ORIGINAL ARTICLE

Preserved Subliminal Processing and Impaired Conscious Access in Schizophrenia

Antoine Del Cul, MD; Stanislas Dehaene, PhD; Marion Leboyer, MD, PhD

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

Objective: To test the hypothesis that the backward-masking deficit in schizophrenia corresponds to a deficit in the late stages of conscious perception, whereas the subliminal processing of masked stimuli is fully preserved.

Design: Twenty-eight patients with schizophrenia and 28 normal control subjects performed 2 backward-masking experiments. We used Arabic digits as stimuli and varied quasi-continuously the interval with a subsequent mask, thus allowing us to progressively unmask the stimuli. We finely quantified their degree of visibility using objective and subjective measures to evaluate the threshold duration for access to consciousness. We also studied the priming effect caused by the variably masked numbers in a comparison task performed on a subsequently presented and highly visible target number.

Results: The threshold delay between the digit and mask necessary for the conscious perception of the masked stimulus was longer in patients compared with controls. This higher consciousness threshold in patients was confirmed by an objective and a subjective measure, and both measures were highly correlated for the patients and controls. However, subliminal priming of masked numbers was effective and identical in patients and controls.

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

Arch Gen Psychiatry. 2006;63:1313-1323

Author Affiliations: Institut National de la Santé et de la Recherche Médicale (INSERM), Cognitive Neuroimaging Unit, Service Hospitalier Frédéric Joliot, Commissariat à l'Energie Atomique, Orsay, France (Drs Del Cul and Dehaene); Departement hospitalo-universitaire de Psychiatrie, Hôpital Albert Chenevier et Henri Mondor, Assistance Publique–Hôpitaux de Paris (Drs Del Cul and Leboyer), and Unite INSERM U 513, Neurobiologie et Psychiatrie, Hôpital Henri Mondor (Drs Del Cul and Leboyer), Creteil, France; and Collège de France, Paris, France (Dr Dehaene).

A FUNCTIONAL BREAKDOWN of large-scale cortical integrative processes caused by abnormal corticocortical and corticosubcortical long-range connectivity is postulated in schizophrenia.[1-14] A crucial issue concerns whether, in addition to this deficit at the level of cognitive integration, patients with schizophrenia also have other possibly unrelated deficits of a lower and more modular nature.[15-22] Indeed, some experimental results arising from studies of visual backward masking have suggested a low-level visual deficit. In visual backward masking, the visibility of a briefly presented stimulus is reduced by a mask presented shortly after the stimulus.[23,24] Patients with schizophrenia consistently show a deficit in the perception of backward-masked stimuli. Compared with normal control subjects, they require a longer interval between the stimulus and mask to identify the stimulus.[25-27]

Breitmeyer and Ogmen[23,24] have proposed a model in which masking depends on the interactions between transient (magnocellular) and sustained (parvocellular) channels within the early visual pathways. In that model, backward masking would occur when the transient channels of the mask interfere with the sustained channels of the stimulus and therefore interrupt the formation of the percept. Abnormal masking in schizophrenia would be linked to deficits in transient magnocellular channels.[25,28-32] An additional deficit in sustained channels (causing abnormal gamma-range activity) has also been proposed.[33,34]

More recently, however, new models of masking have appeared, according to

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

The global workplace model, like most current models of masking, suggests that the initial feed-forward processing of masked stimuli can be largely intact, despite their reduced subjective visibility. This hypothesis is largely confirmed by studies of subliminal priming. In those studies, a masked shape called the *prime* is shown to influence the processing of a subsequent target stimulus. Behavioral and neuroimaging studies of subliminal priming suggest that the processing of stimuli made subjectively invisible by masking is extensive and can include visual recognition, but also lexical and even semantic levels.[49-53] In particular, Dehaene et al[54] demonstrated a nonconscious motor conflict induced by masked primes during a number comparison task. Most relevant to present purposes, they showed that patients with schizophrenia showed a normal masked priming effect, but became disproportionately slower and showed an absence of conflict, relative to controls, when the primes were unmasked.[55] These data, which suggested intact low-level visual processes and abnormal higher-level executive control in schizophrenia, were related to a major hypoactivation of prefrontal and anterior cingulate cortices. Dehaene et al[55] tentatively suggested that the lack of top-down amplification from these areas might jointly explain the higher-level cognitive deficits and the change in the visual masking threshold in patients with schizophrenia.

The main purpose of the present study was to provide a further test of the hypothesis that the backward-masking deficit in schizophrenia corresponds to a deficit in the late stages of conscious perception. Our aim was to evaluate whether the bottom-up subliminal processing of masked stimuli is preserved by studying whether normal subliminal priming could be observed in schizophrenia. We used a new form of masking with a component of spatial attention, inspired by Vorberg et al[56] and Di Lollo et al,[44,45] in which the stimulus and mask shapes are not overlapping. Using Arabic digits as stimuli, we varied quasi-continuously the interval between a digit and the subsequent mask, thus allowing us to progressively unmask the stimulus. This manipulation allowed us to study the subliminal priming effect caused by these variably masked numbers, as well as their degree of visibility, and to precisely quantify the threshold duration for access to consciousness. Based on the global neuronal workplace model of conscious access, the following predictions were made: (1) Masking should affect conscious visibility in an all-or-none manner, ie, either the stimulus is fully consciously perceived or it is not perceived at all. (2) The threshold for conscious access should be higher in patients than in controls, ie, a longer interval between stimulus and mask should be necessary for them to identify the stimulus. (3) The subliminal processing of nonconsciously perceived stimuli, measured by their priming effect, should be preserved and identical in the 2 groups. Thus, we expected response times to be faster when the prime provided some valid information about the target, ie, about its exact identity (repetition priming) or about the nature of the forthcoming response (response priming). The preservation of both priming effects would constitute strong evidence in favor of preserved fast bottom-up perceptual processing in schizophrenia.

METHODS

PARTICIPANTS

Twenty-eight patients with schizophrenia (mean age, 34 years; age range, 18-53 years; 9 women and 19 men) participated in the study. All were native French speakers. Patients met *DSM-IV* criteria for schizophrenia 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. Twenty-two patients were treated with atypical antipsychotics and 6 with typical antipsychotics. This treatment had been unchanged for at least 3 weeks. The comparison group consisted of 28 subjects (mean age, 32 years; age range, 18-55 years; 18 men and 10 women). Comparison subjects were excluded for history of any psychotic disorder, bipolar disorder, schizotypal or paranoid personality disorder, and recurrent depression. Patients and controls with a history of brain injury, epilepsy, alcohol or other drug abuse, or other neurological or ophthalmologic disorders were excluded. Patients and controls did not differ significantly in sex, age, or level of education.

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

STIMULI

In our material, a first number, the prime, was masked by a shape containing in its structure a second number, the target (**Figure 1**). We varied quasi-continuously the interval between the prime and the subsequent mask, thus allowing us to progressively unmask the stimulus digit. The delay between the onset of the prime and the onset of the mask could take 1 of 8 values (0, 16, 33, 50, 66, 83, 100, and 150 milliseconds). For the delay of 0 milliseconds, the prime and the mask had the same onset, but the mask persisted after the prime had disappeared.

The stimulus set consisted of 16 pairs of prime and target numbers. The pairs consisted of the numbers 1, 4, 6, and 9 written in Arabic format. As a consequence, the following factors could be analyzed: target distance (close to or far from 5), tar-

get size (larger or smaller than 5), response congruity (whether or not the prime and target fell on the same side of 5), and repetition (within the congruent trials, whether or not the prime and target were the same number).

PROCEDURE

One part of the experiment was dedicated to a measurement of objective and subjective thresholds. We measured an objective visibility threshold by examining subjects' ability to perform a number comparison task on the prime. We also measured a subjective threshold by collecting introspective ratings of prime visibility on a subjective continuous scale identical to the one used in previous studies of the attentional blink.[40,47,48] The experiment consisted of 20 training trials followed by 20 trials for each delay, for a total of 180 randomly presented trials.

