Spatial Selective Attention and Inhibition in Schizophrenia Patients during Acute Psychosis and at 4-Month Follow-Up

Sohee Park, Jörg Püschel, Barbara H. Sauter, Markus Rentsch, and Daniel Hell

Background: Attentional abnormalities may lie at the core of cognitive symptoms in schizophrenia, but it is unclear how they relate to symptoms. The major aim of our study was to understand the relation between spatial attention and clinical symptoms from acute to chronic state.

Methods: Thirty-six acutely psychotic schizophrenia patients and 42 matched control subjects were assessed on three spatial attention measures: target location detection, interference (concurrent inhibition of distractor), and negative priming (subsequent inhibition of distractor). Symptoms were assessed by the Positive and Negative Syndrome Assessment Scale. Four months later, the same subjects were re-tested, and symptoms were re-assessed.

Results: Symptoms were significantly reduced at the follow-up. Schizophrenia patients were slower at detecting target location than control subjects, but they improved significantly over time. Schizophrenia patients and control subjects did not differ on the interference task. Negative priming was abolished during acute psychosis, but 4 months later it was restored. Positive symptoms were correlated with reduced negative priming but not with interference, nor with target detection. Negative priming during acute psychosis was significantly correlated with the clinical symptoms at the follow-up.

Conclusions: These results suggest that reduced negative priming may be associated with increased clinical symptoms especially the positive symptoms. Biol Psychiatry 2002;51:498–506 © 2002 Society of Biological Psychiatry

Key Words: Schizophrenia, attention, inhibition, positive and negative symptoms

Introduction

Abnormalities of attention and inhibition form the core of cognitive symptoms in schizophrenia. For example, an inability to focus on the relevant stimuli while ignoring the irrelevant is a cardinal feature of acute schizophrenia (McGhie and Chapman 1962; Shakow 1962). Patients with schizophrenia display weakened inhibition in a wide range of tasks: impaired sensory gating (McDowd et al 1993), reduced prepulse inhibition (Braff et al 1992), reduced latent inhibition (Baruch et al 1988), diminished Kamin blocking effect (Jones et al 1992), increased interference on the Stroop task (Carter et al 1997), increased errors on the antisaccade task (Fukushima et al 1988), and reduced or abolished negative priming (Beech et al 1990; Park et al 1996). Disrupted inhibition presumably allows irrelevant stimuli to intrude during information processing (e.g., Claridge 1967; Frith 1993; Hemsley 1987) and contribute to the increased distractibility observed in schizophrenia patients at all levels of cognitive processing. Indeed, impaired attentional or cognitive inhibition has been associated with some of the positive symptoms of schizophrenia (Gray et al 1991).

Cognitive or attentional inhibition can be assessed by a very simple paradigm known as negative priming, which was originally developed to assess the inhibitory component of selective attention (Tipper 1985). Selective attention is hypothesized to be achieved by at least two mechanisms: one involving an excitatory process associated with the target stimulus and the other an inhibitory mechanism that is associated with the ignored stimulus (Neill and Westberry 1987). The negative priming paradigm involves two steps. The initial stage involves an exposure to irrelevant stimuli that are to be ignored. When a stimulus is ignored during a selective attention task, its internal representation is hypothesized to be associated with inhibitory processes. The second step involves the selection of previously ignored stimuli. One important consequence of such inhibitory influences is that the later selection of the ignored stimulus increases the reaction
time. Previous exposure retards (rather than facilitates) later response. Thus, negative priming effect refers to the increased latency to respond to a stimulus that had been recently inhibited (Tipper 1985).

