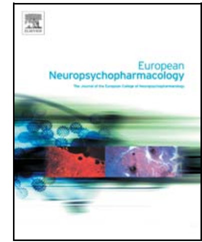
European Neuropsychopharmacology (2006) 16, S109–S118

www.elsevier.com/locate/euroneuro



Generalized anxiety disorder: A comorbid disease

David Nutt*, **Spilos Argyropoulos**, **Sean Hood**, **John Potokar**

Psychopharmacology Unit, University of Bristol, Bristol, United Kingdom

KEYWORDS:
Generalized anxiety disorder;
Comorbidity;
Prevalence;
Burden;
Diagnosis;
Neurobiologic mechanisms

Abstract Generalized anxiety disorder (GAD) frequently occurs comorbidly with other conditions, including depression and somatic complaints. Comorbid GAD sufferers have increased psychologic and social impairment, request additional treatment, and have an extended course and poorer outcome than those with GAD alone; therapy should alleviate both the psychic and somatic symptoms of GAD without negatively affecting the comorbid condition. The ideal treatment would provide relief from both GAD and the comorbid condition, reducing the need for polypharmacy. Physicians need suitable tools to assist them in the detection and monitoring of GAD patients—the GADI, a new, self-rating scale, may meet this requirement. Clinical data have shown that various neurobiologic irregularities (e.g., in the GABA and serotonin systems) are associated with the development of anxiety. Prescribing physicians must take into account these abnormalities when choosing a drug. Effective diagnosis and treatment should improve patients' quality of life and their prognosis for recovery.
© 2006 Elsevier B.V. and ECNP. All rights reserved.

1. Introduction

Generalized anxiety disorder (GAD) is one of the most common conditions that occurs comorbidly with other disorders, particularly other anxiety and depressive disorders. Indeed, comorbidity of mood and anxiety disorders is a hallmark feature of GAD (Judd et al., 1998; Ninan, 2001). Research into GAD is far behind that of many other psychiatric disorders, the main reason being that until fairly recently many eminent physicians still believed that GAD was not a separate disorder, but rather a variant of depression. This misapprehension arose because GAD often occurs comorbidly with depression, which can mask the symptoms of GAD. Consequently it has taken some time to establish that GAD does occur as a discreet condition, and that it definitely is not a form of depression. This was, and still can be, a big hindrance to the progression of research into this important, although somewhat neglected, psychiatric condition.

GAD is frequently comorbid with major depressive disorder (MDD), panic disorder (PD), social anxiety disorder (SAD), specific phobia (SP), and post-traumatic stress disorder (PTSD), and is additionally associated with chronic pain conditions, medically unexplained somatic symptoms, and sleep disorders—in fact many physicians believe that much of the insomnia reported by their patients is actually a variant of GAD. These patterns of comorbidity increase the individual and economic burden of GAD and add to the challenge of treatment. Indeed, comorbidity should be thought of as a challenge rather than a nuisance—it is very important clinically, both when considering neurobiologic disorders and the individual comorbidities. This article will discuss the issues surrounding GAD and its various comorbidities. In addition, we will also address the need for appropriate tools to aid the diagnosis of this condition, and appraise the potential role of various neurobiologic mechanisms in the development and treatment of GAD.

* Corresponding author. Psychopharmacology Unit, Dorothy Hodgkin Building, Whitson Street, Bristol, BS1 3NY, United Kingdom. Tel./fax: +44 117 331 3143.
E-mail address: david.j.nutt@bristol.ac.uk (D. Nutt).

0924-977X/$ - see front matter © 2006 Elsevier B.V. and ECNP. All rights reserved.
doi:10.1016/j.euroneuro.2006.04.003

2. Prevalence of psychiatric comorbidity

Many studies have reported a high prevalence of comorbidity with psychiatric disorders as well as with general medical conditions, both of which lead to a complex clinical presentation. Data from a large general population survey in the USA (the National Comorbidity Survey, NCS) suggest the vast majority (90%) of people with lifetime GAD have a lifetime history of at least one other psychiatric diagnosis (Table 1) (Wittchen et al., 1994). Among individuals with current GAD (defined as the most recent 6-month period of anxiety still ongoing in the 30 days prior to interview), 66% had at least one other concurrent psychiatric disorder: 39% had MDD, 27% agoraphobia, 25% simple phobia, 23% SAD, and 23% PD (Table 1) (Wittchen et al., 1994). Of those diagnosed as having met criteria for GAD within the preceding 12 months, 58% had also experienced an episode of MDD in the previous 12 months; in another US survey (the Midlife Development in the United States Survey, MDUSS), this figure was 70% (Kessler et al., 1999). A representative sample of adults in Germany (the German National Health Interview and Examination Survey-Mental Health Supplement, GHS) showed similar patterns of comorbidity; this survey focused on the 12-month prevalence rates with a requirement that all diagnostic criteria were fully present in the 12 months prior to interview (Wittchen et al., 2000; Carter et al., 2001). In the GHS, 40% of all 12-month GAD cases had current (within the preceding 30 days) depression, 59% had experienced an episode of MDD within the preceding 12 months, and 56% met criteria for any other anxiety disorder within the preceding 12 months (Carter et al., 2001). These incidence rates reinforce how prevalent comorbid GAD is within the population as a whole.