Another part evaluated subliminal and supraliminal priming. Subjects were asked to compare each target number with 5, pressing the right-hand key as fast as possible for numbers larger than 5 and the left-hand key for numbers smaller than 5. This experiment consisted of 20 training trials followed by 320 experimental trials (8 blocks of 40 trials, with 1 block for each delay). The different delays were presented in random order but in different blocks to facilitate the subject's task. If the delays had been randomly mixed, we believed it would have been too difficult for patients to avoid responding to the prime on conscious trials. Blocking helped them to learn to focus on the target and neglect the prime, regardless of its visibility. For similar reasons, the priming experiment, which was the most difficult, was always run before threshold measurement.

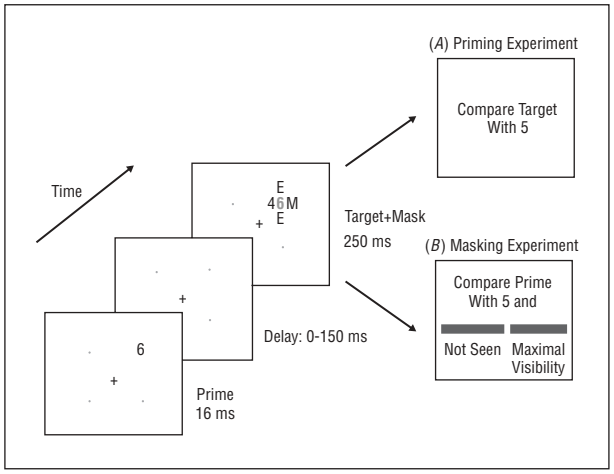

Figure 1. Experiment design. The prime was presented for 16 milliseconds at 1 of 4 positions (1.4° above or below and 1.4° to the right or to the left of the fixation cross). The mask (duration of presentation, 250 milliseconds) was composed of 3 letters (*M*, *M*, and *E*) and the target number (1° from the fixation cross). Those 4 symbols surrounded the prime number without touching it. In the first experiment, referred to as the priming experiment, subjects were asked to compare each target number with 5, pressing the right-hand key as fast as possible for numbers larger than 5 and the left-hand key for numbers smaller than 5. The second experiment aimed at measuring the consciousness threshold in 2 different ways. We measured an objective visibility threshold by examining the subjects' ability to perform the number comparison task on the prime. We also measured a subjective threshold by collecting introspective ratings of prime visibility, on a subjective continuous scale.

RESULTS

MEASURING THE THRESHOLD FOR ACCESS TO CONSCIOUSNESS

Figure 2 and **Figure 3** show the distributions of visibility scores in each group and for each delay on prime-present trials. In both groups, we observed a bimodal repartition of scores, with a first set of responses close to maximal visibility (scale score, >75%) and a second set of responses peaking at zero visibility (score, <25%). Responses ranging from 25% to 75% were rare (<10%). Thus, in both groups, increasing delays did not lead to a progressive increase in subjective experience of prime visibility, but to a shift in the probability of reporting 1 of 2 discrete subjective states ("seen" or "not seen").

Based on this bimodal distribution, we arbitrarily defined seen trials as those in which the visibility score was above the middle of the scale (>50%). **Figure 4**B shows the proportion of seen trials as a function of delay. The proportion increased steadily with delay, but at a slower rate in the patients than in the controls. This pattern was evaluated with an analysis of variance (ANOVA) on the proportion of seen trials, with factors of group and delay. The proportion of seen trials was significantly higher in the controls than in the patients ($F_{1,54}$=12.90 [P<.001]). We also found a significant delay effect ($F_{7,378}$=270.64 [P<.001]) and a group × delay interaction ($F_{7,378}$=8.17 [P<.001]). At all delays longer than 33 milliseconds, the proportion of seen trials was significantly lower in patients (all, P<.05).

A similar analysis was applied to the objective measure of prime processing. For each subject and each delay, we calculated the proportion of correct responses in the prime comparison task (Figure 4A). Again, this measure increased nonlinearly with delay, at a slower rate for the patients than for the controls. An ANOVA indicated that performance was significantly higher in the controls than in the patients (78.2% vs 59.6% correct, $F_{1,54}$=87.53 [P<.001]). There was a main effect of delay ($F_{7,378}$=100.63 [P<.001]) and a group × delay interaction ($F_{7,378}$=5.02 [P<.001]). At each delay, the controls outperformed the patients (all, P<.05). In the controls, performance was significantly superior to chance at all of the delays. However, in the patients, performance became superior to chance only for delays of 50 milliseconds and longer.

In summary, objective and subjective measures of prime conscious perception indicated lower performance in the patients. To characterize for each subject a subjective and an objective threshold for access to consciousness, we used nonlinear regression to fit the curves in Figure 4 with a sigmoid defined in the following equation:

$$f(x) = \alpha_1 + \frac{\alpha_2}{1 + e^{-\alpha_3(x-\alpha_4)}},$$

where the αs represent free parameters. The threshold was defined as the delay for which the sigmoid curve reached its inflexion point, ie, parameter α_4. In all subjects, the fit provided an excellent account of the data (mean r^2=0.95; range, 0.87-1.00). The mean objective threshold was 59 (SD, 13.8; range, 43.0-91.5) milliseconds for controls and 90 (SD, 32.6; range, 47.0-163.5) milliseconds for patients. This threshold was signifi-

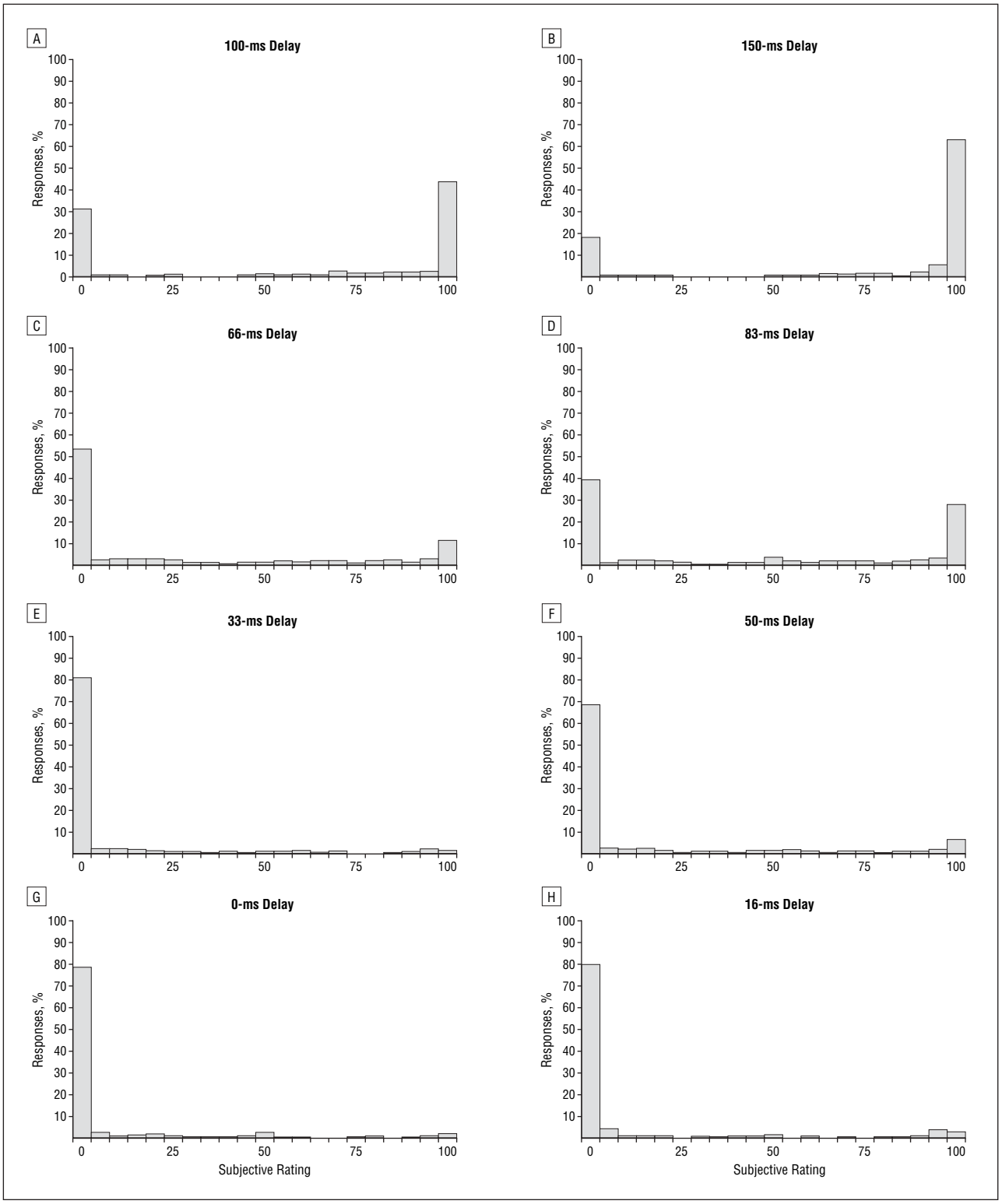

Figure 2. Distribution of subjective visibility ratings in the patient group. In both the patient and control (Figure 3) groups, we observed a bimodal repartition of scores, with a first set of responses close to maximal visibility (scale score, >16) and a second set of responses peaking at zero visibility (score, <6). Responses ranging from 6 to 16 were rare (<10%). More not-seen responses were observed in patients than in controls, particularly at short delays.

