8

Anxiety and Anxiety Syndromes

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CONTENTS

8.1 Vignettes

1. An emergency psychiatric consultation was requested for a 48-year-old man who was admitted to the coronary care unit (CCU) with massive myocardial infarction (MI). He was reported to be acutely agitated, and he wanted to sign out against medical advice. The reason for consultation was to determine the patient's competence to sign out. When the consultant arrived in the CCU, a number of staff members were surrounding the patient as he attempted to exit the cubicle. He shouted, "I want to get out! You cannot hold me here!"

The consultant told him, "I am a psychiatrist, and I am here to help you. I think it might be possible for you to leave if you wish, but I need to speak with you first."

"Not here, not in this room!" replied the patient.

"OK, would it be OK if we talked in the waiting room?"

The patient agreed. He was placed in a gurney and wheeled to the waiting room.

The consultant said, "Since you became quite anxious and flushed, I would like the nurse to give you a sedative to help you relax as we talk." Lorazepam 1 mg IV was administered, which calmed the patient considerably. In the interview, the consultant learned that the patient became panicky when he was rushed into the particular cubicle in the CCU, as it was the same cubicle in which his father had died of an MI some 4 months prior to the patient's own admission. The patient was convinced that he would die in that cubicle just as his father did. When the patient was offered another cubicle, he gladly accepted it without any hesitation. He recovered uneventfully.

2. A 73-year-old woman was admitted for pain in the lumbar area associated with a mass found on a computed tomography (CT) scan. She had a history of major depression in the past but was currently on no medications. A psychiatric consultation was requested as the staff thought the patient was depressed. The patient denied current depression, but admitted to having insomnia and panicky feelings. She was a retired executive, who had "always been on top of things." The patient felt quite apprehensive and out of control as she did not know what was happening to her physically. She stated that the doctors did not explain anything to her, saying only that they needed to do more tests. She was afraid to ask questions because she felt that the doctors were withholding information from her so as to not upset her. When the consultant asked her if she would like the doctors to explain to her exactly what they found and what they were planning to do, she agreed. It turned out that the doctors had not yet found the time to have an in-depth conversation with the patient simply because they had been busy with other patients, not because they were afraid of upsetting her. In fact, the mass turned out to be benign and the patient was discharged without any antidepressant or antianxiety medications.

3. Psychiatric consultation was requested for a 34-year-old man who had undergone a magnetic resonance imaging (MRI) scan and panicked while he was positioned in the narrow confines of the imaging apparatus. On examination, the patient turned out to have claustrophobia. As the MRI was a medical necessity, lorazepam 2 mg po was administered 30 minutes prior to the next scheduled MRI. Though apprehensive, he was able to complete the MRI scan.

8.2 Anxiety

8.2.1 The Function of Anxiety

The most prominent subjective features of anxiety are *fear, a sense of dread,* and *apprehension*. This fearful feeling is usually vague and diffuse, but it may also focus on a specific idea, such as fear of dying, or of cardiac arrest, or of having a serious disease such as cancer. It may also arise under specific situations, such as being in closed spaces, as in the final vignette cited above. Physiological changes are part of anxiety. They are mediated by activation of the sympathetic outflow and of the hypothalamic-pituitary-adrenal (HPA) system. Thus, the manifestations may include rapid pulse, increased blood pressure, excessive sweating, changes in bowel function, changes in appetite, trouble sleeping, and difficulty breathing. Subjective feelings of dread and fear accompanied by symptoms and signs of appropriate physiologic changes indicate the presence of anxiety. The brain structures associated with anxiety include the sensory and association cortices for processing the anxiety signal, the limbic system, particularly the amygdala and the anterior cingulate gyrus, the reticular activating system, and locus ceruleus (see Chapter 6).

Anxiety clearly has adaptive value both for the individual and in an evolutionary sense. Fear is essential in learning to avoid dangerous situations. Fear with associated physiologic arousal, when followed by resolution through mastery, such as successfully avoiding or overcoming the feared object, can also be associated with pleasure and euphoria, explaining thrill-seeking behavior. Genes coding for a low threshold for anxiety and fear might have conferred survival

advantage for our ancestors who needed to be fleet on their feet to avoid predators (see Chapter 6). In the modern age, individuals endowed with such genes might be diagnosed with a generalized anxiety disorder.

