TITLE: Brain Electrical Activity Mapping for Diagnosing Psychiatric Disorders: A Review of the Clinical Evidence

DATE: 4 November 2014

CONTEXT AND POLICY ISSUES

The etiology of diseases affecting the brain has been linked to various neurotransmitters such as acetylcholine, dopamine, gama aminobutyric acid (GABA) and serotonin. For instance, Alzheimer’s disease (AD) is reported to have strong links with impairment in acetylcholine, serotonin and GABA systems in certain regions of the brain,1 while psychoses including schizophrenia are associated with aberrant levels and activities of dopamine and serotonin.2 In the absence of specific and reliable markers or a commonly accepted gold standard, diagnosis of neuropsychiatric diseases in living patients is probabilistic and based on clinical diagnostic criteria. Traditionally, the diagnosis of dementia including Alzheimer’s disease has been done through neurolological assessment that combines scores from validated instruments like the mini-mental state examination (MMSE) tool and clinical neurology expertise.3,4 Diagnosis of psychoses is based on criteria from either the Diagnostic and Statistical Manual (DSM) of mental disorders which is used more commonly in North America, or the International Classification of Diseases (ICD) which is used more commonly in Europe and other parts of the world.5,6

Quantitative EEG (qEEG) involves computer-assisted imaging and statistical analysis of the EEG for detecting abnormalities, assisting the physician in making a diagnosis, and other purposes relating to patient care.7 The underlying assumption is that clinically significant neuropsychiatric disturbances may be accompanied by statistically significant abnormalities in the spectral composition of brain electrical activity compared with healthy controls, and that detecting subtle frequency abnormalities in different domains of the brain can alert the clinician and facilitate diagnosis of a specific disease. By nature, EEG is a potential method to assess neuropsychiatric disorders since it reflects summated electrical activity at the level of functional units of the brain with millisecond time resolution.8 In addition, qEEG is relatively inexpensive, and without using ionizing radiation it is able to noninvasively produce images of both excitatory and inhibitory cortical neuronal activity rather than secondary hemodynamic processes, and the spectra can be displayed as statistical probability maps in which brain areas can be made to

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“light up” in proportion to the abnormality of their activity. These maps form vivid illustrations of the clinical point that a brain problem underlies a patient’s symptoms.\(^7\)

It is unclear whether the diagnosis of a neuropsychiatric disorders based on standard traditional criteria is in agreement with results from brain electrical activity mapping. The objective of this report is to review current evidence for using brain electrical activity mapping to assess the levels of acetylcholine, dopamine, GABA and serotonin activity in adult patients, and to evaluate diagnostic accuracy of brain electrical activity mapping for schizophrenia, bipolar disorders, and dementia.

RESEARCH QUESTIONS

1. What is the clinical evidence of brain electrical activity mapping for assessing levels of acetylcholine, dopamine, GABA and serotonin activity in adult patients?

2. What is the diagnostic accuracy of brain electrical activity mapping for schizophrenia?

3. What is the diagnostic accuracy of brain electrical activity mapping for bipolar disorder?

4. What is the diagnostic accuracy of brain electrical activity mapping for dementia?

KEY FINDINGS

Parameters of quantitative electroencephalography (qEEG) such as the theta index, alpha index, and the absolute powers derived from the frequency bands in EEG do not possess sufficient diagnostic ability to individually distinguish between Alzheimer’s Disease AD patients and healthy control patients. However, a combination of the left hemisphere alpha/theta index of the qEEG and Mini-Mental State EXamination (MMSE) achieved improved diagnostic accuracy for AD compared with MMSE alone. Quantitative EEG methods demonstrated poor diagnostic ability for AD in a selected group of patients with various degrees of dementia conditions.

METHODS

Literature Search Strategy

A limited literature search was conducted on key resources including PubMed, The Cochrane Library (2014, Issue 10), University of York Centre for Reviews and Dissemination (CRD) databases, OVID PsycINFO, Canadian and major international health technology agencies, as well as a focused Internet search. No filters were applied to limit the retrieval by study type. Where possible, retrieval was limited to the human population. The search was also limited to English language documents published between January 1, 2004 and October 6, 2014.