cantly higher for patients than for controls (Wilcoxon rank sum test, W+=539 [$P<.001$]). The mean subjective threshold was 62 (SD, 14.7; range, 41-96) milliseconds for controls and 93 (SD, 36.1; range, 47-182) milliseconds for patients. Again, this threshold was significantly higher for patients than for controls (Wilcoxon rank sum test, W+=523 [$P<.001$]).

Figure 5 shows the relation between the individual objective and subjective thresholds. Linear regression showed that the 2 values were highly correlated as a whole

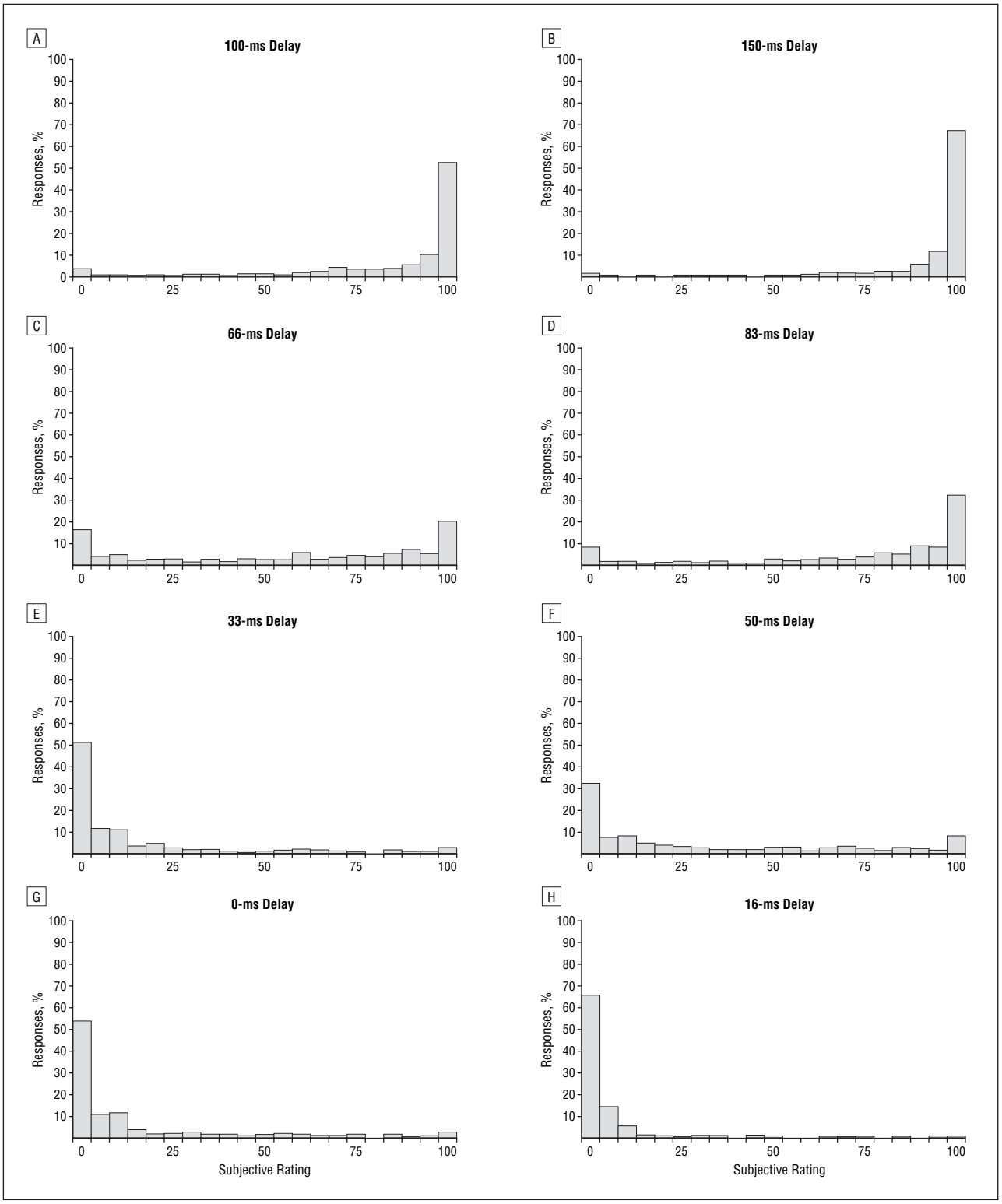

Figure 3. Distribution of subjective visibility ratings in the control group.

(r^2=0.95 [P<.001]), within the controls (r^2=0.83 [P<.001]), and within the patients (r^2=0.96 [P<.001]). In all cases, the slope did not differ from 1, and the intercept was not significant. Thus, the objective and subjective tasks appeared to provide essential identical measures of the threshold for access to consciousness. Those results indicate that our paradigm quantifies this threshold with high cross-task reliability. In the following analyses, we arbitrarily use the objective measure as our index of the conscious access threshold.

Given the large variability in the observed threshold in the patient group, we further studied whether this threshold correlated with the patients' clinical symptoms. To this aim, we used the French translation of the

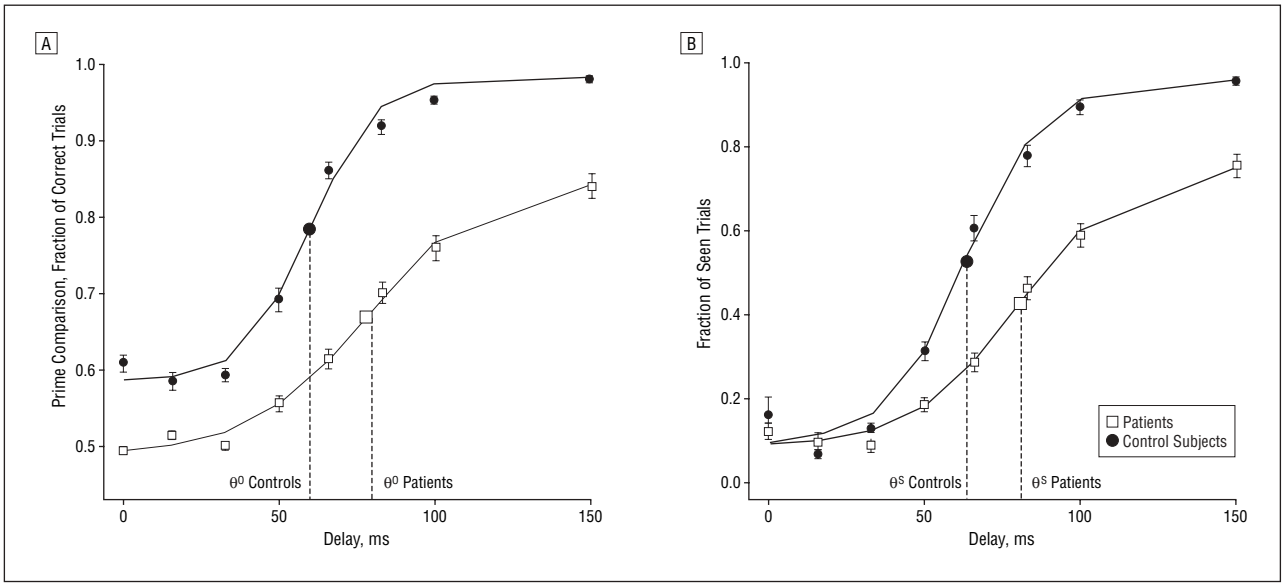

Figure 4. Objective and subjective measures of access to consciousness. A, Percentage of correct responses in the prime comparison with 5 as a function of delay. At each delay, the control subjects outperformed the patients. In controls, performance was significantly superior to chance at all of the delays; in patients, performance became superior to chance only for delays of 50 milliseconds and longer. B, Proportion of trials subjectively rated as "seen" as a function of delay. At all delays longer than 33 milliseconds, the proportion of seen trials was significantly lower in patients. In both graphs, the sigmoid curves fitting the data are represented as continuous lines. The mean objective (θ^o) and subjective (θ^s) thresholds were defined in each group as the delay for which the sigmoid curve reached its inflexion point. Error bars represent the standard error.

