

## Effect of substance misuse in early psychosis

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**Background** Studies examining the temporal relationship between substance use and the onset of psychotic symptoms in schizophrenia are inconclusive.

**Method** Three groups of out-patients with schizophrenia were compared on onset of illness, symptoms and quality of life. Fifty-one subjects had no past or present history of substance misuse, 29 subjects had a history of past substance misuse occurring around the onset of their illness, and 33 subjects were currently misusing substances.

**Results** Current substance misusers had poorer quality of life scores and less negative symptoms than the non-users. Those who had a past history of substance misuse had a significantly earlier age of onset than those with no substance use.

**Conclusions** Attention should be paid to substance misuse present at the first episode. Treatment for schizophrenia should begin even though a diagnosis of drug-induced psychosis cannot be ruled out.

Studies examining the temporal relationship between substance use and the onset of psychotic symptoms in schizophrenia are inconclusive. From the literature there appears to be a high incidence of substance misuse in first-episode samples (Hambrecht & Hafner, 1996). Several reasons for this have been proposed. Substance use may precede the onset of the illness and thus be considered a precipitant or cause. For example, there is evidence to suggest that certain drugs, such as stimulants, can precipitate onset at an earlier age in biologically vulnerable people (Breakey *et al.*, 1974; Tsuang *et al.*, 1982; Richard *et al.*, 1985). Although it is unclear how this may happen it has been suggested that repeated stimulant misuse may alter the dopamine system (Mueser *et al.*, 1992). Substance misuse may follow the onset of the illness and may be seen as an attempt to self-medicate (Schneier & Siris, 1987; Dixon *et al.*, 1991). Thus, in the case of people with first-episode psychosis, early symptom onset may be a risk factor for substance misuse. Substance misuse may accompany the schizophrenia disorder independently, that is in the absence of a causal relationship. This is probably the least likely since the incidence of substance misuse has consistently been reported to be higher in people with schizophrenia compared with control groups (Mueser *et al.*, 1992).

Thus, no studies are conclusive with respect to the relationship between substance use and the onset of psychotic symptoms (Turner & Tsuang, 1990). However a recent study attempts to clarify the position (Hambrecht & Hafner, 1998). In this study the onset and course of schizophrenia and substance misuse were retrospectively assessed in 232 people with first-episode schizophrenia. Alcohol misuse more often followed than preceded the first symptom of schizophrenia. Drug misuse preceded the first symptom in 27.5% of the cases, followed it in 37.9%, and emerged within the same month in 34.6% of the

cases. The mean age at onset of schizophrenia as well as the age at first admission was lower in people who had misused drugs than those without a history of substance misuse.

The incidence of substance misuse in these young people with first episodes generally raises clinical concern. Our attention was further drawn to this issue when two observations were made about data from earlier studies. First, in a sample of 33 individuals diagnosed with schizophrenia and substance misuse (Addington & Addington, 1997) it was noted that approximately 50% had received at least one diagnosis of drug-induced psychosis in the early course of their illness. This fitted with our clinical experience that many young people with schizophrenia first present with what may appear to be a substance-induced psychosis. As a result they may not be offered treatment for schizophrenia until a later admission. This is of concern given recent evidence that suggests a delay in treatment may have an impact on later recovery. Duration of illness before neuroleptic treatment has been found to be significantly associated with time to remission and with level of remission (Wyatt, 1991; Loebel *et al.*, 1992; Szymanski *et al.*, 1996).

The second observation was in a sample of 80 stable out-patients with schizophrenia who were recruited for a social and cognitive functioning study (Addington & Addington, 1998). This sample was representative of an out-patient clinic in a department of psychiatry in a general hospital. Substance misuse in the past year was an exclusion criterion for this study. However, 29 (36%) of the subjects had a past history of substance misuse or dependence. For all of these people the misuse had either occurred up to three years prior to the onset of the schizophrenia or at the most three years after first admission. This suggests that the substance misuse is associated with the onset of schizophrenia.

