Neurasthenia in a longitudinal cohort study of young adults

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SYNOPSIS   This study examines the concept of neurasthenia in a longitudinal cohort of young adults selected from a community sample of the canton of Zurich, Switzerland. The major focus is on the validity of the case definition of neurasthenia. Close approximations of the proposed descriptive and research definitions of the ICD-10 are employed as well as the concept of 'irritable weakness' as described in 1831 by Kraus (1926–1932).

The prevalence of neurasthenia defined according to the ICD-10 criteria was: 1% across 10 years and 0·9% in 1988 for a duration criterion of ≥ 3 months; and 8·1% across 10 years and 12% in 1988 for a duration criterion of ≥ 1 month. The duration criterion of ≥ 3 months appeared to be excessively restrictive to represent individuals with neurasthenia in the community. Subjects with 1 month episodes of neurasthenia exhibited sufficient differences from controls and similarities to subjects with anxiety or depressive disorders to justify a 1 month duration criterion for neurasthenia in community samples.

The clinical significance of neurasthenia was indicated by the magnitude of subjective distress, and occupational and social impairment reported by the majority of the cases. Prospective assessment of the longitudinal course of neurasthenia revealed that approximately 50% of the cases continued to exhibit this disorder at follow-up. Our findings suggest that neurasthenia is equally likely to represent an early manifestation of affective illness as it is a consequence in those neurasthenic subjects who exhibited comorbid affective disorders. The magnitude, chronicity, impairment, longitudinal stability and distinction from anxiety and depression associated with this condition in the general population, suggest that neurasthenia is an important diagnostic entity for which additional validation studies should be undertaken.

INTRODUCTION

With the recent focus on chronic fatigue syndrome, there has been a resurgence of interest in the concept of neurasthenia (Costa e Silva & De Girolamo, 1990; Wessely, 1991). Although Beard, the American neurologist, is credited with the introduction of the term 'neurasthenia' in 1869 to describe a syndrome characterized by exhaustion of the nervous system, various forms of nervous asthenia have been described throughout the history of medicine (Costa e Silva & De Girolamo, 1990).

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Definition

Beard's description of this syndrome included the following criteria: general malaise, debility of all the functions, poor appetite, abiding weakness in the back and spine, fugitive neuralgic pains, hysteria, insomnia, hypochondria, disinclination for consecutive mental labour, severe and weakening attacks of sick headache, and other analogous symptoms. He also required that anaemia and other organic diseases be excluded (Beard, 1869).

The definition of neurasthenia has generally been vague and broad. Although the key features of physical and mental fatigue are generally included in most definitions, the specific concomitant symptoms are highly variable. The

Table 1. *International Classification of Disease-10 criteria for F48.0 neurasthenia*

A Either of the following must be present:
  (1) Persistent and distressing complaints of feelings of exhaustion after minor mental effort (such as performing or attempting to perform everyday tasks that do not require unusual mental effort);
  (2) Persistent and distressing complaints of feelings of fatigue and bodily weakness after minor physical effort.

B At least one of the following symptoms must be present:
  (1) feelings of muscular aches and pains
  (2) dizziness
  (3) tension headaches
  (4) sleep disturbance
  (5) inability to relax
  (6) irritability.

C The patient is unable to recover from the symptoms in criterion A (*1*) or (*2*) by means of rest, relaxation, or entertainment.

D The duration of the disorder is at least 3 months.

E The disorder does not occur in the presence of organic emotionally labile disorder, post-encephalitic syndrome, post-concussional syndrome, mood (affective) disorders, panic disorder, or generalized anxiety disorder.

major difference between some of the more recent definitions of the condition and the descriptions of the neurologists of the nineteenth and early twentieth centuries is the inclusion of 'nervous irritability' as a key feature of the condition. A cluster analysis of the symptoms of subjects from the general community conducted by Angst & Koch (1991) yielded the same three distinct factors that have been the key features of clinical descriptions of neurasthenia, namely, physical exhaustion, mental fatigue and nervous irritability.

Although the symptoms of chronic fatigue syndrome (CFS) are quite similar to those cited above for neurasthenia, the major difference between the two definitions is the requirement of myalgia for CFS (Wessely, 1991). The aetiology of CFS has often been attributed to viral infections as in the post-viral fatigue syndromes (i.e. chronic Epstein–Barr infection, Tobi *et al.* 1982); however, evidence that the characteristic physical and mental fatigue are induced by viral infection is still lacking (Holmes *et al.* 1988).

Aetiological theories of neurasthenia are nearly as numerous as the physicians who described the disease: horseback riding (Hippocrates, in Roccatagliata, 1973); metabolic factors including glucose metabolism, pituitary dysfunction, and thyroid abnormalities

(Mirouze, 1962); life stress (Beard, 1869); drug abuse (Beard, 1869); sexual excesses (Freud, 1895); genetic factors (Möbius, 1894; Costa e Silva & De Girolamo, 1990); personality factors; and psychiatric disorders, particularly depression. However, most contemporary formulations require exclusion of organic abnormalities in order to diagnose neurasthenia.

