Evidence-Based Practice Advisory: The utility of EEG theta/beta power ratio in the diagnosis of ADHD

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Abstract

Objective: To evaluate the evidence published to assess the ability of the EEG theta/beta power ratio to diagnose ADHD, or help in its diagnosis.

Methods: The results of a comprehensive literature search were reviewed and identified published studies relevant to the clinical questions. The studies were classified according to the evidence-based methodology of the American Academy of Neurology.

Results: Two Class I studies looked at the ability of the EEG theta/beta power ratio and EEG frontal beta power to identify patients with ADHD. Together, they correctly identified 167 out of 185 subjects.

Conclusion: It is highly likely that EEG theta/beta power ratio and EEG frontal beta power correctly identifies patients with ADHD (accuracy 89%, 95% CI 85 to 94%) as compared to a clinical evaluation.

Recommendations: The combination of theta/beta ratio and frontal beta power should not be used in place of a standard clinical evaluation, because of the risks of misdiagnosis of 6-15% of patients when using the theta/beta ratio (Level B). There is neither evidence for, nor against the use of theta/beta EEG power ratio either to confirm a diagnosis of ADHD, nor to support further testing after a clinical evaluation (Level U).
Introduction

In 2013, the Food and Drug Administration approved the Neuropsychiatric EEG-Based ADHD Assessment Aid (NEBA) to be used by a clinician as confirmatory support or to pursue further testing after an evaluation for ADHD, in a child aged 6-17. It was not to be used as a stand alone device in the diagnosis of ADHD. The device calculates the ratio of the power of the EEG theta and beta bands at Cz which is the EEG electrode halfway between the inion and the nasion.

A recent review in this area suggested more research was needed before it could be used as a clinical tool.¹ The purpose of this review is to examine the published evidence to determine whether QEEG has utility in the diagnosis of ADHD. We sought to answer the following questions:
1. For patients with ADHD, does the combination of a clinical examination and an examination of the EEG theta/beta power ratio increase diagnostic certainty compared to clinical examination alone?
2. For patients with a possible but uncertain diagnosis of ADHD, how accurately does the EEG theta/beta ratio identify patients with ADHD, as compared to the reference standard of a clinical evaluation?

Description of the Analytic Process

This practice advisory was completed using the methods outlined in the 2011 version of the AAN's guideline development process manual.² We performed a literature search of the Medline, EMBASE, and Central databases, without time constraints, using the following keywords, with associated variants, "ADHD", "EEG", and "Theta/Beta ratio".

The following inclusion/exclusion criteria were utilized:
1. Papers were included which examined theta/beta ratio in patients with ADHD which could answer either of the questions (given in the introduction).
2. Exclusion criteria were the following:
   A. Papers with less than 10 subjects which would have too high a risk of bias,
   B. Class IV papers by AAN criteria,
   C. ADHD which was determined by clinical examination criteria other than DMS-IV (and variants).
   D. Information which was not published in the peer reviewed literature, except see below.
3. There was data provided to the FDA for the NEBA device for which we have a portion of the data that was self-published. This data has not been peer reviewed.² Additional information about the trial was found in the De Novo FDA application.³ We will specifically include what we know about this data, since it is the subject of this review, and include it, regardless of its grading.
The results of a comprehensive literature search (959 abstracts) were reviewed and identified published studies relevant to the clinical questions were classified according to the evidence-based methodology of the American Academy of Neurology. Strength of recommendations were based on the grading of evidence, with consideration of costs, risks, and feasibility, as well as the AAN version of the modified GRADE criteria.

Analysis of evidence

1. For patients with ADHD, does the combination of a clinical examination and an examination of the EEG theta/beta power ratio increase diagnostic certainty compared to clinical examination alone?
The NEBA self-published study examined this question. The information available was rated Class IV. There was not enough information provided by either of the references to properly grade the risk of bias in the study, so as is standard for the AAN Classification, the study is rated Class IV.

Conclusion: There is no evidence above Class IV for or against this question.

Clinical context: The clinical trial registered at Clinicaltrials.gov, NCT00595751, is a prospective cohort trial attempting to answer this question, which ended final data collection for primary outcome measure on June of 2008. The data from this trial was provided to the FDA. It may be that the trial will be rated with a higher Class when it is fully published.