Reduced or abolished negative priming has been demonstrated in schizophrenia patients using Stroop-like interference tasks (e.g., Beech et al 1989; Laplante et al 1992), but others have found no evidence for reduced inhibition (Moritz et al 2000). Spatial negative priming, which minimizes the linguistic and cognitive demands, has also been shown to be impaired in schizophrenia patients (Fuller et al 2000; Park et al 1996). Moreover, reduced cognitive inhibition has been associated with acute psychosis (see Gray et al 1991). For example, differences between acutely psychotic and chronic schizophrenia patients have been found in the studies of negative priming (Park et al 1996), latent inhibition (Baruch et al 1988), and Kamin blocking effect (Jones et al 1992). In these studies, inhibition was reduced or abolished in acutely psychotic patients but restored or improved in chronic state. We have previously reported that acutely psychotic schizophrenia inpatients showed an absence of negative priming, in contrast to chronic schizophrenia outpatients, who displayed normal negative priming (Park et al 1996). Reduced negative priming has also been observed in non-acutely psychotic schizophrenia patients, but the reduction of negative priming seems to depend on the positive symptoms (Fuller et al 2000), and in general positive symptoms are greatly increased during acute psychosis. Positive symptoms are associated with attentional disinhibition (Gray et al 1991) and also with attentional dysfunction per se (Cornblatt et al 1985), but it is not clear whether anomalous attentional inhibition eventually leads to some of the clinical symptoms, such as formal thought disorder, or whether disinhibition occurs in parallel to symptoms. It is also possible that a third variable, such as an abnormal regulation of dopamine, accounts for both.

To better understand the relation between clinical symptoms and attentional inhibition, we investigated spatial selective attention in schizophrenia patients over a period of 4 months, while keeping the medication dose as stable as possible. We employed a nonverbal, spatial attention task to minimize the language-related and cognitive demands generated by tasks that require naming or reading. Negative priming tasks that have been typically used in schizophrenia research require language processing and articulatory responses, but language disturbances during the acute psychotic state may overshadow the underlying attentional and inhibitory abnormalities. Spatial negative priming task is a simple localization task, which generates almost no performance errors. Cognitive demands are low and therefore even acutely psychotic patients can perform this task without generating errors. In addition, it is easier to compare nonverbal, attention task performance across species, which allows us to indirectly infer the neurobiological basis of the task.

In the present study, we investigated three aspects of spatial selective attention and inhibition in relation to clinical symptoms from acutely psychotic state to partial remission at 4-month follow-up: spatial location detection, spatial interference, and spatial negative priming.

Methods and Materials

Subjects

Thirty-six acutely psychotic schizophrenia patients (mean age = 34.8 years, SD = 9.4) were recruited and tested within the first 2 weeks of being admitted to a psychiatric ward. Diagnoses were made by a psychiatrist according to the DSM-III-R criteria (Spitzer and Williams 1987) using a structured clinical interview. Subjects were screened for the following criteria: substance abuse, neurologic disorders, and history of head injury. There were two first-episode patients. All others were relapse patients. The mean duration of illness was 9.8 years (SD = 6.6). The mean age at the first hospitalization and treatment was 24.1 (SD = 7.5). Eight patients were taking atypical antipsychotic drugs. The others were taking typical neuroleptics.

Thirty-one of the original 36 patients participated in the follow-up study 4 months later. Spatial attention and clinical symptoms were re-assessed at the follow-up session, at which point all patients were in partial remission and were clinically stable.

Forty-two normal control participants (mean age = 36.3, SD = 11.3) were recruited from the same city and were re-tested 4-months later. Control subjects had no history of substance abuse or head injury, and no family history of psychiatric illness or neurologic disorders. They were not taking any psychotropic medications.

The two groups did not differ statistically in education level (normal control subjects = 12.8 vs. schizophrenia patients = 12.2 years), age (normal control subjects = 36.3 vs. schizophrenia patients = 34.8 years), and handedness (two left-handers in the patient group vs. three left-handers in the control group).

Clinical interviews and ratings were conducted in the morning and the cognitive experiments in the afternoon at both testing sessions. Informed consent was obtained from all participants.

Clinical Ratings (Positive and Negative Symptoms Scale)

The Positive and Negative Syndrome Assessment Scale (PANSS; Kay et al 1987) was used. The PANSS consists of 30 items. The questions are grouped into three scales to measure negative symptoms (7 items), positive symptoms (7 items), and general psychopathology (16 items). Ratings on the PANSS were completed by a psychiatrist who was blind to the task performance of the subjects.
Spatial Attention Tasks

**APPARATUS AND STIMULI.** A Macintosh computer (Apple, CA) was used. There were four locations on the screen where the target (O) or the distractor (+) could appear. The four positions were placed on the screen so that the horizontal visual angle between the two upper row, outer positions was 8.3 degrees, and that between the two lower row, inner positions was 4.3 degrees. The vertical visual angle between the upper outside and lower inside positions was 1.3 degrees. These locations were spatially analogous to the locations of the keys D, C, K, and M on the computer keyboard. Subject used these four keys to indicate the location of the target. The stimuli (O and +) subtended 0.6 × 0.6 degrees of visual angle. All procedures, designs, and stimuli were adapted from Tipper et al (1991).