Association between neurasthenia and somatic disturbances

A variety of non-psychiatric syndromes have been associated with neurasthenia. Beard (1869) described stomach disturbances, migraine, menstrual disorders, back pain, and respiratory problems. Although most of the diagnostic criteria for neurasthenia rule out discrete organic causes of the syndrome, the above-cited somatic disturbances tend to comprise symptoms rather than pathognomonic manifestations of a specific disease.

Association between neurasthenia and psychiatric disorders

An association between neurasthenia and the 'neurotic' psychiatric disorders has been reported in both descriptive literature and systematic studies of clinical samples. The three most frequently cited disorders are depression, anxiety, and somatization. In the classic essay in which he first described 'Anxiety Neurosis', Freud contended that Beard's formulation of the concept of neurasthenia was too broad to be clinically meaningful. His definition of genuine neurasthenia excluded the hereditary nervous disorders and the 'pseudo-neurasthenias' induced by physical diseases, as well as melancholia and anxiety neurosis (Beard, 1869). Thus, Freud provided the first clear discrimination between neurasthenia and anxiety neurosis and melancholia (Freud, 1895). Freud's observation was recently confirmed by a multivariate analysis by Goldberg *et al.* (1987), who demonstrated that a symptom cluster characterized by fatigue can be distinguished from those with anxiety and depression.

The proportions of neurasthenics who also exhibit a psychiatric disorder range from one-half to three-quarters in psychiatric samples (Allan, 1944; Taerk *et al.* 1987; Manu *et al.* 1988; Strauss, 1988; Swartz, 1988; Kruesi *et al.* 1989; Wessely & Powell, 1989; Hickie *et al.*

1990), and from one-third to one-half in primary care settings (Katon & Walker, 1993). Katon & Walker (1993) reported that the association between fatigue and anxiety and depression increases as one moves from the community to primary care to tertiary care facilities. This suggests that neurasthenics with psychiatric disorders are more likely to seek treatment than those without comorbid conditions.

Previous analyses of this sample revealed that 50 % of the neurasthenic subjects had a history of anxiety or depression. Moreover, the persons with extended neurasthenia had nearly twice the degree of comorbidity with the latter disorders than did those with recurrent brief neurasthenia (Angst & Koch, 1991).

Personality and neurasthenia

In a study of the pre-morbid personality of neurasthenics who had sought treatment for this condition, Nystrom & Lindegard (1975) found that although sub-validity, or psychasthenia, was associated with neurasthenia, even greater associations emerged between psychasthenia and anxiety and depression. This suggests that personality factors comprise non-specific and independent risk factors for the subsequent development of these syndromes. More recently, Blakely *et al.* (1991) examined psychiatric symptoms and personality in patients with CFS and chronic pain compared to normal controls. In classifying the patients on both the symptom and personality scales, they found several clusters of CFS patients, one of which had no evidence of psychiatric or personality disorder. Moreover, their data suggested that emotionality is a predisposing factor rather than a reaction to neurasthenia (Blakely *et al.* 1991). However, these findings require replication in a prospective study of a more systematic sample.

Treatment of neurasthenia

In accordance with the multiple causative factors which have been implicated for neurasthenia, numerous forms of treatment have been suggested as well. For example, Beard (1869) recommended general electrization (i.e. electric shocks applied over the head and spine), whereas Vittoz (1903) applied 'brain control'. Antidepressants are the most widely employed agents in the contemporary treatment of neurasthenia or CFS (Wessely, 1991).

Current studies of neurasthenia

The diagnostic criteria for research on neurasthenia in the most recent version of the International Classification of Disease, Edition 10 (WHO, 1993) are presented in Table 1. The chief criteria are as follows: (*a*) persistent fatigue after ordinary tasks; (*b*) one of six symptoms; (*c*) inability to recover after rest; (*d*) duration of at least 3 months; and (*e*) exclusion of concomitant anxiety and depressive syndromes, and specific organic syndromes. The distinction between neurasthenia and anxiety/depression described by Freud (1895) has been adopted in the ICD-10 as well; concurrent anxiety and depression preclude a diagnosis of neurasthenia.