2. For patients with a possible but uncertain diagnosis of ADHD, how accurately does the EEG theta/beta ratio identify patients with ADHD, as compared to the reference standard of a clinical evaluation?

There were two included trials, both Class I. Please see table one. One was a prospective, blinded cohort study examining 26 children and adolescents who presented with a suspected diagnosis of ADHD. Two quantitative EEG criteria were used for determining children with ADHD: frontal beta power and theta/beta power ratio. Frontal beta power was calculated from 6 EEG sites, using a diagnostic cut-off of 2 standard deviations. The theta/beta power ratio was calculated at Cz using a definition of theta as the frequency 4-7.5 Hz, and beta as 13-20.5 Hz, using a diagnostic cut-off of 1.5 standard deviations. 25 of the 26 were correctly classified according to the EEG compared to the psychiatric evaluation; one child who had ADHD according to the clinical evaluation was not classified correctly. This child had co-morbid conduct disorder. Of note, none of the EEG ADHD diagnoses were made with the frontal power; all were made with excessive theta/beta ratio.

A similar methodology was employed with the other Class I prospective, blinded cohort study, except that it enrolled 160, of which 159 subjects were evaluated. One subject was not included because data for the psychiatric evaluation was incomplete. In the sample of 159, 97 were diagnosed with ADHD by clinical
evaluation; of these, 84 were diagnosed with ADHD by theta/beta ratio, and 1 by frontal power. While it is not given in the paper, the same numbers for false positive EEG evaluations can be calculated from the overall accuracy of 89%: of the 62 who were not diagnosed with ADHD by clinical examination, 5 were incorrectly given the diagnosis of ADHD by EEG.

Conclusion: The combination of theta/beta ratio and frontal beta power should not be used in place of a standard clinical evaluation, because it may lead to misclassification in 6-15% of patients (two class I studies). Frontal beta power alone classified a single person, so seems of little clinical utility (two Class I studies).

Clinical Context: In looking at these two studies in aggregate, the misidentification of 19 subjects in the combined number of 185 children is too high a number for this test to supplant the standard clinical evaluation. Given a positive cut-off of the theta/beta power of 1.5 standard deviations above the mean, it seems unlikely that this test will achieve a higher accuracy without a different approach.

Recommendations:

The combination of theta/beta ratio and frontal beta power should not be used in place of a standard clinical evaluation, because it may lead to misclassification in 6-15% of patients (Level B).

There is neither evidence for, or against, the use of theta/beta EEG power ratio either to confirm a diagnosis of ADHD, nor to support further testing after a clinical evaluation (Level U).

Notes: The lack of generalizability of the two Class I studies (due to the medication washout of three days in the studies being an unlikely to be adhered to clinically, and the exclusion of children on more than one medication) decreased the diagnostic certainty of the replacement of the theta/beta power ratio for the standard clinical evaluation.

Suggestions for further research

Additional research is required to understand why children with ADHD have great theta/beta power at CZ. One prior report has identified positive spikes as a normal variant in children with ADHD. If a normal variant were commonly present in children with ADHD, this might explain the reason for the increased theta/beta power ratio. Moreover, if such were found, it might be possible to increase the accuracy of the theta/beta power ratio by fine-tuning it with the normal variant in mind.

There are EEG normal variants in the theta range, which could affect the theta power at CZ. We give five examples which, if present in children with ADHD, might possibly be the source of the increased theta/beta power ratio. The Cigánek rhythm
is a typically 6 Hz rhythm that is often centered maximally at Cz. Diffuse polymorphic theta (which may include Cz) is a common finding in drowsiness. Rhythmic mid-temporal theta and wickets can have a field with spread to the vertex (Cz). Mu rhythm often includes the vertex.

While a patient with some symptoms of ADHD who presents for evaluation sometimes comes with the specific clinical question of ADHD or not, the clinical question may be more frequently encountered is "What does this child have as a disorder?" The differential diagnosis may include depression, anxiety, learning disabilities, and personality disorders like oppositional defiant disorder.9,10,11 It is not known whether these disorders also have theta-beta ratios that mimic the reported finding in children with ADHD.

References

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<th>Trial</th>
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<th>True Negative</th>
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</table>

Table One: Included study information for question number two. True positives, etc., refers to comparison of the EEG results with the gold standard clinical examination.

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