Altered time course of unconscious response priming in schizophrenia patients

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Dear Editors,

in schizophrenia patients, deficits in conscious stimulus identification (Del Cul et al., 2006) and action control (e.g., Weinberger et al., 2001) are well documented. Despite its clinical importance, only a few studies explored unconscious information processing in this psychiatric disorder (e.g., Del Cul et al., 2006; Kiefer et al., 2009): Altered unconscious processing may impact the conscious domain (Kiefer, 2012) and could underlie symptoms such as disorganization of thought and action.

The masked priming paradigm is suitable for investigating unconscious processing (for a review, see Kiefer, 2012). In masked response priming (Eimer and Schlaghecken, 2003), which probes unconscious visuo-motor processes, responses to visible arrows are faster when preceded by directionally congruent masked prime arrows that cannot be consciously perceived (positive compatibility effect, PCE). Earlier studies in schizophrenia patients using different variants of masked priming paradigms observed intact (Del Cul et al., 2006; Huddy et al., 2009) or even increased unconscious priming (Kiefer et al., 2009), in the presence of deficits in conscious stimulus processing (Del Cul et al., 2006; Huddy et al., 2009; Kiefer et al., 2009) suggesting that unconscious processes remain intact.

It is possible, however, that the temporal dynamics of unconscious processing differ between schizophrenia patients and healthy controls. In healthy participants, masked response priming typically varies as a function of the temporal delay between the prime and the target (stimulus onset asynchrony, SOA) (Eimer and Schlaghecken, 2003): At SOAs ≤ 100 ms, the above described PCE is observed. At SOAs > 100 ms, the PCE decreases or even changes to a negative compatibility effect (NCE) with slower response in the congruent condition, presumably indexing unconscious response inhibition. Although an intact NCE in patients with recent onset schizophrenia was reported (Huddy et al., 2009), the temporal dynamics of unconscious response preparation in schizophrenia deserves further clarification. Here, we therefore investigated the time course of masked response priming in patients with schizophrenia and matched healthy controls by systematically varying the prime-target SOA at three levels (67 ms, 150 ms, 230 ms).

Twenty-one healthy control participants and 21 medicated patients with schizophrenia (20) or schizophreniform disorder (1) according to DSM-IV criteria contributed data to this
study (see also supplementary methods). All participants were right-handed with normal or corrected-to-normal vision and without any signs of neurological illnesses according to a standardized in-house questionnaire (for clinical and demographic data see Supplementary Table 1). Psychiatric diagnoses were based on the Structured Clinical Interview for DSM-IV. Psychopathology of the patients was rated using the Positive and Negative Syndrome Scale, PANSS. Patients were free from other DSM-IV axes I or II disorders. Controls were screened for psychiatric illnesses using Mini-DIPS and SKID-II interviews. Participant groups did not differ significantly with regard to gender, age, years of education and non-verbal intelligence (LPS, scale 3; Horn, 1983). All participants gave written informed consent via the methods approved by the University of Ulm Ethics Committee (No. 150/08).

Participants were presented with left or right pointing arrows as primes and targets (Eimer and Schlaghecken, 2003). They had to press a response key with the index finger of their left or right hand according to the orientation of the target as fast and as accurately as possible. Orientation of the prime and target arrows was either congruent thus requiring the same response or incongruent requiring conflicting responses. Each trial started with a fixation cross for 500 ms, followed by the prime arrow (16.67 ms), a clear screen (16.67 ms), and a pattern mask consisting of lines (66.67 ms). Thereafter, the target arrow was displayed (130 ms), either immediately after the mask, after a clear screen of 50 ms or of 130 ms, resulting in prime-target SOAs of 100 ms, 150 ms or 230 ms. After the response, three hash marks indicated the intertrial interval (1500 ms). Participants were not informed of the presence of the prime. Trial order of the different congruency and SOA conditions (120 trials each) was randomized (see also the supplementary methods).

After the priming experiment, an objective measure of prime visibility was obtained using the same timing parameters as in the main experiment. The only difference was that participants were now instructed to report the orientation of the masked prime. Instructions stressed accuracy over response speed.