The emergence of CFS as a significant disease entity has led to the generation of numerous studies investigating the clinical phenomenology and associated features of this condition. Community studies of fatigue and fatigability have provided preliminary evidence of the magnitude of this complaint in the general population. Although variation in sampling methods precludes derivation of accurate aggregate rates across studies, the current prevalence of fatigue is approximately 24 % in community studies and 15 % in primary care settings (Lewis & Wessely, 1992). Although there is a greater proportion of women with fatigue, there is still a substantial proportion of males who complain of fatigue. The most important finding from these studies is the substantial degree of global dysfunction and chronicity associated with fatigue (Kroenke *et al.* 1988; David *et al.* 1990; Cathébras *et al.* 1992). However, the degree to which the findings regarding the symptom of fatigue generalize with those with the syndrome of neurasthenia needs to be examined.

Although there are several studies currently investigating the prevalence of the ICD-10 disorders in the community and in primary care settings under the auspices of the WHO, to our knowledge, there are no published data from epidemiological samples on the magnitude or correlates of this condition in the general population. The major purpose of the present study is to assess the validity of the case definition of neurasthenia. Close approximations of the proposed descriptive and research definitions of the ICD-10 (WHO, 1993) are employed as well as the concept of 'irritable weakness' as de-

scribed by Kraus (1926–1932). Therefore, the goals of the present study were as follows.

(1) To estimate the magnitude and demographic distribution of neurasthenia in a prospective study of a cohort selected from the general population.

(2) To test the applicability of the ICD-10 definition of neurasthenia in an epidemiological sample through systematic assessment of the inclusion and exclusion criteria and their validity.

(3) To examine the association and longitudinal course of psychiatric disorders and neurasthenia.

(4) To examine the clinical and social manifestations of neurasthenia and its longitudinal stability.

METHOD

Subjects

The subjects of this report are a cohort of 29–30-year-olds from Zurich, Switzerland. The sample was originally selected in 1978 according to scores on a screening test of current symptoms, the Symptom Checklist 90 (SCL-90-R), from which high and low risk groups were selected. The SCL-90-R was developed by Derogatis (1977) as a self-report inventory about current psychiatric symptoms. It is a 90-item multidimensional symptom inventory that yields scores on nine symptom dimensions. The sample was first interviewed in 1979 at age 20, with three subsequent interviews in 1981, 1986, and 1988. The subjects in this report are comprised of 424 subjects (200 males and 224 females) who were interviewed directly in 1988. A more detailed description of the sampling procedures is given by Angst *et al.* (1984) and Merikangas *et al.* (1990).

Procedure

A direct interview, the Structured Psychopathological Interview and Rating of the Social Consequences for Epidemiology (SPIKE), was administered by psychiatric residents and clinical psychologists with extensive clinical training. This interview schedule assesses a number of somatic syndromes, including headache, gastrointestinal, cardiovascular, and respiratory syndromes, as well as psychological syndromes including depression, phobia, obsessive-com-

pulsive, anxiety, and substance abuse (Angst *et al.* 1984). Psychiatric diagnoses were made according to both the DSM-III and the DSM-III-R Criteria (American Psychiatric Association, 1980, 1987). Screening probes were administered for each section and symptoms, duration, frequency, severity, and treatment history and impairment are assessed for every positive answer. Personal and family history of the syndromes were also assessed for all subjects, irrespective of endorsement of the diagnostic screening question for each section.

Symptoms of neurasthenia

Symptoms of neurasthenia were collected at all four interviews. Because the interviews were developed prior to the introduction of the ICD-10, only two of the symptomatic criteria in Section B were collected in the diagnostic interview, namely sleep disturbances and irritability. Therefore, we required at least one of these symptoms for the diagnosis of neurasthenia. The other symptoms of neurasthenia were assessed in the SCL-90, which was administered at the time of each of the four interviews. However, the vast majority of subjects complaining of persistent weakness and fatigue met more than half of the symptomatic criteria for neurasthenia. Organic causes of neurasthenic symptoms could not be excluded in our data.

Impairment and severity were assessed in two ways: (*1*) as an analogue rating from 0–100, with 0 representing no impairment (i.e. no interference with daily activities or the absence of suffering or distress from the symptoms), and a score of 100 representing complete incapacitation or extreme suffering or distress from the symptoms; and (*2*) as a categorical scale from 1–5, with descriptions to anchor each level of severity or impairment.

Assessment of personality

The Freiburg Personality Inventory (FPI) is a 212-item personality questionnaire designed to measure 9 primary factors including nervousness, aggressivity, depressiveness, excitability, sociability, temperament and striving for dominance, inhibition and frankness (Fahrenberg *et al.* 1970). In addition to three secondary factor provided by the test developers, three factors derived from a factor analysis of very large

Table 2. *Weighted longitudinal and 1-year prevalence rates of neurasthenia by components of ICD-10 definition*

Neurasthenia groups	1979	1981	1986	1988	Total
Symptoms* + Duration > 3 months* + Anxiety/depression†	0·7	0·1	1·1	2·1	3·7
Symptoms + Duration > 3 months‡	1·0	0·6	0·2	0·9	1·0
Symptoms + Anxiety/depression	2·3	1·5	5·9	2·5	11·4
Symptoms only*	2·6	1·8	5·4	7·6	7·0
Anxiety/depression, No symptoms*	11·8	17·1	17·3	16·6	25·3
None of the above	81·6	78·9	70·1	70·3	51·6

* One of ICD-10 symptom criteria for neurasthenia.
† DSM-III-R anxiety or affective disorder.
‡ ICD-10 definition of neurasthenia.

samples at the Zurich site were also employed, namely extraversion, autonomic lability, and aggressivity (Angst & Clayton, 1986).