**DESIGN.** Each trial consisted of a pair of prime and probe displays. Each prime display was always followed by a probe display. Participants were asked to locate the target (O) and ignore the distractor (+). There were two types of prime displays: with a distractor or with no distractor (see Figure 1). An interference effect is indicated by an increased reaction time (RT) to locate the target in the distractor condition of the prime display, and it suggests that an irrelevant stimulus has been analyzed and competes with the response to a concurrent target.

There were three types of trials, all consisting of pairs of prime and probe displays: control, ignored repetition, and neutral. The neutral trials contained only the target for both prime and probe displays. In the control trials, the positions of the target and the distractor in the probe and prime displays were all different, whereas in the ignored repetition trials the location of the target in the probe display was identical to the location of the distractor in the prime display (see Figure 1). In other words, in the ignored repetition probe trials, participants were required to respond to a location that they had previously ignored. A negative priming effect is indicated by longer RTs in the ignored repetition probe trial than in the control probe trial and is thought to reflect the inhibitory mechanism that acts on the internal representation of the irrelevant stimulus.

**PROCEDURE.** Participants sat 45 cm from the screen; a chin rest was used to minimize head movement. Participants were told that they must pay attention to the target and ignore the distractor. They were asked to indicate the location of the target (O) by pressing the corresponding key on the keyboard and to ignore the distractor (+). They were asked to identify the target as quickly and as accurately as possible. Participants initiated each block of trials by fixating at the center and then pressing the spacebar. A trial began with the prime display, which stayed on the screen until the participant responded to it by locating the target. Then, there was a 1350 msec pause before the second display (probe) was presented. During the final 800 msec of the pause, the fixation point appeared at the center to prepare participant for the next response. When the participant responded to the probe display by locating the target, a pattern mask was presented and it stayed on the screen. When ready for the next trial, the participant pressed the space bar, after which there was always a 6.4-sec period. Therefore, there was always a rest period of at least 6.4 sec, and in practice the inter-trial interval was about 8–10 sec. This inter-trial interval was necessary because Tipper et al (1991) reported that a negative priming effect may last up to about 7 sec, and we wanted to insure the dissipation of residual priming effects between trials. During the final 800 msec of the pause, a fixation point was presented in the center of the screen to prepare participants for the next prime display (see Figure 2 for a schematic diagram of the procedure).

There were 72 trials (i.e., 72 pairs of prime and probe displays) in each block. Participants were allowed a brief rest after every 18 trials. Each block took about 16–20 min to complete. The order of presentation of different conditions was randomized within each block. Participants were given practice trials before the beginning of the experiment.

**Results**

**Symptoms**

During acute psychosis, average positive symptoms score was 15.3 (SD = 6.3), but it was reduced significantly to 8.3 (SD = 7.0) at 4 months \([F(1,31) = 32.2, p < .0001]\). Negative symptoms were also reduced from 11.9 (SD = 7.0) on the first day to 8.7 (SD = 6.1) 4 months later \([F(1,31) = 7.03, p < .013]\).
Spatial Attention Tasks

The average error rate was less than 1% for all subjects on both testing days. Schizophrenia and control subjects were compared on three measures: location detection, spatial interference, and spatial negative priming. The location detection effect was indexed by the RT to locate a single target in the prime trials (i.e., the first trial of each prime-probe pair for the neutral condition). The spatial interference effect was obtained from the prime trials. The RT to detect a single target (neutral trials) was compared with that for detecting a target in the presence of a distractor. The negative priming effect was indexed by examining the RTs of probe displays following the presentation of the prime displays. The RT to detect a target at a position previously occupied by a distractor was expected to be increased. The ignored repetition condition was compared with the control condition in the probe trials.