Most studies examining correlates or predictors of substance misuse in schizophrenia tend to compare people with schizophrenia who misuse substances with people with schizophrenia with no history of substance misuse. We were concerned about people with first episodes and we wanted to see if there were differences between people with schizophrenia with no history of substance misuse with those whose problems with substances occurred in the period immediately before the onset of their illness

and immediately after. In particular we were interested in differences in age at onset, age at first admission and outcome in terms of symptoms and level of functioning.

## METHOD

### Subjects

Eighty out-patients (54 males, 26 females) with schizophrenia were identified from an out-patient clinic in a general hospital department of psychiatry and a community mental health clinic. They were recruited for a larger study that was examining the relationship between social and cognitive functioning in schizophrenia. These people were divided into two groups. One group consisted of 51 people who had no past or current history of substance misuse or dependence. The other consisted of 29 people who had no current substance misuse or dependence but retrospectively met DSM-III-R criteria (American Psychiatric Association, 1987) for substance misuse or dependence sometime in the three years before or the five years after the onset of their illness. Onset of illness was determined as the time that psychotic symptoms were first apparent. This information was obtained by using the Structured Clinical Interview for DSM-III-R (SCID; Spitzer *et al*, 1990) and chart review.

A third group of 33 out-patients (29 males, 4 females) with schizophrenia who met criteria for substance misuse or dependence were identified from an out-patient clinic in a general hospital department of psychiatry and a community mental health

clinic and were recruited for the present study. The substance misuse group met criteria for dependence of at least one substance. This group was further divided into the following sub-groups: (a) alcohol dependence (12 people); (b) cannabis dependence (five people); (c) alcohol dependence or misuse plus cannabis dependence or misuse (12 people); and (d) other criteria (four people, one with alcohol dependence plus past 'crack' cocaine dependence, one with codeine dependence, one with codeine (in the form of a systemic cough and decongestant preparation) dependence, and one with alcohol and barbiturate dependence). All of the people in the substance misuse group had at one time or other been referred to a substance or dual-diagnosis programme for treatment. The implication is that either care-givers or significant others had perceived these individuals to have a problem with substances. The majority of the subjects were single, lived alone and received governmental financial support.

Diagnoses of schizophrenia and substance misuse or dependence according to DSM-III-R criteria (American Psychiatric Association, 1987) were made, using the SCID interview. Diagnoses were made by D.A. and J.A. Interrater reliability was determined in a separate sample of 10 people by 100% agreement on the diagnosis and at least 80% agreement for symptom presence. All the individuals met criteria for schizophrenia. However, they were excluded if they had: (a) evidence of an organic central nervous system disorder (e.g. epilepsy, traumatic brain injury, infectious or toxic cerebrovascular disease); (b) learning

disability; (c) under 18 or over 65 years of age. The study was described verbally and in writing to each participant. Written informed consent was obtained from each person.

### Measures

The Positive and Negative Syndrome Scale (PANSS; Kay *et al*, 1987) was used to obtain ratings for positive and negative symptoms. The PANSS was administered by J.A. and a clinical research nurse. Interrater reliability was determined in a separate sample of five people to at least 85% reliability on the syndrome scores and no more than one point difference on any individual symptom items.

The Quality of Life Scale (QLS; Heinrichs *et al*, 1984) is a 21-item interviewer rating scale, providing information on functioning during the preceding four weeks. Each item is rated on a seven-point scale and in all but two cases requires a judgement by the clinician. It measures adjustment on four sub-scales: interpersonal relations, instrumental role functioning, intrapsychic foundations (e.g. motivation), and common objects and activities (owning a car, reading a book). The QLS was administered by a clinical research nurse.