Statistical analyses

In the present study, the statistical analyses that were conducted to test the significance of the differences for comparisons of the categorical variables were χ^2 corrected for continuity. Analyses of variance were applied to the continuous variables using the general linear models procedure of the Statistical Analysis System (Reinhardt & Winston, 1985). Group mean differences were compared with the Duncan Multiple Range Test, which corrects for chance (Duncan, 1975).

RESULTS

Assessment of diagnostic criteria

Table 2 presents the weighted and longitudinal rates of neurasthenia according to the step-wise application of the ICD-10 criteria for neurasthenia. The figures in the second row labelled 'symptoms and duration $\geq$ 3 months' represent the subjects who met all of the ICD-10 criteria for neurasthenia (i.e. persistent fatigue, $\geq$ 1 of the 6 symptoms, inability to recover, plus $\geq$ 3 months duration and the absence of concomitant anxiety or depressive disorders) at each of the 4 interviews and across the entire study interval. Inspection of longitudinal trends shown in Table 2 revealed that the rates of neurasthenia were quite stable over 10 years at 1 %. However, there was an increase over time in the proportion of subjects who reported symptoms of neurasthenia as the sample aged from 20 to 30. Inspection of

the sex ratio across the 10 years of follow-up revealed that the prevalence of neurasthenia was equal among males and females during the initial stages of the study, whereas females exhibited 1·6-fold greater rates of neurasthenia than males during the later interviews.

Application of successive criteria of exclusion of subjects with anxiety or depressive disorders and duration of $\geq$ 3 months to the proportion of subjects with neurasthenic symptoms yielded a dramatic decrease in the longitudinal rates of neurasthenia from 23·1 % to 1 %. This indicates that nearly 75 % of individuals complaining of persistent and distressing fatigue and weakness with symptomatic manifestations are excluded from the diagnosis of neurasthenia. Because the 3 month duration criterion yielded groups that were too small for meaningful analysis, a 1 month duration was employed in subsequent analyses. The major focus of this paper is therefore on determining whether differences exist between pure and comorbid cases of neurasthenia. There were no differences between the four groups in demographic characteristics including marital status, education, number of children and social class.

Symptoms

The non-criterial symptoms of neurasthenia collected in the diagnostic interview and self-reported criterial symptoms according to co-morbid anxiety and depression in neurasthenic subject, at the most recent interview are presented in Fig. 1. No major differences in symptom frequencies emerged between the co-morbid and non-comorbid neurasthenics. The large proportion of neurasthenic subjects who
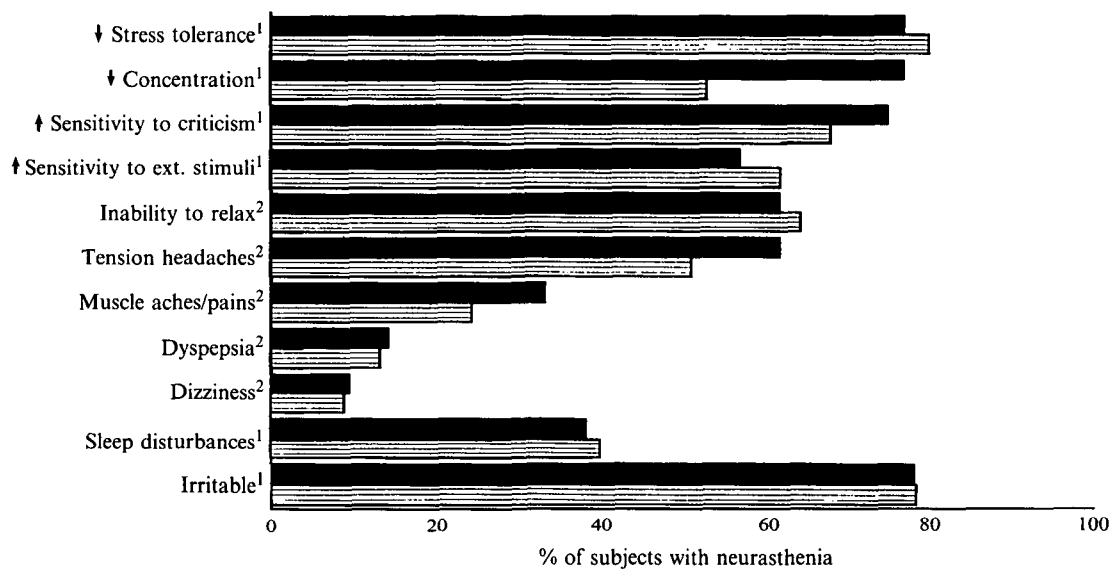
FIG. 1. Symptoms of neurasthenia by neurasthenia comorbidity groups in 1988. (■, Anxiety/depression + neurasthenia; ▤, neurasthenia only; [1] = interview; and [2] = SCL-90 self-report.)