Anxiety has an inverted U relationship with task performance. Too little anxiety results in little motivation and a lackluster performance, whereas too much anxiety leads to paralysis. Mild and transient, barely perceptible anxiety may arise when a stimulus has the potential to reactivate a long-standing psychological conflict that may result in overwhelming anxiety. Such anxiety, called *signal anxiety*, activates automatic psychological defense mechanisms (somewhat akin to a thermostat), such as denial, repression, projection, rationalization, and sublimation, that ward off the perception of the stimulus or its connections to the conflict.

8.2.2 Dysregulation of Anxiety

Anxiety is considered pathologic if it is uncontrollably excessive or persistent so as to affect one's functioning. Such dysregulation of anxiety may occur at several levels: genes, gene-environment interaction in childhood, and recent and current stress, both psychosocial and biological. The final common pathway brain dysfunction in the anxiety circuits underlies the anxiety syndrome (see Chapter 6).

8.3 Anxiety Syndromes

8.3.1 Secondary Anxiety Symptoms and Syndromes

In the consultation-liaison (CL) setting, secondary anxiety syndromes are quite common and should be considered first in diagnosing the patient. Anxiety may be secondary to the stress of hospitalization itself, to the apprehension associated with a serious diagnosis or with procedure such as surgery, or to the biochemical changes secondary to the biochemical changes caused by the medical disease or by the drugs to treat the disease. Patients' lack of information concerning the illness and proposed treatment is another very common cause of anxiety. See Table 6.1 in Chapter 6 for a list of medical diseases that may underlie psychiatric syndromes.

Anxiety symptoms are particularly common in hyperthyroidism, hypoglycemia, Cushing syndrome, pheochromocytoma, and carcinoid tumors. Delirium and drug withdrawal states are almost always associated with anxiety.

The stress of a serious medical disease or of hospitalization tends to heighten the underlying personality traits of an individual. Thus, a patient who has an anxious personality will experience even greater anxiety and may develop general anxiety or phobic symptoms, and an obsessive-compulsive personality may develop heightened obsessive-compulsive symptoms, as discussed below.

8.3.2 Primary Anxiety Syndromes

Once secondary anxiety has been either ruled out or considered as a contributing but not primary factor, the presence of primary anxiety syndrome should be considered. Primary anxiety syndrome usually antedates the illness for which the patient is being treated, though it may be exacerbated by the illness or the stress of hospitalization.

8.3.2.1 Acute Stress Disorder (ASD) and Posttraumatic Stress Disorder (PTSD)

Though classified as primary psychiatric disorders, these two syndromes are secondary to or the sequelae of identifiable stresses. In the CL setting, these disorders are often found in trauma, burn, and rape victims. Others may have an existing posttraumatic stress disorder diagnosis from combat experience and may be hospitalized for an unrelated medical condition. The prevalence of PTSD in combat veterans is considered to be about 25%, and in other traumatized groups, 3% to 60%.

Acute stress disorder and PTSD are differentiated only by how much time has passed since the trauma. A PTSD is diagnosed if the trauma occurred more than a month before the onset of the symptoms, or the symptoms persist for more than a month. The syndromes are characterized by three classes of symptoms and signs: (1) dissociative symptoms, including flashbacks, nightmares, and intrusive thoughts; (2) arousal symptoms, including hypervigilance, hyperarousal, and startle reactions; and (3) avoidance of situations and stimuli that may remind the person of the trauma. In addition to these symptoms, any number of psychiatric symptoms may be associated with PTSD, including brief psychotic episodes with hallucinations and delusions, depression, panic, substance abuse, and suicidal behavior. Memory impairment and learning disability may be prominent. Infact, PTSD may be called the SLE (systemic lupus erythematosus) of psychiatry in the protean symptomatology. Therefore, PTSD should be included in the differential diagnosis of any psychiatric symptom.

The pathophysiology of PTSD involves the limbic system, particularly the amygdala and hippocampus, the locus ceruleus, and the prefrontal cortex. A reduced volume of the hippocampus has been consistently reported in PTSD (Bremner et al., 1995a,b; Uno et al., 1989). Hypercortisolemia associated with acute stress has been postulated to underlie the learning disability and memory impairment associated with PTSD (Bremner et al., 1999; Sapolsky, 1996; Smith et al., 1995) A traumatic childhood may also predispose an individual to adult stress disorders.

