



IJPPR

INTERNATIONAL JOURNAL OF PHARMACY & PHARMACEUTICAL RESEARCH
An official Publication of Human Journals

ISSN 2349-7203



Human Journals

Review Article

February 2018 Vol.:11, Issue: 3

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Relaxation of Contracted Skeletal Muscle in Anxiety Conditions: GABAergic Pathway

			
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Submission:	24 January 2018		
Accepted:	29 January 2018		
Published:	28 February 2018		



HUMAN JOURNALS

www.ijppr.humanjournals.com

Keywords: Anxiety, skeletal muscle contraction, GABA, amygdala.

ABSTRACT

Anxiety is one of the disturbing classes of psychiatric disorders. The number of people being affected by it every year is on a rise especially in females as compared to men. Anxiety has its origin in the amygdala which goes overactive in anxiety conditions. GABA, NE and 5HT are the neurotransmitters involved in it. The neurobiology of anxiety conditions is very complex to understand. GABA (Gamma-aminobutyric acid) is considered the major inhibitory neurotransmitter in the brain. The brain circuits in the amygdala are thought to comprise inhibitory networks of γ -aminobutyric acidergic (GABAergic) interneurons and thus this neurotransmitter is best opted for treating anxiety. Various physiological changes take place in the body in the long run one of which is intense skeletal muscle contraction. But when you're having anxiety for an extensive period of time, your skeletal muscles never leave the contraction phase which leads to discomfort, immobility and adds to the overall anxiety. Following article is the overview of the origin of anxiety, the skeletal muscle contraction phase, physiological changes in body and the implications of the GABAergic pathway which gives one a deeper understanding of the disorder.

INTRODUCTION

Anxiety is a group of emotions coming together often characterized by fear, confusion, state of great disturbances affecting one mentally and physically, accompanied by nervous behavior. Basically, it is the hyperarousal of the central nervous system and intense feelings of worry. Anxiety disorders affect millions of people each year. Clinical signs and symptoms include restlessness, insecurity, worrying about future, nervousness trembling, phobias such as fear of darkness, strangers, fear of animals, fear of being alone, over thinking all night. The different types of anxiety disorders include social anxiety disorder (SAD) which is associated with socially interacting with people, post-traumatic stress disorder (PTSD) occurring after a tragic event, generalized anxiety disorder (GAD) which is mainly associated with extreme muscle tension, panic disorder (PD) marked by sudden and recurrent episodes, obsessive-compulsive disorder (OCD) that involves repetitive behavior or mental acts (for example, checking, washing, counting repeatedly). They are highly prevalent in adult female compared to men. Anxiety conditions are accompanied by intense muscle contraction especially skeletal muscles as skeletal muscles comprise one of the major types. Skeletal muscles get tense and add to the overall anxiety conditions especially Generalized anxiety disorder (GAD). Muscle tension in GAD is poorly understood. [1] Benzodiazepines are the class of psychoactive drugs with anti-anxiety and skeletal muscle relaxant properties. They produce effects centrally in the brain and spinal cord. These drugs depress the pulse transmission in polysynaptic pathways. They target GABA_A component of Supramolecular complex, produce GABAergic effect and enhance the effect of the neurotransmitter GABA. However, they have side effects. [2] Herbal medicines can also be opted for treatment of anxiety via GABAergic pathways such as plants containing constituents like quercetin and sinapic acid. [3] [4] [5] Herbal medicines not only have lesser side effects but have various active constituents which can cure various ailments via GABAergic pathway. [6]

AMYGDALA

The amygdala is an almond-shaped structure located in the limbic system which is involved in the processing of memory, decisions, and emotions. Anxiety has its origin in the amygdala which goes overactive in anxiety conditions and gets disrupted. [7] [8] The reaction begins in the amygdala, which triggers a neural response in the hypothalamus. Corticotropin Releasing Hormone (CRH) is produced by the hypothalamus. The initial reaction is followed by activation of the pituitary gland where adrenocorticotrophic hormone (ACTH) is secreted. The