Table 3. *SCL-90 scores† in neurasthenia by comorbidity groups in 1988*

	Neurasthenia + Anx/dep (N = 32) Mean (S.D.)	Neurasthenia only (N = 51) Mean (S.D.)	Anx/dep only (N = 74) Mean (S.D.)	Neither (N = 267) Mean (S.D.)
Scale scores				
Anxiety	60·3 (11·43)	56·1 (8·3)	55·9 (14·13)	50·4 (11·28)**
Depression	66·1 (11·73)	60·7 (7·2)	61·1 (12·0)	53·8 (10·92)**
Hostility	55·9 (13·96)	55·6 (10·0)	56·3 (10·7)	51·5 (10·33)**
Interpersonal sensitivity	66·4 (13·40)	60·8 (9·14)	60·8 (13·66)	54·9 (11·56)**
Obsessive compulsive	63·3 (13·40)	54·9 (10·8)	56·4 (12·99)	50·9 (11·56)**
Paranoia	62·6 (10·66)	57·1 (10·13)	56·7 (11·62)	53·2 (11·55)**
Phobia	60·9 (11·43)	55·1 (12·4)	55·8 (12·26)	50·3 (11·37)**
Psychoticism	64·2 (11·96)	57·7 (10·04)	57·0 (12·02)	53·1 (10·41)**
Factor scores				
Somatic instability	65·2 (9·68)	53·2 (10·98)	52·8 (10·67)	48·6 (9·42)**
Emotional instability	60·9 (10·14)	55·6 (6·99)	56·3 (9·91)	50·8 (9·43)**
Vegetative instability	58·4 (7·91)	56·1 (8·26)	55·8 (8·79)	51·2 (8·11)**
Global severity index	65·0 (11·30)	58·9 (7·39)	60·2 (11·31)	53·8 (9·17)**

† *t* transformed (mean = 50, S.D. = 10).
** $P < 0.01$.

reported decreased stress tolerance, and increased sensitivity to criticism and to external stimuli (i.e. 82%, 73% and 67%, respectively) suggests that these phenomena may constitute additional features of neurasthenia. In contrast, the criteria of muscle aches and pains, dyspepsia, and dizziness were reported by less than one-third of the subjects with neurasthenia, suggesting that they may not comprise valid clinical features of this condition.

The factor and scale scores of the SCL-90 in the neurasthenia groups and controls are shown in Table 3. All three groups of affected subjects differed significantly from the unaffected subjects on all of the scale scores and factor scores of the SCL-90. The comorbid group exhibited the greatest scores on all scales, whereas the groups of subjects with either neurasthenia alone or anxiety/depression alone had nearly identical scores on all scales. This suggests a lack of

Table 4. *Clinical features of neurasthenia by comorbidity in* 1988

	Neurasthenia + Anx/dep (N = 32)	Neurasthenia only (N = 51)	
Maximal duration/episode (past year %)			
⩽ 1 week	28·1	66·7	
> 1 week–1 month	6·3	19·6	**
⩾ 1 month	65·6	13·7	
Subjective distress			
mean (S.D.)	25·8	53·7	
	(25·7)	(28·0)	
Attribution (%)			
Physical	22·6	30·2	
Psychological	96·8	72·1	**
Impairment (%)			
Occupational	80·6	79·1	
Social	93·5	86·0	
Dimensional rating, mean (S.D.)	39·7	33·9	
	(29·0)	(25·6)	
Professional treatment			
Past year (%)	41·9	23·3	
Lifetime, mean (S.D.)	0·7	0·3	*
	(0·83)	(0·69)	

* $P < 0.05$; ** $P < 0.01$.

specificity of the SCL-90 scale scores for both neurasthenia and affective disorders.

Clinical features

The clinical features of neurasthenia in the two groups of subjects during the year prior to the most recent interview are presented in Table 4. Patterns of duration of neurasthenic episodes differed for the comorbid and non-comorbid groups. The majority of subjects in the non-comorbid group reported episodes of approximately one week, but occurring frequently over the one year period. In contrast, the majority of the comorbid subjects reported longer episodes, lasting an average of 1–2 months, but with less frequency than the non-comorbid group.

