



## Narcolepsy and psychopathology: is there an association?

A. Vourdas<sup>a</sup>, J.M. Shneerson<sup>b</sup>, C.A. Gregory<sup>c</sup>, I.E. Smith<sup>b</sup>, M.A. King<sup>b</sup>,  
E. Morrish<sup>b</sup>, P.J. McKenna<sup>c,\*</sup>

<sup>a</sup>Department of Child Psychiatry, Maudsley Hospital, De Crespigny Park, Denmark Hill, London SE5 8AZ, UK

<sup>b</sup>Respiratory Support and Sleep Centre, Papworth Hospital, Cambridge CB3 8RE, UK

<sup>c</sup>Fulbourn Hospital, Cambridge CB1 5EF, UK

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### Abstract

**Background:** It is widely believed that patients with narcolepsy show high rates of associated psychiatric disturbance, especially schizophrenia and depression. However, surveys have produced conflicting findings and have not addressed the potential confounding effects of stimulant drug treatment.

**Method:** Forty-five patients with narcolepsy attending a sleep disorder clinic and 50 matched normal controls underwent structured psychiatric interview. Using a 'lifetime' approach, psychiatric symptoms and diagnoses were established for both groups.

**Results:** Four of the narcolepsy patients but none of the controls had experienced psychotic symptoms. All four patients were taking amphetamines, and the symptoms resolved when the dose was lowered or treatment was changed to modafinil. The lifetime frequency of various depressive syndromes did not differ significantly between the groups.

**Conclusions:** Contrary to previous claims this study found little to suggest that narcolepsy is associated with schizophrenia. Nor, despite its serious social and occupational consequences, does narcolepsy appear to be associated with an increased frequency of diagnosable depressive disorders. © 2002 Published by Elsevier Science B.V.

**Keywords:** Narcolepsy; Psychosis; Schizophrenia; Depression

### 1. Introduction

Narcolepsy has a time-honoured association with psychiatric disturbance. A prominent and enduring theme in the literature has been the alleged increased rate of schizophrenia [1], which has led to speculation about possible shared pathological mechanisms in the two disorders [2,3]. Depression is also widely considered to be common in narcolepsy, and the occurrence of anxiety, hysterical symptoms, personality abnormalities and sexual disorders has been commented on [4].

The first description of schizophrenia in association with narcolepsy was by Brown in 1908 [5]. He described a 17-year-old man who developed attacks of somnolence associated with poor night-time sleep and vivid dreams. He may also have had cataplexy. Two years later the patient became hallucinated, believing he could hear his schoolfellows' voices transmitted by telephone and telegraph. Later he came to believe the voices were those of staff and patients and he was sometimes violent towards them. Davison and

Bagley [1] reviewed this and 17 other case reports and concluded that schizophrenia-like psychoses occurred in patients with narcolepsy more frequently than chance would predict. In several cases the psychotic symptoms appeared to be related to and grow out of hypnagogic and other narcoleptic hallucinations. For example, Thigpen and Moss [6] described a patient who heard doors banging and people talking during episodes of sleep paralysis and believed that attempts were being made to poison him. These ideas usually disappeared when he was able to open his eyes, but sometimes they persisted for up to 25 h. Cases have also been reported where florid schizophrenic states developed against a background of excessive daytime sleepiness and other narcoleptic phenomena; when these latter symptoms were recognized and treated improvement in the psychosis also took place [2,7,8].

Although depression has occasionally been reported as being uncommon in narcolepsy [9,10], most authors consider it to be frequent [4,11–13]. This is not surprising as narcolepsy is a chronic, disabling condition which is associated with considerable social and occupational dysfunction [12–14]. As with schizophrenia, there have also been suggestions of closer links between the two disor-

\* Corresponding author. Fax: +44-1223-218638.

E-mail address: peter.mckenna@virgin.net (P.J. McKenna).

