

Disclaimer/Publisher's Note: The statements, opinions, and data contained in all publications are solely those of the individual author(s) and contributor(s) and not of MDPI and/or the editor(s). MDPI and/or the editor(s) disclaim responsibility for any injury to people or property resulting from any ideas, methods, instructions, or products referred to in the content.

Short Note

Cannabidiol, NegEnt and Panic Disorder

Tullio Scrimali

University of Catania, Catania Italy and ALETEIA, European School of Cognitive Therapy, Enna, Italy; tscrimact@gmail.com

Abstract: The article presents the potential of liposomal cannabidiol in the treatment of Panic Disorder, when used in integration with Complex Cognitive Psychotherapy. The advantages of the integrated treatment, developed by the Author, and based on the use of liposomal cannabidiol combined with cognitive psychotherapy, are discussed. A new and original tool is presented and described, developed, and tested for the first time by the Author and called NegEnt Panic Blocker.

Keywords: cannabidiol; liposomal cannabidiol; NegEnt; panic disorders; cognitive psychotherapy; alprazolam

1. Introduction

A *Panic Attack* consists of a specific situation, during which there is a sudden onset of intense fear, associated with a feeling of impending catastrophe or death. During the panic episode, the patient perceives marked physical symptoms, such as shortness of breath, palpitations, chest pain or discomfort, nausea or the impulse to vomit. A *panic attack* differs from *an anxiety attack* in that, in the latter case, the patient acknowledges that they are experiencing intense discomfort, but not that it's life threatening. On the other hand, in the state of panic, the person really believes that they are on the verge of death. Another important difference between anxiety and panic is that the former is almost always in answer to external threats and activates the fight or flight response. On the other hand, panic is triggered by altered perceptions of vital activities, which are considered to lead to heart problems, heart attack and death and is associated with derealisation and depersonalisation (Scrimali, Alaimo, Grasso 2007).

Since panic attacks are a *traumatic experience*, it leaves an intense and persistent traces in the emotional memories after each episode, triggering the ongoing, nagging worry that another episode may recur at any time. The patient then begins to exhibit an anxious state – one that is increasingly present and painful – of being able to feel ill and the scenario is soon complicated by *agoraphobia*, where the subject tries not to leave their home and well-known locations where they believe they can receive help and support. In turn, they develop a marked *relational dependence*, in the sense that they insist on asking not to be alone, and to always be accompanied and helped by someone they consider reassuring.

2. Neurobiology

Neuroscience today provides sufficient evidence for the development of a psychobiological conceptualisation of Panic Disorder. One of the brain structures most involved in panic attack is the dorsal portion of the periaqueductal gray matter, an archaic neural system, located in the midbrain. Electrical stimulation of this system can produce symptoms very similar to panic attacks, with feelings of terror and imminent death, accompanied by increased heart rate and widespread pain in the face and chest. The role of a structure called the *insula cortex* that is involved in processing information from the body's vital systems is also important. The insula is made up of a portion of the cerebral cortex that lies within the sulcus, of fissure, that separates the temporal lobe from the frontal lobe. The role of the amygdala, which is important in other anxiety disorders but hasn't always been found to be hyperactive in Panic Disorder (Goodkind, Etkin, 2018), remains unclear.



3. Aetiology and Psychopathology

Important for the understanding of Panic Disorder are the contributions provided by *Attachment Theory* that studies how caregiving, which every human being has received in the developmental period of their lives, can determine how the mind organises its processes (Bowlby, 1988). According to Attachment Theory, subjects who exhibit Panic Disorder have received care throughout their developmental history from parents, or other caregivers, who were excessively emotional, apprehensive and controlling. In this way they have developed the deep conviction of being fragile and vulnerable, as well as being able to easily get sick, or even die, from a sudden illness (Guidano, Liotti, 1983).

In psychotherapy these patients clearly recall memories of the mother who told them: Don't run, you'll get sweaty! Feel your heart pounding! You're too hot! Look how you're breathing! You're almost gasping! -.

