

1 **Preserved subliminal processing and**
2
3 **impaired conscious access in Schizophrenia.**

4
5
6
7
8 **Authors:**

9
10 Antoine Del Cul¹², Stanislas Dehaene¹³, and Marion Leboyer²

11
12
13 **4495 words**

14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30

¹ Institut National de la Santé et de la Recherche Médicale, Cognitive Neuroimaging Unit, Service Hospitalier Frédéric Joliot, Commissariat à l'Energie Atomique, 4, place du Général Leclerc, 91401 Orsay Cedex, France.

² Département hospitalo-universitaire de Psychiatrie, Hôpital Albert Chenevier et Henri Mondor (AP-HP), 40 rue Mesly, 94000 Créteil, France; Unité INSERM U 513, "Neurobiologie et Psychiatrie", Hôpital Henri Mondor, 94000 Créteil, France.

³ Collège de France, Place Marcelin Berthelot, Paris, France

31 **Abstract**

32

33

34 **Background**

35 Studies of visual backward masking have frequently revealed an elevated masking
36 threshold in schizophrenia. This finding has frequently been interpreted as indicating a low-
37 level visual deficit. However, more recent models suggest that masking may also involve late
38 and higher-level integrative processes, while leaving intact early “bottom-up” visual
39 processing.

40 **Objectives**

41 We tested the hypothesis that the backward masking deficit in schizophrenia
42 corresponds to a deficit in the late stages of conscious perception, whereas the subliminal
43 processing of masked stimuli is fully preserved.

44 **Method**

45 28 patients with schizophrenia and 28 normal controls performed two backward-
46 masking experiments. We used Arabic digits as stimuli and varied quasi-continuously the
47 interval with a subsequent mask, thus allowing us to progressively “unmask” the stimuli. We
48 finely quantified their degree of visibility using both objective and subjective measures to
49 evaluate the threshold duration for access to consciousness. We also studied the priming
50 effect caused by the variably masked numbers on a comparison task performed on a
51 subsequently presented and highly visible target number.

52

53 **Results**

54 The threshold delay between digit and mask necessary for the conscious perception of
55 the masked stimulus was longer in patients compared to control subjects. This higher
56 consciousness threshold in patients was confirmed by an objective and a subjective measure,

57 and both measures were highly correlated for patients as well as for controls. However,
58 subliminal priming of masked numbers was effective and identical in patients compared to
59 controls.

60 **Conclusions**

61 Access to conscious report of masked stimuli is impaired in schizophrenia, while fast
62 bottom-up processing of the same stimuli, as assessed by subliminal priming, is preserved.
63 These findings suggest a high-level origin of the masking deficit in schizophrenia, although
64 they leave open for further research its exact relation to previously identified bottom-up visual
65 processing abnormalities.

66
67

68 **Introduction**

69

70 A functional breakdown of large-scale cortical integrative processes, caused by
71 abnormal cortico-cortical and cortico-subcortical long-range connectivity is postulated in
72 schizophrenia [1-14]. A crucial issue concerns whether, in addition to this deficit at the level
73 of cognitive integration, patients with schizophrenia also suffer from other, possibly unrelated
74 deficits of a lower and more modular nature [15-22]. Indeed, some experimental results
75 arising from studies of visual backward masking have suggested a low-level visual deficit. In
76 visual backward masking, the visibility of a briefly presented stimulus is reduced by a mask
77 presented very shortly after the stimulus [23, 24]. Patients with schizophrenia consistently
78 show a deficit in the perception of backward-masked stimuli: compared with healthy controls,
79 they require a longer interval between stimulus and mask in order to identify the stimulus.
80 [25-27]

81 Breitmeyer and Ganz have proposed a model where masking depends on the
82 interactions between transient (magnocellular) and sustained (parvocellular) channels within

83 the early visual pathways. In that model, backward masking would occur when the transient
84 channels of the mask interfere with the sustained channels of the stimulus and therefore
85 interrupt the formation of the percept. [23, 24]. Abnormal masking in schizophrenia would be
86 linked to deficits in transient magnocellular channels [25, 28-32]. An additional deficit in
87 sustained channels (causing abnormal gamma range activity) has also been proposed [33, 34].

88 More recently, however, new models of masking have appeared, according to which
89 this phenomenon may also involve late and higher-level integrative processes [35-43]. Enns
90 and Di Lollo, for instance, suggest that some forms of masking may be caused by a disruption
91 in the integration between bottom-up inputs and a top-down attentional signal [44, 45].
92 Similarly, the global neuronal workspace model of conscious perception [39-41, 46]
93 postulates that conscious access is associated with recurrent interactions between distant brain
94 areas. Top-down feedback from prefrontal and parietal areas to lower-level sensory regions
95 would establish a self-amplified reverberant neuronal assembly associated with conscious
96 reportability. During masking, a stimulus would fail to reach consciousness if the mask
97 replaces the stimulus before this recurrent activity has become stable. Simulations show that
98 this process is stochastic and may fail due to random fluctuations in prestimulus spontaneous
99 activity. The model therefore predicts an all-or-none, bimodal distribution of subjective
100 visibility scores and of event-related brain activation measures, which was recently observed
101 experimentally during the attentional blink. [40, 47, 48]

102 The global workspace model, like most current models of masking, suggests that the
103 initial feedforward processing of masked stimuli can be largely intact, in spite of their reduced
104 subjective visibility. This hypothesis is largely confirmed by studies of subliminal priming. In
105 those studies, a masked shape called the “prime” is shown to influence the processing of a
106 subsequent target stimulus. Behavioral and neuroimaging studies of subliminal priming
107 suggest that processing of stimuli made subjectively invisible by masking is extensive and can

108 include visual recognition, but also lexical and even semantic levels. [49-52] [53]. In
109 particular, Dehaene et al demonstrated a non-conscious motor conflict induced by masked
110 primes during a number comparison task. [54] Most relevant to present purposes, they showed
111 that patients with schizophrenia showed a normal masked priming effect, but became
112 disproportionately slower and showed an absence of conflict, relative to controls, when the
113 primes were unmasked [55]. These data, which suggested intact low-level visual processes
114 and abnormal higher-level executive control in schizophrenia, were related to a major
115 hypoactivation of prefrontal and anterior cingulate cortices. Dehaene et al. tentatively
116 suggested that the lack of top-down amplification from these areas might jointly explain both
117 the higher-level cognitive deficits and the change in visual masking threshold in patients with
118 schizophrenia.