Table 1  
Rates of schizophrenia and depression in patients with narcolepsy

| Study                  | Method (%)                          | Sample (%)               | Diagnosis of narcolepsy | Schizophrenia | Depression | Comment   |
|------------------------|-------------------------------------|--------------------------|-------------------------|---------------|------------|---|
| Sours [11]             | Case note review; interview in some | 75 patients              | Clinical                | 13            | 20         | Schizophrenia considered to be stimulant-drug-induced in 3 out of 10 patients |
| Roy [16]               | Interview                           | 20 patients              | Clinical                | 5             | 5          | –   |
| Zarcone and Fuchs [17] | Case note review                    | 130 patients             | Clinical                | 0             | 5          | Amphetamine psychosis in 3 patients   |
| Kales et al. [18]      | Interview                           | 50 patients, 50 controls | Clinical + laboratory   | 0             | 30         | Patients had higher scores than controls on MMPI schizophrenia scale          |
| Krishnan et al. [19]   | Case note review                    | 24 patients              | Clinical                | 0             | 21         | Psychiatric diagnoses made according to DSM III                               |

ders. Thus patients have been described whose narcolepsy became worse when they were depressed, or in whom narcoleptic symptoms only appeared during periods of depression [9,10,15].

Formal surveys of psychiatric disorders in narcoleptic patients [11,16–19] are summarized in Table 1. It can be seen that schizophrenia has been found at rates ranging from 0 to 14%. The frequency of depression has been found to be similarly variable, but overall somewhat higher at 5–30%. As also indicated in Table 1, only one of these studies employed controls. Some of the studies had other methodological weaknesses including small sample size [16,19] or assessment based wholly or partly on case notes [11,17,18]. Another difficulty facing these studies is that until recently amphetamine and related drugs were the mainstay of treatment for narcolepsy. These drugs themselves have a well-documented capacity to induce schizophrenia-like psychosis [20,21], and they have also been associated with other symptoms including anxiety, obsessions, compulsions and depression [22,23]. None of the above surveys was able to fully address this potential confounding factor.

The aim of this study was to identify the frequency of major and minor psychiatric disorder among patients with narcolepsy as compared to a group of matched normal individuals. The study also took advantage of the recent introduction of a new wake-promoting drug, modafinil, for narcolepsy. This is a non-amphetamine stimulant which probably promotes vigilance via a non-dopaminergic/adrenergic mechanism; it has a low abuse potential [24,25] and appears to induce psychosis only rarely [26].

## 2. Method

### 2.1. Subjects

The sample was drawn from out-patients attending the clinic at the Papworth Hospital Sleep Centre, which serves

Cambridge and surrounding areas and also receives referrals from across the United Kingdom. Inclusion criteria were: age 18 years or over and diagnosis of narcolepsy meeting the criteria of the International Classification of Sleep Disorders (ICSD) [27]. Patients were excluded if they had a history of other neurological disease or disabling non-neurological illness or if their original referral to the sleep disorders clinic had been from a psychiatric service. This was done in order to avoid ascertainment bias – there would be several potential reasons for an over-representation of psychiatric disorder in such patients. (In fact, only one patient was excluded on this basis; see below.)

Of 61 patients registered with the Papworth Hospital Sleep Centre as having a diagnosis of narcolepsy, it proved possible to interview 45 (two patients had stopped attending and 14 attended yearly or less frequently). No patients refused to be interviewed. All the patients had undergone polysomnography and multiple sleep latency testing (MSLT) and most had had HLA testing. The age range of the patients was 20–88 years, (mean 46.4). Twenty-four were female and 21 male.

A control group of 50 normal individuals, recruited by advertisement from the Cambridge area, consisted of 29 women and 21 men with an age range of 19–82 years (mean 43.8). Exclusion criteria were the same as for the study group. The controls did not differ significantly from the narcolepsy patients on either variable.

### 2.2. Procedure

The patients were approached and invited to participate in the study during their regular appointment at the clinic. They and the control subjects gave written informed consent.