The degree of subjective distress attributed to neurasthenia was similar for the two groups of subjects. The magnitude of the distress was rated on an analogue scale from 0, indicating no distress, to 100 for extreme distress. The high mean levels found in both groups suggest that the symptoms of neurasthenia are associated with a severe degree of distress in all of the subjects who meet the criteria for this syndrome.

Likewise, there was a remarkable degree of subjective and occupational impairment associated with neurasthenia among all affected persons. Approximately 80 % of the cases reported that neurasthenia symptoms interfered with their ability to pursue their usual occupational activities. The mean level of 80 (range 0–100) suggests that the complications of neurasthenia were sufficient to inhibit routine daily activities. Similar findings emerged for the dimensional measures of impairment in both occupation and social activity.

The proportion of subjects who had sought treatment differed significantly between the comorbid and non-comorbid groups. The treatment rates among the comorbid cases were similar to those of the anxiety and depression group, with 42 % reporting having sought

Table 5. *Rates of somatic and psychiatric disorders by neurasthenia comorbidity groups in* 1988

	Neurasthenia + Anx/dep (N = 32)	Neurasthenia only (N = 57)	Anx/dep only (N = 74)	Neither (N = 267)
Somatic disturbances (%)				
Back	50·0	37·3	37·8	31·8
Circulation	21·9	23·5	13·5	9·4**
Menstrual (females only)	52·9	35·1	44·4	34·3
Migraine	32·0	43·8	25·8	23·3*
Respiratory/heart	28·1	15·7	10·8	6·7**
Stomach	43·8	25·5	20·3	10·5**
Psychiatric disorders (%)				
Alcoholism	9·4	3·9	8·1	2·3*
Cannabis abuse	3·1	2·0	2·8	0·4
Tobacco dependence	62·6	41·2	41·7	25·8**
Agoraphobia	6·3	2·0	2·8	1·5
Simple phobia	6·3	11·8	10·8	8·6
Social phobia	9·4	3·9	4·2	2·7

* $P < 0.05$; ** $P < 0.01$.

Table 6. *FPI scores by neurasthenia comorbidity groups in* 1988

	Neurasthenia + Anx/dep (N = 32) Mean (S.D.)	Neurasthenia only (N = 51) Mean (S.D.)	Anx/dep only (N = 74) Mean (S.D.)	Neither (N = 267) Mean (S.D.)
Scale scores				
Nervousness	22·9 (8·77)	20·5 (7·63)	18·5 (7·25)	15·1 (5·52)**
Aggressiveness	21·5 (7·51)	16·4 (5·92)	18·3 (6·95)	15·2 (6·82)**
Depression	22·0 (8·30)	16·6 (6·98)	17·4 (8·04)	12·1 (6·33)**
Irritability	25·9 (8·07)	23·0 (8·04)	21·9 (8·18)	19·5 (8·00)**
Sociability	20·3 (7·63)	18·6 (8·16)	19·5 (8·03)	20·6 (7·28)
Resilience	13·4 (9·41)	13·7 (7·76)	12·8 (8·82)	16·6 (7·57)**
Aggressive reaction	19·1 (7·63)	17·1 (6·97)	17·3 (7·16)	15·4 (7·43)**
Inhibition	21·9 (9·01)	21·7 (8·89)	21·4 (8·67)	18·2 (8·40)**
Openness	19·7 (6·14)	19·0 (7·55)	18·0 (8·01)	16·7 (8·06)
Factor scales				
Aggressiveness	22·2 (7·72)	18·9 (6·74)	18·8 (7·07)	16·6 (7·20)**
Extraversion	17·3 (8·08)	16·3 (8·00)	17·1 (7·96)	19·2 (7·59)*
Neuroticism (autonomic lability)	23·4 (7·65)	20·1 (7·44)	18·5 (7·31)	14·7 (5·92)***

† *t* transformed (mean = 20, S.D. = 8).
* $P < 0.05$; ** $P < 0.01$; *** $P < 0.001$.

1979		1988

Neurasthenia only (N=33)
14% Neurasthenia + Affective/anxiety disorder
31% Neurasthenia only
21% Affective/anxiety disorder only
34% Neither

