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*Ismail Hani Shoeb, MB, BCh, MRCPsych, *formerly Consultant Psychiatrist and Chief Medical Officer, Abha Psychiatric Hospital, Abha, Assir Region, Saudi Arabia, now Barnet Clinical Lecturer, Department of Psychiatry, University College and Middlesex School of Medicine, Riding House Street, London W1N 8AA*; Gamal Ahmed Hassan, MB, BCh, MRCPsych, *formerly Consultant Psychiatrist, Abha Psychiatric Hospital, Abha, Assir Region, Saudi Arabia, now Consultant Psychiatrist, Frimley Park Hospital, Frimley, Surrey*

*Correspondence

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Panic Attacks in Chronic Schizophrenia

NICHOLAS ARGYLE

Of 20 patients attending a clinic for maintenance therapy of schizophrenia, seven had regular panic attacks, and these were often associated with agoraphobia and social phobia. Similar fears and avoidance in other cases were associated with paranoid ideas and negative symptoms. The relationship of panic to psychotic symptoms varied greatly. In two patients neuroleptics were associated with an increase in panic attacks.

Since its inclusion in DSM-III (American Psychiatric Association, 1980), panic disorder has been the subject of great research interest, both clinically and in the laboratory. In DSM-III-R (American Psychiatric Association, 1987) panic disorder has taken precedence over agoraphobia in the diagnostic hierarchy – reflecting the adoption by many authors of Klein's (1980) model of panic and agoraphobia. At the same time it is becoming clear that panic attacks occur in patients with all the anxiety disorders, depression, and personality disorders, and the distinction of panic disorder as a diagnostic category has been questioned (e.g. Argyle & Roth, 1989). In particular the relationship of panic disorder to depression remains a matter of dispute. DSM-III-R now allows both diagnoses to be made. Boyd (1986) describes how commonly panic disorder occurs

with other diagnoses, and suggests panic attacks lead to seeking treatment in other disorders.

There has been little attention paid to any relationship between panic attacks or panic disorder and schizophrenia. Sandberg & Siris (1987) reported one chronic schizophrenic in whom panic attacks responded to alprazolam. Kahn *et al* (1988) treated seven patients with schizophrenia and panic attacks with alprazolam and found improvement in both positive and negative symptoms. Kahn *et al* (1987) also suggest panic may contribute to the pathogenesis of schizophrenic symptoms. Benzodiazepines are generally recognised as having only a minor role in the treatment of schizophrenia, where they may reduce both anxiety symptoms and psychotic symptoms in some cases (Donaldson *et al*, 1978).

This study describes the incidence and phenomenology of panic attacks and phobias in a group of 20 patients with chronic schizophrenia.

Method

Twenty consecutive patients attending an out-patient clinic for chronic maintenance treatment of schizophrenia were interviewed. All had previous in-patient admissions and the shortest time since first psychiatric episode was four years. Diagnosis was made by clinical interview and review of extensive medical notes. All patients met both ICD-9 (World Health Organization, 1978) and DSM-III-R (American Psychiatric Association, 1980) criteria for schizophrenia and had had a chronic course of illness. Seven were of paranoid type and 13 of hebephrenic or disorganised type. None had had acute psychotic exacerbations in the last three months, but eight had residual positive psychotic symptoms. Three patients were in remission, no positive or negative schizophrenic symptoms being present. All except two were on neuroleptics. Six were living with spouses or parents, four lived in sheltered or supervised accommodation, and ten lived alone. Nine were working at least part time.

All subjects were interviewed by the author using both a clinical interview and a structured interview (SCID-UP; Spitzer & Williams, 1983) to establish DSM-III-R (American Psychiatric Association, 1987) diagnoses of panic disorder and anxiety states and depressive illness. Schizophrenia was not used as an exclusion criteria, but the relation of psychotic symptoms to anxiety symptoms was noted. All subjects had at least four follow-up interviews over 12 months to record changes in their symptoms.

Results

The average age of the 20 patients was 39.9 (range 20–62) years, and 15 were men. Four men and three women reported panic attacks, with a frequency ranging from once a week to once a day (average 2.4 per week). One of these had an excessive caffeine intake, which excluded a primary diagnosis of panic disorder.