All subjects were assessed using the Present State Examination, 9th Edition (PSE) [28]. Interviews were carried out by the three psychiatrists involved in the study, who were trained in its use, and who worked in pairs. The PSE is a

225 detailed structured psychiatric diagnostic interview which  
226 establishes the presence or absence of many different types  
227 of psychotic and neurotic symptoms (only symptoms related  
228 to eating disorders and post-traumatic stress symptoms are  
229 not covered). All symptoms are rated as absent, present, or  
230 present in severe degree on a 0–1–2 scale, assisted by anchor  
231 points and a glossary of definitions. The PSE has been widely  
232 used in psychiatric studies and is of established reliability and  
233 validity for schizophrenia and affective disorder [29,30]. It  
234 has also been used to investigate psychiatric symptoms in  
235 association with organic brain syndrome [31], Parkinson's  
236 disease [32], epilepsy [33] and multiple sclerosis [34].

237 Like other diagnostic interviews, the PSE can be used to  
238 assess not only current psychopathology but also, by means  
239 of a 'lifetime' version, past episodes of illness [35]. The  
240 lifetime approach was used for the purposes of this study:  
241 both the patients and controls were assessed for periods of  
242 psychiatric symptomatology occurring during the whole  
243 adult life.

244 It should be noted that hypnagogic/hypnopompic halluci-  
245 nations are rated in the PSE as 'delirious hallucinations' (i.e.  
246 occurring in a state of impaired consciousness) and there-  
247 fore do not contribute to psychiatric diagnosis. During the  
248 course of the study a number of patients were encountered  
249 who experienced isolated brief episodes of visual and/or  
250 auditory hallucinations, reported as occurring while wide  
251 awake (see below). As these otherwise closely resembled  
252 hypnagogic phenomena they were not rated as psychotic  
253 symptoms.

### 255 2.3. Data analysis

256  
257 In the PSE, symptoms are combined into 'PSE  
258 syndromes': groups of individual symptoms which are intu-  
259 itively related and/or commonly co-occur. These PSE  
260 syndromes formed the main focus of comparison between  
261 the patient and control groups in this study. One example of  
262 a PSE syndrome is *nuclear syndrome*, which includes eight  
263 items from the so-called first rank symptoms of schizophre-  
264 nia (thought insertion, thought broadcast, thought commen-  
265 tary, thought withdrawal, voices discussing patient,  
266 delusions of control, delusions of alien penetration, primary  
267 delusions). Fourteen PSE syndromes cover other aspects of  
268 psychosis, including various categories of delusions, hallu-  
269 cinations, catatonia and mania. There are three PSE  
270 syndromes related to depression. *Simple depression*  
271 includes depressed mood, plus inefficient thinking, hope-  
272 lessness, suicidal ideas and plans, and depression on exam-  
273 ination. *Other features of depression* and *special features of*  
274 *depression* respectively cover the biological symptoms of  
275 depression and depressive cognitions such as guilt and self-  
276 deprecation. There are two PSE syndromes related to anxi-  
277 ety, *generalized anxiety* and *situational anxiety* (e.g. agor-  
278 aophobia). Typically, positive ratings on two or more  
279 individual symptoms in a category are required for a PSE  
280 syndrome to be counted as present.

281 Diagnoses for schizophrenia and major depression were  
282 assigned according to DSM IV [36] on the basis of PSE  
283 symptom ratings. DSM IV criteria for schizophrenia require  
284 presence of at least one major class of schizophrenic symp-  
285 tom, such as auditory hallucinations or bizarre delusions,  
286 plus evidence of deterioration in social and occupational  
287 functioning and duration of symptoms of more than 6  
288 months. When clear-cut schizophrenic symptoms are  
289 present but have not lasted 6 months and/or there has been  
290 no decline in function, the category *schizophreniform disor-*  
291 *der* is used instead. Other psychotic diagnoses include *delu-*  
292 *sional disorder*, for patients who have delusions as their  
293 only symptom, and *psychotic disorder not otherwise speci-*  
294 *fied*, for psychotic symptoms which are not sufficient for any  
295 of these categories. *Major depression*, according to DSM  
296 IV, requires persistent depressed mood for at least two  
297 weeks, coupled with loss of interest and at least three  
298 other depressive symptoms. There are a number of other  
299 depressive categories, including *depressive disorder not*  
300 *otherwise specified*.