8.3.2.2 Obsessive-Compulsive Disorder (OCD)

The characteristic feature of this disorder is recurrent obsessive thoughts or compulsive acts. Obsessive thoughts are ideas, images, or impulses that enter the individual's mind again and again in a stereotyped form. They are almost invariably distressing (ego-dystonic) as they are violent or obscene or senseless, and the patient often tries to resist them—to no avail. These recurrent thoughts are recognized as the patient's own thoughts. Compulsive acts or rituals are stereotyped, repeated behaviors. They are neither inherently enjoyable nor result in the completion of inherently useful tasks. The patient often views them as preventing some objectively unlikely event. Patients usually recognize the compulsive acts to be pointless, and repeated attempts are made to resist them. If the individual is unable to perform the compulsive act, or resists it, unbearable anxiety may build up.

Onset is usually in childhood or early adulthood, and about 1% to 4% of the population is affected. Obsessive-compulsive disorder occurs equally in men and women and often develops in individuals who have obsessive-compulsive (anankastic) personality traits.

Patients with OCD often have depressive symptoms, and patients suffering from depression often develop obsessive thoughts during depressive episodes. In severe cases OCD may be crippling, as the patient may be unable to leave home

without performing endlessly repetitive compulsive acts such as rearranging furniture and checking the locks. It is important to note that in the CL setting, the stress of the medical condition or the delirium or dementia associated with the medical condition or treatment may exaggerate a patient's obsessive-compulsive personality traits. For example, the development of OCD following brain injury is well documented (Coetzer, 2004). Such OCD symptoms may resolve once the underlying delirium or stress is resolved.

8.3.2.3 Panic Disorder with or without Agoraphobia

In panic syndrome, there are recurrent attacks of intense anxiety under unpredictable circumstances. There is often a sudden onset of palpitations, sweating, chest pain, choking sensations, dizziness, nausea, chills, chest pain or discomfort, and feelings of unreality (depersonalization or derealization). There is also a secondary fear of dying, losing control, or going mad. These attacks usually peak within 10 minutes and usually result in the patient's hurried exit from the place in which the attack occurs. A panic attack is often followed by a persistent fear of having another attack. Frequent and unpredictable panic attacks produce fear of being alone or going into public places where escape may be difficult (panic disorder with agoraphobia). There is evidence of decreased 5-hydroxytryptamine 1A (5-HT_{1A}) receptors in anterior cingulate, posterior cingulate, and raphe nuclei in panic disorder patients (Neumeister et al., 2004).

The onset of panic disorder is usually in early to middle childhood, affecting about 1% to 3% of the population. It occurs more commonly among females and is often associated with depression (Weissman et al., 1997)

8.3.2.4 Specific Phobias

These phobias denote marked and persistent fear that is excessive or unreasonable, cued by the presence or anticipation of a specific object or situation such as particular animals, heights, thunder, darkness, flying, being in closed spaces, urinating or defecating in public toilets, eating certain foods, undergoing dental work, the sight of blood or injury, and the fear of exposure to specific diseases. The onset is usually in childhood or early adulthood. The seriousness of the condition depends on how easy it is for the patient to avoid the phobic situation. Disease phobias (e.g., HIV/AIDS, radiation sickness) and needle phobias are common in CL settings. The phobic object may be a conditioned stimulus to fear.

8.3.2.5 Social Phobia

Social phobia is characterized by marked and persistent fear of one or more social or performance situations in which the person is exposed to unfamiliar people or to possible scrutiny by others. Individuals with social phobia fear that they will act in a way that will be humiliating or embarrassing, and consequently they avoid such social situations. The phobia may be restricted to eating in public, to public speaking, or to encounters with the opposite sex, or it may be generalized, that is, involving almost all social situations outside the family circle. The onset is usually in childhood or adolescence, and it is more common in females. About 6% of the population have full social phobia, while up to 24% have symptoms of social phobia. There are more females with diagnosed social phobia, though the symptoms may be equally distributed between the sexes (Merikangas et al., 2002).

8.3.2.6 Generalized Anxiety Disorder (GAD)

In this syndrome, there is generalized and persistent free-floating anxiety that is not tied to a particular situation. The symptoms may include nervousness, shakiness, muscular tension, sweating, light-headedness, palpitations, and

stomach discomfort. There may be vague apprehension and forebodings of dreadful accidents or illness happening to them or to loved ones. Generalized anxiety disorder affects about 2% of the adult population, is more common in women, and is often associated with chronic stress. Up to 10% of the primary care population may have GAD (Lieb et al., 2005).