119 The main purpose of the present work is to provide a further test of the hypothesis that
120 the backward masking deficit in schizophrenia corresponds to a deficit in the late stages of
121 conscious perception. Our aim was to evaluate whether the bottom-up subliminal processing
122 of masked stimuli is preserved by studying whether normal subliminal priming could be
123 observed in schizophrenia. We used a new form of masking, with a component of spatial
124 attention, inspired by Vorberg et al. [56] and Di Lollo et al. [44, 45], where the stimulus and
125 mask shapes are not overlapping. Using Arabic digits as stimuli, we varied quasi-continuously
126 the interval between a digit and the subsequent mask, thus allowing us to progressively
127 “unmask” the stimulus. This manipulation allowed us to study both the subliminal priming
128 effect caused by these variably masked numbers, as well as their degree of visibility, and to
129 precisely quantify the threshold duration for access to consciousness. Based on the global
130 neuronal workspace model of conscious access, the following predictions were made. 1)
131 Masking should affect conscious visibility in an “all or none” manner: either the stimulus is
132 fully consciously perceived or it is not perceived at all. 2) The threshold for conscious access

133 should be higher in patients than in controls, i.e. a longer interval between stimulus and mask
134 should be necessary for them to identify the stimulus. 3) The subliminal processing of non-
135 consciously perceived stimuli, measured by their priming effect, should be preserved and
136 identical in the two groups. Thus, we expected response times to be faster when the prime
137 provided some valid information about the target, either about its exact identity (repetition
138 priming) or about the nature of the forthcoming response (response priming). The
139 preservation of both priming effects would constitute strong evidence in favour of preserved
140 fast bottom-up perceptual processing in schizophrenia.

141

142 **Method**

143 **Participants**

144

145 Twenty eight patients with schizophrenia (mean age, 34yr, range 18-53, 9 women and
146 19 men) participated in the study. All were native French speakers. Patients met DSM-IV
147 criteria for schizophrenia and were recruited from the psychiatric department of Creteil
148 University Hospital (Assistance Publique, Hôpitaux de Paris). They had a chronic course and
149 were stable at the time of the experiment. 22 patients were medicated by atypical
150 antipsychotics and 6 with typical antipsychotics. This treatment had been unchanged for at
151 least three weeks. The comparison group consisted of twenty eight subjects (mean age, 32yr,
152 range 18-55, 18 men and 10 women). Comparison subjects were excluded for history of any
153 psychotic disorder, bipolar disorder, schizotypal or paranoid personality disorder, recurrent
154 depression. Patients and controls with a history of brain injury, epilepsy, alcohol or substance
155 abuse, or other neurological or ophthalmologic disorders were excluded. Patients and controls
156 did not differ significantly in sex, age and level of education.

157 All experiments were approved by the French regional ethical committee for
158 biomedical research (Hôpital de la Pitié Salpêtrière), and subjects gave written informed
159 consent.

160 **Stimuli**

161 In our material, a first number, that we will call the “prime”, was masked by a shape
162 containing in its structure a second number, the “target” (see figure 1). We varied quasi-
163 continuously the interval between the prime and the subsequent mask, thus allowing us to
164 progressively unmask the stimulus digit. The delay between the onset of the prime and the
165 onset of the mask could take one out of eight values (0, 16, 33, 50, 66, 83, 100 and 150 ms).
166 For the delay of 0 ms, the prime and the mask had the same onset, but the mask persisted after
167 the prime had disappeared.

168 The stimulus set consisted of 16 pairs of prime and target numbers, consisting in all
169 pairs of the numbers 1, 4, 6 and 9 written in Arabic format. As a consequence, the following
170 factors could be analyzed: target distance (close or far from 5), target size (larger or smaller
171 than 5), response congruity (whether or not the prime and target fell on the same side of 5),
172 and repetition (within the congruent trials, whether or not the prime and target were the same
173 number).

174 **Procedure**

175 One part of the experiment was dedicated to a measurement of both objective and
176 subjective thresholds. We measured an objective visibility threshold by examining subjects’
177 ability to perform a number comparison task on the prime. We also measured a subjective
178 threshold by collecting introspective ratings of prime visibility, on a subjective continuous
179 scale, identical to the one used in previous studies of the attentional blink (see refs. [40, 47,
180 57] for detailed instructions). The experiment consisted in 20 training trials followed by 20
181 trials for each delay, for a total 180 randomly presented trials.

182 Another part evaluated subliminal and supraliminal priming. Subjects were asked to
183 compare each target number with 5, pressing the right-hand key as fast as possible for
184 numbers larger than 5 and the left hand key for numbers smaller than 5. This experiment
185 consisted in 20 training trials followed by 320 experimental trials (8 blocks of 40 trials, one
186 block for each delay). The different delays were presented in random order but in different
187 blocks in order to facilitate the subject's task. It was felt that, if the delays had been randomly
188 mixed, it would have been too difficult for patients to avoid responding to the prime on
189 conscious trials. Blocking helped them to learn to focus on the target and neglect the prime,
190 regardless of its visibility. For similar reasons, the priming experiment, which was the most
191 difficult, was always run prior to threshold measurement.

192 **Results**

193 **Measuring the threshold for access to consciousness**

194 Figure 2 shows the distributions of visibility scores in each group and for each delay
195 on prime-present trials. In both groups, we observed a bimodal repartition of scores, with a
196 first set of responses close to maximal visibility (scale score > 75%) and a second set of
197 responses peaking at zero visibility (score < 25%). Responses between 25% and 75% were
198 rare (< 10%). Thus, in both groups, increasing delays did not lead to a progressive increase in
199 subjective experience of prime visibility, but to a shift in the probability of reporting one of
200 two discrete subjective states ("seen" or "not seen").

201 Based on this bimodal distribution, we arbitrarily defined "seen" trials as those whose
202 visibility score was above the middle of the scale (>50%). Figure 3b shows the proportion of
203 "seen" trials as a function of delay. The proportion increased steadily with delay, but at a
204 slower rate in patients than in the controls. This pattern was evaluated with an ANOVA on the
205 proportion of "seen trials", with factors of group and delay. The proportion of "seen" trials
206 was significantly higher in controls than in patients ($F(1,54)=12.90$; $p<0.001$). We also found

207 a significant delay effect ($F(7,378)=270.64$; $p<0.001$) and a group by delay interaction
208 ($F(7,378)=8.17$; $p<0.001$). At all delays above 33 ms, the proportion of “seen” trials was
209 significantly lower in patients (all $p<0.05$).

210 A similar analysis was applied to the objective measure of prime processing. For each
211 subject and each delay, we calculated the proportion of correct responses in the prime
212 comparison task (Figure 3a). Again, this measure increased non-linearly with delay, at a
213 slower rate for patients than for controls. An ANOVA indicated that performance was
214 significantly higher in controls than in patients (78.2% against 59.6% correct; $F(1,54)=87.53$;
215 $p<0.001$). There was a main effect of delay ($F(7,378)=100.63$; $p<0.001$) and a group by delay
216 interaction ($F(7,378)=5.02$; $p<0.001$). At each delay, the controls outperformed the patients
217 (all $p<0.05$). In the controls, performance was significantly superior to chance at all the
218 delays. However, in the patients, performance only became superior to chance for delays of
219 50 ms and above.

