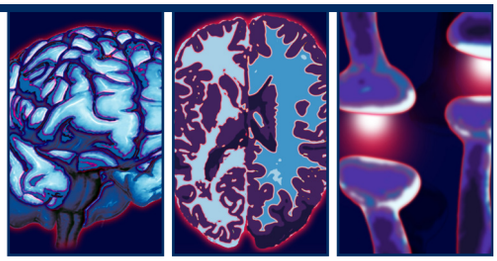

Should nonpharmacological treatments of anxiety be considered first systematically?

Geneviève Belleville[†1]

Martin D Provencher[1]

"...cost analysis studies have demonstrated that, for anxiety disorders, cognitive behavioral therapy administered by a psychologist is more cost effective than pharmacotherapy..."

Anxiety disorders are widely prevalent. It is estimated that 28.8% of the US population will suffer from an anxiety disorder at some point in their lives, and half of them will have more than one [1]. Anxiety disorders, the most common of all mental disorders, include panic disorder with or without agoraphobia, post-traumatic stress disorder, acute stress disorder, generalized anxiety disorder, obsessive–compulsive disorder, social anxiety disorder (social phobia) and specific phobia. Furthermore, the manifestations of anxiety are common in mood, psychotic, cognitive, eating, somatoform, sleep and personality disorders. In fact, most mental illnesses, and a number of physical ones, are likely to provoke anxiety.

Accordingly, the use of anti-anxiety agents is very common. Pharmacotherapy often represents the first line of treatment for anxiety symptoms and disorders. Medications used to alleviate anxiety include (but are not limited to) benzodiazepines, antidepressants with sedative properties, anticonvulsants and β-blockers. The use of anti-anxiety agents is widespread and increasing. For example, 20% of the Canadian population has reported using a minor tranquilizer or a sleeping pill at least once in a 12-year period [2]. In Europe, 9.8% of the population uses anxiolytics [3]. In Australia, 2.4% of the population uses sedative drugs on a daily basis [4].

Physicians prescribe these medications – and patients specifically ask for them – because to some extent, they work. Anti-anxiety medications decrease the physiological and cognitive arousal associated with anxiety [5], they provide fast and often immediately noticeable relief and are easily accessible. Owing to the significant investments pharmaceutical companies make in promoting their products compared with advocates of nonpharmacological options, medications are familiar treatment options. Physicians can easily obtain a wealth of information on medications (e.g., regarding their efficacy and

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[1]École de Psychologie, Université Laval, Pavillon Félix-Antoine-Savard, Bureau 1334, 2325 rue des Bibliothèques, Québec, G1V 0A6, Canada

[†]Author for correspondence: Tel.: +1 418 656 2131 ext. 4226; Fax: +1 418 656 3646; genevieve.belleville@psy.ulaval.ca

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how they work) and have the training and knowledge they need to understand and use the information available.

However, an important downside of anti-anxiety medication is the wide range of well-known undesirable side effects that are associated with their use. Undesirable effects of benzodiazepines include cognitive and psychomotor impairment, higher risk of accidents and falls, risk of dependence, and rebound anxiety and insomnia upon discontinuation [6–8]. Undesirable side effects associated with antidepressants vary according to the specific agent that is used, but can include nausea, dizziness, headaches, sleep disturbances and agitation [9–11]. A significant problem is that these side effects are somatic symptoms to which people with anxiety have a typical low tolerance. As a result, they often interpret these side effects as a worsening of the anxiety problem, leading to low adherence to the treatment plan.

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The repeated observation that the use of anti-anxiety agents is associated with increased mortality hazard is another serious cause for concern. In 2010, one of the authors analyzed data from the Canadian National Population Health Survey, a population-based sample of 14,117 people aged 18–102 years, with data collected every second year from 1994 to 2007 [2]. The odds of mortality for respondents who reported anxiolytic or hypnotic drug use in the past month were 3.22-times higher than for those who did not. After controlling for confounding sociodemographic, lifestyle and health factors (including depression), the odds ratio was reduced but remained significant. It was concluded that sedative drug use is uniquely associated with a 36% increase in mortality risk. These observations added to a growing number of studies indicating increased mortality risk among anti-anxiety medication users [12,13]. Although the mechanisms through which the use of sedative drugs leads to an increased mortality rate are far from understood, these findings cannot be ignored. Physicians should be aware that they are prescribing drugs that can potentially put their patients at higher risk for death. Before prescribing the drug, they may wish to ask themselves whether they believe that the risk of mortality for this particular patient would be higher without recourse to anti-anxiety medication.

Another important fact to keep in mind is that, when the differential efficacy of pharmacological and nonpharmacological strategies to treat anxiety are compared, nonpharmacological strategies often win [14–17]. In the short term, nonpharmacological strategies are often shown to be as efficacious as, or more efficacious than, pharmacological ones. More importantly, nonpharmacological strategies produce durable therapeutic gains that are maintained, and even continue to increase, once therapy is completed. The same cannot be said for most anti-anxiety agents.