301 Frequencies of PSE syndromes and major diagnostic  
302 categories were compared using 2 × 2 chi-squared tests.  
303 When numbers in any category were small, Fisher's exact  
304 test was used instead.

### 307 3. Results

308  
309 All 45 patients had a primary complaint of excessive  
310 daytime sleepiness. All patients had also experienced cata-  
311 lepsy. Forty-nine percent had sleep paralysis and 24% had  
312 hypnagogic/hypnopompic hallucinations. From sleep inves-  
313 tigations 69% had sleep latency of less than 10 min; 51%  
314 had REM sleep latency of less than 20 min; 80% had two or  
315 more sleep onset REM periods; 75% had an MSLT mean  
316 latency of less than 5 min. Forty of the patients had under-  
317 gone HLA testing and all of these were positive for HLA  
318 DR15/DR2. None of the patients failed to meet ICSD  
319 criteria for narcolepsy.

320 Fifteen (33%) of the patients and nine (18%) of the  
321 controls had other medical conditions. These are summar-  
322 ized in Table 2. Thirty-six patients were currently taking  
323 modafinil without amphetamine or other stimulants; six  
324 were taking amphetamine or related stimulants; one was  
325 taking both; two patients were taking neither drug. Most  
326 (71%) of the patients had been treated with amphetamine  
327 or related stimulant drugs at some point in the past. Twenty-  
328 six patients (58%) were taking anticataleptic medication at  
329 the time of interview (clomipramine in 20, other tricyclic  
330 antidepressants in two, and fluoxetine or other non-tricyclic  
331 antidepressants in four).

332 Lifetime frequencies of PSE syndromes in the two groups  
333 are shown in Fig. 1. Three patients (7%) had persecutory  
334 delusions, two (4%) had auditory hallucinations (occurring  
335 in both the second and third person, and so also meeting the  
336 requirements for *nuclear syndrome*) and two (4%) had

Table 2  
Other medical disorders in narcolepsy patients and controls

|  | Narcolepsy patients<br>(n = 45) | Normal controls<br>(n = 50) |
|--|---------------------------------|-----------------------------|
| Hypertension                           | 6                               | 2                           |
| Diabetes                               | 2                               | –                           |
| Ischaemic heart disease/<br>arrhythmia | 2                               | 1                           |
| Cardiac arrhythmia                     | 1                               | 2                           |
| Pulmonary embolism                     | –                               | 1                           |
| Thyroid disease                        | 2                               | 1                           |
| Cancer                                 | 1                               | –                           |
| Asthma                                 | 1                               | 2                           |
| Arthritis                              | 1                               | 3                           |
| Irritable bowel syndrome               | –                               | 1                           |
| Alcohol/drug use                       | 2                               | 1                           |

minor or non-specific symptoms of psychosis. Two controls had experienced psychotic symptoms, visual hallucinations in both cases. Depression and neurotic symptoms were, on the other hand, frequent in both groups. The lifetime frequency of the PSE syndrome *simple depression* was 11/45 (24%) in the patients and 15/50 (30%) in the controls. Comparison of rates of individual PSE syndromes between patients and controls (chi-squared or Fisher’s exact test) revealed no significant differences for any syndrome.