Four of these seven patients had spontaneous panic attacks, that is, not occurring in, or before entering, phobic situations, with rapid escalation to four or more symptoms within ten minutes, and at least one attack per week over the last four weeks, and therefore met full criteria for DSM-III-R panic disorder, apart from the coexistence of schizophrenia. On close questioning of these four, two had attacks precipitated by anxious cognitions associated with overvalued paranoid ideas, and one had attacks clearly precipitated by physical sensations (which were not psychotic in nature).

Three patients had panic attacks in situations related to agoraphobic fears of a typical nature – fear of being alone, unsafe, away from home. Two of these three had spontaneous attacks also; one had only situational attacks. Of the 13 patients not experiencing panic attacks, one patient had typical agoraphobic fears and four others had travel fears related to paranoid ideas.

Social avoidance was present in 13 cases. In five this was associated with negative symptoms of loss of interest and motivation; in four paranoid ideation was the apparent cause; in four typical social phobia with fear of appearing anxious and being humiliated was found. Three of this latter group had full (four or more symptoms) panic attacks in social situations, two also having spontaneous attacks and meeting criteria for panic disorder.

One patient with panic also met criteria for major depressive episode (DSM-III-R).

Follow-up and summaries

The seven cases with panic attacks are briefly summarised.

- (a) A 33-year-old man, living with his parents, with residual auditory hallucinations and thought disorder, had panic attacks which were judged to be precipitated by excessive caffeine intake (10–20 cups of coffee or tea per day plus caffeine tablets). He could not be persuaded to reduce his caffeine intake and panic attacks continued. He remained socially withdrawn and agoraphobic.
- (b) A 25-year-old single man with residual paranoid delusions, working as a part-time cleaner, had his antipsychotic medication increased to reduce his delusions and sleep disturbance. At the same time his panic attacks became much less frequent and the moderate agoraphobia and social withdrawal both improved.
- (c) A 34-year-old delivery man living with his mother, with residual paranoid ideation and ideas of reference, unilaterally stopped his antipsychotic medication and his panic attacks stopped. After several weeks he became increasingly agitated, paranoid, and socially avoidant. On restarting his antipsychotics (fluphenazine 25 mg i.m. three-weekly), panic attacks recurred even though his paranoid ideas and agitation were reduced. Panic attacks did not respond to a change in antipsychotics and he was unwilling to take any other drugs.
- (d) A 26-year-old single man working as a nursing assistant was in remission from schizophrenia but had marked social phobia with panic disorder. These responded to behavioural instruction and low-dose benzodiazepines (diazepam 2.5 mg t.d.s.).
- (e) A 32-year-old unemployed lady living with her mother, whose schizophrenic illness had always been associated with anxiety, panic attacks, and social phobia, had few residual ideas of reference and overvalued ideas but marked negative symptoms – lack of confidence, indecisiveness, and lack of motivation – which were unresponsive to medication. Alprazolam (0.5 mg t.d.s.) reduced the frequency of her panics but had no effect on her behaviour.
- (f) A 60-year-old single lady living alone practised severe social avoidance related to paranoid ideas and agoraphobia associated with typical ideas of collapsing or being away from safety. She was also depressed. Panic attacks occurred mainly at home, apparently precipitated by minor bodily symptoms such as dizziness, fleeting pains, or breathlessness or

palpitations. Her paranoid ideas were resistant to increased doses of antipsychotics (flupenthixol 60 mg i.m. fortnightly). Panic attacks became more frequent with the increase in antipsychotics and less frequent, though not absent, with diazepam (5 mg b.d.). She did not tolerate a trial of antidepressants. She would not attempt behavioural or cognitive therapy and remained phobic of social and travel situations.

- (g) A 38-year-old lady living alone, with residual paranoid ideas and infrequent auditory hallucinations, whose social avoidance was directly attributed to paranoid ideas and fluctuated with their intensity, became more psychotic and agitated when her panic attacks became more frequent. Increased antipsychotic medication reduced the frequency. Panic attacks occurred not in phobic situations but following paranoid ideation, which made her anxious.

Discussion

Panic attacks were found to be common, occurring in seven of this sample of 20 patients. Because of the overshadowing importance of psychotic symptoms earlier in the course of illness, panic and phobic phenomena may be relatively ignored by clinicians dealing with schizophrenia. For the subgroup of seven patients who had panic attacks, panic and phobic avoidance accounted for a significant part of their current distress and disability.

The relationship between panic attacks and phobic avoidance was more complex than in other patients with anxiety states, because both negative symptoms and paranoid ideas were also found as causes of social withdrawal or avoidance behaviour.