Selection Criteria and Methods

One reviewer screened citations and selected studies. In the first level of screening, titles and abstracts were reviewed and potentially relevant articles were retrieved and assessed for inclusion. The final selection of full-text articles was based on the inclusion criteria presented in Table 1.
Table 1: Selection Criteria

<table>
<thead>
<tr>
<th>Population</th>
<th>Adults presenting with neuropsychiatric disorders that require a differential diagnosis</th>
</tr>
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<tbody>
<tr>
<td>Intervention</td>
<td>Brain electrical activity mapping (BEAM), quantitative electroencephalography (qEEG)</td>
</tr>
</tbody>
</table>
| Comparator | Clinical history, CT scan, MRI, neuropsychological assessments  
| | No comparator |
| Outcomes | Clinical benefit:  
| | - Appropriate quantification of neurotransmitter activity (acetylcholine, dopamine, GABA, serotonin)  
| | - Appropriate diagnosis of psychiatric conditions (schizophrenia, bipolar disorder, dementia) |
| Study Designs | Health Technology Assessment (HTA)/ Systematic Review (SR)/Meta-Analysis (MA), Randomized Controlled Trials (RCT), Non-Randomized Studies |

Exclusion Criteria

Studies were excluded if they did not satisfy the selection criteria, if they were duplicate publications, or were published prior to January 1, 2004.

Critical Appraisal of Individual Studies

The methodological quality of the studies included in this report was assessed using the Downs and Black checklist for measuring study quality. The strengths and limitations of the individual studies have been summarized and presented in tabular form in Appendix 3.

SUMMARY OF EVIDENCE

Quantity of Research Available

A total of 293 citations were identified in the literature search. Following screening of titles and abstracts, 277 citations were excluded and 16 potentially relevant reports from the electronic search were retrieved for full-text review. A grey literature search did not find any publications that were potentially relevant to this review. Of the 16 potentially relevant articles identified, 14 publications were excluded for not meeting the inclusion criteria listed in Table 1, while two publications which met the inclusion criteria were included in this report. Appendix 1 describes the PRISMA flowchart of the study selection.

Summary of Study Characteristics

Characteristics of included studies have been summarized in Appendix 2.

Country of origin

One of the included studies was conducted in Brazil and the other was from Sweden.

Study setting

None of the included studies was a randomized controlled trial (RCT). Although the design was not specified, the study from Brazil appeared to have a prospective design and recruited...
patients consecutively from the outpatient department of a neurology clinic. The study from Sweden\(^1\) was described as a retrospective analysis of patients referred to a memory clinic who had qEEG as part of the diagnostic procedure.

**Patient population**

Thirty-four patients diagnosed with dementia and Alzheimer’s disease (AD), and a control group (CG) of 30 people with no history of cognitive impairment or neuropsychiatric disability participated in one study.\(^6\) The mean ± standard deviation (SD) age of patients in the AD group (ADG) was 73.59 ± 5.81 years and their MMSE score (mean ± SD) was 17.17 ± 4.54 points. The mean ± SD age of the CG in the study\(^1\) was 71.6 ± 4.26 years and they had mean ± SD MMSE scores of 26.8 ± 2.09 points. The CG group was constituted by preferentially selecting amongst the spouses of the patients attending the outpatient clinic. The ADG had similar proportion of males and females as the CG. Patients were excluded if they suffered from co-morbidities with significant reductions in life expectancy; were under treatment with acetylcholinesterase inhibitors, memantine, and antipsychotic or benzodiazepine medication; showed a score below 4 on the Hachinski scale (a commonly used questionnaire for diagnosis of vascular dementia); showed focal injuries in neurological examination; or had clinical dementia rating (CDR) score indicating severe AD.

The other study\(^2\) involved 104 patients with various degrees of dementia, or cognitive impairment including AD, AD co-existing with vascular dementia (AD/VaD) and mild cognitive impairment (MCI). Their mean ± SD age was 67.5 ± 9.9 years, and their mean ± SD MMSE score was 26.5 ± 3.6 points. According to the investigators a strict exclusion criteria was not applied. Therefore, only patients with extensive substance abuse or serious psychiatric symptoms who are usually referred to a psychogeriatric outpatient clinic but not memory clinics may have been excluded.