Baseline Reaction Time to Detect a Single Target during Acute Psychosis and 4 Months Later

The neutral condition consisted of trials with a single target for detection. Therefore the mean RTs for the neutral condition in the prime trials were taken as an index of the baseline RT. There were no errors in locating the target in the neutral trials. A repeated measures analysis of variance (ANOVA) showed that there was a main effect of the diagnosis \[ F(1,71) = 26.2, p < .0001 \]. Schizophrenia patients were slower than the control subjects on Day 1 \[ F(1,71) = 19.7, p < .0001 \] and at the follow-up \[ F(1,71) = 26.6, p < .0001 \]. There was a significant main effect of the time of testing \[ F(1,71) = 10.9, p < .0015 \]. There was also a diagnosis-by-time of testing interaction \[ F(1,71) = 9.8, p < .0026 \]. The reduction in baseline RT over time was greater for the schizophrenia patients (35.3% decrease) than for the control subjects (6.5%) (see Figure 3).

Spatial Interference Effect: Concurrent Inhibition of Distractor

Reaction time to locate the target in the prime trial was the variable of interest. The accuracy in locating the target was above 99%. Trials in which the target was not located correctly were excluded in the computation of the interference score.

Interference effect refers to the difference in RTs to locate the target in the neutral trials (single target) compared with when the stimulus display consisted of the target and the distractor. Interference effect is present if concurrent presence of the distractor increases the RT for detecting the target.

A raw interference score was calculated by averaging the mean RT for prime trials with target and distractor and then subtracting the mean RTs of prime trials with single target. Interference effect is indicated by a score greater than zero. Both groups showed interference effect as indicated by the positive score (see Figure 4). Repeated measures ANOVA showed that there was no main effect of diagnostic groups \[ F(1,71) = 1.02, p > .32 \], no main
effect of the time of testing \[ F(1,71) = 1.69, \ p > .20 \], and no group-by-time of testing interaction \[ F(1,71) = 0.08, \ p > .78 \].

Because there was a group difference in the baseline RT, we calculated percent interference score to account for the possible individual differences in baseline RTs (% Interference Score = 100 × (Raw Interference Score/RT for neutral prime trials). There was no main effect of the diagnosis \[ F(1,71) = 0.05, \ p > .82 \]. Schizophrenia patients and the control subjects did not differ significantly on their ability to ignore the concurrent distractor, either on Day 1 \[ F(1,71) = .039, \ p > .84 \] or at the follow-up session \[ F(1,71) = .28, \ p > .60 \]. There was no main effect of the time of testing \[ F(1,71) = 1.74, \ p > .19 \]. There was no interaction between the diagnosis and the time of testing \[ F(1,71) = .25, \ p > .62 \]. Thus, schizophrenia patients did not experience a different degree of spatial interference compared with the control subjects, and the concurrent inhibition of distractors was not altered by chronic or acute state of schizophrenia (see Figure 4).

Spatial Negative Priming: Subsequent Inhibition of Distractor

Reaction time to locate the target in the probe trial was the variable of interest. The accuracy in locating the target was above 99%. Trials in which the target was not located correctly for either the prime or probe display were not included in the computation of the negative priming score.

Negative priming score was computed by comparing the RTs of the probe displays of the ignored repetition trials and the RTs of the probe displays of the control trials. A raw negative prime score was first calculated by subtracting the mean RT of ignored repetition probe trials from the mean RT of control probe trials. A negative score indicates the presence of negative priming, whereas a positive score indicates absence of negative priming (disinhibition). A repeated measures ANOVA showed that there was a significant main effect of diagnosis \[ F(1,71) = 4.60, \ p < .035 \]. Schizophrenia patients showed reduced negative priming compared with the control subjects. There was also a significant main effect of the time of testing \[ F(1,71) = 6.66, \ p < .012 \], such that both groups showed increased negative priming at the 4 month follow-up. There was a significant interaction between diagnosis and the time of testing \[ F(1,71) = 9.82, \ p < .0045 \] but not with the location detection RT \[ r = .51, \ p < .0045 \] but not with the location detection RT \[ r = .51, \ p < .0045 \] but not with the location detection RT \[ r = .19, \ p > .27 \] nor with the location detection RT \[ r = .19, \ p > .27 \] nor with the location detection RT \[ r = .36 \]. Those with more positive symptoms tended to show greater abnormalities of negative priming (i.e., greater positive scores). During...
acute psychosis, negative symptoms were not associated with the negative priming effect \( (r = .28, p > .12) \) nor with the interference effect \( (r = .06, p > .73) \), but they were significantly associated with the baseline RT \( (r = .50, p < .005) \), such that those patients with more negative symptoms tended to be slower at detecting the single target.