8.3.3 Anxiety-Related Physical Symptoms / Psychophysiologic Syndromes

Some patients manifest more prominent physical symptoms than the subjective feelings of anxiety. Only by careful questioning does one discern that the symptoms are associated with stress or stressful situations. Common such physical symptoms are palpitations, choking sensation, sweating, frequency of urination, nausea, vomiting, and constipation. Less common but more serious conditions include hyperventilation syndrome, irritable bowel syndrome, neurodermatitis, and fainting. Any physical symptom associated with a physical disease may become exaggerated or exacerbated by anxiety, for example, tremors, seizures, migraine, and back pain.

8.3.4 Management and Treatment of Anxiety Syndromes

In general, anxiety, regardless of cause, may be reduced by the use of antianxiety drugs, cognitive behavioral techniques, and environmental means. In secondary anxiety syndrome, the underlying cause should be identified and treated in conjunction with management of anxiety per se.

General pharmacologic treatment for anxiety involves the use of γ-aminobutyric acid (GABA) agonists such as benzodiazepines, selective serotonin reuptake inhibitors (SSRIs) for attenuation and prevention, and antipsychotic drugs for severe anxiety, especially when associated with dissociative or psychotic symptoms, sedative antihistaminics such as hydroxyzine, and beta-blockers such as propranolol, or for physiologic symptoms such as palpitation. Tricyclic antidepressants, for example, imipramine and amitriptyline, and monoamine oxidase inhibitors (MAOIs) may also be used in place of SSRIs.

General nonpharmacologic treatments include cognitive-behavioral therapy (CBT), reassurance, supportive psychotherapy, relaxation training, mindfulness training, and self-hypnosis.

8.3.4.1 Acute Stress Disorder and Posttraumatic Stress Disorder

8.3.4.1.1 Pharmacotherapy: The SSRIs are considered to be the first line of treatment. For acute stress disorder (ASD) with nightmares or insomnia, olanzapine in small doses (e.g., 2.5 to 5 mg) hs for 1 month may be particularly helpful. For nightmares associated with PTSD, the α-adrenergic blocker prazosin (1 mg hs gradually increased up to 6 mg) has been shown to be useful. Benzodiazepines may also be used for reducing anxiety. For PTSD, the treatment is always symptomatic, as the symptoms may range from depression, to impulsivity, to psychotic symptoms, to panic. Thus, in addition to SSRIs and antipsychotics, mood stabilizers such as valproic acid and lithium, and beta-blockers may be indicated.

8.3.4.1.2 Psychotherapy: Remembering the traumatic event within 24 hours after it occurred has been shown to be a predictor of future PTSD, whereas amnesia concerning the event is a predictor of not developing PTSD (Gil et al., 2005).

Thus, when a patient who suffered an acute stress, such as a motor vehicle accident or assault, has no memory of the incident, it is prudent for the medical staff not to encourage the patient to remember it. Psychological debriefing and critical incident debriefing, in which the individual relives in detail the traumatic experience in a group situation, have been shown to be ineffective or even detrimental and more likely to result in PTSD (Litz et al., 2005). Cognitive-behavioral therapy has been shown to be effective in PTSD, as has psychoeducation and supportive therapy.

8.3.4.2 Obsessive-Compulsive Disorder

As discussed earlier, the stress of illness and hospitalization and the cognitive deficits associated with head injury, medications, and mild delirium can accentuate personality traits such as obsessiveness. Uncertainties regarding diagnosis or proposed treatment may render a person to appear obsessive-compulsive. As it is rare for patients to develop OCD de novo in a hospital, every effort should be made to reduce the situational anxiety or the cognitive deficit accompanying the behavior.

8.3.4.2.1 Pharmacotherapy: In patients with diagnosed OCD, the treatment of choice is an SSRI, increased gradually to a very high dose (e.g., fluoxetine 80 mg per day). Second-generation antipsychotics may also be used if indicated.

8.3.4.2.2 Psychotherapy: Cognitive-behavioral therapy has been shown to be effective.

8.3.4.3 Panic Disorder

8.3.4.3.1 Pharmacotherapy: Antidepressant drugs (SSRIs, tricyclics, and MAOIs) and high-potency benzodiazepines have been shown to be effective for panic disorder with or without agoraphobia. Commonly used SSRIs include fluoxetine, paroxetine, and sertraline, and high-potency benzodiazepines include alprazolam and clonazepam.

