EEG Variability in Anxiety Disorders

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Anxiety is one among the most prevalent mental health problems in the United States [1]. Anxiety disorders include the following five subclasses:

Generalized anxiety disorder (GAD)

Generalized anxiety disorder (GAD) is a highly disabling condition whose disrupting effects on day-to-day living are often underestimated. In the United States, GAD affects 3.1% of the general population every year and can affect up to 5.7% of a patient's lifetime [1], with women receiving a diagnosis almost twice as often as men [2].
Research shows that GAD can be associated with **altered cardiovascular function** [3]**, increased risk for suicide** [4] **and increased risk for death** [5]**.**

Symptoms of GAD include continued, difficult to control worry (e.g., about finances, family, health, and the future), accompanied by restlessness, chronic fatigue, reduced attention, irritability, chest pain, headache, shortness of breath, muscle tension, increased sweating or sleep disturbances).

Social anxiety disorder (SAD)

Another leading cause of impairment and distress in the general population is **social anxiety disorder** (SAD) [6, 7]. SAD has a high economic burden on the self, family and society, because it negatively affects social life, academic performance, and work productivity [8].

Obsessive-Compulsive Disorder (OCD)

Obsessive-Compulsive Disorder (OCD) is characterized by unwanted thoughts (obsessions) and/or regularly occurring behaviors (compulsions). Repetitive behaviors such as hand washing, searching for patterns in the environment, and house cleaning are often performed in the hope of releasing or at least calming the feeling of uneasiness associated to the obsessive thoughts.

Performing these behaviors as some sort of rituals, however, offers only temporary relief from anxiety, which increases if the patient is forced not to act on the obsessive thoughts [9].

Panic disorder

Panic disorder is an anxiety disorder where patients experience unexpected intense fear, with dramatic changes in normal physiology. Symptoms may include chest pain, heart palpitations, high blood pressure, sweating, shortness of breath, dizziness, or greatly increased bowel activity [10].

Post-Traumatic Stress Disorder (PTSD)

Post-Traumatic Stress Disorder (PTSD) can develop after the exposure to inescapable psychological or physical challenges. Traumatic events include violent assaults to the self, disasters, accidents, or wars [11].

Treatments of anxiety disorders: Advantages and limitations

Treatments of anxiety disorders considered to be effective include **psychotherapy** (e.g., cognitive behavioral therapy) and **pharmacotherapy**, employing selective serotonin reuptake inhibitors (SSRIs), serotonin- norepinephrine reuptake inhibitors (SNRIs), or benzodiazepines [12].

However, **in many cases, these treatments have only limited or no effect** on anxiety symptoms [13, 14] and can **induce adverse effects** [12], increasing patient's distress [15]. In particular, the use of benzodiazepines for more than 6 months has been associated greater risk of death [16], dependency [17] and dementia. Further, **benzodiazepines have no significant effects on depression,** which is often a comorbid condition in anxiety disorders in which case, their use has been linked to an increased risk for suicide [18].

Finally, studies with ketamine have shown that while there is some evidence of ameliorating effects on anxiety levels [19], in other cases it exerts only partial effects on the overall range of symptoms [19].

Using electroencephalogram (EEG) to monitor or predict the outcome of pharmacotherapy in anxiety and depressive disorders

Anxiety and depression share similar features in terms of associated EEG changes [20] and antidepressant treatment has mixed effects on EEG activity. Overall, however, there is evidence that **specific EEG changes are linked to a positive treatment outcome** [21].

For example, measuring alpha band (frequency range: 8-12 Hz) changes in the posterior (occipital) brain region, Ulrich and colleagues [22] found differences between responders and non-responders after four weeks of treatment with tricyclic antidepressants (TCA). Responders showed greater activity before treatment and a decrease after week 4. In a follow-up study with major depression patients, the same group compared EEG activity after the administration of TCAs with different mechanisms of action (clomipramine and maprolitine) and found that **early changes in alpha band EEG activity after the first TCA dose were associated with a favorable treatment response at three weeks** [23, 24]. In another study with depressed subjects, increases in alpha activity and decreases in theta activity were found in responders to a six-week treatment with paroxetine [25]

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In a study by Bruder and colleagues [25, 26] only non-responders exhibited reduced alpha activity over the right hemisphere before treatment with fluoxetine for 12 weeks. Importantly, this study also suggested a significant gender effect, suggesting that that this biomarker is more likely to distinguish responders and non-responders in women but not in men.

Other evidence indicates a **link between antidepressant treatment and changes in frontal EEG measures in the theta band** (4–8 Hz) [24, 25], in line with earlier research suggesting a role of this frequency band in emotion regulation [27-29].

Further, in patients treated with the antidepressant paroxetine [25], a positive treatment outcome was associated with a reduction of beta band activity (frequency range, 12 to 30 Hz), a measure that has been proposed to be linked to focus in the lower range (12-15 Hz) and to active, busy, or anxious thinking in the higher range (15-40 Hz) [30].

Finally, some studies suggest that baseline parameters acquired using quantitative EEG (qEEG) may predict the occurrence of treatment adverse effects, including suicidal ideation [31-33].

A question pertains then to how EEG-based technology can be employed by clinicians to optimize treatment response in patients with anxiety disorders and often comorbid depression.

Although the technology may not directly assist clinicians in the selection of the most appropriate treatments, it may still offer crucial information on treatment responses to quickly evaluate the effects of pharmacotherapy and ultimately reach an acceptable treatment outcome.

Conclusions

Anxiety disorders widely occur in the general population, with significant disruption of the quality of life. While psychotherapy can offer some support in the treatment of anxiety symptoms, pharmacotherapy requires careful calibration, which is most often achieved through a trial and error approach. EEG-based technologies offer the advantage to improve the prediction of treatment response and to more effectively optimize treatment outcome.

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