One in two cases (b and g) were panic attacks clearly associated with global severity of illness, fluctuating with levels of psychosis, sleep disturbance, and other symptoms. In both cases they were reduced by antipsychotics. Increased arousal may be the simple connection here. Arousal is known to be high in phobic anxiety and panic (Lader & Mathews, 1968) and in some cases of schizophrenia (Gruzelier & Venables, 1972), and would be reduced by antipsychotics. While there does appear to be a specific genetic predisposition to panic there are probably many non-specific factors, such as arousal, which also increase the likelihood of panic.

In one case panic was associated with a high caffeine intake which is not uncommon in schizophrenia and which is easily overlooked. The importance of caffeine as a harmful drug is probably underestimated in the general population also (Ashton, 1987).

The phenomenology of the panic attacks themselves was the same as that found in pure anxiety states, with a high number of symptoms, usually six or more,

and the same spectrum of symptoms, with one exception. None of these patients had the cognition that they were going crazy, insane, or losing control, possibly because they had had previous experience of really becoming psychotic. This supports the hypothesis that the cognitive aspect of panic, which consists of catastrophic interpretation, can be modified, in this case by prior experience (Argyle, 1988). (The subjects studied by Kahn *et al* (1988) did report the fear of going crazy, which appears to have been justified as they also experienced sudden increases in psychotic symptoms with their panic attacks; the difference may be explained by their sample being actively psychotic, chronically hospitalised, and low functioning.)

A different interpretation was remembered by two patients in this sample; when they had been more psychotic they had attributed their panic attacks to interference by external forces which reinforced their paranoid delusions. This is distinct from the occurrence of panic during the anxiety associated with paranoid delusions or ideas.

The seven patients with panic attacks did report other anxiety symptoms, particularly insomnia and poor concentration, but these were also present in several of the remaining 13 patients and could well have been related to either their schizophrenia or antipsychotic medication. Depersonalisation or derealisation were present in six of the seven panic patients and five of the other 13. However, none of the 13 reported sudden or intense episodes; periods of anxiety were described by nine of these patients but these did not have the sudden onset nor large number of symptoms seen in panic attacks.

A previous history of being misdiagnosed as schizophrenic is not too uncommon in panic disorder, and may be associated with the difficulty in describing depersonalisation/derealisation, plus the extreme nature of panic anxiety. This may give rise to descriptions of symptoms which have a forcefulness reminiscent of delusional illness. Anxiety and panic symptoms may be among the presenting symptoms of a schizophrenic illness. They may be seen either as part of a more general psychophysiological disturbance or as an understandable psychological reaction to psychotic experiences.

Patients with panic disorder misdiagnosed as psychosis or who have failed to respond to other drugs may be given antipsychotics. There is no evidence to support this treatment in pure panic disorder and many patients clinically report that their illness was exacerbated by taking antipsychotics, some describing a dramatic deterioration. In this study two cases had worsening of panic with the reintroduction or increasing of antipsychotics.

This could be due to some central effects of the medication or to misinterpretation of the peripheral side-effects and possible autonomic instability. The latter seemed to be a factor in case (f).

Conclusion

These cases provide further evidence for the occurrence of panic attacks outside of pure panic disorder, with or without agoraphobia. Their relationship to the patients' other, schizophrenic, symptoms varied from running a closely parallel course to being apparently independent. It is suggested that antipsychotics may increase panic attacks in some cases.

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Nicholas Argyle, MB, BS, MRCPsych, *formerly at Cambridge University Medical School, now c/o Physiology Department, MIU, Fairfield, Iowa 52556, USA*

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Schizophrenia and Marfan Syndrome

PINKHAS SIROTA, MOSHE FRYDMAN and LEA SIROTA

Five index patients and three of their first-degree relatives were affected both by schizophrenia and Marfan syndrome. Since the association appears statistically significant, the possibility of linkage disequilibrium between adjacent genes or a cytogenetic abnormality causing both disorders is suggested. These hypotheses are testable and hold promise in attempting to map the 'schizophrenia susceptibility gene' by the candidate-gene approach.

Marfan syndrome (MS) is a dominantly inherited disorder of connective tissue. Typically, the patients are tall and have an asthenic body build. Stretching

of the zonula with dislocation of the lenses, dilatation of the aortic root, prolapse of the mitral valve, and often fatal dissection of the aorta are the most