Signs and Symptoms of Psychotic Illness Scale.[57,58] The consciousness threshold was positively correlated with psychomotor poverty (Pearson r^2=0.55 [P<.001]), depression (r^2=0.47 [P=.02]), and disorganization (r^2=0.46 [P<.01]). We also found a significant correlation with reality distortion (r^2=0.46 [P=.02]) and, inside this cluster of symptoms, a positive correlation with hallucinations (r^2=0.63 [P<.001]) and delusion (r^2=0.40 [P=.047]).

OCCASIONAL MISMATCH BETWEEN SUBJECTIVE AND OBJECTIVE MEASURES

We further analyzed the rare trials in which subjective and objective measures did not match. One potential cause for such a mismatch is a capacity for subliminal performance in the objective number comparison task, which is known to be partly feasible under subliminal conditions.[51,54,59] As previously shown in Figure 4, for short delays (<50 milliseconds), subjective visibility was around zero and did not differ between groups, but objective performance was above chance for controls only, thus creating a significant difference between the 2 groups. To study whether this phenomenon was imputable to subliminal processing in the control subjects, we analyzed objective performance while restricting ourselves solely to subjectively defined not-seen trials, the latter being defined using a conservative criterion (subjective score, ≤25%).

Figure 6C shows, across delays, the objective performance in each group for not-seen trials, and Figure 6A shows this performance for each delay. Averaged across delays, objective performance on not-seen trials was significantly above chance (50%) in controls (objective performance, 0.60 [P<.001]), indicating some capacity for subliminal number comparison, but not in patients (objective performance, 0.52 [P=.10]). An ANOVA indicated that this performance was significantly superior in controls compared with patients ($F_{1,44}$=19.69 [P<.001]). There was a main effect of delay ($F_{6,230}$=2.70 [P=.02]), indicating that performance increased with delay, without a delay × group interaction ($F_{6,230}$=1.55 [P=.16]).

Another potential cause for mismatch between objective and subjective measures might be a propensity for illusory perception. To objectify the impression that patients had more such illusory perceptions than controls, we analyzed prime comparison performance during subjectively defined seen trials (conservatively defined as a subjective score >75%). The objective performance was 97.1% correct in controls and 90.5% correct in patients (Figure 6B), indicating the presence of comparison errors in both groups, as is usual in response-time experiments. However, using an ANOVA on these percentages, we found that objective performance was significantly higher for controls than for patients ($F_{1,42}$=13.61 [P<.001]). There was a main effect of delay ($F_{6,192}$=16.19 [P<.001]) without a delay × group interaction ($F_{6,192}$=1.06 [P=.39]), indicating that erroneous objective performance was particularly frequent in the controls and in the patients at short delays of 50, 66, and 83 milliseconds.

It seems likely that, at those delays, several patients with schizophrenia experienced illusory perception of the primes, which led them to respond erroneously in the comparison task. Indeed, performance within seen trials averaged across delays was only negatively correlated with hallucinations (r^2=–0.40 [P=.03]), indicating that clinical hallucinations likely were accompanied by visual illusions of seeing the masked prime.

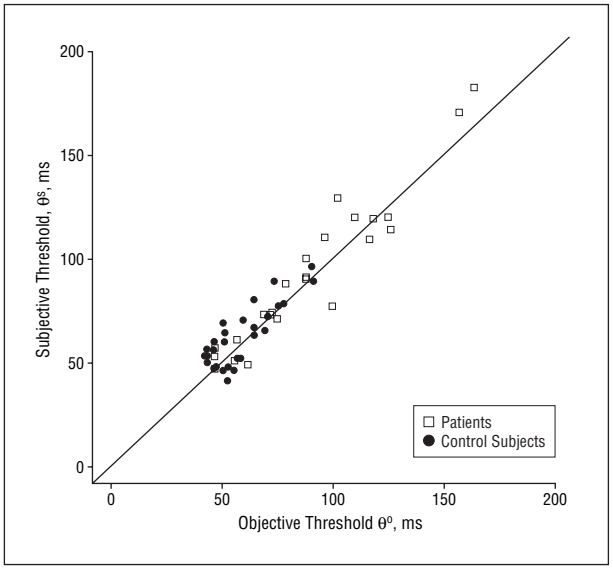

Figure 5. Positive correlation between objective and subjective consciousness thresholds across subjects. The 2 values were highly correlated as a whole (r^2=0.95 [P<.001]), within the control subjects (r^2=0.83 [P<.001]), and within the patients (r^2=0.96 [P<.001]). In all cases, the slope did not differ from 1, and the intercept was not significant.

SUBLIMINAL AND CONSCIOUS PRIMING EFFECTS

We now turn to the priming experiment, in which we measured the ability of the subliminal number prime to influence the processing of the subsequent conscious target. We performed an ANOVA on the error rate and mean reaction time (RT) from all trials with RTs less than 1000 milliseconds (representing 1.5% [SD, 1.7%] of all the trials for the controls and 3.6% [SD, 4.7%] of all the trials for the patients), with factors of group, prime-target relation (congruent repeated, congruent nonrepeated, and incongruent), distance of the target number to 5, and delay.

First, we tested whether the patients and controls differed on number comparison processes. For a similar distance effect, they answered faster for a large distance than for a small distance (37 milliseconds for patients, $F_{1,25}$=130.63 [P<.001]; 46 milliseconds for controls, $F_{1,25}$=144.36 [P<.001]) without a significant distance × group interaction ($F_{1,49}$=2.19 [P=.15]). Furthermore, the error rate in target comparison with 5 was nonsignificantly different between the patients and controls (5.0% vs 4.9% errors [P=.91]). We found a significant effect of delay ($F_{7,364}$=4.46 [P<.001]), indicating that the subjects made more errors for longer delays, without a significant difference between groups ($F_{7,364}$=0.70 [P=.67]).

Figure 7A shows the mean RT for each group, for each condition of prime-target relation and for each delay. Overall, patients were slower than controls (618 vs 513 milliseconds, $F_{1,52}$=21.46 [P<.001]). The main effect of delay was globally significant ($F_{7,364}$=20.59 [P<.001]): RT increased with delay, particularly at the longer delays in which the prime becomes conscious. The main effect of the prime-target relation was significant overall ($F_{2,104}$=91.06 [P<.001]), and a significant delay × relation interaction ($F_{14,728}$=5.33 [P<.001]) indicated that the