220 In summary, both objective and subjective measures of prime conscious perception
221 indicated lower performance in the patients. In order to characterize, for each subject, a
222 subjective and an objective threshold for access to consciousness, we used non-linear
223 regression to fit the curves in figure 3 with a sigmoid defined as $f(x) = \alpha_1 + \frac{\alpha_2}{1 + e^{-\alpha_3(x-\alpha_4)}}$,
224 where the α_i are free parameters. The threshold was defined as the delay for which the
225 sigmoid curve reached its inflexion point, i.e. parameter α_4 . In all subjects, the fit provided an
226 excellent account of the data (mean $r^2 = 0.948$, range=0.871-0.996). The mean objective
227 threshold was 59 ms (SD: 13.76; range: 43-91.5) for controls and 90 ms (SD: 32.62; range:
228 47-163.5) for patients. This threshold was significantly higher for patients than for controls.
229 (Wilcoxon test: $W = 539$, $p<0.001$). The mean subjective threshold was 62 ms (SD: 14.68
230 range: 41 -96) for controls and 93 ms (SD: 36.11 range: 47-182) for patients. Again, this

231 threshold was significantly higher for patients than for controls. (Wilcoxon test: $W = 523$,
232 $p < 0.001$).

233 Figure 4 shows the relation between the individual objective and subjective thresholds.
234 Linear regression showed that the two values were highly correlated, both as a whole ($r^2 =$
235 0.951 , $p < 0.001$), within the controls ($r^2 = 0.834$, $p < 0.001$) and within the patients ($r^2 = 0.955$
236 $p < 0.001$). In all cases, the slope did not differ from 1, and the intercept was not significant.
237 Thus, the objective and subjective tasks appeared to provide essential identical measures of
238 the threshold for access to consciousness. Those results indicate that our paradigm quantifies
239 this threshold with high cross-task reliability. In the following, we arbitrarily use the objective
240 measure as our index of the conscious access threshold.

241 Given the large variability in the observed threshold in the patient group, we further
242 studied whether this threshold correlated with the patients' clinical symptoms. To this aim, we
243 used the French translation of the Signs and Symptoms of Psychotic Illness (SSPI) scale. [58,
244 59] The consciousness threshold was positively correlated with psychomotor poverty
245 (Pearson's $r^2 = 0.551$, $p < 0.001$), depression ($r^2 = 0.473$, $p = 0.017$), and disorganization ($r^2 =$
246 0.459 , $p < 0.01$). We also found a significant correlation with reality distortion ($r^2 = 0.459$,
247 $p = 0.021$) and inside this cluster of symptoms, a positive correlation with hallucinations ($r^2 =$
248 0.629 , $p < 0.001$) and delusion ($r^2 = 0.4$, $p = 0.047$).

249 **Occasional mismatch between subjective and objective measures**

250 We further analyzed the rare trials in which subjective and objective measures did not
251 match. One potential cause for such a mismatch is a capacity for subliminal performance in
252 the objective number comparison task, which is known to be partly feasible under subliminal
253 conditions [51, 54, 60]. As previously shown in figure 3, for short delays (inferior to 50 ms),
254 subjective visibility was around zero and did not differ between groups, but objective
255 performance was above chance for controls only, thus creating a significant difference

256 between the two groups. To study whether this phenomenon was imputable to subliminal
257 processing in the control subjects, we analyzed objective performance while restricting
258 ourselves solely to subjectively defined “not seen” trials, the latter being defined using a
259 conservative criterion (subjective score smaller or equal to 25%).

260 Figure 5c shows, across delays, the objective performance in each group for “not seen
261 trials” and Figure 5a shows this performance for each delay. Averaged across delays,
262 objective performance on “not seen” trials was significantly above chance (50%) in controls
263 (objective performance= 0.6; $p<0.001$), indicating some capacity for subliminal number
264 comparison, but not in patients (objective performance= 0.52; $p=0.099$). An ANOVA
265 indicated that this performance was significantly superior in controls than in patients
266 ($F(1,44)=19.69$, $p<0.001$). There was a main effect of delay ($F(6,230)=2.695$; $p=0.015$),
267 indicating that performance increased with delay, without delay by group interaction
268 ($F(6,230)=1.551$; $p=0.163$).

269 Another potential cause for mismatch between objective and subjective measures
270 might be a propensity for illusory perception. To objectify the impression that patients had
271 more such illusory perceptions than controls, we analyzed prime comparison performance
272 during subjectively defined “seen” trials (conservatively defined as a subjective score greater
273 than to 75%). The objective performance was 97.12 % correct in controls and 90.5 % correct
274 in patients (Figure 5b), indicating the presence of comparison errors in both groups, as is
275 usual in response time experiments. However, using an ANOVA on these percentages, we
276 found that objective performance was significantly higher for controls than for patients
277 ($F(1,42)=13.61$, $p<0.001$). There was a main effect of delay ($F(6,192)= 16.191$; $p<0.001$)
278 without delay by group interaction ($F(6,192)= 1.06$; $p= 0.388$) indicating that erroneous
279 objective performance was particularly frequent in the controls and in the patients at short
280 delays of 50, 66 and 83 ms.

281 It seems likely that, at those delays, several schizophrenic patients experienced illusory
282 perception of the primes, which led them to respond erroneously in the comparison task (see
283 discussion). Indeed, performance within “seen” trials averaged across delays was only
284 negatively correlated with hallucinations ($r^2 = -0.402$, $p=0.034$), indicating that clinical
285 hallucinations likely were accompanied by visual illusions of seeing the masked prime.

286 **Subliminal and conscious priming effects**

287 We now turn to the priming experiment, in which we measured the ability of the
288 subliminal number prime to influence the processing of the subsequent conscious target. We
289 performed an analysis of variance (ANOVA) on error rate and on mean RT from all trials
290 with RTs below 1000 ms (representing 1,5%, $SD = 1.7$, of all the trials for the controls and
291 3.6%, $SD = 4.7$, for the patients), with factors of group, prime-target relation (congruent
292 repeated, congruent non-repeated, and incongruent), distance of the target number to five, and
293 delay.

294 First, we tested that patients and controls did not differ on number comparison
295 processes: first, they were affected by a similar distance effect: they answered faster for large
296 than for small distance (37 ms for patients: $(1,25)=130.63$ $p<0.001$, and 46 ms for controls:
297 $F(1,25)=144.36$ $p<0.001$) without significant distance*group interaction; $F(1,49)=2.191$
298 $p=0.145$). Furthermore, the error rate in target comparison to 5 was non-significantly different
299 between patients and controls (5.017% versus 4.91% errors, $p=0.905$). We found a significant
300 effect of delay ($F(7,364)= 4.463$ $p<0.001$) indicating that subjects made more errors for longer
301 delays, without significant difference between groups ($F(7,364)= 0.705$; $p=0.668$).

