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# Negative priming in amphetamine psychosis

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ABSTRACT

Amphetamine abuse may lead to a psychotic state, its symptomatology being very similar to what is seen in paranoid schizophrenia. Failure of attentional inhibition of irrelevant information is thought to be associated with the psychotic symptoms in schizophrenia. Negative priming (NP) paradigm is believed to measure this impairment. Several studies have shown impaired NP in schizophrenia. In the present study a spatial NP task was used to assess attentional inhibition in a group of amphetamine-induced psychosis patients. Nineteen patients with amphetamine-induced psychotic disorder and 20 healthy subjects participated in this study. Severity of psychotic symptoms was measured prior to testing using the Brief Psychiatric Rating Scale (BPRS). Patients showed no deficit in NP, and the amount of their NP effect was not significantly different from healthy subjects. Besides, we did not find any correlation between the amount of NP effect and severity of symptoms. Our results may indicate that cognitive mechanisms underlying NP might not be affected in amphetamine psychosis.



## 1. Introduction

Abuse of amphetamine may lead to a psychotic state which is typically identified with persecutory delusions and/or hallucinations. Contents of these delusions and hallucinations are very similar to those seen in paranoid schizophrenia (Bell, 1965; Snyder, 1973). Cognitive abnormalities have been well researched in schizophrenia. It has been observed that schizophrenic patients seem distractible and have a hard time focusing on a stimulus. Such observations have led to a hypothesis that the symptoms of schizophrenia such as hallucinations and delusions may be due to deficits in inhibitional processes (Frith, 1979). Since then, deficits in inhibitory processing of irrelevant information have been shown by a variety of paradigms (Baruch et al., 1988; Braff et al., 1992; Elkins and Cromwell, 1994; McDowd et al., 1993; Nestor et al., 1992; Steffy and Galbraith, 1974).

One of the paradigms used to investigate these processes is called negative priming (NP) (Tipper, 1985). NP is a normal phenomenon in which responses to an object are slower when the object is previously ignored (Tipper, 1985). Depending on the type of NP task, this slowing of reaction times (RTs) can occur due to conflicts between for example locations or identities of the target and the previous distractor. In a spatial NP task, when a target is presented in the location of the distractor of the previous trial, response time to that target will increase (Tipper and Cranston, 1985).

There are many studies showing reduced NP in schizophrenia patients (Beech et al., 1989; MacQueen et al., 2003; Park et al., 1996, 2002; Peters et al., 2000; Tipper et al., 1995; Ungar et al., 2010). There are also several studies showing that such impairments are associated with positive symptomatology in schizophrenia (Park et al., 2002; Peters et al., 2000; Williams, 1996).

As mentioned earlier, the symptomatology of amphetamine psychosis is similar to schizophrenia. Besides, amphetamine acts through the neurotransmitters such as dopamine (the most important), norepinephrine, and serotonin. This hyperdopaminergic state caused by amphetamine is similar to the dopamine hypothesis of schizophrenia. Based on studies like Gray et al. (1991), it is thought that dopaminergic action in limbic system plays an important role in attentional inhibition. Hyperdopaminergic state in schizophrenia and increased dopamine neurotransmission following amphetamine (a dopamine agonist) use may lead to a reduced level of inhibition (Gray et al., 1991, 1992). Taking these similarities into account, it seems necessary to examine attentional inhibition in amphetamine psychosis.

In some earlier studies, positive effects of amphetamine on cognitive performance such as in learning have been reported (Kornetsky et al., 1959; Seashore and Ivy, 1953; Soetens et al., 1995). However, this improvement of functioning has been observed only when the subjects were functioning below their potential level (like when subjects were fatigued). Moreover, in such studies, tasks have been conducted after acute brief administration of amphetamine. Thus, the mentioned positive effects in

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street amphetamine users who use amphetamine in much higher doses are not to be expected. On the other hand, there are many research studies that have examined cognitive deficits in amphetamine abusers, and have shown that they have impaired functioning in many cognitive tasks such as memory, decision making and manipulation of information tasks (Ornstein et al., 2000; Rogers et al., 1999; Simon et al., 2000; Volkow et al., 2001). Nevertheless, fewer studies have assessed NP in these people. Salo et al. (2002) and Dafters (2006) examined NP as a measure of inhibitional processing in amphetamine users (methamphetamine and methylenedioxyamphetamine (MDMA), respectively). They used a color-word Stroop task for this purpose and compared two measures between patients and controls: Stroop interference and NP. As mentioned earlier, NP is the increased response time to a stimulus in a trial, following previous exposure to that stimulus in the previous trial. In contrast, color-word Stroop interference occurs when the ink color is different from the color name in one trial; this difference results in prolonged RT. Salo compared a group of methamphetamine dependent individuals, which were abstinent for the last 2–4 months, to a control group. She showed intact NP and increased Stroop interference in amphetamine dependents. Dafters did the same comparison between 3 groups: MDMA users, cannabis and ecstasy users, and non-drug users. MDMA users exhibited reduced level of NP, and no difference in Stroop interference was observed between the three groups. These studies were both done regardless of the presence or absence of psychotic symptoms.

In the present study a spatial NP task was used to assess attentional inhibition in a group of amphetamine-induced psychosis patients. Knowing their similarities to schizophrenia and the dopaminergic effects of amphetamine, we hypothesized that patients with amphetamine-induced psychotic disorder would show some level of NP impairment.