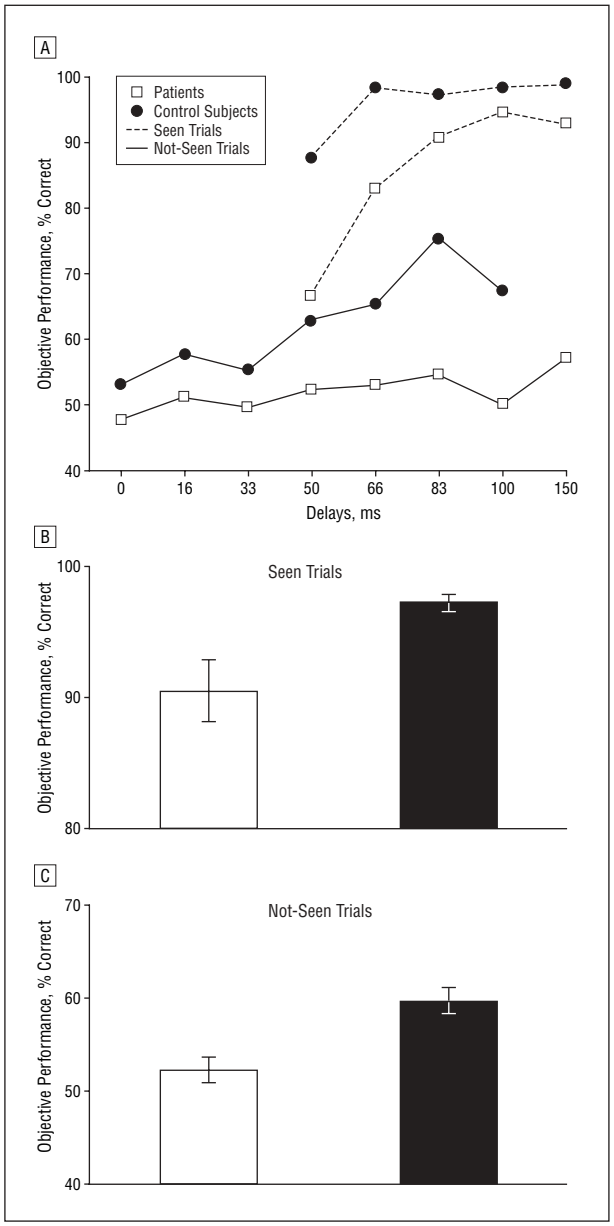

Figure 6. Measures of objective performance in prime comparison in each group for "seen" trials (conservatively defined as a subjective score >16) and "not-seen" trials (subjective score, ≤5). A, Performance at each delay and performance averaged across delays. B, Results for seen trial. C, Results for not-seen trials. The results demonstrate in control subjects a capacity for objective prime processing, even on trials subjectively rated as not seen (subliminal perception) and, conversely, in patients an invalability of objective information on some trials judged as seen (hallucinations). Error bars represent the standard error.

priming effect tended to increase with delay. Crucially, none of these effects interacted with the group. There was no interaction of delay and group ($F_{7,364}$=1.10 [P=.36]) or of prime-target relation and group ($F_{2,104}$=0.02 [P=.99]) or any triple interaction ($F_{14,728}$=1.14 [P=.32]). At each delay, we found no significant difference between groups for the prime-target relation effect. Furthermore, the overall prime-target relation effect was significant in both groups (all, P<.001).

The effect of prime-target relation on RT could be decomposed into the following 2 distinct effects: response

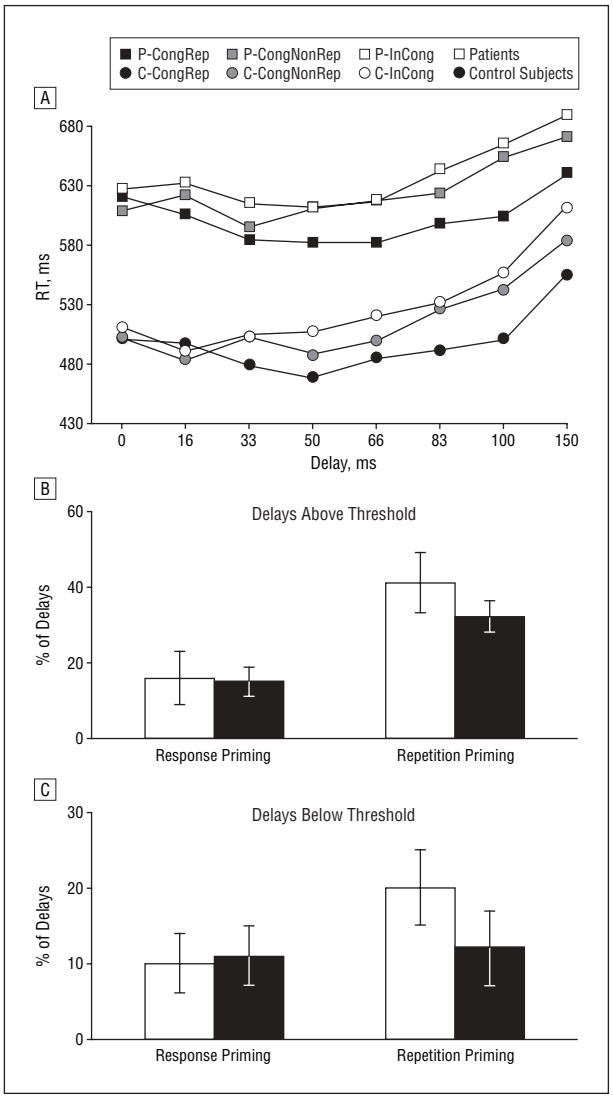

Figure 7. Measures of priming during the target number comparison task. A, Mean reaction time (RT) for each group, each condition of prime-target relation, and each delay. Response priming was defined as the difference in reaction time between incongruent (InCong) and congruent nonrepeated (CongNonRep) trials and repetition priming as the difference between CongNonRep and congruent repeated (CongRep) trials. Both effects were significant across and within each group without significant difference between groups. B and C, Delays were sorted into 2 categories, according to whether they fell above (B) or below (C) the previously measured consciousness thresholds. C indicates control subjects; P, patients. Error bars represent the standard error.

priming and repetition priming. Both effects were significant across and within each group (all, $P<.05$) without significant difference between groups. We then separated the delays into those above and those below the consciousness threshold (60 milliseconds in controls and 90 milliseconds in patients). In both cases, however, priming was not significantly different between groups for repetition priming or for response priming (Figure 7C).

COMMENT

Overall, our results demonstrate the nonlinear character of conscious access, as postulated in the global workplace theory. In both patients and controls, the bimodal distribution of subjective visibility ratings suggests that conscious access corresponds to a discontinuous all-or-none process (with a higher threshold in patients). All subjects were instructed to report even minimal changes in visibility, clarity, or brightness. Indeed, previous research[47] established that normal subjects could do so with remarkable sensitivity, and with continuous changes in their ratings, in a pattern-masking paradigm in which prime duration was manipulated. On the contrary, the bimodal distribution observed herein does not seem attributable to a failure to comply with the instructions but may correspond to a genuine discontinuity in perception during the present object substitution paradigm, as previously observed in an attentional blink paradigm.[47,48] In both cases, the lack of conscious access may be imputable to the all-or-none availability of central top-down attention.

Our experiment allowed us to measure an objective and a subjective threshold within each subject, and we found a good correlation of these 2 measures within each subject and in both groups. Therefore, the variability found in the masking thresholds was not noise but could be considered a genuine interindividual difference between subjects. Furthermore, this threshold captured some of the clinical variability in schizophrenia because we found a positive correlation between conscious threshold and psychomotor poverty dimension, depression, hallucinations, and disorganization. The tight correlation between objective and subjective measures indicates that patients possessed an excellent ability for introspection or metacognition about their vision.

Our results were similar to those of previous studies,[25-34] which also found a backward-masking performance deficit in patients. However, we also demonstrate that the subliminal priming effect is identical between patients and controls. Our results corroborate findings of normal or even enhanced repetition and semantic priming effects in schizophrenia.[60-62] In particular, they replicate previous results in which intact subliminal priming was found for numbers written both in word and in Arabic formats.[55] The preservation of nonconscious repetition and response priming in schizophrenia suggests that the fast feed-forward processing stages that are thought to support these priming effects are largely intact, including early visual analysis, as well as numerical comparison and automatic response programming. On the contrary, the deficit of the patients in perceiving backward-masked stimuli would then be due to a dysfunction in the late stages of conscious perception. Compatible with this interpretation, an auditory masking deficit involving central processes and contrasting with preserved low-level masking has been reported in schizophrenia and was attributed to a deficient central cross-modal stage.[63]

Our finding that even subtle measures of automatic visual processing can be preserved in schizophrenia has to be discussed in the context of the many studies that support a low-level visual dysfunction of the magnocellular pathway in schizophrenia.[20,64,65] Our experiment studied the subliminal processing of stimuli, relying principally on the parvocellular pathway (high-contrast digits and letters). It did not assess the integrity of the magnocellular

response to the stimuli and/or to the mask. Therefore, we cannot exclude the fact that an abnormal bottom-up magnocellular response to the mask contributes to the stronger masking effect in patients, as previously postulated.[20,28-32,66,67] Such a deficit would not affect the processing in the parvocellular pathway, known to project predominantly to ventral visual areas, whereas it might affect the speed or strength of activity in dorsal stream areas where the magnocellular pathway is known to project predominantly. In turn, such a weaker dorsal input may lead to a slower orientation of spatial attention, thus leading to a prolonged period of susceptibility to substitution masking.[44,45] Foxe et al[68,69] and Doniger et al[70] have reported a decrease in a dorsal parietal subcomponent of the visual evoked potential P1, contrasting with preserved processing in the visual ventral stream. Whether this early magnocellular visual impairment and the higher-level conscious access deficit are linked or independent remains uncertain. According to Foxe et al,[68,69] the magnocellular impairment would lead to a deficit in later effortful conceptual processing requiring intact dorsal stream input. Alternatively, the deficit observed with low-contrast visual stimuli and imputed to a magnocellular impairment could be an indirect consequence of impaired parietofrontal networks for top-down effortful processing in schizophrenia, which would induce a deficient top-down amplification of lower-level processing crucial for such tasks. Those 2 possibilities are not necessarily incompatible and remain open for further research.