302 Figure 6a shows the mean RT for each group, for each condition of prime-target
303 relation and for each delay. Overall, patients were slower than controls (618 ms versus 513
304 ms, $F(1,52)=21.461$, $p<0.001$). The main effect of delay was globally significant
305 ($F(7,364)=20.589$; $p<0.001$): RT increased with delay, particularly at the longer delays where

306 the prime becomes conscious. The main effect of prime-target relation was significant overall
307 ($F(2,104)=91.059$, $p<0.001$), and a significant delay by relation interaction ($F(14,728)=5.332$;
308 $p<0.001$) indicated that the priming effect tended to increase with delay. Crucially, none of
309 these effects interacted with group. There was no interaction of delay and group
310 ($F(7,364)=1.105$; $p=0.359$), of prime-target relation and group ($F(2,104)=0.017$; $p=0.983$), nor
311 any triple interaction ($F(14,728)=1.139$; $p=0.319$). At each delay, we found no significant
312 difference between groups for the prime-target relation effect. Furthermore, the overall prime-
313 target relation effect was significant in both groups (all $p<0.001$).

314 The effect of prime-target relation on RT could be decomposed into two distinct
315 effects: response priming and repetition priming. Both effects were significant across and
316 within each group (all $p<0.05$) without significant difference between groups. We then
317 separated the delays into those above and those below the consciousness threshold (60ms in
318 controls and 90ms in patients). In both cases, however, priming was not significantly different
319 between groups, neither for repetition priming nor for response priming (Figure 6c).

320
321

322 **Discussion**

323 Overall, our results demonstrate the non-linear character of conscious access, as
324 postulated in the global workspace theory. In both patients and controls, the bimodal
325 distribution of subjective visibility ratings suggests that conscious access corresponds to a
326 discontinuous” all-or-none” process (with a higher threshold in patients). Note that all
327 subjects were instructed to report even minimal changes in visibility, clarity or brightness.
328 Indeed, previous research established that normal subjects could do so with remarkable
329 sensitivity, and with continuous changes in their ratings, in a pattern masking paradigm where
330 prime duration was manipulated [47]. *A contrario*, the bimodal distribution observed here
331 does not seem attributable to a failure to comply with the instructions, but may correspond to

332 a genuine discontinuity in perception during the present object substitution paradigm, as
333 previously observed in an attentional blink paradigm [47, 48]. In both cases, the lack of
334 conscious access may be imputable to the all-or-none availability of central top-down
335 attention.

336 Our experiment allowed us to measure both an objective and a subjective threshold
337 within each subject, and we found a good correlation of these two measures within each
338 subject and in both groups. Therefore, the variability found in the masking thresholds was not
339 noise but could be considered as a genuine inter-individual difference between subjects.
340 Furthermore, this threshold captured some of the clinical variability in schizophrenia, as we
341 found a positive correlation between conscious threshold and psychomotor poverty
342 dimension, depression, hallucinations, and disorganization. The tight correlation between
343 objective and subjective measures indicates that patients possessed an excellent ability for
344 introspection or metacognition about their vision.

345 Our results were similar to those of previous studies which also found backward
346 masking performance deficit in patients. However, we also demonstrate that subliminal
347 priming effect is identical between patients and controls. Our results corroborate findings of
348 normal or even enhanced repetition and semantic priming effects in schizophrenia [61-63]. In
349 particular, they replicate previous results where intact subliminal priming was found for
350 numbers written both in word and in Arabic formats [55]. The preservation of non-conscious
351 repetition and response priming in schizophrenia suggests that the fast feedforward processing
352 stages that are thought to support these priming effects are largely intact, including early
353 visual analysis, but also numerical comparison and automatic response programming. A
354 contrario, the deficit of the patients in perceiving backward masked stimuli would then be due
355 to a dysfunction in the late stages of conscious perception. Compatible with this
356 interpretation, an auditory masking deficit involving central processes and contrasting with

357 preserved “low level” masking has been reported in schizophrenia and was attributed to a
358 deficient central cross-modal stage. [64]

359 Our finding that even subtle measures of automatic visual processing can be preserved
360 in schizophrenia has to be discussed in the context of the many studies which support a low-
361 level visual dysfunction of the magnocellular (M) pathway in schizophrenia [20, 65, 66]. Our
362 experiment studied the subliminal processing of stimuli relying principally on the
363 parvocellular (P) pathway (high contrast digits and letters). It did not assess of the integrity of
364 the magnocellular response to the stimuli and/or to the mask. Therefore, we cannot exclude
365 that an abnormal “bottom up” magnocellular response to the mask contributes to the stronger
366 masking effect in patients, as previously postulated.[20, 28-32, 67, 68] Such a deficit would
367 not affect the processing in the P pathway, known to project predominantly to ventral visual
368 areas, whereas it might affect the speed or strength of activity in dorsal stream areas where the
369 M pathway is known to project predominantly. In turn, such a weaker dorsal input may lead
370 to a slower orientation of spatial attention, thus leading to a prolonged period of susceptibility
371 to substitution masking. [44, 45] Foxe et al [69-71] have reported a decrease in a dorsal
372 parietal subcomponent of the visual evoked potential P1, contrasting with preserved
373 processing in the visual ventral stream. Whether this early magnocellular visual impairment
374 and the higher-level conscious access deficit are linked or independent remains uncertain.
375 According to Foxe et al, the magnocellular impairment would lead to a deficit in later
376 “effortful conceptual processing requiring intact dorsal stream input”. Alternatively, the
377 deficit observed with low-contrast visual stimuli, and imputed to a magnocellular impairment,
378 could be an indirect consequence of impaired parieto-frontal networks for top-down effortful
379 processing in schizophrenia, which would induce a deficient top-down amplification of lower-
380 level processing crucial for such tasks. Those two possibilities are not necessarily
381 incompatible and remain open for further research.

382 The hypothesis of a perturbed central stage associated with conscious cognitive
383 control [55, 72-77] may explain, not only the elevated threshold for perception of masked
384 stimuli, but also the observed difference in the ability to exploit subliminal information below
385 that threshold. Normal subjects performed the objective prime comparison task better than
386 chance, even on trials where they reported not seeing the prime; patients, however, remained
387 at chance level on those trials (see figure 3). We speculate that, during this experiment,
388 normal subjects are able to concentrate on the masked stimulus even though there are many
389 trials in which this stimulus cannot be seen. This considerable effort of top-down attention
390 may enable them to subliminally extract some information about the stimulus. Indeed, other
391 experiments have shown that attention can modulate and enhance subliminal processing [78].
392 This ability to maintain a strong top-down task set in the absence of any visible stimulus, a
393 function which depends particularly on prefrontal resources, may be impaired in
394 schizophrenia [79, 80].

