synchrony (Rivolta et al., 2015; Uhlhaas and Singer, 2014; van Kerkoerle et al., 2014). Recently, they have been shown to play a specific role in top-down cortico-cortical connectivity and the late amplification of sensory signals (Herrero et al., 2013; Moran et al., 2015; Self et al., 2012; van Loon et al., 2016). In particular, NMDA-receptor antagonists leave intact the feedforward propagation of visual information, and selectively impact on late recurrent processing (Self et al., 2012). NMDA receptor dysfunction could therefore be a plausible cause for the anomaly in conscious perception observed in the present work.

Conclusion

Our study aimed to disentangle how sensory information processing is modulated by bottom-up (SOA) and top-down (attention) factors. We found that, in the absence of attention, bottom-up information still weakly modulated sensory information processing, while attention enabled a strong amplification of sensory signals that, in its late stages, played a decisive part in conscious access. The abnormal consciousness threshold in schizophrenia

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seems tightly linked to a dysfunction of the latter top-down attentional amplification mechanisms.

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