**Interventions and comparators**

In both studies,\(^6,\)\(^2\) qEEG assessment was compared with standard clinical neurological assessment to distinguish AD patients. Electroencephalographic oscillations are measured and categorized into frequency bands which reflect cognitive and memory performance.\(^1\) For instance, research has shown that significantly higher theta power is involved in encoding of words which can be remembered in a later recall task, compared with words which could not be remembered later. In contrast to the theta band, alpha band power decreased during encoding.\(^3\) Furthermore, the alpha frequency power is positively related to cognitive performance and brain maturity and the extent of alpha power suppression correlates positively with cognitive performance and memory performance during actual task demands. Conversely, theta power decreases from early childhood to adulthood and is enhanced during actual task demands.\(^1\) The alpha band is reported to be the dominant frequency in the human scalp EEG of adults and has a frequency range of about 7.5 to 12.5Hz. In humans, the theta band lies between a frequency of about 4 to 7.5 Hz.\(^1\) In patients with a variety of different neurological disorders, alpha power is lowered while theta power is enhanced.\(^1\) In a physiological sense, EEG power reflects the number of neurons that discharge synchronously.\(^1\) A comprehensive discussion of qEEG processes and terminology is beyond the scope of this report. One study\(^6\) evaluated the ability of qEEG to discriminate AD patients from health controls under two conditions: one while awake but resting with eyes closed; and the other awake with eyes open. The qEEG analyses used 18 to 26 epochs free of artifacts, each lasting 2.56 seconds, and a Fast Fourier Transform was applied to study frequency bands including the theta (4.9 to
7.7 Hz) and alpha (8.2 to 12.5 Hz). The absolute power averages were calculated for all the electrodes together (global average), and for the left hemisphere, the right hemisphere, occipital regions, and the frontal regions.

The second study\textsuperscript{11} assessed the ability of qEEG to discriminate AD, AD/VaD, and MCI patients from patients with various dementia disorders. Thus, a healthy control group was not used in this study; rather the ability of qEEG to distinguish between patients with different categories of dementia was assessed. A digital EEG recording was performed for 5 minutes during rest with eyes closed, and then for 5 minutes with alternating cycles of 30 seconds with eyes closed and 30 seconds with eyes open. The sampling rate was 1,035 Hz. An amplifier with a low-pass anti-aliasing filter and a cut-off frequency at 268 Hz was used.

**Outcome Measures**

Following the EEG procedure, one study\textsuperscript{10} measured the comparative differences in absolute theta and alpha powers, theta and alpha reactivity indices, and alpha/theta index between ADG and CG. The theta reactivity index on opening the eye was defined as the ratio between the absolute theta power with eyes open and that with eye closed. The outcome measures are defined by the following:

1. \[
\text{Theta reactivity index} = \frac{\text{Absolute theta power, eye open}}{\text{Absolute theta power, eyes closed}}
\]
2. \[
\text{Alpha reactivity index} = \frac{\text{Absolute alpha power, eye open}}{\text{Absolute alpha power, eyes closed}}
\]
3. \[
\text{Alpha/Theta index} = \frac{\text{Alpha reactivity index}}{\text{Theta reactivity index}}
\]

The other study\textsuperscript{11} determined the comparative AD index of patients diagnosed with pure AD and those with other dementia conditions. A statistical program, (Statistical Pattern Recognition [SPR]) was applied to a set of 28 features (not reported in this review) made up of various frequency bands and other EEG parameters, the reliability of which, according to the investigators, had been previously validated to derive an optimal decision boundary that best separates the AD from the non-AD patients. For each new EEG that was entered for a given patient, the distance from the derived optimal boundary was measured as the AD index with a range of 0 to 100. An AD index of 100 means meant the EEG was identical to EEG of an AD patient while a zero AD index was consistent with an EEG of a person without AD. The intermediate was described as non-conclusive. Outcomes were reported using three models: model 1 compared pure AD patients with the remaining dementia patients, model 2 compared a combination of pure AD and AD/VaD patients with the remaining dementia patients, and model 3 compared MCI +AD/VaD +AD patients to the remaining dementia patients.

