COGNITION™ Therapeutics

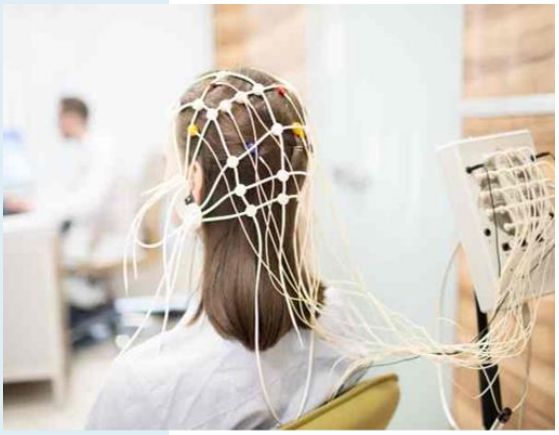
Quantitative EEG – a Primer

SEQUEL Study (n=16)

- Double-blind, placebo-controlled, cross-over trial in adults with mild-to-moderate Alzheimer's disease

Outcomes include:

- Change in the brain's electrical activity as measured by quantitative EEG following treatment of CT1812, an experimental candidate for
- Supported by $3.3M NIA grant award (AG057553)
- NCT04735536



HYPOTHESIS

- Given the substantial evidence that Aβ oligomers impair synaptic and neuronal activity, will the displacement of Aβ oligomers from synapses as a result of treatment with CT1812 lead to a detectable change in EEG in this short-term pilot study?

NOTES

* *Hertz (Hz) is a measure of the frequency of brain waves. Compact brain wave patterns indicate a healthy amount of brain activity, whereas broad wider-spaced waves in the 1-8 Hz range can indicate cognitive impairment.*

What is an EEG?

An electroencephalogram (EEG) is a sensitive test that measures the electrical activity of neurons in the brain by placing a matrix of small discs (electrodes) on the scalp. Each electrode measures the summed activity of the brain region underneath, each of which contains millions of neurons.

The resulting EEG readout (as pictured in Figure 1) will appear as a series of wave forms representing the activity of specific brain regions. The number of waves per second, their amplitude (height of waves), and the presence of irregular spikes or other abnormalities may be useful in diagnosing central nervous system (CNS) disorders.

In current clinical practice, EEG is a standard assessment tool in diagnosing epilepsy, cerebrovascular disease, dementia and encephalopathy. In other disease states, EEG is used in conjunction with other assessments to determine extent of damage in TBI or stroke or to confirm a diagnosis of ADHD, depression, autism, bipolar disorder, schizophrenia, or Parkinson's disease.

Quantitative EEG

Quantitative EEG (qEEG) involves the analysis of recorded digital EEG signals using sophisticated mathematical algorithms. Compared to traditional EEG, qEEG possesses enhanced sensitivity that can identify and differentiate between wave pattern nuances. Recently, interest has increased in the potential for qEEG as a non-invasive tool for measuring changes in the speed and coordination of synaptic function in neurocognitive disorders. By so doing, qEEG may be able to differentiate between Alzheimer's disease and other dementias, and to predict the progression of MCI to Alzheimer's disease.

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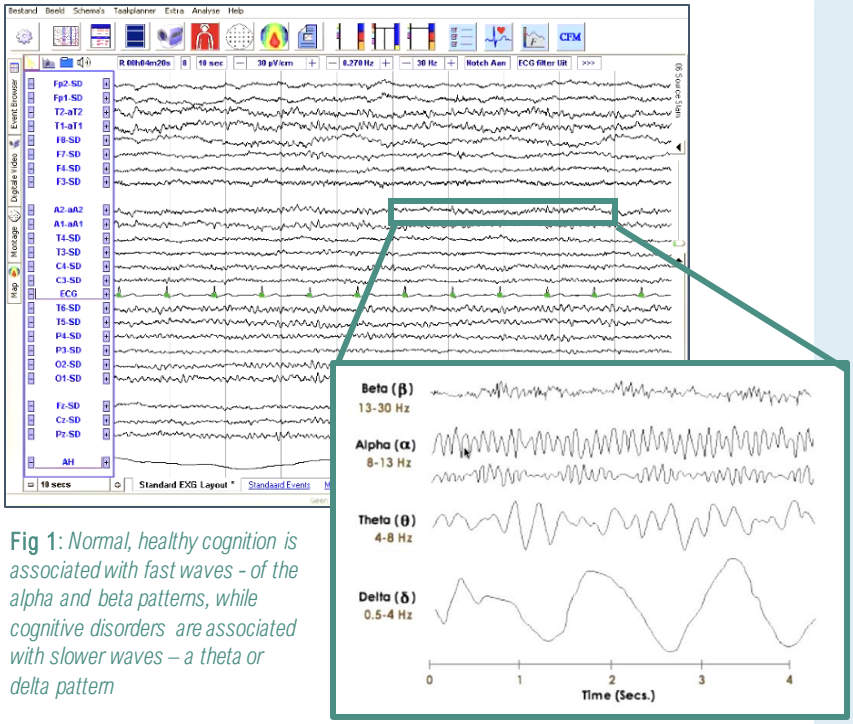

Fig 1: *Normal, healthy cognition is associated with fast waves - of the alpha and beta patterns, while cognitive disorders are associated with slower waves – a theta or delta pattern*

EEG Fast Facts

- Electroencephalography (EEG) was discovered in 1929 by the German psychiatrist, Hans Berger, who later identified and described alpha waves (so named because they were identified first) and published descriptions of EEG changes associated with epilepsy and cerebral injury
- In 1937, Davis and Lennox published a correlation between EEG findings and epileptic convulsions
- By 1940, EEG became established as a standard diagnostic tool in clinical practice for children with epilepsy
- In the 1990s, computing and digital data capacity enabled continuous EEG monitoring

Why is Cognition Therapeutics interested in EEG?

Cognition is conducting a biomarker study (SEQUEL) to determine if differences in synaptic function can be measured in CT1812- versus placebo-treated participants using quantitative EEG.

In cognitively normal individuals in a restful but awake state, the dominant posterior brainwaves will be in the 8-13 Hz* range. These waves, termed "alpha" waves, have high amplitudes and are close together and are considered to be part of the normal background rhythm of a healthy brain.

In the brain of an Alzheimer's patient, as synapses are lost and neurons lose connectivity with other regions, alpha waves lose their dominance and are gradually replaced by slower oscillating, lower-amplitude "theta" waves.

It is not uncommon for the slow shift from alpha to theta waves to begin before Alzheimer's symptoms arise, making this non-invasive tool an appealing prospect for diagnosing early-stage disease.

In addition, besides local brain activity, qEEG can also provide insight into the communication strength between brain regions. This 'functional connectivity' gradually breaks down in Alzheimer's disease.

References

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