## RESULTS

Seven one-way ANOVAs were conducted to compare the three groups on age, age at first admission, age at onset, symptoms and quality of life total scores. The significant results were that people with past substance misuse were significantly younger at age of

**Table 1** Differences among groups in study

	No substance misuse group, <i>n</i> =51 mean (s.d.)	Past substance misuse group, <i>n</i> =29 mean (s.d.)	Current substance misuse group, <i>n</i> =33 mean (s.d.)	<i>F</i> d.f. (110,2)
Gender (male : female)	31 : 20	23 : 6	29 : 4	
Age	38.1 (9.6) <sup>1</sup>	31.2 (7.7) <sup>1</sup>	34.3 (7.7)	6.2**
Age at onset	24.7 (7.3) <sup>1</sup>	20.4 (4.5) <sup>1</sup>	23.0 (7.02)	4.1*
Age at first admission	26.0 (7.8)	22.4 (8.6)	24.2 (6.6)	NS
PANSS (positive)	13.6 (5.6)	13.8 (5.5)	15.3 (5.5)	NS
PANSS (negative)	17.1 (6.7) <sup>1</sup>	16.1 (5.4)	14.0 (4.0) <sup>1</sup>	2.9*
PANSS (GPS)	26.5 (7.3)	28.4 (8.0)	28.0 (6.1)	NS
Quality of life	76.3 (16.9)	75.0 (17.7)	59.8 (20.6) <sup>2</sup>	8.9***

PANSS, Positive and Negative Syndrome Scale; GPS, General Psychopathology Scale.

1. Significantly different from each other.

2. Significantly different from the other two groups.

\**P* < 0.05, \*\**P* < 0.01, \*\*\**P* < 0.001.

onset than those with no history of substance misuse. Those who were currently misusing substances had poorer quality of life scores than the other two groups and less negative symptoms than the non-misuser group. Results are presented in Table 1.

In the group of current misusers, of the four people in the sub-group 'other criteria', none of the PANSS or QLS scores were more than two s.d.s above or below the means for the substance misusing group as a whole.

## DISCUSSION

Results of this study suggest that individuals with schizophrenia and substance misuse function at a lower level than their peers in the non-misusing group with schizophrenia in areas of interpersonal relationships, motivation, role functioning, activities and ownership of possessions. They also have lower levels of negative symptoms. However, the most notable difference among the three groups is that the people with past substance misuse had a significantly younger age of onset than those people in the non-misuser group. This was not accounted for by gender differences. It is possible that for the past misuse group the first psychotic episode was exacerbated by the use of drugs and/or alcohol or that early onset symptoms are a risk factor for using substances. Although not significant the past misuse group had a younger age of onset than the people in the current misuse group.

Retrospectively, people who would have been diagnosed with substance misuse in the early stages of the schizophrenic illness fall into two groups in the later stages of the illness. First, those who continue to use substances and second those whose substance misuse occurred immediately prior to and/or immediately after the onset of schizophrenia. For the latter group there are several possibilities. It may be that drug and alcohol misuse is part of the poor premorbid history that is evident in many individuals with schizophrenia. However, substance misuse is not

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uncommon and for those with a vulnerability to schizophrenia the substance misuse may act as a trigger to the onset of the illness. Third, the substance misuse may occur in either the prodromal stage or with the onset of psychotic symptoms as a means to either cope with the illness or to self-medicate the symptoms. The substance misuse may then ameliorate once the illness is stabilised. Finally, those individuals who have an early onset of symptoms could be more vulnerable to substance misuse.

This study clearly has limitations. Diagnoses of past substance misuse were done retrospectively. The age of onset was determined by interviewing the individuals and chart review. There is a greater risk of inaccuracy in determining the time of onset if the individual is using substances. Although only seven ANOVAs were conducted there are dangers in carrying out multiple analyses in this way. Despite these tentative results, there are some implications for clinical management. Regardless of the potentially different reasons for misusing substances in people with first-episode psychosis substance use should be routinely assessed and treatment should be immediately available if required. This also raises the possibility that prophylactic pharmacotherapy may have the potential to reduce relapse rates even though drug-induced psychosis cannot initially be ruled out.

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