8.3.4.3.2 Psychotherapy: Cognitive-behavioral therapy is effective, particularly in combination with pharmacotherapy. The cognitive component may include, for example, reevaluating the symptoms as being due to anxiety and not due to a heart attack, and the behavioral component may include *exposure and response prevention;* that is, the patient is exposed to a panic-producing situation and the patient learns to "ride out" the panic until it passes.

8.3.4.4 Specific Phobias

8.3.4.4.1 Psychotherapy: Behavior therapy, consisting of desensitization through gradual exposure, is usually effective for specific phobias. Other psychotherapeutic techniques include relaxation training, flooding, and exploratory psychotherapy.

8.3.4.5 Social Phobia/Anxiety

8.3.4.5.1 Pharmacotherapy: Antidepressants (SSRIs, MAOIs, tricyclics) as well as antianxiety drugs (e.g., clonazepam, gabapentin) have been shown to be effective, particularly combined with behavioral therapy. Paroxetine, an SSRI, may be used in doses of 20 to 50 mg per day. Propranolol in small doses (e.g. 10 mg po 30 minutes before exposure) may be particularly effective for performance/social anxiety.

8.3.4.5.2 Psychotherapy: Behavioral therapy, guided exposure, CBT with social skills training, and group therapy have been shown to be effective.

8.3.4.6 Generalized Anxiety Disorder

Generalized anxiety disorder is a chronic illness, and a realistic goal of treatment is to reduce anxiety symptoms sufficiently for functioning, not total elimination.

8.3.4.6.1 Pharmacotherapy: Benzodiazepines, buspirone, and gabapentin are some of the antianxiety drugs that may be effective for GAD. Antidepressants, including SSRIs and tricyclics, may be helpful. Venlafaxine, a serotonin-norepinephrine reuptake blocker, has been reported to be particularly helpful (Davidson et al., 2001).

8.3.4.6.2 Psychotherapy: Psychoeducation, CBT, supportive psychotherapy, relaxation training, meditation, and self-hypnosis may be useful in GAD.

8.3.4.7 Anxiety-Related Physical Symptoms and Psychophysiologic Syndromes

Treatment of the physical symptoms associated with anxiety should be geared to both the physical symptoms and the underlying anxiety. Thus, paper-bag rebreathing to reduce the hypocapnea is an effective treatment for *hyperventilation syndrome*, and anticholinergic drugs may be effective for *irritable bowel syndrome*.

8.3.4.7.1 Pharmacotherapy: Benzodiazepines or antidepressants may be used to control/reduce anxiety. In psychophysiologic syndromes, there may be excessive physiologic arousal in the presence of only moderate anxiety, and such arousal may be treated with antianxiety agents. There is no evidence that prolonged use of moderate to large doses of benzodiazepines to control such physical symptoms results in tolerance and the need for more benzodiazepines. The pharmacologic and psychotherapeutic measures described for GAD are also applicable for psychophysiologic syndromes.

References

Bremner JD, Randall PR, Capelli S, et al. The neurobiology of posttraumatic stress disorder: an integration of animal and human research. In: Saigh P, Bremner JD, eds. Posttraumatic Stress Disorder: A Comprehensive Text. New York: Allyn & Bacon, 1999:103–143.

Bremner JD, Randall PR, Capelli S, Scott T, McCarthy G, Charney DS. Deficits in short-term memory in adult survivors of childhood abuse. Psych Res 1995a;59:97–107.

Bremner JD, Randall PR, Scott TM, et al. MRI-based measurement of hippocampal volume in posttraumatic stress disorder. Am J Psychiatry 1995b;152:973–981.

Coetzer BR. Obsessive-compulsive disorder following brain injury: a review. Int J Psychiatry Med 2004;34(4):363–377.

Davidson JR. Pharmacotherapy of generalized anxiety disorder. J Clin Psychiatry 2001;62 Suppl 11:46–50.

Gil S, Caspi Y, Zilberman Ben-Ari I, Koren D, Klein E. Does memory of a traumatic event increase the risk for posttraumatic stress disorder in patients with traumatic brain injury? A prospective study. Am J Psychiatry 2005;162:963–969.