The hypothesis of a perturbed central stage associated with conscious cognitive control[55,71-76] may explain the elevated threshold for perception of masked stimuli and the observed difference in the ability to exploit subliminal information below that threshold. Normal controls performed the objective prime comparison task better than chance, even on trials for which they reported not seeing the prime; patients, however, remained at chance level in those trials (Figure 4). We speculate that, during this experiment, the normal controls are able to concentrate on the masked stimulus, although there are many trials in which this stimulus cannot be seen. This considerable effort of top-down attention may enable them to subliminally extract some information about the stimulus. Indeed, other experiments have shown that attention can modulate and enhance subliminal processing.[77] This ability to maintain a strong top-down task set in the absence of any visible stimulus, a function that depends particularly on prefrontal resources, may be impaired in schizophrenia.[78,79]

Some patients (approximately 13) occasionally seemed to experience an erroneous perception of the masked stimuli. On a few trials, they reported seeing a number but were wrong when they compared this number with 5, thus suggesting that their introspection did not correspond to reality. Given the design of the experiment, we cannot exclude that some of these responses were merely errors in the comparison task. However, for several reasons, we believe that the phenomenon goes beyond this interpretation. First, during the experiment, although their task only required comparing the prime with 5, some patients verbally reported the prime identity and occasionally gave a verbal response that did not correspond to the digit that was actually presented. Second, such errors on seen trials decreased with delay (Figure 6A) and were frequent only at the intermediate delays of 50 and 66 milliseconds. This pattern would not be expected if the errors resulted merely from a failure to compare a consciously seen digit. Third, across subjects, the occurrence of such errors correlated with a high hallucination score and with an elevated consciousness threshold. What could be the mechanism for such erroneous perceptions? In recent simulations of the global neuronal workplace model, spontaneous activity of neural populations was shown to compete with the entry of external inputs.[80] Thus, for some trials and obviously only for some patients, it is possible that local, spontaneously activated internal representations competed with the concurrent visual input for access to consciousness. Elevated spontaneous activity could simultaneously explain both the elevated threshold and the intrusion of hallucinated digits.

A previous study from our laboratory[55] had revealed impaired conscious priming in patients with schizophrenia. When the prime was made visible by removing the masks, response priming was reduced, whereas repetition priming remained unchanged. In the present study, however, there was no difference between patients and controls at any of the delays, including delays that were supposedly above the consciousness thresholds. A possible explanation is that, even at the longest delays, the mask was always present. This might have helped patients focus their attention on the mask and neglect the prime. Because of this neglect of the prime in the priming task, we think that there was hardly ever a conscious conflict between prime and target for most of the patients, even for the primes presented at the longest delay.

CONCLUSIONS

Our results suggest that the process of access to conscious report of masked stimuli is impaired in schizophrenia, whereas some fast bottom-up processes of visual perception and number comparison are fully preserved. This deficit could be due to anomalies in the recurrent interactions between visual and higher-level associative areas necessary for conscious access. Indeed, a functional disconnection hypothesis of schizophrenia has been proposed, based on abnormal patterns of long-distance correlation in functional neuroimaging studies[4,81,82] and on structural anomalies observed with diffusion tensor imaging in the long-distance white matter bundles, particularly in the frontocingular cortices, the uncinate fasciculus area, and the corpus callosum.[83-91] Although these functional and anatomical anomalies can be plausibly related to an impaired global workplace associated with conscious processing, further experiments are needed to clarify the exact relation between this high-level masking deficit and the lower-level visual abnormalities previously described in schizophrenia.

Submitted for Publication: September 29, 2005; final revision received March 9, 2006; accepted March 10, 2006.
Correspondence: Antoine Del Cul, MD, PhD, Institut National de la Santé et de la Recherche Médicale, Unit 562,

Cognitive Neuroimaging, Service Hospitalier Frédéric Joliot, Commissariat à l'Energie Atomique, 4 place du General Leclere, Orsay, CEDEX 91401, France (antoine.delcul@cea.fr).

Financial Disclosure: None reported.

Funding/Support: This work was supported by grant PHRC AOM98152 from the Assistance Publique–Hôpitaux de Paris, grants from the Fondation pour la Réchèrché Médicale and INSERM, and a centennial fellowship from the McDonnell donation (Dr Dehaene).

Acknowledgment: We thank the following individuals for their help and useful comments: Bertrand Audoin, MD, PhD, Laurent Cohen, MD, PhD, Raphaël Gaillard, MD, Caroline Huron, MD, PhD, Alexandre Meary, MD, Lionel Naccache, MD, PhD, Christophe Pallier, PhD, Jean-Philippe Ranjeva, PhD, Françoise Reuter, Jerome Sackur, PhD, Franck Schürhoff, MD, PhD, Claire Sergent, PhD, and Andrei Szocke, MD, PhD.