Affective or anxiety disorder only (N=110)
8% Neurasthenia + Affective/anxiety disorder
25% Neurasthenia only
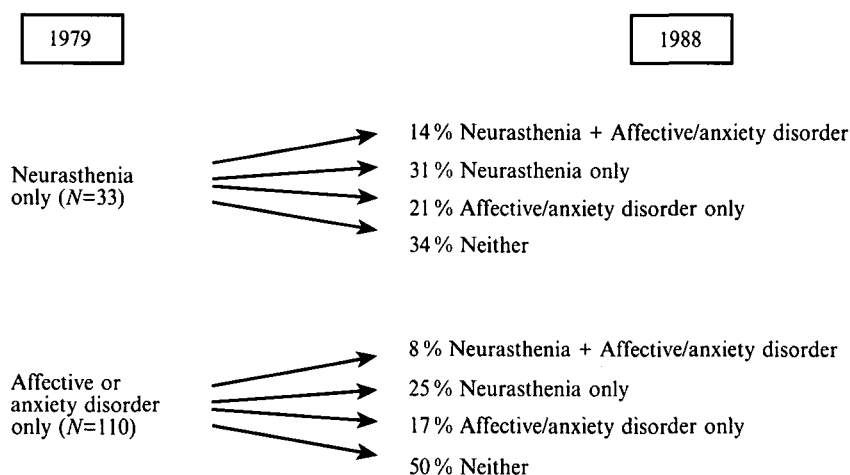17% Affective/anxiety disorder only
50% Neither

FIG. 2. Ten-year follow-up of subjects with neurasthenia only or affective/anxiety disorder only.

professional treatment for their condition. In contrast, only 23% of the pure neurasthenics had sought professional treatment.

Comorbidity

Table 5 presents the cross-sectional association between neurasthenia and other somatic and psychiatric syndromes at age 30. Because the concept of neurasthenia includes both physical and mental weakness, the SPIKE interview, which assessed a variety of somatic conditions as well as psychological conditions, was an ideal source of data on this condition. Neurasthenia was associated with numerous somatic conditions including migraine, stomach disturbances, circulation problems, cardiac and respiratory disturbances. However, other conditions assessed, including back problems, were not associated with neurasthenia, thereby suggesting that these subjects are not simply exhibiting a tendency to somaticize across all systems.

The associations between neurasthenia and the major psychiatric disorders are also shown in Table 5. Because major depression, dysthymia, panic disorder, and generalized anxiety were included in the group definitions, the analyses

shown in this table include only the phobic disorders and substance abuse. Alcoholism was elevated only among the subjects with depression/anxiety disorders with or without neurasthenia, with a four-fold elevation in the rates of alcoholism compared to that of controls. For all other disorders except simple phobia, the non-comorbid groups exhibited intermediate rates between the comorbid and the controls.

Personality

The factor and scale scores on the FPI at the most recent interview according to the neurasthenic comorbidity groups are shown in Table 6. The neurasthenics had elevated scores on nearly all scales with the exception of the depression score. The results of the factor score analyses revealed that the neurasthenics were characterized by somatic symptoms, autonomic instability, and irritability. The comorbid group exhibited higher scores on all of these dimensions than the pure neurasthenics. These findings validate the symptoms endorsed by the subjects during the diagnostic interview, because they were assessed completely independently of the subjects report of the cluster of symptoms which characterized neurasthenia.

Course

The course of neurasthenia among subjects without comorbidity at the initial interview in 1979 is presented in Fig. 2. Neurasthenia was much more stable over the longitudinal course than the affective disorders. Nearly one-half of the persons with neurasthenia at the time of the initial interview continued to exhibit neurasthenia at the follow-up, whereas only 25% of the subjects with affective disorders reported affective disorders at the follow-up. In contrast, subjects with pure neurasthenia were equally likely to develop an affective or anxiety disorder during the follow-up (i.e. 35%) as were those with only an affective or anxiety disorder at the initial interview (i.e. 33%).

Another indicator of the course of neurasthenia assessed in the interview was the number of years over the entire study that the subjects reported symptoms of neurasthenia. The average duration of neurasthenia across the entire 10-year-period was about 4 years, with the comorbid group reporting longer duration (mean = 4·5 years) than the non-comorbid group

(mean = 3·5 years). The age of onset of neurasthenia was also assessed retrospectively at the most recent interview. The average age of onset was estimated to be significantly earlier among the comorbid than in the pure neurasthenics, with the comorbid subjects reporting an average age of onset of 17·9 and the non-comorbid subjects reporting an average of 19·7.

DISCUSSION

The prevalence of neurasthenia defined according to the ICD-10 criteria was 1% across 10 years and 0·9% in 1988 for a duration of ≥ 3 months, and 8·1% across 10 years and 12% in 1988 for a duration of ≥ 1 month. The duration criterion of ≥ 3 months appeared to be excessively restrictive to represent individuals with neurasthenia in the community. Subjects with 1 month episodes of neurasthenia exhibited sufficient differences from controls and subjects with anxiety or depressive disorders alone to justify a 1 month duration criterion for neurasthenia in community samples. However, differences between neurasthenia alone and those with comorbid anxiety or depressive disorders supported the exclusion of these conditions from the criteria for neurasthenia. Although there was an excess of females over the longitudinal course, cross-sectional data indicate that a substantial proportion of males also suffer from this condition.