395 Some patients (about thirteen) occasionally seemed to experience an erroneous
396 perception of the masked stimuli. On a few trials, they reported to have seen a number but
397 were wrong when comparing this number to 5, thus suggesting that their introspection did not
398 correspond to reality. Given the design of the experiment, we cannot exclude that some of
399 these responses were merely errors in the comparison task. However, for several reasons, we
400 believe that the phenomenon goes beyond this interpretation. First, during the experiment,
401 although their task only required comparing the prime with 5, some patients verbally reported
402 the prime identity and occasionally gave a verbal response that did not correspond to the digit
403 that was actually presented. Furthermore, such errors on “seen” trials decreased with delay
404 (figure 5a), and were frequent only at the intermediate delays of 50 and 66 ms. This pattern
405 would not be expected if the errors resulted merely from a failure in comparison of a
406 consciously seen digit. Third, across subjects, the occurrence of such errors correlated with a

407 high hallucination score and with an elevated consciousness threshold. What could be the
408 mechanism for such erroneous perceptions? In recent simulations of the global neuronal
409 workspace model, spontaneous activity of neural populations was shown to compete with the
410 entry of external inputs. [81] Thus, for some trials and obviously only for some patients, it is
411 possible that local, spontaneously activated internal representations competed with the
412 concurrent visual input for access to consciousness. Elevated spontaneous activity could
413 simultaneously explain both the elevated threshold and the intrusion of hallucinated digits.

414 Our previous study [35] had revealed impaired conscious priming in patients with
415 schizophrenia: when the prime was made visible by removing the masks, response priming
416 was reduced whereas repetition priming remained unchanged. Here, however, there was no
417 difference between patients and controls at any of the delays, including delays that were
418 supposedly above the consciousness thresholds. A possible explanation is that, in the present
419 study, even at the longest delays, the mask is always present. This might have helped patients
420 focus their attention on the mask and neglect the prime. Because of this neglect of the prime
421 in the priming task, we think that there was hardly ever for most of the patients a conscious
422 conflict between prime and target even for the primes presented at the longest delay.

423 In conclusion, our results suggest that the process of access to conscious report of
424 masked stimuli is impaired in schizophrenia, while some fast bottom-up processes of visual
425 perception and number comparison are fully preserved. This deficit could be due to anomalies
426 in the recurrent interactions between visual and higher level associative areas necessary for
427 conscious access. Indeed, a functional disconnection hypothesis of schizophrenia has been
428 proposed, based on abnormal patterns of long-distance correlation in functional neuroimaging
429 studies [4, 82, 83] and on structural anomalies observed with diffusion tensor imaging in the
430 long-distance white matter bundles, particularly in the fronto-cingular cortices, the uncinate
431 fasciculus area and corpus callosum. [84-92]. Although these functional and anatomical

432 anomalies can be plausibly related to an impaired “global workspace” associated with
433 conscious processing, further experiments are needed to clarify the exact relation between this
434 high-level masking deficit and the lower-level visual abnormalities previously described in
435 schizophrenia..

436

437 ***Acknowledgements***

438

439 This work was supported by grants from the Assistance Publique-Hôpitaux de Paris
440 (PHRC AOM98152), the Fondation pour la Recherche Médicale and the Institut de la Santé et
441 de la Recherche Médicale (INSERM) and a centennial fellowship from the McDonnell
442 donation to S.D. We are grateful to the following individuals for their help and useful
443 comments: Bertrand Audoin, Laurent Cohen, Raphaël Gaillard, Caroline Huron, Alexandre
444 Meary, Lionel Naccache, Christophe Pallier, Jean-Philippe Ranjeva, Françoise Reuter, Jerome
445 Sackur, Franck Schürhoff, Claire Sergent and Andrei Szocke.

446 ***Figure Legends***

447 **Figure 1: Experiment design.**

448 The prime was presented for 16 ms at one of four positions (1.4 degrees above or below
449 and 1.4 degrees right or left to the fixation cross). The mask (duration of presentation 250ms)
450 was composed of three letters (M, M, E) and the target number (1 ° from the fixation cross).
451 Those four symbols surrounded the prime number without touching it.

452 In the first experiment, referred to as the “priming experiment”, subjects were asked to
453 compare each target number with 5, pressing the right-hand key as fast as possible for
454 numbers larger than 5 and the left hand key for numbers smaller than 5.

455 The second experiment aimed at measuring the consciousness threshold in two
456 different ways. We measured an objective visibility threshold by examining subjects’ ability

457 to perform the number comparison task on the prime. We also measured a subjective
458 threshold by collecting introspective ratings of prime visibility, on a subjective continuous
459 scale.

460

461 **Figure 2: Distribution of subjective visibility ratings.**

462 In both groups, we observed a bimodal repartition of scores, with a first set of
463 responses close to maximal visibility (scale score > 16) and a second set of responses peaking
464 at zero visibility (score < 6). Responses between 6 and 16 were rare (< 10%). More not seen
465 responses were observed in patients than in controls, particularly at short delays.

466

467 **Figure 3: Objective and subjective measures of access to consciousness.**

468 a) Percentage of correct responses in prime comparison to 5 as a function of delay. At
469 each delay, the controls outperformed the patients. In controls, performance was significantly
470 superior to chance at all the delays whereas in patients, performance only became superior to
471 chance for delays of 50 ms and above.

472 b) Proportion of trials subjectively rated as “seen” as a function of delay. At all delays
473 above 33 ms, the proportion of “seen” trials was significantly lower in patients.

474 In both graphs, the sigmoid curve fitting the data is represented as a continuous line.
475 The mean objective θ^o and subjective θ^s thresholds were defined in each group as the delay
476 for which the sigmoid curve reached its inflexion point.

477 Error bars represent the standard error.

478

479

480

481

482 **Figure 4: Positive correlation between objective and subjective consciousness thresholds**
483 **across subjects.**

484 The two values were highly correlated, both as a whole ($r^2 = 0.951$, $p < 0.001$), within
485 the controls ($r^2 = 0.834$, $p < 0.001$) and within the patients ($r^2 = 0.955$, $p < 0.001$). In all cases,
486 the slope did not differ from 1, and the intercept was not significant.

487

488 **Figure 5**

489 Objective performance in prime comparison in each group respectively for “seen
490 trials” (conservatively defined as a subjective score greater than to 16) and “not seen” trials
491 (subjective score smaller or equal to 5). a) Performance at each delay b) and c) performance
492 averaged across delays.

493 The results demonstrate, in normal subjects a capacity for objective prime processing
494 even on trials subjectively rated as “not seen” (subliminal perception); and, conversely, in
495 patients, an inavailability of objective information on some trials judged as “seen”
496 (hallucinations).