## 2. Methods

### 2.1. Subjects

Demographic characteristics of the patients and the controls are shown in Table 1. The patients group consisted of 19 amphetamine-induced psychosis patients (mean age: 33.42 years (S.D.=5.02); 15 males) (after exclusions). Diagnoses were made by attending psychiatrists according to DSM-IV criteria (American Psychiatric Association, 1994), and confirmed by Persian version of Structured Clinical Interview [SCID] (Sharifi et al., 2009). All patients were on treatment with antipsychotic agents; fourteen on risperidone (dose range 2–4 mg/day), four on olanzapine (5–15 mg/day), two on haloperidol (10–20 mg/day), and one on trifluoperazine (5–15 mg/day). They were abstinent for a minimum of 7 days and a maximum of 15 days. Patients outside the age range 18–40 were excluded from the study; any change in the diagnosis and any use of amphetamine during the hospitalization also led to exclusion. Twenty normal subjects (mean age: 30.85 (S.D.=5.82); 14 males) took part as the control group. They were recruited from medical students, service staff, and catering staff of the hospital. Participants in the control group had to have no history of a major psychiatric illness (based on their own report) and not to use any substance at the time of the experiment (with the exception of nicotine or caffeine). Two subjects from the patients group were excluded because the diagnoses at discharge were different from the initial diagnoses. Two other patients were also eliminated from the analysis due to high error rates (>25%). The initial patients sample size was 23. None of the controls was excluded. No subject was excluded for RTs longer than 2 s. The two groups were not significantly different in male to female ratio, age ($t=1.48$, d.f.=37, $P=0.15$) or education years ($t=-1.31$, d.f.=37, $P=0.20$).

Informed consent was obtained in accord with institutional and national guidelines for human subjects' safety and confidentiality.

**Table 1**
Demographic characteristics of the subjects.

| Variable | Patients ($n=19$) | Controls ($n=20$) | $P$-value |
|---|---|---|---|
| Age (years)[a] | 33.42 (±5.02) | 30.85 (±5.82) | 0.15 |
| Gender (male: female) | 14: 5 | 14: 6 | |
| Education (years)[a] | 10.32 (±2.36) | 12.35 (±6.39) | 0.20 |
| Duration of amphetamine abuse (years)[a] | 2.99 (±2.25) | – | |

[a] Mean (±S.D.).

### 2.2. Measures and procedures

#### 2.2.1. Negative priming

The NP was measured with a spatial NP task which was adapted from the spatial NP task by Vink et al. (2005) and Tipper et al. (1995). Stimuli were presented to the subjects on the computer screen placed in front of them. The task consisted of a block of 80 trials; a separate practice block (10 trials) was also run before the main block. After pressing a start button by participants, the four marker circles were presented. These circles formed the background that was displayed continuously throughout the task. Five hundred millisecond later, the first trial started. In each trial, two filled white dots of different sizes were presented within the outer circles. The subjects had to press a button on the keyboard corresponding to the location of the target (i.e. the larger dot) as quickly as possible; the smaller dot would be the distractor. The RTs of the responses were recorded. The white dots disappeared as soon as the response was made. Between each two trials the marker circles were presented for 500 ms. In 24 of the 80 trials the target was in the location of the distractor of the previous trial (i.e. spatial NP condition). In the rest of the trials the location of the target was not the same as the location of the distractor of the previous trial (i.e. no spatial NP condition) (Fig. 1). All trials were developed and run with E-prime version 1.

#### 2.2.2. Severity of psychotic symptoms

Psychotic symptoms were measured prior to testing using the 24-item Brief Psychiatric Rating Scale (BPRS) (Overall and Gorham, 1962). Total BPRS scores were calculated by summing all the 24 items and were used for determining the overall severity of symptoms. Four of the BPRS items (Grandiosity, suspiciousness, hallucinations, and unusual thought content) were summed as the BPRS positive scores. Another four items (Blunted affect, emotional withdrawal, motor retardation, and mannerisms and posturing) were summed and used as the BPRS negative scores (Nicholson et al., 1995). Total scores equal or greater than 31, 41, and 53 were considered as “mildly”, “moderately”, and “severely” ill, respectively (Leucht et al., 2005).

### 2.3. Statistical analysis

Statistical analyses were performed using the Statistical Package for Social Sciences (SPSS), version 17.0 for Windows. Analysis of RTs included only correct responses and the responses with RTs less than 2 s. A repeated measures analysis of variances (ANOVA), Pearson's correlation, and a series of $t$-tests were used to study associations between measures. Significance level was set at 0.05.

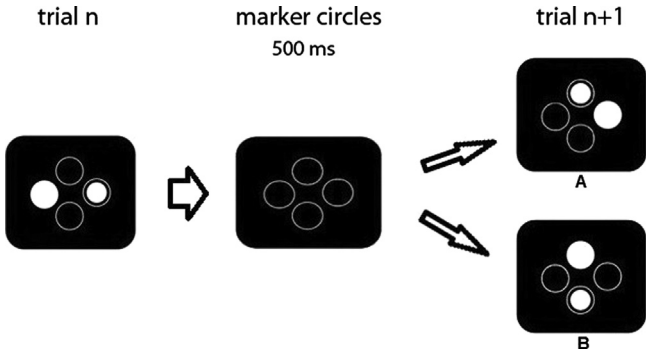


**Fig. 1.** In each trial two filled white dots of different sizes were presented within the outer circles. The subjects had to press a button on the keyboard corresponding to the location of the target (i.e. the larger dot); the smaller dot would be the distractor. The RTs of the responses were recorded. The white dots disappeared as soon as the response was made. Between each of the two trials the marker circles were presented for 500 ms. In NP conditions (A) the target was in the location of the distractor of the previous trial. In no-NP conditions (B) the location of the target was not the same as the location of the distractor of the previous trial.