REFERENCES

1. Meyer-Lindenberg A, Poline JB, Kohn PD, Holt JL, Egan MF, Weinberger DR, Berman KF. Evidence for abnormal cortical functional connectivity during working memory in schizophrenia. *Am J Psychiatry*. 2001;158:1809-1817.
2. Fletcher P, McKenna PJ, Friston KJ, Frith CD, Dolan RJ. Abnormal cingulate modulation of fronto-temporal connectivity in schizophrenia. *Neuroimage*. 1999; 9:337-342.
3. Haraldsson HM, Ferrarelli F, Kalin NH, Tononi G. Transcranial magnetic stimulation in the investigation and treatment of schizophrenia: a review. *Schizophr Res*. 2004;71:1-16.
4. Lawrie SM, Buechel C, Whalley HC, Frith CD, Friston KJ, Johnstone EC. Reduced frontotemporal functional connectivity in schizophrenia associated with auditory hallucinations. *Biol Psychiatry*. 2002;51:1008-1011.
5. Tononi G, Edelman GM. Schizophrenia and the mechanisms of conscious integration. *Brain Res Brain Res Rev*. 2000;31:391-400.
6. Fuster JM. Synopsis of function and dysfunction of the frontal lobe. *Acta Psychiatr Scand Suppl*. 1999;395:51-57.
7. Friston K. Disconnection and cognitive dysmetria in schizophrenia. *Am J Psychiatry*. 2005;162:429-432.
8. Friston KJ. The disconnection hypothesis. *Schizophr Res*. 1998;30:115-125.
9. Friston KJ. Schizophrenia and the disconnection hypothesis. *Acta Psychiatr Scand Suppl*. 1999;395:68-79.
10. Friston KJ, Frith CD. Schizophrenia: a disconnection syndrome? *Clin Neurosci*. 1995;3:89-97.
11. Spencer KM, Nestor PG, Niznikiewicz MA, Salisbury DF, Shenton ME, McCarley RW. Abnormal neural synchrony in schizophrenia. *J Neurosci*. 2003;23:7407-7411.
12. Spencer KM, Nestor PG, Perlmutter R, Niznikiewicz MA, Klump MC, Frumin M, Shenton ME, McCarley RW. Neural synchrony indexes disordered perception and cognition in schizophrenia. *Proc Natl Acad Sci U S A*. 2004;101:17288-17293.
13. Andreasen NC, Nopoulos P, O'Leary DS, Miller DD, Wassink T, Flaum M. Defining the phenotype of schizophrenia: cognitive dysmetria and its neural mechanisms. *Biol Psychiatry*. 1999;46:908-920.
14. Andreasen NC, Paradiso S, O'Leary DS. "Cognitive dysmetria" as an integrative theory of schizophrenia: a dysfunction in cortical-subcortical-cerebellar circuitry? *Schizophr Bull*. 1998;24:203-218.
15. Judd LL, McAdams L, Budnick B, Braff DL. Sensory gating deficits in schizophrenia: new results. *Am J Psychiatry*. 1992;149:488-493.
16. Braff DL, Geyer MA. Sensorimotor gating and schizophrenia: human and animal model studies. *Arch Gen Psychiatry*. 1990;47:181-188.
17. Braff DL, Grillon C, Geyer MA. Gating and habituation of the startle reflex in schizophrenic patients. *Arch Gen Psychiatry*. 1992;49:206-215.
18. Braff DL, Swerdlow NR, Geyer MA. Gating and habituation deficits in the schizophrenia disorders. *Clin Neurosci*. 1995;3:131-139.
19. Braff DL, Light GA. Preattentional and attentional cognitive deficits as targets for treating schizophrenia. *Psychopharmacology (Berl)*. 2004;174:75-85.
20. Butler PD, Zemon V, Schechter I, Saperstein AM, Hoptman MJ, Lim KO, Revheim N, Silipo G, Javitt DC. Early-stage visual processing and cortical amplification deficits in schizophrenia. *Arch Gen Psychiatry*. 2005;62:495-504.
21. Meincke U, Light GA, Geyer MA, Braff DL, Gouzoulis-Mayfrank E. Sensitization and habituation of the acoustic startle reflex in patients with schizophrenia. *Psychiatry Res*. 2004;126:51-61.
22. Lindstrom L, Klockhoff I, Svedberg A, Bergstrom K. Abnormal auditory brainstem responses in hallucinating schizophrenic patients. *Br J Psychiatry*. 1987; 151:9-14.
23. Breitmeyer BG. *Visual Masking: An Integrative Approach*. New York, NY: Oxford University Press; 1984.
24. Breitmeyer BG, Ogmen H. Recent models and findings in visual backward masking: a comparison, review, and update. *Percept Psychophys*. 2000;62:1572-1595.
25. Cadenhead KS, Serper Y, Braff DL. Transient versus sustained visual channels in the visual backward masking deficits of schizophrenia patients. *Biol Psychiatry*. 1998;43:132-138.
26. Green M, Walker E. Symptom correlates of vulnerability to backward masking in schizophrenia. *Am J Psychiatry*. 1986;143:181-186.
27. Rund BR. Backward-masking performance in chronic and nonchronic schizophrenics, affectively disturbed patients, and normal control subjects. *J Abnorm Psychol*. 1993;102:74-81.
28. Butler PD, DeSanti LA, Maddox J, Harkavy-Friedman JM, Amador XF, Goetz RR, Javitt DC, Gorman JM. Visual backward-masking deficits in schizophrenia: relationship to visual pathway function and symptomatology. *Schizophr Res*. 2003; 59:199-209.
29. Schechter I, Butler PD, Silipo G, Zemon V, Javitt DC. Magnocellular and parvocellular contributions to backward masking dysfunction in schizophrenia. *Schizophr Res*. 2003;64:91-101.
30. Bedwell JS, Brown JM, Miller LS. The magnocellular visual system and schizophrenia: what can the color red tell us? *Schizophr Res*. 2003;63:273-284.
31. Green MF, Nuechterlein KH, Mintz J. Backward masking in schizophrenia and mania, II: specifying the visual channels. *Arch Gen Psychiatry*. 1994;51:945-951.
32. Green MF, Nuechterlein KH, Mintz J. Backward masking in schizophrenia and mania, I: specifying a mechanism. *Arch Gen Psychiatry*. 1994;51:939-944.
33. Green MF, Mintz J, Salveson D, Nuechterlein KH, Breitmeyer B, Light GA, Braff DL. Visual masking as a probe for abnormal gamma range activity in schizophrenia. *Biol Psychiatry*. 2003;53:1113-1119.
34. Green MF, Nuechterlein KH, Breitmeyer B, Mintz J. Backward masking in unmedicated schizophrenic patients in psychotic remission: possible reflection of aberrant cortical oscillation. *Am J Psychiatry*. 1999;156:1367-1373.
35. Shelley-Tremblay J, Mack A. Metacontrast masking and attention. *Psychol Sci*. 1999;10:508-515.
36. Williams MC, Weisstein N. Spatial frequency response and perceived depth in the time-course of object superiority. *Vision Res*. 1981;21:631-646.
37. Lamme VA, Roelfsema PR. The distinct modes of vision offered by feedforward and recurrent processing. *Trends Neurosci*. 2000;23:571-579.
38. Lamme VA, Zipser K, Spekreijse H. Masking interrupts figure-ground signals in V1. *J Cogn Neurosci*. 2002;14:1044-1053.
39. Dehaene S, Naccache L. Towards a cognitive neuroscience of consciousness: basic evidence and a workspace framework. *Cognition*. 2001;79:1-37.
40. Dehaene S, Sergent C, Changeux JP. A neuronal network model linking subjective reports and objective physiological data during conscious perception. *Proc Natl Acad Sci U S A*. 2003;100:8520-8525.
41. Dehaene S, Changeux JP. Neural mechanisms for access to consciousness. In: Gazzaniga M, ed. *The Cognitive Neurosciences*. 3rd ed. New York, NY: WW Norton Co Inc; 2004:1145-1157.
42. Ramachandran VS, Cobb S. Visual attention modulates metacontrast masking. *Nature*. 1995;373:66-68.
43. King DL, Mose JF, Nixon NS. One line decreases the visibility of a simultaneous identical distant second line. *Percept Psychophys*. 1995;57:393-401.
44. Di Lollo V, Enns JT, Rensink RA. Competition for consciousness among visual events: the psychophysics of reentrant visual processes. *J Exp Psychol Gen*. 2000; 129:481-507.
45. Enns JT, Di Lollo V. What's new in visual masking? *Trends Cogn Sci*. 2000;4:345-352.
46. Dehaene S, Kerszberg M, Changeux JP. A neuronal model of a global workspace in effortful cognitive tasks. *Proc Natl Acad Sci U S A*. 1998;95:14529-14534.
47. Sergent C, Dehaene S. Is consciousness a gradual phenomenon? evidence for an all-or-none bifurcation during the attentional blink. *Psychol Sci*. 2004;15: 720-728.
48. Sergent C, Baillet S, Dehaene S. Timing of the brain events underlying access to consciousness during the attentional blink. *Nat Neurosci*. 2005;8:1391-1400.
49. Dehaene S. The neural bases of subliminal priming. In: Kanwisher N, Duncan J, eds. *Functional Neuroimaging of Visual Cognition (Attention and Performance Series, 20)*. New York, NY: Oxford University Press; 2004.
50. Dehaene S, Jobert A, Naccache L, Ciuciu P, Poline JB, Le Bihan D, Cohen L.