497 Error bars represent the standard error.

498

499

500 **Figure 6: Measures of priming during the target number comparison task.**

501 a) Mean RT for each group, for each condition of prime-target relation and for each
502 delay. Response priming was defined as the difference in reaction time between incongruent
503 (InCong) and congruent non-repeated (CongNonRep) trials, and repetition priming as the
504 difference between congruent non-repeated and congruent repeated (CongRep) trials. Both
505 effects were significant across and within each group without significant difference between
506 groups.

507 b) and c) Delays were sorted into two categories according whether they fell below
508 and above the previously measured consciousness thresholds.

509 Error bars represent the standard error.

510 **References**

- 511
512
- 513 1. Meyer-Lindenberg, A., et al., *Evidence for abnormal cortical functional connectivity*
514 *during working memory in schizophrenia*. Am J Psychiatry, 2001. **158**(11): p. 1809-
515 17.
 - 516 2. Fletcher, P., et al., *Abnormal cingulate modulation of fronto-temporal connectivity in*
517 *schizophrenia*. Neuroimage, 1999. **9**(3): p. 337-42.
 - 518 3. Haraldsson, H.M., et al., *Transcranial Magnetic Stimulation in the investigation and*
519 *treatment of schizophrenia: a review*. Schizophr Res, 2004. **71**(1): p. 1-16.
 - 520 4. Lawrie, S.M., et al., *Reduced frontotemporal functional connectivity in schizophrenia*
521 *associated with auditory hallucinations*. Biol Psychiatry, 2002. **51**(12): p. 1008-11.
 - 522 5. Tononi, G. and G.M. Edelman, *Schizophrenia and the mechanisms of conscious*
523 *integration*. Brain Res Brain Res Rev, 2000. **31**(2-3): p. 391-400.
 - 524 6. Fuster, J.M., *Synopsis of function and dysfunction of the frontal lobe*. Acta Psychiatr
525 Scand Suppl, 1999. **395**: p. 51-7.
 - 526 7. Friston, K., *Disconnection and cognitive dysmetria in schizophrenia*. Am J Psychiatry,
527 2005. **162**(3): p. 429-32.
 - 528 8. Friston, K.J., *The disconnection hypothesis*. Schizophr Res, 1998. **30**(2): p. 115-25.
 - 529 9. Friston, K.J., *Schizophrenia and the disconnection hypothesis*. Acta Psychiatr Scand
530 Suppl, 1999. **395**: p. 68-79.
 - 531 10. Friston, K.J. and C.D. Frith, *Schizophrenia: a disconnection syndrome?* Clin
532 Neurosci, 1995. **3**(2): p. 89-97.
 - 533 11. Spencer, K.M., et al., *Abnormal neural synchrony in schizophrenia*. J Neurosci, 2003.
534 **23**(19): p. 7407-11.
 - 535 12. Spencer, K.M., et al., *Neural synchrony indexes disordered perception and cognition*
536 *in schizophrenia*. Proc Natl Acad Sci U S A, 2004. **101**(49): p. 17288-93.
 - 537 13. Andreasen, N.C., et al., *Defining the phenotype of schizophrenia: cognitive dysmetria*
538 *and its neural mechanisms*. Biol Psychiatry, 1999. **46**(7): p. 908-20.
 - 539 14. Andreasen, N.C., S. Paradiso, and D.S. O'Leary, *"Cognitive dysmetria" as an*
540 *integrative theory of schizophrenia: a dysfunction in cortical-subcortical-cerebellar*
541 *circuitry?* Schizophr Bull, 1998. **24**(2): p. 203-18.
 - 542 15. Judd, L.L., et al., *Sensory gating deficits in schizophrenia: new results*. Am J
543 Psychiatry, 1992. **149**(4): p. 488-93.
 - 544 16. Braff, D.L. and M.A. Geyer, *Sensorimotor gating and schizophrenia. Human and*
545 *animal model studies*. Arch Gen Psychiatry, 1990. **47**(2): p. 181-8.
 - 546 17. Braff, D.L., C. Grillon, and M.A. Geyer, *Gating and habituation of the startle reflex in*
547 *schizophrenic patients*. Arch Gen Psychiatry, 1992. **49**(3): p. 206-15.
 - 548 18. Braff, D.L., N.R. Swerdlow, and M.A. Geyer, *Gating and habituation deficits in the*
549 *schizophrenia disorders*. Clin Neurosci, 1995. **3**(2): p. 131-9.
 - 550 19. Braff, D.L. and G.A. Light, *Preattentional and attentional cognitive deficits as targets*
551 *for treating schizophrenia*. Psychopharmacology (Berl), 2004. **174**(1): p. 75-85.

- 552 20. Butler, P.D., et al., *Early-stage visual processing and cortical amplification deficits in*
553 *schizophrenia*. Arch Gen Psychiatry, 2005. **62**(5): p. 495-504.
- 554 21. Meincke, U., et al., *Sensitization and habituation of the acoustic startle reflex in*
555 *patients with schizophrenia*. Psychiatry Res, 2004. **126**(1): p. 51-61.
- 556 22. Lindstrom, L., et al., *Abnormal auditory brain-stem responses in hallucinating*
557 *schizophrenic patients*. Br J Psychiatry, 1987. **151**: p. 9-14.
- 558 23. Breitmeyer, B.G., *Visual Masking: An Integrative Approach*. 1984: Oxford University
559 Press.
- 560 24. Breitmeyer, B.G. and H. Ogmen, *Recent models and findings in visual backward*
561 *masking: a comparison, review, and update*. Percept Psychophys, 2000. **62**(8): p.
562 1572-95.
- 563 25. Cadenhead, K.S., Y. Serper, and D.L. Braff, *Transient versus sustained visual*
564 *channels in the visual backward masking deficits of schizophrenia patients*. Biol
565 Psychiatry, 1998. **43**(2): p. 132-8.
- 566 26. Green, M. and E. Walker, *Symptom correlates of vulnerability to backward masking in*
567 *schizophrenia*. Am J Psychiatry, 1986. **143**(2): p. 181-6.
- 568 27. Rund, B.R., *Backward-masking performance in chronic and nonchronic*
569 *schizophrenics, affectively disturbed patients, and normal control subjects*. J Abnorm
570 Psychol, 1993. **102**(1): p. 74-81.
- 571 28. Butler, P.D., et al., *Visual backward-masking deficits in schizophrenia: relationship to*
572 *visual pathway function and symptomatology*. Schizophr Res, 2003. **59**(2-3): p. 199-
573 209.
- 574 29. Schechter, I., et al., *Magnocellular and parvocellular contributions to backward*
575 *masking dysfunction in schizophrenia*. Schizophr Res, 2003. **64**(2-3): p. 91-101.
- 576 30. Bedwell, J.S., J.M. Brown, and L.S. Miller, *The magnocellular visual system and*
577 *schizophrenia: what can the color red tell us?* Schizophr Res, 2003. **63**(3): p. 273-84.
- 578 31. Green, M.F., K.H. Nuechterlein, and J. Mintz, *Backward masking in schizophrenia*
579 *and mania. II. Specifying the visual channels*. Arch Gen Psychiatry, 1994. **51**(12): p.
580 945-51.
- 581 32. Green, M.F., K.H. Nuechterlein, and J. Mintz, *Backward masking in schizophrenia*
582 *and mania. I. Specifying a mechanism*. Arch Gen Psychiatry, 1994. **51**(12): p. 939-44.
- 583 33. Green, M.F., et al., *Visual masking as a probe for abnormal gamma range activity in*
584 *schizophrenia*. Biol Psychiatry, 2003. **53**(12): p. 1113-9.
- 585 34. Green, M.F., et al., *Backward masking in unmedicated schizophrenic patients in*
586 *psychotic remission: possible reflection of aberrant cortical oscillation*. Am J
587 Psychiatry, 1999. **156**(9): p. 1367-73.
- 588 35. Shelley-Tremblay, J. and A. Mack, *Metacontrast Masking and Attention*.
589 Psychological Science, 1999. **10**(6): p. 508-515.
- 590 36. Williams, M.C. and N. Weisstein, *Spatial frequency response and perceived depth in*
591 *the time-course of object superiority*. Vision Res, 1981. **21**(5): p. 631-46.
- 592 37. Lamme, V.A. and P.R. Roelfsema, *The distinct modes of vision offered by feedforward*
593 *and recurrent processing*. Trends Neurosci, 2000. **23**(11): p. 571-9.
- 594 38. Lamme, V.A., K. Zipser, and H. Spekreijse, *Masking interrupts figure-ground signals*
595 *in V1*. J Cogn Neurosci, 2002. **14**(7): p. 1044-53.
- 596 39. Dehaene, S. and L. Naccache, *Towards a cognitive neuroscience of consciousness:*
597 *Basic evidence and a workspace framework*. Cognition, 2001. **79**: p. 1-37.
- 598 40. Dehaene, S., C. Sergent, and J.P. Changeux, *A neuronal network model linking*
599 *subjective reports and objective physiological data during conscious perception*. Proc
600 Natl Acad Sci U S A, 2003. **100**: p. 8520-8525.