For the analysis of reaction times (RT), mean RT of the correct responses was calculated for each condition. In order to account for the overall slowing in patients, we analyzed relative priming scores defined as percentage of facilitation (Spitzer et al., 1993):

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PRI = \left( \frac{RT_{\text{congruent}} - RT_{\text{incongruent}}}{RT_{\text{congruent}}} \right) \times 100.
\]

Prime scores were submitted to a repeated-
measures analysis of variance with the within-subject factor SOA and the between-subject factor group. Using multiple regression, we assessed whether priming scores of the different SOA conditions in the patient group were modulated by clinical (PANSS scores, dose of antipsychotic medication in CPE, duration of illness, number of hospitalizations) and demographic variables (age, education and intelligence).

Identification of the masked primes did not differ from chance level (see also Supplementary Results). Error rate in the target task was low (2.8 %) demonstrating that participants performed the task successfully. Analysis of priming scores (Figure 1) yielded an interaction between group and SOA \( (F(2,80) = 8.98, \text{MS} e = 10.56, p < .0001) \). Subsequent two-tailed one-sample t-tests revealed in controls priming scores significantly greater than zero at SOAs of 100 ms \( (t(20) = 4.73, p < .001) \) and 150 ms \( (t(20) = 3.41, p < .01) \), whereas in patients priming was greater than zero at the SOAs of 150 ms \( (t(20) = 2.70, p < .05) \) and 230 ms \( (t(20) = 2.93, p < .01) \). Between-group comparisons showed that masked priming was larger in controls than in patients at the SOA of 100 ms \( (t(40) = 2.66, p < .05) \). Further analyses confirmed a differential linear trend of priming in the patient and control groups \( (F(1,40) = 11.19, \text{MS} e = 16.06, p < .01) \). Although the NCE was not significant at the SOA=230 ms in the control group, significantly more controls (11) exhibited an NCE than patients (4; \( \chi^2(1) = 5.08, p < .05 \)). Multiple regression analyses did not reveal significant influences of demographic or clinical variables on masked priming. For an analysis of absolute RTs and a regression analysis relating masked priming to prime visibility, see the supplementary results.

Our results indicate a different time course of unconscious response priming in schizophrenia patients compared with healthy controls suggesting deficits in unconscious visuo-motor processing. Schizophrenia patients showed an increase of masked response priming (PCE) as a function of the SOA. Controls, in contrast, exhibited a decrease of the PCE with increasing SOA. The later onset of masked response priming in schizophrenia patients indicates that unconscious visuo-motor processing is delayed, presumably due to a
slower accumulation of prime-related activity in the visuo-motor system (Vorberg et al., 2003). Furthermore, the PCE in the patient group at the longest SOA and the small number of patients with an NCE indicates unconscious response inhibition deficits. Although the NCE was not significant in the control group in contrast to our pilot study, presumably due to an age-related decline of the NCE in older aged participants (Schlaghecken and Maylor, 2005), significantly more controls than patients exhibited an NCE.

The presently observed deficits in unconscious response priming in schizophrenia contrasts with earlier findings of intact unconscious visuo-motor processing (Del Cul et al., 2006; Huddy et al., 2009). This discrepancy in results can be explained by differences in the masking procedure: In these earlier studies, the prime was presented longer than in the present study (>32 ms vs. 16 ms here) or was masked with a non-overlapping mask in contrast to the present pattern mask. Probably, deficits in unconscious visual processing are more apparent in schizophrenia patients when the visual input is relatively weak and strongly masked as in the present experiment so that the signal within the visuo-motor system is small. As our patients were medicated, future studies should explore unconscious processing in unmedicated patients or in high-risk populations.

In conclusion, the present results suggest an altered time course of unconscious visuo-motor processing and action control in schizophrenia patients. Preparation of a motor response induced by an unconscious prime started later and lasted longer in the patient than in the control group. This prolonged response activation in schizophrenia patients indicates unconscious response inhibition deficits similar to the conscious domain (e.g., Huddy et al., 2009; Weinberger et al., 2001).

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References

Del Cul, A., Dehaene, S., & Leboyer, M., 2006. Preserved subliminal processing and impaired conscious access in schizophrenia. Archives of General Psychiatry, 63, 1313-1323.


Huddy, V., Aron, A., Harrison, M., Barnes, T., Robbins, T., & Joyce, E., 2009. Impaired conscious and preserved unconscious inhibitory processing in recent onset schizophrenia. Psychological Medicine, 39, 907-916.


Figure captions

Figure 1: Priming scores (percentage of facilitation) for schizophrenia patients and healthy control participants as a function of the SOA. Note the different time course of unconscious response priming in patients and controls.