**FOLLOW-UP AT 4 MONTHS.** The correlation between positive symptoms and negative priming was still significant at 4 months \( (r = .38, p < .04) \), but the positive symptoms were not associated with the interference effect \( (r = .09, p > .61) \) nor with the baseline RT \( (r = .13, p > .47) \). The correlation between negative symptoms and the negative priming effect was not significant \( (r = .23, p > .19) \). In addition, neither the interference effect \( (r = .28, p > .13) \) nor the baseline RT \( (r = .22, p > .22) \) was associated with the negative symptoms. Therefore, at the follow-up, when all the patients are in partial remission with significantly reduced PANSS scores, the only association between clinical symptoms and the measures of spatial selective attention remains that between the negative priming score and the positive symptoms.

Is it possible to predict the degree of positive and negative symptoms at the 4-month follow-up from the performance on the spatial attention tasks during acute psychosis? We examined the relationship between the performance on the spatial attention tasks during the acute psychotic episode and the clinical symptoms at the follow-up stage. The negative priming score during acute psychosis was significantly correlated with the positive symptoms \( (r = .380, p < .034) \) and with the negative symptoms \( (r = .382, p < .033) \) at the follow-up. This suggests that those patients who experienced greater disinhibition (i.e., more positive negative priming score) during the acute psychotic episode tended to have more positive and negative symptoms at the follow-up. Interference effect during acute psychosis was not associated with positive symptoms \( (r = -.23, p > .20) \) nor with negative symptoms \( (r = .10, p > .57) \) at the follow-up session. Similarly, the baseline RT during acute psychosis was not correlated with the positive symptoms 4 months later \( (r = -.05, p > .77) \), but there was a trend toward an association between the baseline RT to detect a target during acute psychosis and the negative symptoms at the follow-up \( (r = .31, p < .08) \), such that those patients who were slower during the acute stage tended to have more negative symptoms 4 months later.

We also carried out regression analyses, with the symptoms at follow-up as dependent variables and the three spatial attention measures at acute state as independent variables. Only negative priming score at acute state was associated with the positive \( (R = .33, p < .0064) \) and negative symptoms \( (R = .23, p < .035) \) at the follow-up session. Positive symptoms at the follow-up were not associated with the interference \( (R = .029, p > .78) \) nor with the baseline RT \( (R = -.001, p > .34) \) at the acute state. Similarly, neither the interference \( (R = .12, p > .19) \) nor RT \( (R = .002, p > .17) \) at the acute state was associated with the negative symptoms 4 months later. These results suggest that only the negative priming during the acute psychotic state may predict symptoms at a later date.

**Antipsychotic Drug Effects**

There was not a significant change in the drug dose over the 4 months \( [F(1,31) = .47, p > .49] \). During the acute psychotic episode, the average Chlorpromazine (CPZ) equivalent was 302.8 mg \( (SE = 56) \). Four months later, the CPZ equivalent was 330.3 mg \( (SE = 58) \). We examined the relationship between the antipsychotic drug dose (CPZ equivalent) and the performance on the spatial attention tasks, but there were no significant correlations.

**Discussion**

In this study, we examined spatial location detection, spatial interference, and spatial negative priming over a period of 4 months in schizophrenia patients and control subjects.

Schizophrenia patients were slower than control subjects in locating a target in space in both acute and chronic states, but they showed a significant improvement at the
follow-up session. Increased reaction time in schizophrenia patients is a common finding (Heinz et al 1998). During acute psychosis, patients with more negative symptoms tended to be slower on the target location detection task. One core feature of negative symptoms is a difficulty in initiating action, and schizophrenia patients’ increased RT to locate spatial targets may be a reflection of this problem. It is interesting to note that the performance on this simple spatial localization task was able to discriminate the two groups very well and was sensitive to group-by-time of testing interaction. Is it possible that increased RTs may have caused reduced negative priming? Overall, slower subjects (e.g., schizophrenia patients) tend to show greater loss of negative priming than faster subjects (e.g., control subjects). Within the schizophrenia group, however, the correlation between baseline RT and negative priming was not significant during acute state ($r = .25, p > .13$) nor at the follow-up ($r = -.11, p > .53$). Although the simple target detection task discriminated the two groups very well, it was not a reliable predictor of symptoms, as can be seen in the regression analysis.

