

Research Update

rTMS for Treatment of Anxiety – Research Protocol Review and rTMS System Configuration

Regulatory Note: rTMS for the treatment of Anxiety is not included in the Intended Use for MagPro stimulators. The use of MagPro stimulators for applications outside the approved intended use in a given country is the responsibility of the researchers performing the studies. For USA: Please consult MagVenture.

1. What is Anxiety

Anxiety is a normal human emotion that everyone experiences at times. Many people feel anxious, or nervous, when faced with a problem at work, before taking a test, or making an important decision. Anxiety disorders, however, are different. They can cause such distress that it interferes with a person's ability to lead a normal life. An anxiety disorder is a serious mental illness. For people with anxiety disorders, worry and fear are constant and overwhelming, and can be crippling. The following disorders are referred to as anxiety:

- **Generalized Anxiety Disorder (GAD)** is characterized by excessive, exaggerated anxiety and worry about everyday life events with no obvious reasons for worry. People with symptoms of generalized anxiety disorder tend to always expect disaster and can't stop worrying about health, money, family, work, or school. In people with GAD, the worry is often unrealistic or out of proportion of the situation. Daily life becomes a constant state of worry, fear, and dread. Eventually, the anxiety so dominates the person's thinking that it interferes with daily functioning, including work, school, social activities, and relationships.
- **Social Anxiety Disorder**, also called social phobia (SAD), is an anxiety disorder in which a person has an excessive and unreasonable fear of social situations. Anxiety (intense nervousness) and self-consciousness arise from a fear of being closely watched, judged, and criticized by others. A person with social anxiety disorder is afraid that he or she will make mistakes, look bad, and be embarrassed or humiliated in front of others. The fear may be made worse by a lack of social skills or experience in social situations. The anxiety can build into a panic attack. As a result of the fear, the person endures certain social situations in extreme distress or may avoid them altogether. In many cases, the person is aware that the fear is unreasonable, yet is unable to overcome it.



- **Panic Disorder (PD)** is different from the normal fear and anxiety reactions to stressful events in our lives. Panic disorder is a serious condition that strikes without reason or warning. Symptoms of panic disorder include sudden attacks of fear and nervousness, as well as physical symptoms such as sweating and a racing heart. During a panic attack, the fear response is out of proportion of the situation, which often is not threatening. Over time, a person with panic disorder develops a constant fear of having another panic attack, which can affect daily functioning and the general quality of life. Panic disorder often occurs along with other serious conditions, such as depression, alcoholism, or drug abuse.
- **Obsessive Compulsive Disorder (OCD)** is treated in a separate Research Update.
- **Post-Traumatic Stress Disorder (PTSD)** is treated in a separate Research Update.

2. Basic TMS Theories in Anxiety

TMS is likely to have a therapeutic effect on the anxiety disorders Generalized Anxiety Disorder, Social Anxiety Disorder, and Panic Disorder. Anxiety–depression comorbidity has been characterized by more right than left frontal activity in Major Depression Disorder patients, consistent with a key role of right DLPFC in anxiety disorders. These findings have led to the hypothesis that inhibitory low frequency repetitive transcranial magnetic stimulation (rTMS) of the right prefrontal cortex may be helpful to balance the lateralized hyperexcitability and relieve symptoms of anxiety and depression.

Clinical Studies

Generalized Anxiety Disorder (GAD)

GAD is very little explored. Only one small study including 10 patients has looked at the effect of rTMS on GAD. Results from Bystrisky et al. suggest that rTMS may indeed be beneficial in the treatment of GAD. The study, however, is of limited size and further work is very much encouraged to take place.

GAD	Study	Number of subjects	Number of sessions	Number of pulses Per treatment	Pulse intensity (RMT)	rTMS parameters	Outcome
	Bystrisky et al., 2008	10	6 (2 per week)	900	90%	1 Hz rTMS right DLPFC	↓ anxiety symptoms