From an empirical point of view, fear is one of the most well-understood emotions. We possess an extended, historically rich and ever-expanding understanding of the acquisition and maintenance of fear and anxiety. The causes of anxiety are multidimensional and involve predisposing factors, such as genetic contributions to personality traits prone to anxiety, but also – and more importantly – precipitating and perpetuating factors, where the role of learning is omnipresent. Fear can be acquired through classical conditioning, an automatic type of learning in which a stimulus acquires the capacity to evoke a response that was originally evoked by another stimulus. For example, an anxiety reaction following a sharp, unexpected pain while receiving dental care can condition other stimuli in the dentist's office – the dentist's chair, the smell of the disinfectant or the sound of the drill – and elicit anxiety at the next visit. Anxiety can also be maintained through operant conditioning, where a behavior's antecedent and/or its consequence influence its occurrence and form. An individual can learn that avoidance of a feared situation results in pleasant relief from the anxiety sensations (negative reinforcement). For example, an anxious student who fears academic failure can avoid studying for an exam by surfing the internet, hence not having the catastrophic thoughts and anxious feelings associated with opening her books to study. The avoidance of a feared situation also prevents people with anxiety from learning that the situation may not be as bad as anticipated. For example, an anxious worker may avoid presenting his point of view in meetings, thus never learning that, although the situation makes him nervous, he is able to get through it. Furthermore, anxiety can be acquired as well as maintained by social learning (i.e., by observing a family member or a peer showing fear or by being repeatedly told that a situation is dangerous). A young adult who worries constantly about potential financial problems may remember a recurrent fear

of becoming homeless in her childhood, triggered by anxious exchanges between her parents regarding the family budget. Fear and anxiety occur when an individual learns that a situation is dangerous and that he/she has no power over it. The key point here is that fear and anxiety are learned behaviors, learned reactions.

Anxiety and fear also have a great influence on how the brain processes information. The perception of a situation has a greater influence on the anxiety reaction than the situation itself. Accordingly, anxious individuals remember past unpleasant experiences more readily and more vividly than people without anxiety. They direct more attention to fear-provoking stimuli in the environment. They anticipate situations with greater details and overestimate the probability that a feared catastrophe is really going to happen. They closely monitor their environment to detect the feared stimuli. When recalling a past experience, they are more likely to remember the unpleasant sensations of fear that occurred before engaging in the situation than the actual sequence of events. These particular attention and memory biases, and many others, contribute directly to maintaining fear.

Building on this knowledge, nonpharmacological strategies targeting anxiety focus on providing the anxious person new learning experiences and increasing awareness of how thoughts regarding a situation, more than the situation itself, provoke fear. The most powerful and empirically tested nonpharmacological strategies used in anxiety disorders involve exposure and cognitive restructuring (or cognitive defusion, i.e., the acceptance and abandonment of control over thoughts). Gradual and repeated exposure to a feared situation, when collaboratively planned and executed to promote a sense of mastery, leads to the extinction of anxiety by triggering the habituation response and by providing an opportunity to reappraise its dangerousness. Cognitive strategies involve identifying the attention and memory biases that lead to catastrophizing and overly self-critical ways of thinking, as well as learning ways to modify the internal dialog (cognitive restructuring) or to detach oneself from it (cognitive defusion). These strategies act directly on the most important causes of anxiety.

Empirically supported therapies exist for all of the anxiety disorders, employing strategies largely based on exposure and cognitive techniques, but with specific adaptations for each anxiety disorder [18]. These therapies have been empirically demonstrated to be efficacious and efficient, both in the short and long term. Their strategies may be adapted to be used in several formats, ranging from one brief session to longer interventions of 15–20 weekly sessions. They can also be delivered in multiple modalities (e.g., individual, group, self-help and internet) and offered by providers with different clinical backgrounds (given proper training). They can be administered to people who suffer from anxiety coexisting with other psychiatric or medical conditions. Furthermore, contrary to common perception, they also represent a good financial investment. Indeed, cost analysis studies have demonstrated that, for anxiety disorders, cognitive behavioral therapy administered by a psychologist is more cost effective than pharmacotherapy [19,20].

We would like to conclude by envisioning a significant breakthrough in the treatment of anxiety disorders. Let us all imagine a new drug that would work directly on the major causes of anxiety, provide improvement within the first few weeks of treatment, need to be taken for only a few months (with some longer but less intensive follow-up for more severe cases), have no serious side effects and be discontinued without a return of symptoms. If such a drug existed, would anyone question whether it should be used as a first line of treatment for anxiety disorders? Fortunately, such a treatment does exist: nonpharmacological treatments involving exposure and cognitive strategies, such as cognitive behavioral therapy, have been proven to do exactly that. So, should the nonpharmacological treatment of anxiety systematically be considered first? Empirical evidence and best practices indicate that it should be. The question we are left to ponder is why it is not always the case.

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