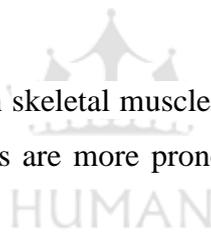
adrenal gland is activated releasing the hormone adrenaline thereby releasing the hormone cortisol, which increases blood pressure, blood sugar, and suppresses the immune system. Adrenaline, as you know, is the “fight or flight” hormone, When your fight or flight system is activated - which occurs during times o stress and anxiety - your muscles contract. [11][7][8][9]

PHYSIOLOGICAL CHANGES IN BODY

The physiological changes that occur during the fight or flight response in anxiety conditions are as follows:-

- Increased blood flow to the muscles.
- Increased blood pressure, heart beat rate, blood sugars, and fats.
- Increase in The blood clotting function of the body
- Increased muscle tension

Muscle tension can be associated with skeletal muscle, cardiac muscle and smooth muscle or either of it intensely. Skeletal muscles are more prone since they account one of the major muscle types. [11][10]



SKELETAL MUSCLE CONTRACTION IN ANXIETY

Skeletal muscle (striated muscles) is one of three major muscle types, the others being cardiac muscle and smooth muscle. They are attached to bones by bundles of collagen fibers known as tendons. Skeletal Muscle tension is a critical aspect of anxiety conditions especially Generalized anxiety disorder (GAD) [11]

This is what happens within a skeletal muscle when it contracts in anxiety –

An electrical signal when travels down a nerve cell causes it to release a neurotransmitter acetylcholine into the synapse. The neurotransmitter then crosses the synapse, binds to a receptor on the muscle-cell membrane thus stimulating the membranes of muscle fibers to contract and thus causes an action potential in the muscle cell. The electrical signal spreads along the muscle cell and enters the cell through the T-tubule opening the gates in the sarcoplasmic reticulum. Calcium ions move into the cytoplasm, where the actin and myosin

filaments are present and start binding to troponin-tropomyosin molecules located in the grooves of the actin filaments thus exposing the binding sites, Myosin interacts with actin by cycling cross bridges. The skeletal muscle thereby creates force and shortens. During anxiety, skeletal muscle fibers tend to contract by 30 to 40 percent of their original length. Skeletal muscles are attached to bones with the help of tendons which are bands of fibrous tissues that need rest and enough oxygen. The entire process takes about 1 millisecond. But when one is having anxiety for prolonged duration, skeletal muscles never leave the contraction phase. Eventually, this tension causes pain, discomfort and immobility at times. [12]

TREATMENT INVOLVING GABAergic PATHWAY

GABA (Gamma-aminobutyric acid) is considered the major inhibitory neurotransmitter in the brain. GABA- benzodiazepine receptors are widely distributed in the brain and spinal cord. They are particularly concentrated in portions of the brain thought to be involved in anxiety, including the medial PFC, amygdala, and hippocampus, and results from several studies have indicated abnormalities in this system in patients with anxiety disorders. Low levels of GABA a neurotransmitter that reduce activity in the central nervous system contributes to anxiety. There are two types of GABA receptors GABAA and GABAB. GABA molecule when released into the synapse travels across the synapse binds with GABA receptors postsynaptically on the amygdala. It actually opens the ion channels and lets chloride ion flow in which inhibits neurotransmission postsynaptically and reduces the hyperactivity of the amygdala. Benzodiazepines bind to the benzodiazepine receptor on the complex located on the postsynaptic neuron. Some oral supplements when taken like Diazepam or herbal constituents like Sinapic acid and Quercetin present in plant bind along with GABA on the GABA receptor and block the reuptake of GABA thereby increasing the GABA concentration. More binding to the postsynaptic receptor leads to more Cl⁻ ion channel opening and inhibition of amygdala. Therefore anxiety decreases even more. [1][13][14]

Since Spinal cord is a part of the central nervous system, electrical signals from the brain move down to the spinal cord, these neurons become motor nerves that run out towards the body's muscles. These oral supplements act as GABA agonist that work to hyperpolarize neurons in the central nervous system and depress them so that they do not secrete acetylcholine or less acetylcholine is secreted. Thus the motor neurons will not receive the message to activate the muscle cell and so the skeletal muscle which was first contracted due

to anxiety goes calm and relaxed. [15] This is how the CNS and Muscular system are interconnected and contracted skeletal muscles get relaxed in anxiety conditions.