Two supplementary analyses were carried out on these PSE data. First, rates of PSE syndromes were compared in the patients and controls aged 65 years or less, on the grounds that recall of past episodes of illness may have been compromised in some of the elderly subjects. There were 40 patients and 45 controls in this age group, and they remained matched for age and sex. Once again, no

significant difference was found for any PSE syndrome. Secondly, it seemed possible that, although the patients and controls showed similar rates of psychopathology over their whole adult lives, the patients might have experienced more episodes of illness occurring after the onset of narcolepsy than had the controls over a corresponding time period. To investigate this possibility, age of first occurrence of psychiatric symptoms was established for all subjects who met DSM IV criteria for any disorder. The mean age of first onset of psychiatric symptoms was 27.9 years in 14 of the 16 narcoleptic patients (in two patients the onset was not dateable) and in the 10 controls it was 30.4; this difference was not significant ( $t = -0.57$ ).

When diagnoses rather than symptoms were considered, four patients had experienced episodes meeting criteria for definite or probable psychotic disorder according to DSM IV, in contrast to none of the controls – a significant difference (Fisher’s exact test,  $P = 0.047$ ). Of these four patients, one had a presentation consistent with *schizophreniform disorder*, one for *delusional disorder*, and the remaining two had unclear clinical pictures which would only meet criteria for *psychosis not otherwise specified*. The presentations of these patients are summarized in Table 3.

However, there were clear indications that the psychotic symptoms experienced by all four of these patient were related to amphetamine, since they remitted promptly when the dose of this drug was lowered or medication was changed to modafinil (the DSM IV diagnosis would therefore strictly be *psychotic disorder, drug-induced* in all cases).

Seven (16%) of the narcoleptic patients and nine (18%) of the controls had experienced one or more episodes meeting

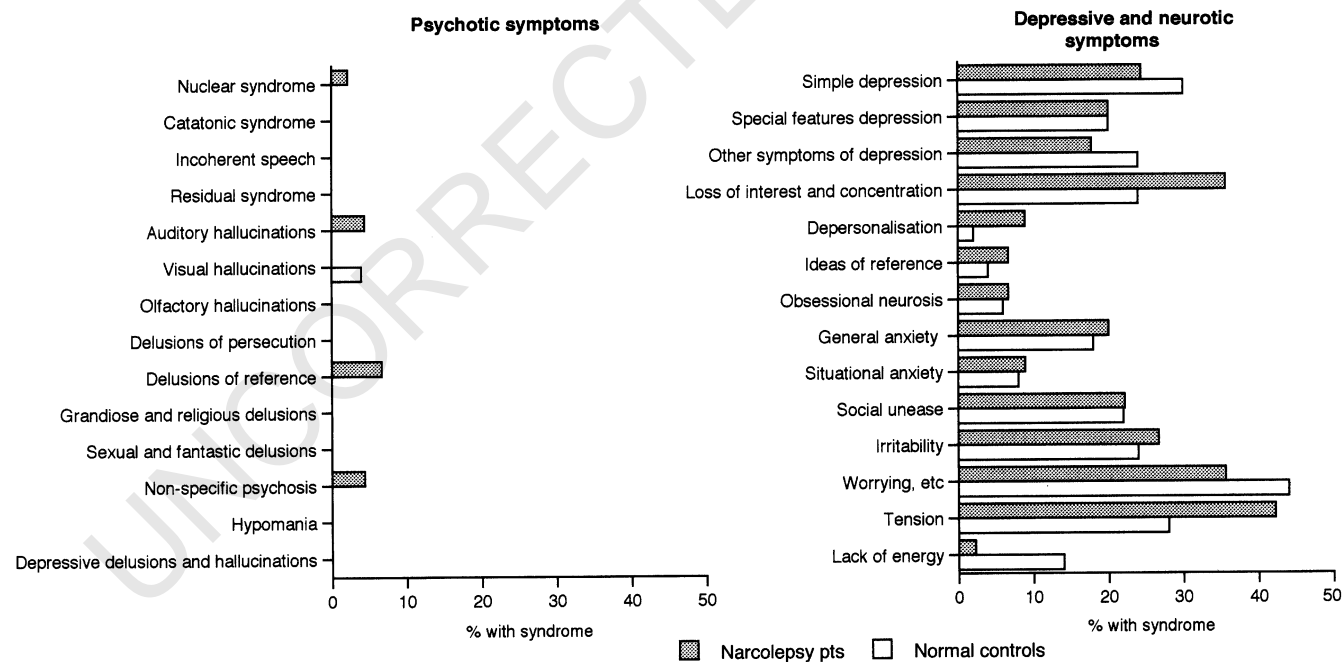


Fig. 1. Frequencies of PSE syndromes in 45 patients with narcolepsy and 50 controls.