**Summary of Critical Appraisal**

Appendix 3 provides further details of the critical appraisal of individual studies. Both of the studies included in this report\textsuperscript{10,11} had clearly described objectives, interventions and comparators, and outcomes of interest. In addition, all the studies clearly described the main study findings. In one study,\textsuperscript{10} the baseline demographic characteristics were reported separately for the different participating groups showing a balance across treatment groups, and the MMSE score sufficiently deliated patents with AD from the healthy controls. In the other
study,\textsuperscript{11} mean values of demographic measures were reported for the whole group without differentiating between the different classes of patients. However, it is not likely that this will affect the outcomes since it is not likely to influence the diagnostic procedures that were compared in a selective manner. Though the baseline MMSE and other scores in this study\textsuperscript{11} were reported for the various dementia patients in the second study,\textsuperscript{10} there was no indication of validated cut-offs to enable an appraisal of how well the groups had been differentiated on these scales. For both studies,\textsuperscript{10,11} it is unknown whether they had sufficient power to detect clinically significant differences because none of them performed a calculation to determine sample sizes that provide power for the used analysis to detect the differences.

Although both studies,\textsuperscript{10,11} reported that patients were diagnosed with clinical neurological assessment tools by experts based on standardized criteria, only one of the studies\textsuperscript{11} indicated that two experts independently diagnosed the patients and resolved disagreement through consensus. The other study\textsuperscript{10} did not provide any details about how many experts were involved in the diagnosis and whether or not a consensus approach was used. In the area of dementia disorders where diagnosis is probabilistic because of the absence of specific and reliable marker of etiologically different dementia syndromes, preference for consensus diagnosis, after initial diagnosis performed independently by more than one expert, is likely to reduce bias in clinical studies.

Both studies reported that clinical diagnosis based on neurological assessment and standard criteria preceded the qEEG evaluation. However, there was no report concerning whether the individuals involved in evaluating the qEEG had knowledge of the clinical diagnosis of the study participants. Moreover, none of the studies reported the time lag between the two evaluations which could be an indicator of whether or not a significant change in the disease states had occurred between the time points. Even so, it is unlikely that the reported outcomes were influenced by these observation since previous knowledge of clinical diagnosis is unlikely to influence the EEG spectra and the qEEG derived mathematically from it. Furthermore, neuropsychiatric disorders are progressive in nature so that a longer time lag is expected to result in a worsened condition to favor the qEEG score, which is not supported by the inferior outcomes reported by the qEEG.

One study\textsuperscript{11} stated that it included patients without strict exclusion criteria to mimic real-life clinical practice. While this may be good for generalizability, it also increases the possibility of co-existing medical conditions and/or medication being taken by some patients interfering with the diagnostic potential of the test being evaluated.

Both studies were conducted outside Canada, so it is uncertain how generalizable the findings would be in clinical settings in Canada.

Summary of Findings

1. What is the clinical evidence of brain electrical activity mapping for assessing levels of acetylcholine, dopamine, GABA and serotonin activity in adult patients?

There was no study found from literature search that met the inclusion criteria for this review which assessed the clinical evidence of brain electrical activity mapping for assessing levels of acetylcholine, dopamine, GABA and serotonin activity in adult patients.
2. What is the diagnostic accuracy of brain electrical activity mapping for schizophrenia?

There was no study found from literature search that met the inclusion criteria for this review which assessed the diagnostic accuracy of brain electrical activity mapping for schizophrenia.

3. What is the diagnostic accuracy of brain electrical activity mapping for bipolar disorder?

There was no study found from literature search that met the inclusion criteria for this review which assessed the diagnostic accuracy of brain electrical activity mapping for bipolar disorder.