Despite the low prevalence of neurasthenic episodes of greater than 3 months duration, all of the subjects reported chronicity of the condition. That is, the average case with > 1 month duration reported the presence of neurasthenic symptoms during an average of 4 years of the 10 years of the study. This is quite remarkable in light of the relatively youthful age of this cohort.

The results of the present study also suggest that the validity of the definition would be enhanced by the inclusion of the dimension of sensitivity to stress. The interview data from the present study confirmed the results of an earlier cluster analysis (Angst & Koch, 1991) which suggested that neurasthenia should be broadened to include the concept of stress intolerance, which characterized the majority of persons with neurasthenia.

The stability of the sub-typing according to

comorbidity for anxiety and depression was confirmed by prospective data on the longitudinal course over a decade. The pure neurasthenics were discriminated from the comorbid group by differences in treatment rates, patterns of comorbidity, and the longitudinal stability of neurasthenia. In contrast to the majority of previous studies of clinical samples which consider neurasthenia as a manifestation of underlying depression and anxiety syndromes (e.g. Wilson *et al.* 1983), these findings suggest that there is no characteristic pattern of the order of onset of neurasthenia and affective and anxiety disorders. In the present study, the onset of neurasthenia was equally likely to pre-date as it was to post-date the onset of these comorbid conditions. In contrast to most previous clinical studies, Hickie *et al.* (1990) reported that the onset of psychological disturbances tended to post-date the onset of fatigue in patients with CFS.

The severity of neurasthenia was indicated by the magnitude of subjective distress, and both occupational and social impairment which was reported by 80% of the cases. Likewise, in a study of the treated prevalence of CFS, Lloyd *et al.* (1990) reported that 43% of the patients with this syndrome were completely incapacitated. Kroenke *et al.* (1988) also noted the striking degree of dysfunction associated with fatigue in their primary care sample. Indeed, the impact of fatigue was similar to that of survivors of myocardial infection, sudden cardiac death and hypothyroidism. Aside from the magnitude of the suffering experienced by persons with this condition, the medical expenses and decreased occupational productivity are associated with an enormous indirect cost as well.

The chronicity of neurasthenia was demonstrated by the continued manifestation of disorders in more than half of the subjects over a decade, at an average duration of 4 to 5 years. Similar findings emerged from 1 year prospective follow-ups of primary care patients with complaints of fatigue. Kroenke *et al.* (1988) found that fatigue persisted in 72% of their patients after 1 year and Cathébras *et al.* (1992) estimated that 50–66% of their sample exhibited chronicity over 1 year. The magnitude, chronicity and impairment associated with this condition in the general population, as well as the substantial proportion of persons in whom manifestation of

this syndrome is distinct from anxiety of depressive disorders, suggest that neurasthenia is a valid diagnostic entity, and should be considered for inclusion in American diagnostic systems.

Neurasthenia is frequently encountered in diverse medical specialities including neurology, psychiatry, internal medicine, cardiology, gastro-enterology, and rheumatology, with no speciality claiming neurasthenia within its sole domain. This is not surprising because the disorder itself has moved between specialities since it was first described. For example, Beard (1869) was a neurologist, Griesinger (1845) an internist, Freud (1895) a psychiatrist and neurologist and Kielholz (1957) a psychiatrist. Although heterogeneous aetiology is likely given the magnitude and protean manifestations of this condition, the treatment of choice is currently antidepressant medications, after detectable somatic aetiologies have been excluded by appropriate clinical or laboratory tests (Wessely & Powell, 1989).

Despite severe levels of impairment and distress, however, few of the pure neurasthenics had actually consulted a professional of any speciality for this disorder. This explanation is supported by the finding that the neurasthenics with affective disorders in the present study had sought treatment more often, either because of the severity of the concomitant manifestations of symptoms in both domains, or the relative availability of treatment and public awareness of depression. The small proportion of pure neurasthenics who seek treatment may be associated with the mixture of somatic and psychological features of this syndrome. In contrast to subjects from treated samples (see Wessely & Powell, 1989), the majority of the neurasthenics in the present study attributed their symptoms to psychological and somatic factors. The psychological manifestations, when taken together with a lack of disturbance in a specific organ system, may impede identification of an appropriate source of treatment. Resistance to psychiatric treatment may also be an important component of the infrequency with which these individuals seek professional help.

These findings underscore the need for empirical data on this syndrome from both epidemiological and treatment settings. Epidemiological data on a wider age range of subjects

are critical to investigate the magnitude, impact, and comorbidity in order to identify sources of heterogeneity in its expression, as well as for planning for health services. Further work is necessary to study the case definition across diverse settings. There is also a critical need for systematic treatment studies and prospective follow-up studies of clinical samples. The current follow-up of this sample at age 35 will yield information on the stability of neurasthenia and differential patterns of course among persons with underlying psychiatric disorders.

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