Table 3

Narcoleptic patients with psychotic symptoms

*Female, age 21 (schizophreniform disorder<sup>a</sup>)*

Narcolepsy diagnosed two years previously. For the last 18 months, while on treatment with amphetamine, c/o 'paranoia and panic attacks'. Heard people talking about her, e.g. in night clubs, saying things like "I've had enough of her". Also would hear her parents "putting me down" in another room; they would refer to her in the third person. All symptoms disappeared 6 weeks after changing to modafinil

*Female, age 25 (delusional disorder<sup>a</sup>)*

While taking dextedrine 80 mg/day, mind racing, "on the go all the time", felt she wasn't doing her job properly, it looked like there was frosted glass between her and the world, objects and people looked bigger. Everyone at work was talking about her, convinced this was real. Also believed the management were deliberately creating artificial situations to test her out. All symptoms ceased within weeks of changing to modafinil

*Male, age 51 (psychosis not otherwise specified<sup>a</sup>)*

This patient was known to abuse amphetamine and other prescribed medication. When interviewed described depression, racing thoughts, and various neurotic symptoms. Also stated that for an unspecified period he had been hearing a voice in his head saying things like "you would do better with a spade" when gardening. Also experienced vivid images in his mind's eye when he picked up small objects; he believed these to be stored memories of historical events. Gave descriptions of strange sensations in his hands "as though something wants to communicate with me", and the so-called delusion of presence – he intermittently sensed people in the room with him, sometimes seeming to enter his body

*Female, age 28 (psychosis not otherwise specified<sup>a</sup>)*

This patient had a 6-month period where she thought everyone was staring at her. If she walked into a room she would think that everyone was talking about her. If people laughed they would be laughing at her. The whole office was talking about her. Thought people were deliberately excluding her from things. Really believed this to be true. She once confronted someone on the train because of this. She found herself listening to her flatmate talking (e.g. on the telephone) to see if this could be about her. All symptoms disappeared when she was changed from amphetamine to modafinil

<sup>a</sup> DSM IV diagnosis strictly psychotic disorder, drug-induced.

DSM IV criteria for major depression. Three (7%) of the narcoleptic patients and one (2%) of the controls met DSM IV criteria for *depressive disorder not otherwise specified*. Finally, two patients and none of the controls met DSM IV criteria for *anxiety disorder not otherwise specified*. None of these differences was significant.

In the 36 patients who were taking modafinil, the treatment period ranged from 1 to 32 months (mean 15.7). None of these patients showed psychotic symptoms over this period. Two patients met criteria for *depressive disorder not otherwise specified* while taking modafinil, and one met DSM IV criteria for *major depression* (however, this patient had had similar symptoms for two years prior to starting modafinil). No patients on modafinil met criteria for anxiety or obsessional disorders.

An incidental finding of the study was the description, by some patients, of isolated, complex perceptual abnormalities. These were similar to hypnagogic hallucinations in character, but were reported as occurring when the patient was fully awake, or during cataplexy or sleep paralysis. Examples of these are shown in Table 4.

The single patient who was excluded from the study on the basis of having been originally referred from psychiatric services had psychotic symptoms (bizarre delusions and incoherence of speech). He was a 39-year-old man with narcolepsy following encephalitis at age 9 years, who had been on treatment with amphetamine since childhood. His psychotic symptoms probably first appeared in his late twenties. When amphetamine was replaced by modafinil, the patient improved to the point that his speech became coherent and he no longer spontaneously mentioned his delusions.