- 601 41. Dehaene, S. and J.P. Changeux, *Neural mechanisms for access to consciousness*, in
602 *The cognitive neurosciences, 3rd edition.*, M. Gazzaniga, Editor. 2004, Norton: New
603 York. p. 1145-1157.
- 604 42. Ramachandran, V.S. and S. Cobb, *Visual attention modulates metacontrast masking*.
605 *Nature*, 1995. **373**(6509): p. 66-8.
- 606 43. King, D.L., J.F. Mose, and N.S. Nixon, *One line decreases the visibility of a*
607 *simultaneous identical distant second line*. *Percept Psychophys*, 1995. **57**(3): p. 393-
608 401.
- 609 44. Di Lollo, V., J.T. Enns, and R.A. Rensink, *Competition for consciousness among*
610 *visual events: the psychophysics of reentrant visual processes*. *J Exp Psychol Gen*,
611 2000. **129**(4): p. 481-507.
- 612 45. Enns, J.T. and V. Di Lollo, *What's new in visual masking?* *Trends Cogn Sci*, 2000.
613 **4**(9): p. 345-352.
- 614 46. Dehaene, S., M. Kerszberg, and J.P. Changeux, *A neuronal model of a global*
615 *workspace in effortful cognitive tasks*. *Proc Natl Acad Sci U S A*, 1998. **95**(24): p.
616 14529-34.
- 617 47. Sergent, C. and S. Dehaene, *Is consciousness a gradual phenomenon? Evidence for an*
618 *all-or-none bifurcation during the attentional blink*. *Psychol Sci*, 2004. **15**(11): p. 720-
619 8.
- 620 48. Sergent, C., S. Baillet, and S. Dehaene, *Timing of the brain events underlying access*
621 *to consciousness during the attentional blink*. *Nat Neurosci*, 2005. **8**(10): p. 1391-400.
- 622 49. Dehaene, S., *The neural bases of subliminal priming*, in *Functional Neuroimaging of*
623 *Visual Cognition (Attention and Performance Series, 20)*, N. Kanwisher and J.
624 Duncan, Editors. 2004, Oxford University Press: New York.
- 625 50. Dehaene, S., et al., *Letter binding and invariant recognition of masked words:*
626 *behavioral and neuroimaging evidence*. *Psychol Sci*, 2004. **15**(5): p. 307-13.
- 627 51. Naccache, L. and S. Dehaene, *Unconscious semantic priming extends to novel unseen*
628 *stimuli*. *Cognition*, 2001. **80**(3): p. 215-29.
- 629 52. Greenwald, A.G., S.C. Draine, and R.L. Abrams, *Three cognitive markers of*
630 *unconscious semantic activation*. *Science*, 1996. **273**(5282): p. 1699-702.
- 631 53. Dehaene, S., et al., *Cerebral mechanisms of word masking and unconscious repetition*
632 *priming*. *Nat Neurosci*, 2001. **4**(7): p. 752-8.
- 633 54. Dehaene, S., et al., *Imaging unconscious semantic priming*. *Nature*, 1998. **395**: p. 597-
634 600.
- 635 55. Dehaene, S., et al., *Conscious and subliminal conflicts in normal subjects and patients*
636 *with schizophrenia: the role of the anterior cingulate*. *Proc Natl Acad Sci U S A*,
637 2003. **100**(23): p. 13722-7.
- 638 56. Vorberg, D., et al., *Different time courses for visual perception and action priming*.
639 *Proc Natl Acad Sci U S A*, 2003. **100**(10): p. 6275-80.
- 640 57. Sergent, C., S. Baillet, and S. Dehaene, *Timing of the brain events underlying access*
641 *to consciousness during the attentional blink*. *Nature Neuroscience*, 2005(In Press).
- 642 58. Liddle, P.F., *The symptoms of chronic schizophrenia: a re-examination of the positive-*
643 *negative dichotomy*. *British Journal of Psychiatry*, 1987. **151**: p. 145-151.
- 644 59. Liddle, P.F., et al., *Signs and Symptoms of Psychotic Illness (SSPI): a rating scale*. *Br*
645 *J Psychiatry*, 2002. **180**: p. 45-50.
- 646 60. Koechlin, E., et al., *Primed numbers: Exploring the modularity of numerical*
647 *representations with masked and unmasked semantic priming*. *Journal of*
648 *Experimental Psychology: Human Perception and Performance*, 1999. **25**: p. 1882-
649 1905.