Lieb R, Becker E, Altamura C. The epidemiology of generalized anxiety disorder in Europe. Eur Neuropsychopharmacol 2005;15(4):445–452.

Litz B, Gray M, Bryant R, Adler A. Early intervention for trauma: current status and future directions. A National Center for PTSD Fact Sheet, 2005.

Merikangas KR, Avenevoli S, Acharyya S, Zhang H, Angst J. The spectrum of social phobia in the Zurich cohort study of young adults. Biol Psychiatry 2002;51(1):81–91.

Neumeister A, Bain E, Nugent AC, et al. Reduced serotonin type 1_a receptor binding in panic disorder. J Neurosci 2004;24(3):589–591.
Sapolsky RM. Why stress is bad for your brain. Science 1996;273:749–750.
Smith MA, Makino S, Kvetnansky R, Post RM. Stress and glucocorticoids affect the expression of brain-derived neurotrophic factor and neurotrophin-3 mRNA in the hippocampus. J Neurosci 1995;15:1768–1777.
Uno H, Tarara R, Else JG, Suleman MA, Sapolsky RM. Hippocampal damage associated with prolonged and fatal stress in primates. J Neurosci 1989;9:1705–1711.
Weissman MM, Bland RC, Canino GJ, et al. The cross-national epidemiology of panic disorder. Arch Gen Psychiatry 1997;54(4):305–309.

Bibliography

Albano AM, Marten PA, Holt CS, Heimberg RG, Barlow DH. Cognitive-behavioral group treatment for social phobia in adolescents. A preliminary study. J Nerv Ment Dis 1995;183(10):649–656.
Beidel DC, Turner SM, Morris TL. Behavioral treatment of childhood social phobia. J Consult Clin Psychol 2000;68(6):1072–1080.
Davidson JR, DuPont RL, Hedges D, Haskins JT. Efficacy, safety, and tolerability of venlafaxine extended release and buspirone in outpatients with generalized anxiety disorder. J Clin Psychiatry 1999;60(8):528–535.
Davidson JR, Potts N, Richichi E, et al. Treatment of social phobia with clonazepam and placebo. J Clin Psychopharmacol 1993;13(6):423–428.
Gorman JM. Treatment of generalized anxiety disorder. J Clin Psychiatry 2002;63 (suppl 8):17–23.
Gray MJ, Litz BT. Behavioral interventions for recent trauma: empirically informed practice guidelines. Behav Modif 2005;9(1):189–215.
Nesse RM. The smoke detector principle natural selection and the regulation of defensive responses. Ann NY Acad Sci 2001;935:75–85.
Pollack MH, Zaninelli R, Goddard A, et al. Paroxetine in the treatment of generalized anxiety disorder: results of a placebo-controlled, flexible-dosage trial. J Clin Psychiatry 2001;62(5):350–357.
Spence SH, Donovan C, Brechman-Toussaint M. The treatment of childhood social phobia: the effectiveness of a social skills training-based, cognitive-behavioural intervention, with and without parental involvement. J Child Psychol Psychiatry 2000; 41:713–726.
Stein MB, Liebowitz MR, Lydiard RB, Pitts CD, Bushnell W, Gergel I. Paroxetine treatment of generalized social phobia (social anxiety disorder): a randomized controlled trial. JAMA 1998;280(8):708–713.
Ursano RJ, Bell C, Eth S, Friedman M, Norwood A, Pfefferbaum B, Pynoos JD, Zatzick DF, Benedek DM, McIntyre JS, Charles SC, Altshuler K, Cook I, Cross CD, Mellman L, Moench LA, Norquist G, Twemlow SW, Woods S, Yager J. Work Group on ASD and PTSD; Steering Committee on Practice stress disorder and posttraumatic stress disorder. Am J Psychiatry 2004 Nov;161(11 Suppl):3–31.
van Vliet IM, den Boer JA, Westenberg HG. Psychopharmacological treatment of social phobia; a double blind placebo controlled study with fluvoxamine. Psychopharmacology (Berl) 1994;115(1–2):128–134.
Zai G, Arnold P, Burroughs E, Barr CL, Richter MA, Kennedy JL. Evidence for the gamma-amino-butyric acid type B receptor 1 (GABBR1) gene as a susceptibility factor in obsessive-compulsive disorder. Am J Med Genet B Neuropsychiatr Genet 2005;134(1):25–29.