I myself, having been born and raised in Sicily, a place which is notoriously hot in summer, remember that I was systematically terrified by my mother with phrases like: *Don't sweat too much because then the sweat will freeze on your body, and you'll get sick*. So, unfortunately, when I played in the street, downstairs, in a small street in the historic part of Enna, which was still cobbled just like an ancient Roman street, I, perfectly at ease with the Latin name of Tullio, was set upon by my mother with a towel, a spare tank top, and talcum powder. After the *treatment*, I was left whiter than a zombie and smelling of talc like a sweet violet. Meanwhile, my friends had finished the game without me! In short, my mother built in my mind the belief that sweating was not a beneficial physiological function, indispensable to ensure thermal homeostasis, but a menacing warning of diseases! Fortunately for me, I didn't exhibit any biological vulnerability or inclination to become a phobic! In fact, dysfunctional parenting is not enough to create psychological discomfort: we need the presence of other factors, including, most importantly, biological vulnerability.

Without realising it, people who later develop panic attacks start *body scanning*: a kind of nagging, obsessive monitoring of the somatic state. Any information about changes in physical conditions, like a harmless extrasystole or a slight increase in heart rate, or a slight discomfort in the retrosternal area, perhaps due to poor digestion, is perceived and tagged as an incoming heart attack. Hence the consistent statement of one of my phobic patients: *Masturbation is a death risk!* - Trying to analyse, and then restructure, this dysfunctional belief, using Socratic dialogue, we came to the following consistent but absurd syllogism, well rooted in the mind of that patient: *When I masturbate I feel my heart accelerate, especially if I reach orgasm. An increase in heart rate means the threatening harbinger of a cardiovascular problem, perhaps a heart attack. Therefore, masturbation causes a heart attack!*

The patient, when he perceives any anomaly in a vital process, feels anxious and immediately becomes the victim of a vicious circle, since anxiety causes hyperpnea (deep breathing), sweating, tachycardia (fast heart rate), digestive blockages, with possible nausea, which are perceived as confirmation of an incoming heart attack. He truly feels in mortal danger, so he begins to panic, which, as we have seen, is connected to the fear of dying. The subject almost always goes to the nearest emergency room to ask for help, believing that he is really about to dramatically say goodbye to the world.

4. Epidemiology

Panic disorder is fairly common, with an estimated prevalence rate of about 9%, and often occurs in conjunction with other anxiety disorders and a range of mental disorders such as depression and substance use disorder.

5. Treatment

Since panic disorder was included in DSM III, the third edition of the US manual for the classification of mental disorders in the 1980s, a very large business has developed that has seen the great US pharmaceutical company Upjohn, which was very timely in presenting its new benzodiazepine, alprazolam, at the same time, become the leading

player. Immediately afterwards, thanks to a self-assured, hyped-up health marketing campaign, they convinced people that it was a therapy specifically for Panic Disorder. With the brand name of Xanax, and on the wings of the cultural and scientific colonisation of the Western world by the USA, which it also implemented through the DSM statistical and diagnostic manual of mental disorders, doctors and patients around the world were led to believe that Xanax was the specific and suitable therapy for Panic Disorder. To date, Xanax is the product most prescribed by primary care physicians and specialists and that is unquestioningly believed to be an effective treatment of Panic Disorder.

But this isn't the case. Alprazolam, i.e., Xanax, isn't an adequate treatment of Panic Disorder, only a *symptomatic therapy* that isn't always effective, nor accepted by the patient. The person who takes Xanax will be sedated, and may not experience panic attacks for a certain period of time, but as soon as they stop the treatment, the panic attacks will return, this time more violent and frustrating than before.

Let's hasten to clarify that the treatment of Panic Disorder must primarily be psychotherapeutic and can use any benzodiazepine, not just alprazolam, and only as a temporary tool for managing panic.

As part of my studies on the treatment of psychological distress and the complex integration between psychotherapy and pharmacological treatments, I have developed an original and innovative approach to the treatment of Panic Disorder (Scrimali, 2008).

In the short term, the patient will receive a drug prescription to be taken daily to reduce basic anxiety and significantly decrease the likelihood of a panic attack occurring. However, the will primarily have to learn to stop obsessive body scanning, and, in the event that anxiety arises, they will be able to regulate it without becoming terrified and consequently losing control. This is achieved in our ALETEIA Clinical Centres by implementing self-control training based on the systematic practice of biofeedback implemented with the instrumentation that I have made, called the MindLab Set (Scrimali, 2012).

Furthermore, as part of an integrated protocol, which I have called Daedalus, the recommendation to the patient to always carry an orally dissolving tablet of lorazepam with them and to dissolve it under the tongue in case of warning signs of a panic attack, plays an important role. The patient, reassured by the power to successfully face any emergency, begins to deal positively with situations that previously caused agoraphobia and resumes exploring, agreeing to leave their home to resume the normal attitude of moving in the outside environment.

