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Sympathetic activation in broadly defined generalized anxiety disorder

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Abstract

The definition of generalized anxiety disorder (GAD) has been narrowed in successive editions of DSM by emphasizing intrusive worry and deemphasizing somatic symptoms of hyperarousal. We tried to determine the clinical characteristics of more broadly defined chronically anxious patients, and whether they would show physiological signs of sympathetic activation. A group whose chief complaint was frequent, unpleasant tension over at least the last six weeks for which they desired treatment, was compared with a group who described themselves as calm. Participants were assessed with structured interviews and questionnaires. Finger skin conductance, motor activity, and ambient temperature were measured for 24 h. Results show that during waking and in bed at night, runs of continuous minute-by-minute skin conductance level (SCL) declines were skewed towards being shorter in the tense group than in the calm group. In addition, during waking, distributions of minute SCLs were skewed towards higher levels in the tense group, although overall mean SCL did not differ. Thus, the tense group showed a failure to periodically reduce sympathetic tone, presumably a corollary of failure to relax. We conclude that broader GAD criteria include a substantial number of chronically anxious and hyperaroused patients who do not fall within standard criteria. Such patients deserve attention by clinicians and researchers.

Keywords: Tension; Anxiety; Generalized anxiety disorder; Sympathetic activation; Skin conductance; Autonomic nervous system; Sleep

1. Introduction

Whether psychiatric diagnostic categories are distinct biological entities or the artificial product of classificatory logic has long been a matter of debate. The absence of firm biological foundations for most psychiatric diagnoses has weakened arguments for biological categories and encouraged logical ones. From a logical point of view, anxiety disorders should be assigned to categories on the basis of the presence or absence of sets of features. To qualify for a disorder, the anxiety should be excessive, more than the anxiety of the average person under similar circumstances and severe enough to impair functioning. Essential for categorization as an *anxiety* disorder is that anxiety be a primary aspect of the diagnosis and not secondary to other diagnoses such as psychosis or depression. After that, further classification is attempted on the basis of further qualitative or quantitative descriptors of the anxiety. Features usually considered are whether the anxiety is acute or chronic, whether it is in response to identifiable external stimuli, whether there was a history of traumatic events, and what behavior or thinking accompanies the anxiety.

Based on these considerations, diagnostic systems have usually identified a category of chronic anxiety where external stimuli, traumatic events, and psychotic thought processes have not played a major role. In the current diagnostic system, this category is Generalized Anxiety Disorder (GAD), the evolution of which through DSM editions is instructive of classificatory logic. Patients diagnosed with DSM-III GAD were often given other diagnoses by clinicians ostensibly following the same

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diagnostic definitions, which challenged the distinctness and thereby the legitimacy of this category. To improve separation from other mood and anxiety disorders, DSM-III-R made worry that included topics different from those typical of other anxiety disorders, a required symptom (reviewed by Barlow et al., 1986). Extending the requirement in DSM-IV to be that the worry had to be difficult to control, further improved this separation. At the same time, many of the symptoms of autonomic hyperactivity were dropped because DSM-III-R defined GAD patients endorsed these symptoms infrequently and inconsistently (Marten et al., 1993).

We suspected as have others that the changes in the definition of GAD might have left undiagnosed a substantial number of patients with general persistent anxiety who do not have intrusive worry as a prominent symptom (e.g., Rickels and Rynn, 2001). If this less worrying group properly belongs to a valid category of chronic anxiety, it should show signs of sympathetic activation, perhaps even more so than in currently defined GAD, since worriers as a subgroup of chronic anxiety patients may be anomalous in having little physiological arousal. Evidence for this comes from experiments in which worry was manipulated: heart rate increases to phobic imagery were diminished in the high worry condition (e.g., Borkovec and Hu, 1990). That may be a reason why GAD patients are often found to show a narrowed range of physiological activation, "diminished physiological flexibility" (Hoehn-Saric et al., 1989), rather than increased activation. A recent ambulatory study confirmed this by showing that DSM-IV defined GAD patients had neither higher heart rates nor skin conductance than controls (Hoehn-Saric et al., 2004). On the other hand, a number of studies have found autonomic changes associated with GAD and worry. In one, heart rate was elevated and respiratory sinus arrhythmia (a measure of vagal tone) was reduced in a GAD sample at baseline (Thayer et al., 1996). Others reported a similar pattern of heart rate changes (reviewed by Brosschot et al., 2006).

With the study reported here we attempted to determine what kinds of chronically anxious people are being left out by the current DSM-IV GAD criteria, and whether a more broadly defined group would show physiological signs of sympathetic activation, a cardinal biological characteristic of fear. In rats, for example, the neural pathways of fear have been traced from the central amygdaloid nucleus to the lateral hypothalamic area and from there down the sympathetic branch of the autonomic nervous system (LeDoux et al., 1988). We recruited people whose chief complaint was frequent, unpleasant tension over at least the last six weeks for which they desired treatment. After casting this wider net, we examined our catch for symptoms and signs of anxiety, and established where they fell among DSM-IV categories. Unlike most diagnostic endeavors, we supplemented the participants' verbal report of anxiety and its symptoms with a psychophysiological assessment of anxiety repeated over a 24-h period. Using finger skin conductance, we measured sympathetic autonomic activation less inferentially than from reports of activation symptoms. Since skin conductance is affected by temperature and physical activity, we measured these variables along with it.

2. Methods

2.1. Participants

Participants who might be suffering from persistent anxiety were recruited and selected with broader and simpler criteria than DSM-IV defined GAD. We posted advertisements in newspapers, flyers, and the internet for the following: "Have you recently been suffering from so much tension that it is distressing you or interfering in your daily life? Has this been going on for 6 weeks or more? Are you between 18 and 65 years old? Researchers at Stanford University and the Palo Alto VA Health Care System are offering free physiological evaluations of your tension and a seminar in ways of reducing it." To be included, applicants had to answer "yes" to the following questions at phone screening:

1. "Do you often feel tense?" The word "tense" was chosen rather than "anxious" or "afraid" as being a more general description of negatively felt hyperarousal. In factor analytic studies of moods as self-reported in terms of adjectives, a bipolar dimension emerges that loads on the words "tense," "jittery," "fearful" vs. "calm," "quiet," "placid," showing that tension and fear are closely associated semantically and in life, and that tension is not at all restricted to muscle sensations (reviewed by Thayer, 1989).
2. "Does the tension interfere with your life or is it greater than with other people?"
3. "Have you felt this way more than half the days in the last 6 weeks?" Questions 2 and 3 were meant to exclude applicants whose tension did not rise above that occasionally experienced in daily life by ordinary people. In DSM-III GAD symptoms had to last only 1 month, while in DSM-III-R this was increased to 6 months to reduce co-morbidity, with the intention of making the disorder less overlapping with other disorders and less like a situational stress reaction. However, a recent analysis of a US household sample of almost 10,000 people has shown that GAD symptom episodes of 1–5 months do not differ from >6 month episodes in onset, persistence, impairment, co-morbidity, parental GAD, or sociodemographic correlates (Kessler et al., 2005). Thus, we chose 6 weeks as a broader criterion than DSM-IV's 6 months.
4. "Do you find these feelings unpleasant?"
5. "Are you interested in learning how to be less tense and to relax?" Questions 4 and 5 were meant to establish that the feeling had a negative valence. Psychophysiological studies show that heightened arousal accompanies both positive and negative emotions (Lang, 1995), although ordinarily it is only the latter that are sources of subjective distress.