Comparable rates of comorbidity with those observed in general population surveys have been reported in clinical samples, overall rates of comorbidity are high with 45–98% of patients with GAD having lifetime comorbid anxiety, depressive, or substance use disorders (Noyes, 2001). As in the general population, MDD is the most common disorder occurring comorbidly with GAD in these samples (Noyes, 2001). One study of patients with GAD, which excluded those with concurrent MDD, found that 42% had experienced at least one major depressive episode during their lifetime (Brawman-Mintzer et al., 1993). A prospective study indicated that 39% of patients with GAD had a comorbid diagnosis of MDD at intake, with the rate increasing as the study progressed (Fig. 1) (Bruce et al., 2001). Comorbid anxiety disorders occur with GAD in a substantial proportion of patients with up to 59% of GAD patients having a lifetime history of SAD, and up to 56% a history of SP (Noyes, 2001). PD is also a prevalent comorbidity with GAD. However, many studies of patients with GAD specifically exclude those with PD, so rates of lifetime comorbidity found in such studies are likely to underestimate the true prevalence of comorbid PD (Noyes, 2001). In a study of patients with current GAD, 48% of those also had current PD with or without agoraphobia (Massion et al., 1993); in another study of patients with PD, 63% had GAD (Cassano et al., 1990). In the Harvard/Brown Anxiety Disorders Research Program (HARP), a longitudinal study of over 700 treatment-seeking patients, 62% of those with a diagnosis of lifetime GAD had lifetime PD (14% without and 48% with agoraphobia) (Goisman et al., 1995). Prevalence of comorbidity with PTSD is less well established than other conditions; 39% of a sample of patients with PTSD in primary care had comorbid GAD (Stein et al., 2000).

Although in general the prevalence of GAD in children and adolescents is relatively low in relation to other anxiety disorders, when GAD is present in these groups, high rates of comorbidity similar to those seen in adults, are observed (Masi et al., 2001; Wagner, 2001; Masi et al., 2004). A recent study of 157 children and adolescents (7–18 years, mean age 13.4 years) with GAD, who attended an outpatient clinic between 1997 and 2002, found comorbid anxiety disorders in 75% and depressive disorder in 56% (Masi et al., 2004). Although the prevalence of other anxiety disorders appears to diminish with age that of GAD is maintained or even increased in elderly populations (Krasucki et al., 1998). Again, there is considerable comorbidity, with depression in particular, but GAD may be more likely to be secondary to depression in elderly patients (Flint, 1994; Noyes, 2001). A community-based sample of over 4000 elderly patients found

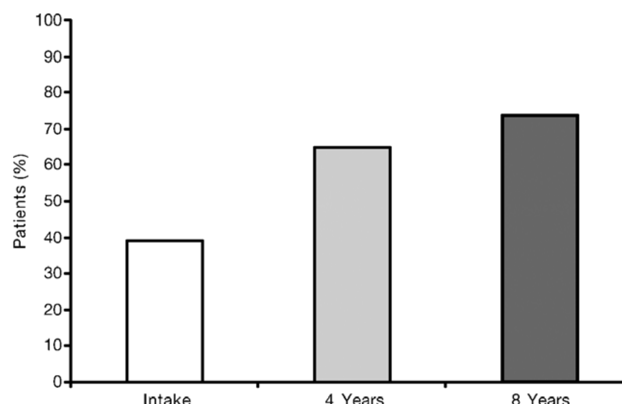


Figure 1 Increase in comorbidity of GAD and MDD over time in a prospective study (Bruce et al., 2001).

Table 1 Lifetime prevalence of disorders comorbid with GAD in the National Comorbidity Survey (NCS)

Comorbid disorder	Current GAD[a] (%)	Lifetime GAD[b] (%)
Any of the following	66.3	90.4
Major depression	38.6	62.4
Agoraphobia	26.7	25.7
Simple phobia	24.5	35.1
Social anxiety disorder	23.2	34.4
Panic disorder	22.6	23.5
Dysthymia	22.1	39.5
Mania	12.1	10.5
Alcohol abuse	11.2	37.6
Drug abuse	5.1	27.6

Adapted from Wittchen et al. (1994), with the kind permission of JAMA.

[a] 30-day prevalence of other disorders among respondents with 30-day GAD, defined as the most recent 6-month period of anxiety still ongoing in the 30 days prior to interview.

[b] Lifetime prevalence of other disorders among respondents with lifetime GAD.

Download English Version:

https://daneshyari.com/en/article/322264

Download Persian Version:

https://daneshyari.com/article/322264

Daneshyari.com