In recent years I have begun to study cannabidiol and, in particular, the product, developed by me, which I have called NegEnt (from Negative Entropy), based on nanometric liposomal cannabidiol, for the treatment of panic disorder.

A recent review of the scientific literature, which included both experimental studies in laboratory animals and clinical studies in humans, investigated the anti-panic properties of CBD. All scientific studies taken into account in the review clearly suggest cannabidiol's anxiolytic effect, both in animals and in humans. Based on this scientific review, it seemed to me that cannabidiol could be a promising drug for the treatment of panic disorder.

In addition to this, the pharmacodynamic profile of CBD is particularly promising and suitable here. Unlike benzodiazepines, cannabidiol does not exhibit any sedative action, only a tranquilising one. Essentially, cannabidiol *calms without sedating*. Patients afflicted by Panic Disorder don't like the feeling of relaxation and sedation caused by benzodiazepines because they associate it with fainting, collapsing and, in any case, a loss of control. The use of CBD in phobic patients is therefore very well accepted, since it doesn't cause any negative somatic sensation that would immediately put them on the alert. On top of that, phobics are plagued by the dysfunctional belief that plant-based remedies are safer and more tolerated than synthetic ones. This belief is, of course, unfounded and will need to be restructured in the course of psychotherapy. However, at the beginning of treatment, it can play a role in encouraging them to take cannabidiol.

I have thus developed an innovative way of using NegEnt, nanometric liposomal cannabidiol, as a basic treatment, integrated with cognitive psychotherapy, to be systematically taken three times a day, at the rate of 5 sublingual drops at breakfast, lunch and dinner (Scrimali, 2022).

However, I have recently developed, and already positively tested, a new medical device, based on NegEnt, called the *NegEnt Panic Blocker*.

It is a 50 mg dose of NegEnt, placed in a hermetic syringe container that the patient can keep in their pocket so that it is always with them. In case they get any signs of panic, (the patient is trained to recognise the first warning signs during psychotherapy) they can use the *NegEnt Panic Blocker* to deposit 50 mg of immediately bioavailable nanometric liposomal cannabidiol under the tongue on the mucus membrane that can prevent the onset of the real panic attack. Absorbed through the mucus membrane and the sublingual vein, liposomal cannabidiol immediately enters the circulation and acts in a very short amount of time. Thanks to the availability of this new effective coping tool, the patient being to feel more confident (mastery and coping are significantly improved!) and gradually abandons phobic avoidance, once again beginning to explore their environment.

6. Conclusions

NegEnt, liposomal cannabidiol, used in an integrated and complex approach, as well as an extemporaneous device, named *Panic Blocker*, within the framework of complex cognitive-behavioural psychotherapy protocols, seems to be a possible new innovative therapy for Panic Disorder, which is very effective and lacks any side effects. In addition to this, as NegEnt is an over-the-counter aromatherapy product on the Internet, (www.herb-alneurocare.it), it can also be prescribed and used by patients of psychotherapists who are psychology graduates who can't prescribe benzodiazepines or any other psychopharmaceutical.

References

1. Bowlby, J. (1988). *A secure base: Parent-child attachment and healthy human development*. London: Routledge.
2. Goodkind, M.S., Etkin, A. (2018). Functional Neurocircuitry and Neuroimaging Studies of Anxiety Disorders. In: Charney, D.S., Buxbaum, J.D., Sklar, P., Nestler, E.J. (Eds) *Neurobiology of Mental Illness*. Oxford: Oxford University Press.
3. Guidano, V.F., Liotti, G. (1983). *Cognitive Processes and Emotional Disorders*. New York: Guilford Press.
4. Scrimali, T. (2008). *Entropy of Mind and Negative Entropy*. London: Karnac Books
5. Scrimali, T. (2012). *Neuroscience-based Cognitive Therapy*. Chichester: Wiley
6. Scrimali, T. (2020). NegEnt: A cannabidiol-based herbal medicine. Theoretical aspects, pharmacology, clinical and research perspectives, economic and social implications. *International Journal of Herbal Medicine*, 8 (5): 143-151
7. Scrimali T. (2022). NegEnt. Liposomal cannabidiol in human and veterinary medicine. ALETEIA Publisher, Enna.
8. Scrimali, T., Alaimo M., Grasso, F. (2007) *Dal sintomo ai processi. L'orientamento costruttivista e complesso in psicodiagnostica. (From symptom to process: Constructivist and complex orientation in psychodiagnostics)* Milan: FrancoAngeli Publishing.