Letter binding and invariant recognition of masked words: behavioral and neuroimaging evidence. *Psychol Sci*. 2004;15:307-313.
51. Naccache L, Dehaene S. Unconscious semantic priming extends to novel unseen stimuli. *Cognition*. 2001;80:215-229.
52. Greenwald AG, Draine SC, Abrams RL. Three cognitive markers of unconscious semantic activation. *Science*. 1996;273:1699-1702.
53. Dehaene S, Naccache L, Cohen L, Bihan DL, Mangin JF, Poline JB, Riviere D. Cerebral mechanisms of word masking and unconscious repetition priming. *Nat Neurosci*. 2001;4:752-758.
54. Dehaene S, Naccache L, Le Clec'H G, Koechlin E, Mueller M, Dehaene-Lambertz G, van de Moortele PF, Le Bihan D. Imaging unconscious semantic priming. *Nature*. 1998;395:597-600.
55. Dehaene S, Artiges E, Naccache L, Martelli C, Viard A, Schurhoff F, Recasens C, Martinot ML, Leboyer M, Martinot JL. Conscious and subliminal conflicts in normal subjects and patients with schizophrenia: the role of the anterior cingulate. *Proc Natl Acad Sci U S A*. 2003;100:13722-13727.
56. Vorberg D, Mattler U, Heinecke A, Schmidt T, Schwarzbach J. Different time courses for visual perception and action priming. *Proc Natl Acad Sci U S A*. 2003;100:6275-6280.
57. Liddle PF. The symptoms of chronic schizophrenia: a re-examination of the positive-negative dichotomy. *Br J Psychiatry*. 1987;151:145-151.
58. Liddle PF, Ngan ET, Duffield G, Kho K, Warren AJ. Signs and Symptoms of Psychotic Illness (SSPI): a rating scale. *Br J Psychiatry*. 2002;180:45-50.
59. Koechlin E, Naccache L, Block E, Dehaene S. Primed numbers: exploring the modularity of numerical representations with masked and unmasked semantic priming. *J Exp Psychol Hum Percept Perform*. 1999;25:1882-1905.
60. Minzenberg MJ, Ober BA, Vinogradov S. Semantic priming in schizophrenia: a review and synthesis. *J Int Neuropsychol Soc*. 2002;8:699-720.
61. Condray R, Siegle GJ, Cohen JD, van Kammen DP, Steinhauer SR. Automatic activation of the semantic network in schizophrenia: evidence from event-related brain potentials. *Biol Psychiatry*. 2003;54:1134-1148.
62. Baving L, Wagner M, Cohen R, Rockstroh B. Increased semantic and repetition priming in schizophrenic patients. *J Abnorm Psychol*. 2001;110:67-75.
63. Kallstrand J, Montnemery P, Nielzen S, Olsson O. Auditory masking experiments in schizophrenia. *Psychiatry Res*. 2002;113:115-125.
64. Keri S, Kelemen O, Janka Z, Benedek G. Visual-perceptual dysfunctions are possible endophenotypes of schizophrenia: evidence from the psychophysical investigation of magnocellular and parvocellular pathways. *Neuropsychology*. 2005;19:649-656.
65. Kim D, Wylie G, Pasternak R, Butler PD, Javitt DC. Magnocellular contributions to impaired motion processing in schizophrenia [published online ahead of print December 1, 2005]. *Schizophr Res*. 2006;82:1-8 Medline:16325377.
66. Green MF, Nuechterlein KH, Breitmeyer B. Backward masking performance in unaffected siblings of schizophrenic patients: evidence for a vulnerability indicator. *Arch Gen Psychiatry*. 1997;54:465-472.
67. Butler PD, Schechter I, Zemon V, Schwartz SG, Greenstein VC, Gordon J, Schroeder CE, Javitt DC. Dysfunction of early-stage visual processing in schizophrenia. *Am J Psychiatry*. 2001;158:1126-1133.
68. Foxe JJ, Doniger GM, Javitt DC. Early visual processing deficits in schizophrenia: impaired P1 generation revealed by high-density electrical mapping. *Neuroreport*. 2001;12:3815-3820.
69. Foxe JJ, Murray MM, Javitt DC. Filling-in in schizophrenia: a high-density electrical mapping and source-analysis investigation of illusory contour processing. *Cereb Cortex*. 2005;15:1914-1927.
70. Doniger GM, Foxe JJ, Murray MM, Higgins BA, Javitt DC. Impaired visual object recognition and dorsal/ventral stream interaction in schizophrenia. *Arch Gen Psychiatry*. 2002;59:1011-1020.
71. Carter CS, Mintun M, Nichols T, Cohen JD. Anterior cingulate gyrus dysfunction and selective attention deficits in schizophrenia: $[^{15}O]H_2O$ PET study during single-trial Stroop task performance. *Am J Psychiatry*. 1997;154:1670-1675.
72. Cohen JD, Braver TS, O'Reilly RC. A computational approach to prefrontal cortex, cognitive control and schizophrenia: recent developments and current challenges. *Philos Trans R Soc Lond B Biol Sci*. 1996;351:1515-1527.
73. Frith CD, Blakemore S, Wolpert DM. Explaining the symptoms of schizophrenia: abnormalities in the awareness of action. *Brain Res Brain Res Rev*. 2000;31:357-363.
74. Frith C, Dolan R. The role of the prefrontal cortex in higher cognitive functions. *Brain Res Cogn Brain Res*. 1996;5:175-181.
75. 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;351:1505-1512.
76. Frith CD. Consciousness, information processing and schizophrenia. *Br J Psychiatry*. 1979;134:225-235.
77. Naccache L, Blandin E, Dehaene S. Unconscious masked priming depends on temporal attention. *Psychol Sci*. 2002;13:416-424.
78. Goldman-Rakic PS. The physiological approach: functional architecture of working memory and disordered cognition in schizophrenia. *Biol Psychiatry*. 1999;46:650-661.
79. Goldman-Rakic PS. Working memory dysfunction in schizophrenia. *J Neuropsychiatry Clin Neurosci*. 1994;6:348-357.
80. Dehaene S, Changeux JP. Ongoing spontaneous activity controls access to consciousness: a neuronal model for inattentional blindness [published online ahead of print April 12, 2005]. *PLoS Biol*. 2005;3:e141. doi:10.1371/journal.pbio.0030141. Accessed April 12, 2005.
81. Breakspear M, Terry JR, Friston KJ, Harris AW, Williams LM, Brown K, Brennan J, Gordon E. A disturbance of nonlinear interdependence in scalp EEG of subjects with first episode schizophrenia. *Neuroimage*. 2003;20:466-478.
82. Lee KH, Williams LM, Breakspear M, Gordon E. Synchronous gamma activity: a review and contribution to an integrative neuroscience model of schizophrenia. *Brain Res Brain Res Rev*. 2003;41:57-78.
83. Lim KO, Hedehus M, Moseley M, de Crespigny A, Sullivan EV, Pfefferbaum A. Compromised white matter tract integrity in schizophrenia inferred from diffusion tensor imaging. *Arch Gen Psychiatry*. 1999;56:367-374.
84. Burns J, Job D, Bastin ME, Whalley H, Macgillivray T, Johnstone EC, Lawrie SM. Structural disconnectivity in schizophrenia: a diffusion tensor magnetic resonance imaging study. *Br J Psychiatry*. 2003;182:439-443.
85. Wolkin A, Choi SJ, Szilagyi S, Sanfilipo M, Rotrosen JP, Lim KO. Inferior frontal white matter anisotropy and negative symptoms of schizophrenia: a diffusion tensor imaging study. *Am J Psychiatry*. 2003;160:572-574.
86. Wang F, Sun Z, Cui L, Du X, Wang X, Zhang H, Cong Z, Hong N, Zhang D. Anterior cingulum abnormalities in male patients with schizophrenia determined through diffusion tensor imaging. *Am J Psychiatry*. 2004;161:573-575.
87. Kubicki M, McCarley R, Westin CF, Park HJ, Maier S, Kikinis R, Jolesz FA, Shenton ME. A review of diffusion tensor imaging studies in schizophrenia [published online ahead of print May 3, 2005]. *J Psychiatr Res*. doi:10.1016/j.jpsychires.2005.05.005. Accessed May 3, 2005.
88. Kubicki M, Park H, Westin CF, Nestor PG, Mulkern RV, Maier SE, Niznikiewicz M, Connor EE, Levitt JJ, Frumin M, Kikinis R, Jolesz FA, McCarley RW, Shenton ME. DTI and MTR abnormalities in schizophrenia: analysis of white matter integrity. *Neuroimage*. 2005;26:1109-1118.
89. Kubicki M, Westin CF, Nestor PG, Wible CG, Frumin M, Maier SE, Kikinis R, Jolesz FA, McCarley RW, Shenton ME. Cingulate fasciculus integrity disruption in schizophrenia: a magnetic resonance diffusion tensor imaging study. *Biol Psychiatry*. 2003;54:1171-1180.
90. Kubicki M, Westin CF, Maier SE, Frumin M, Nestor PG, Salisbury DF, Kikinis R, Jolesz FA, McCarley RW, Shenton ME. Uncinate fasciculus findings in schizophrenia: a magnetic resonance diffusion tensor imaging study. *Am J Psychiatry*. 2002;159:813-820.
91. Szeszko PR, Ardekani BA, Ashtari M, Kumra S, Robinson DG, Sevy S, Gunduz-Bruce H, Malhotra AK, Kane JM, Bilder RM, Lim KO. White matter abnormalities in first-episode schizophrenia or schizoaffective disorder: a diffusion tensor imaging study. *Am J Psychiatry*. 2005;162:602-605.