- 650 61. Minzenberg, M.J., B.A. Ober, and S. Vinogradov, *Semantic priming in schizophrenia: a review and synthesis*. J Int Neuropsychol Soc, 2002. **8**(5): p. 699-720.
- 651
- 652 62. Condray, R., et al., *Automatic activation of the semantic network in schizophrenia: evidence from event-related brain potentials*. Biol Psychiatry, 2003. **54**(11): p. 1134-48.
- 653
- 654
- 655 63. Baving, L., et al., *Increased semantic and repetition priming in schizophrenic patients*. J Abnorm Psychol, 2001. **110**(1): p. 67-75.
- 656
- 657 64. Kallstrand, J., et al., *Auditory masking experiments in schizophrenia*. Psychiatry Res, 2002. **113**(1-2): p. 115-25.
- 658
- 659 65. Keri, S., et al., *Visual-perceptual dysfunctions are possible endophenotypes of schizophrenia: evidence from the psychophysical investigation of magnocellular and parvocellular pathways*. Neuropsychology, 2005. **19**(5): p. 649-56.
- 660
- 661
- 662 66. Kim, D., et al., *Magnocellular contributions to impaired motion processing in schizophrenia*. Schizophr Res, 2005.
- 663
- 664 67. Green, M.F., K.H. Nuechterlein, and B. Breitmeyer, *Backward masking performance in unaffected siblings of schizophrenic patients. Evidence for a vulnerability indicator*. Arch Gen Psychiatry, 1997. **54**(5): p. 465-72.
- 665
- 666
- 667 68. Butler, P.D., et al., *Dysfunction of early-stage visual processing in schizophrenia*. Am J Psychiatry, 2001. **158**(7): p. 1126-33.
- 668
- 669 69. Foxe, J.J., G.M. Doniger, and D.C. Javitt, *Early visual processing deficits in schizophrenia: impaired P1 generation revealed by high-density electrical mapping*. Neuroreport, 2001. **12**(17): p. 3815-20.
- 670
- 671
- 672 70. Doniger, G.M., et al., *Impaired visual object recognition and dorsal/ventral stream interaction in schizophrenia*. Arch Gen Psychiatry, 2002. **59**(11): p. 1011-20.
- 673
- 674 71. Foxe, J.J., M.M. Murray, and D.C. Javitt, *Filling-in in schizophrenia: a high-density electrical mapping and source-analysis investigation of illusory contour processing*. Cereb Cortex, 2005. **15**(12): p. 1914-27.
- 675
- 676
- 677 72. Carter, C.S., et al., *Anterior cingulate gyrus dysfunction and selective attention deficits in schizophrenia: [15O]H2O PET study during single-trial Stroop task performance*. Am J Psychiatry, 1997. **154**(12): p. 1670-5.
- 678
- 679
- 680 73. Cohen, J.D., T.S. Braver, and R.C. O'Reilly, *A computational approach to prefrontal cortex, cognitive control and schizophrenia: recent developments and current challenges*. Philos Trans R Soc Lond B Biol Sci, 1996. **351**(1346): p. 1515-27.
- 681
- 682
- 683 74. Frith, C.D., S. Blakemore, and D.M. Wolpert, *Explaining the symptoms of schizophrenia: abnormalities in the awareness of action*. Brain Res Brain Res Rev, 2000. **31**(2-3): p. 357-63.
- 684
- 685
- 686 75. Frith, C. and R. Dolan, *The role of the prefrontal cortex in higher cognitive functions*. Brain Res Cogn Brain Res, 1996. **5**(1-2): p. 175-81.
- 687
- 688 76. Frith, C., *The role of the prefrontal cortex in self-consciousness: the case of auditory hallucinations*. Philos Trans R Soc Lond B Biol Sci, 1996. **351**(1346): p. 1505-12.
- 689
- 690 77. Frith, C.D., *Consciousness, information processing and schizophrenia*. Br J Psychiatry, 1979. **134**: p. 225-35.
- 691
- 692 78. Naccache, L., E. Blandin, and S. Dehaene, *Unconscious masked priming depends on temporal attention*. Psychological Science, 2002. **13**: p. 416-424.
- 693
- 694 79. Goldman-Rakic, P.S., *The physiological approach: functional architecture of working memory and disordered cognition in schizophrenia*. Biol Psychiatry, 1999. **46**(5): p. 650-61.
- 695
- 696
- 697 80. Goldman-Rakic, P.S., *Working memory dysfunction in schizophrenia*. J Neuropsychiatry Clin Neurosci, 1994. **6**(4): p. 348-57.
- 698

- 699 81. Dehaene, S. and J.P. Changeux, *Ongoing spontaneous activity controls access to*
700 *consciousness: a neuronal model for inattentive blindness*. PLoS Biol, 2005. **3**(5): p.
701 e141.
- 702 82. Breakspear, M., et al., *A disturbance of nonlinear interdependence in scalp EEG of*
703 *subjects with first episode schizophrenia*. Neuroimage, 2003. **20**(1): p. 466-78.
- 704 83. Lee, K.H., et al., *Synchronous gamma activity: a review and contribution to an*
705 *integrative neuroscience model of schizophrenia*. Brain Res Brain Res Rev, 2003.
706 **41**(1): p. 57-78.
- 707 84. Lim, K.O., et al., *Compromised white matter tract integrity in schizophrenia inferred*
708 *from diffusion tensor imaging*. Arch Gen Psychiatry, 1999. **56**(4): p. 367-74.
- 709 85. Burns, J., et al., *Structural disconnectivity in schizophrenia: a diffusion tensor*
710 *magnetic resonance imaging study*. Br J Psychiatry, 2003. **182**: p. 439-43.
- 711 86. Wolkin, A., et al., *Inferior frontal white matter anisotropy and negative symptoms of*
712 *schizophrenia: a diffusion tensor imaging study*. Am J Psychiatry, 2003. **160**(3): p.
713 572-4.
- 714 87. Wang, F., et al., *Anterior cingulum abnormalities in male patients with schizophrenia*
715 *determined through diffusion tensor imaging*. Am J Psychiatry, 2004. **161**(3): p. 573-
716 5.
- 717 88. Kubicki, M., et al., *A review of diffusion tensor imaging studies in schizophrenia*. J
718 Psychiatr Res, 2005.
- 719 89. Kubicki, M., et al., *DTI and MTR abnormalities in schizophrenia: analysis of white*
720 *matter integrity*. Neuroimage, 2005. **26**(4): p. 1109-18.
- 721 90. Kubicki, M., et al., *Cingulate fasciculus integrity disruption in schizophrenia: a*
722 *magnetic resonance diffusion tensor imaging study*. Biol Psychiatry, 2003. **54**(11): p.
723 1171-80.
- 724 91. Kubicki, M., et al., *Uncinate fasciculus findings in schizophrenia: a magnetic*
725 *resonance diffusion tensor imaging study*. Am J Psychiatry, 2002. **159**(5): p. 813-20.
- 726 92. Szeszko, P.R., et al., *White matter abnormalities in first-episode schizophrenia or*
727 *schizoaffective disorder: a diffusion tensor imaging study*. Am J Psychiatry, 2005.
728 **162**(3): p. 602-5.
729
730
731
732