#### 4. Discussion

This study of psychiatric disorder in narcolepsy found little evidence for an increased frequency of any class of symptom. However, with only 45 patients and similar numbers of controls, this negative finding has to be regarded as provisional rather than definitive. Other limitations of the study were that the patients were not individually yoked to controls on demographic variables such as age and sex, and that the two groups were not explicitly matched for factors like education and socio-economic status. Also, the study used a control group drawn from the general population and so cannot provide information about the relative frequency of psychiatric disability in narcolepsy compared to other patient groups with chronic medical or neurological illnesses.

Perhaps the most surprising finding of the present study was the small number of narcoleptic patients – four out of 45 – who had experienced psychotic symptoms. Furthermore, it seemed highly likely that in all four cases the psychosis was due to amphetamine or related stimulant drug treatment, as it remitted when this medication was reduced or withdrawn. In these circumstances it may be instructive to re-examine the 18 case reports of schizophrenia associated with narcolepsy collected by Davison and Bagley [1]. Three of the patients in these case reports were taking amphetamine or related drugs [37,38], and one [39] was taking piperidol, which also has amphetamine-like properties. Two further reports [40,41] unusually failed to mention any drug treatment despite the fact that amphetamine was established as a treatment for narcolepsy at the time. Three cases would not nowadays be accepted as narcolepsy: two had somnolence

Table 4

Non-hypnagogic perceptual experiences in narcoleptic patients

*Hypnagogic-like visual hallucinations when wide awake*

“I’m awake but tired, I may see a wall in front of me. I stretch out my hands ahead to convince myself”

*Out of body experiences lasting half an hour, occurring several times over a period of months*

“I was sitting on the bed and I saw myself leaving my body and moving around the house. Then I walked back to the bedroom where I saw my body. I was not asleep and I could stop it any time”

*Hypnagogic-like visual hallucinations when wide awake*

While in McDonald’s saw a fisherman placing maggots on his line. Tried to point him out to a friend. Lasted 3–4 min. Often fleetingly sees car doors open, and similar

*Hypnagogic hallucination-like experiences when wide awake*

“A person climbed into bed with me, it was very frightening, my heart was pounding. I was too frightened to look round. Eventually (after about half an hour) I fell asleep”

*Complex perceptual experience during cataplexy*

Feels someone “smelly” may be in the doorway. He then sits on her and squeezes all the air out of her body. Very frightening, “It’s so real”

*Hypnagogic hallucination-like experiences when wide awake*

Hears knocking, voice calling name, approximately twice a day, when wide awake. Also hears talking up to 5 min at a time, “usually when I’m a little bit tired”; “although I’m not asleep I seem to wake up”. Also fleeting visual hallucinations, e.g. cats in garden or climbing up curtains, “usually when I’m tired”

related to pituitary tumours [42,43] and one had had encephalitis lethargica [44]. Other case reports gave no description of schizophrenic symptoms, only hypnagogic hallucinations or similar phenomena [9,45,46]. Nevertheless, five reports gave reasonably detailed and convincing descriptions of schizophrenia occurring in apparently typical cases of narcolepsy [5,47–50].

In several of these case reports it is apparent that the diagnosis of schizophrenia was made despite concurrent stimulant drug treatment, apparently on the basis that the patient was taking only modest doses of amphetamine, or had been on treatment for a long time without adverse effects, or that the features of the psychosis went beyond the typical paranoid-hallucinatory state of amphetamine psychosis. In reality, amphetamine psychosis does not show any simple relationship with dosage and duration of drug use – it may develop after a single large dose of amphetamine, or only supervene after months or years of regular use [20]. Nor does stimulant-drug-induced psychosis always take the form of paranoid-hallucinatory state; cases have been documented which reproduce most or all the symptoms of schizophrenia including thought disorder and negative symptoms [20,22].