Normal control subjects and schizophrenia patients did not differ on the spatial interference effect. Both groups showed interference effect, indicating that they processed the irrelevant distractor, and that this process competed with the response to the concurrent target. It is interesting to note that even during floridly psychotic episode, schizophrenia patients do not necessarily experience a greater degree of spatial interference compared with normal control subjects.

In contrast, spatial negative priming was abolished in schizophrenia patients during acute psychosis. Positive symptoms and negative priming were correlated, such that those with more positive symptoms tended to show greater abolition of negative priming. At the follow-up session, negative priming was normalized in schizophrenia patients, but the correlation between positive symptoms and negative priming score was still significant. These results are in agreement with previous studies implicating the relationship between positive symptoms and cognitive disinhibition (Beech et al 1991; Peters et al 1994). In addition, abnormal negative priming during acute psychosis was associated with greater positive and negative symptoms at the follow-up session. From the present study, it is not possible to deduce whether greater loss of negative priming during a psychotic episode predicts worse outcome at a later stage, but it is a possibility that should be explored in a future study.

The tasks in this study generated almost no errors, and therefore the performance difference between the patients and the control subjects cannot reasonably be attributed to a global, generalized cognitive deficit. Moreover, schizophrenia patients and control subjects did not differ on the spatial interference performance.

It has been suggested that negative priming and attentional inhibition may be mediated by the dopaminergic system, but the direction of effect is not clear. It has also been suggested that the absence of negative priming can be “restored” or “normalized” by the neuroleptic treatment. Attentional inhibition in animals and humans can be abolished or reduced by dopamine agonists (Gray et al 1992a, b; Weiner et al 1988, 1990) and increased or restored by dopamine antagonists (Beech et al 1990; Weiner et al 1990); however, contradictory results have also been reported (e.g., David 1995; Williams et al 1998). Williams et al (1998) found that inhibition was absent in nonneuroleptic-treated patients but present in patients who were naive to antipsychotics. They concluded that the reduced attentional inhibition in acute schizophrenia may stem from the antipsychotic treatment rather than from the disorder. But we do not know much about the clinical symptoms of these patients and need a fuller account concerning the relation between the psychotic symptoms, antipsychotic medication, and inhibition before we can draw any firm conclusions.

It is interesting to note that in the absence of antipsychotic medication, abnormal negative priming has been observed in healthy individuals who may carry latent liability for schizophrenia. Negative priming is reduced or abolished in the first-degree relatives of schizophrenia patients (Park et al 1996), as well as in schizotypal subjects (Beech and Claridge 1987; Beech et al 1991; Park et al 1996; Peters et al 1994; Watson and Tipper 1997). Moreover, behavioral signs that are similar to the positive symptoms of schizophrenia are correlated with reduced negative priming in these individuals (Park et al 1996; Peters et al 1994). To summarize, the relation between positive symptomatology, hyperdopaminergia, and negative priming is unclear, but the studies of schizotypal subjects suggest that anomalous negative priming can occur in the absence of psychotropic medications. It is, of course, unknown whether a subtle, internal dysregulation of the dopamine system in the healthy but schizotypic subjects leads to abnormal negative priming. We found that negative priming was abolished during acute psychosis but restored 4 months later. At both testing sessions, the patients were receiving comparable doses of antidopaminergic medication. It seems unlikely that the reduced negative priming effect that we observed during acute psychosis reflects a simple antidopaminergic drug effect.

A major limitation of the study is that we do not know whether reduction of negative priming during acute psychosis is specific to schizophrenia or to positive symptoms. If it were the latter case, bipolar patients during acute psychosis should also show reduction or abolition of
negative priming. This is a distinct possibility and should be tested.

In sum, we investigated spatial selective attention and inhibition during acute and chronic states of schizophrenia using a very simple location detection paradigm and a within-subjects design. Our major goal was to examine the relationship between spatial attention and clinical symptoms. We found that reduced negative priming is associated with positive symptoms and that negative priming was normalized at the 4-month follow-up. Although we do not yet know what causes abolition of negative priming during psychotic episode, future studies will be able to further specify cognitive and pharmacologic mechanisms underlying abnormalities of attention and inhibition in schizophrenia.

This work was supported in part by Human Frontiers of Science (SP), NARSAD (SP), and Swiss National Science Foundation (SP, JP, DH).

References