DISCUSSION

Anxiety has its origin in the amygdala. The brain circuits in the amygdala are thought to comprise inhibitory networks of γ -aminobutyric acidergic (GABAergic) interneurons. GABA (Gamma-aminobutyric acid) thus plays a key role in treating anxiety and the contracted skeletal muscles in anxiety condition. GABA is considered the major inhibitory neurotransmitter in the brain. [13] Benzodiazepines have various side effects such as sedation, drowsiness, ataxia, impaired judgment, depression of the respiratory system on increased doses. [16] Herbal supplements such as Quercetin and sinapic acid present in plants are known for its anti-anxiety activity and treating contracted skeletal muscles in anxiety conditions. via GABAergic effect. [3][4][5][6]

CONCLUSION

Herbal medicines are the need of the hour. They not only have lesser side effects but can be used for treating multiple ailments and act via GABAergic effect. The future remains optimistic for those who struggle with anxiety.

REFERENCES

1. Arya Ashwani, Kumar Tarun, Malik Ajay and Hooda Anil. Anxiety disorders: A Review. International Research Journal of Pharmacy. ISSN 2230-8407.
2. Available from: Benzodiazepines as Centrally Acting Skeletal Muscle Relaxants .howmed.net > Pharmacology.
3. Preeti, Milind Parle, Monu and Kailash Sharma, Medicinal plants possessing anxiolytic activity: A brief review. Pelagia Research Library Der Pharmacia Sinica, 2015, 6(5):1-7.
4. Ji Wook Jung and Seungheon Lee, Anxiolytic Effects of Quercetin: Involvement of GABAergic System. Journal of Life Science 2014 .24.(3). 290~296.
5. Yoon BH, Jung JW, Lee JJ, Cho YW, Jang CG, Jin C, Oh TH, Ryu JH. Anxiolytic-like effects of sinapic acid in mice. Article in Life Sciences 2007;81(3):234-40.
6. Amita Pandey, Shalini Tripathi, Katyayni Bajpeyi. A Review on Receptor in the Brain Responsible for Anxiety and List of Higher Plants for Treatment Anxiety. IJRPLS, 2014, 2(1): 167-175.
7. Available from: Amygdala - Wikipedia <https://en.wikipedia.org/wiki/Amygdala>.
8. Available from: The Amygdala: The Body's Alarm Circuit - Dana Foundation. www.dana.org/news/brainwork/detail.aspx?id=1338
9. Available from: Fight-or-flight-response-Wikipedia. en.wikipedia.org/wiki/Fight-or-flight_response.
10. Peter Sainsbury and J. G. Gibson, Symptoms of Anxiety and Tension and the Accompanying Physiological Changes in the Muscular System. J. Neurol. Neurosurg. Psychiat, 1954;17,216.
11. Available from: Skeletal muscle - Wikipedia https://en.wikipedia.org/wiki/Skeletal_muscle
12. Available from: Muscle contraction - Wikipedia https://en.wikipedia.org/wiki/Muscle_contraction.

13. Philippe Nuss, Anxiety disorders and GABA neurotransmission: a disturbance of modulation. *Neuropsychiatric Disease and Treatment*, Dovepress 2015;11 165–175.
14. Available from: How The Neurotransmitter GABA Works For Anxiety In The Brain. https://youtu.be/M_QQD9NdJcU.
15. Available from: Muscle Relaxants. <https://youtu.be/FmWAVChLKWQ>.
16. Available from: Diazepam used for anxiety, insomnia and muscle spasms. www.netdoctor.co.uk/medicines/depression/a6560.