It is also evident from these case reports that the hypnagogic and other hallucinations of narcolepsy have occasionally caused difficulties with the differential diagnosis from schizophrenia. In general, the distinction between hypnagogic and schizophrenic hallucinations should not cause problems: the former are primarily visual whereas the latter are typically auditory, and visual hallucinations are usually considered to be uncommon or rare in schizophrenia. Confusion may, however, arise in cases where narcoleptic hypnagogic experiences are complex, non-visual or multi-

modal in nature. Thus hypnagogic hallucinations have been reported which took the form of demons appearing from clouds of smoke, waves of rats running over the patient, hands manipulating the genitals, music, threatening speech, feelings of levitation, and out-of-body experiences [2,51,52]. Sleep paralysis can also be associated with complex hallucinations [51,53] – one of the patients of Douglass et al. [2] who was originally diagnosed as schizophrenic but improved on treatment for narcolepsy had hallucinations of being raped by escaped criminals at night, “hands and feet tied down, and under anaesthesia”. Our study also suggests that a minority of patients with narcolepsy may even experience otherwise typical hallucinations which take place against a background of wakefulness rather than when half-asleep.

Perhaps as surprising as the lack of an increased rate of psychosis in narcolepsy was the present study’s failure to find that depression was more prevalent than in an age- and sex-matched sample of the normal population. This finding seems counter-intuitive since depression is frequent in medically ill patients [54], and narcolepsy has not previously been thought to be an exception to this rule. Thus Broughton et al. [12] found that 51% of 180 narcoleptic patients reported recurrent depression, and Daniels et al. [14] found 57% of 500 patients contacted in a postal survey had scores in the mildly, moderately or severely depressed range on the Beck Depression Inventory (BDI).

One possible reason for the discrepancy between these rates and the 24% rate of simple depression in our study is that we measured depression using a structured psychiatric interview rather than by means of a self-report scale such as the BDI. Like other structured psychiatric interviews, the PSE requires depression to be present to a clinically signifi-

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673 cant degree, based on a combination of frequency and sever-  
 674 ity of symptoms as well as objective evidence of depressed  
 675 mood, in contrast to subjective depressive complaints,  
 676 which are common without necessarily being clinically  
 677 significant. In fact the 24% rate of simple depression we  
 678 found agrees quite well with those of 20–30% [11,18,55]  
 679 found in other surveys of narcolepsy patients in which  
 680 presence of depression was based on clinical diagnosis.  
 681 The rate is also similar to that found in a study which  
 682 used the PSE to assess depression in another chronic,  
 683 disabling central nervous system disorder: Brown and  
 684 McCarthy [32] found that the PSE syndrome of simple  
 685 depression was present in 25% of a sample of 40 moderately  
 686 to severely disabled out-patients with Parkinson's disease.

687 It is accepted that many if not all chronic medical disor-  
 688 ders are associated with a higher than normal rate of depres-  
 689 sion [54] and it is difficult to explain our failure to find this  
 690 to be the case in narcolepsy. Depression was frequent  
 691 among the normal controls in our study, with 30% having  
 692 the PSE syndrome of simple depression and 18% having  
 693 met at some time criteria for major depression. However,  
 694 while this rate may seem high, it has to be remembered that  
 695 depression is a common disorder: according to a recent  
 696 nationwide survey [56] 17% of the United States population  
 697 aged 15–54 years will have experienced an episode severe  
 698 enough to have met criteria for major depression – and this  
 699 excludes elderly patients who are at more risk. Another  
 700 possible explanation could lie in the drugs used to treat  
 701 narcolepsy: amphetamine has mood-elevating properties  
 702 and antidepressants are commonly prescribed for cataplexy.  
 703 However, the limited available evidence suggests that this is  
 704 probably not a contributing factor. Merritt et al. [57] found  
 705 that depression in narcolepsy was unrelated to pharmaco-  
 706 logical treatment, and Daniels et al. [14] found that patients on  
 707 both stimulants and antidepressant drugs had significantly  
 708 higher BDI scores than those on either drug alone or on  
 709 neither drug.

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