4. What is the diagnostic accuracy of brain electrical activity mapping for dementia?

One study\textsuperscript{10} found that neither the absolute powers derived from the frequency bands nor the theta and alpha indices could, of themselves, distinguish between AD patients and the healthy control patients. However, when the left hemisphere alpha/theta index of the qEEG derived from the ratio of alpha and theta indices was combined with MMSE the diagnostic accuracy improved from 92.2% for MMSE alone to 95.3% for the combination. In addition, the combination resulted in improvement of the specificity and sensitivity obtained from MMSE alone. The respective improvement for left hemisphere alpha/theta index of the qEEG combined with MMSE and MMSE alone were 96.6% versus 93.3% for sensitivity, and 94.1 % versus 91.2% for specificity. However, the accuracy of the alpha/theta index by itself was lower than MMSE alone (75.0% versus 92.2%), attaining inferior specificity and sensitivity score compared with MMSE alone (70.0% versus 96.6%; and 79.4% versus 94.1%, respectively).

In the other study,\textsuperscript{11} a statistically significant association between the diagnosis of AD as determined by clinical neurological assessment and the qEEG diagnosis of AD was not achieved for any of the three models tested. The chi-squares for models 1 to 3 were 2.543 ($P = 0.111$), 3.655 ($P = 0.056$) and 3.293 ($P = 0.70$), respectively. Furthermore, each of models 1 to 3 had low scores for sensitivity (73%, 73% and 68%, respectively) and low specificity (46%, 48% and 51%, respectively); and each of them obtained an area under the receiver operator characteristic (ROC) curve below 0.5, the point where the finding could be attributed to chance, indicating the diagnostic ability of qEEG as determined by this study was worse than chance.

Limitations

This report is limited by the fact that two studies were found through literature search that met the inclusion criteria for the review and both studies addressed one of the four questions this review had purposed to answer. Limitations of the included studies were the fact that neither was a randomized controlled trial and there was no information regarding samples size calculations to provide sufficient power for analysis to detect clinically relevant difference between the means of assessment. Additionally, both studies depended on expert opinion for diagnosis using standard clinical neurological assessment. Since a gold standard test for demntia diagnosis does not exist currently, opinions of experts are required and are subject to variability. In addition to these shared limitations, one of the studies\textsuperscript{10} investigated the comparative ability of qEEG to discriminate AD patients from healthy group. Therefore it is unknown whether qEEG as applied in that study could differentiate AD patients from patients with other memory conditions. For the second study,\textsuperscript{11} while a liberal inclusion criteria was an advantage because it was more representative of real-life clinical setting, it was also a limitation in that it is unclear whether co-existing medical conditions and/or medication use in some patients had influenced the outcomes reported.
CONCLUSIONS AND IMPLICATIONS FOR DECISION OR POLICY MAKING

In one study\textsuperscript{10} it was demonstrated that using the left hemisphere alpha/theta index derived from qEEG in addition to MMSE achieved an increment in the diagnostic accuracy for AD in relation to MMSE. However, the other qEEG parameters showed inferior discrimination in comparison with the accuracy obtained using the MMSE score alone. In the second study,\textsuperscript{11} the qEEG was poor at diagnosing AD, as it produced many false-positive results. Therefore, evidence gathered from the studies included in this report is not sufficient to support the diagnostic utility of qEEG as a stand-alone instrument in dementia.

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REFERENCES


Appendix 1: Selection of Included Studies

293 citations identified from electronic literature search and screened

→ 277 citations excluded

16 potentially relevant articles retrieved for scrutiny (full text, if available)

→ 0 potentially relevant reports retrieved from other sources (grey literature, hand search)

16 potentially relevant reports

→ 14 reports excluded:
  - irrelevant population (6)
  - irrelevant outcomes (4)
  - other (review articles, editorials) (4)

→ 2 reports included in review
## Appendix 2: Characteristics of Included Studies

<table>
<thead>
<tr>
<th>First Author, Publication year, Country</th>
<th>Study Design</th>
<th>Patient Characteristics</th>
<th>Intervention</th>
<th>Comparator</th>
<th>Clinical Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fonseca, 10 Brazil 2011</td>
<td>NRS</td>
<td>Thirty-four patients diagnosed with dementia and AD (ADG), aged 73.59 ± 5.81 years and with MMSE score of 17.17 ± 4.54; and a control group (CG) of 30 people with no history of cognitive impairment or neuropsychiatric disability, aged 71.6 ± 4.26 years and with MMSE score 26.8 ± 2.09 and of similar gender</td>
<td>qEEG</td>
<td>Clinical neurological assessment incorporating the MMSE</td>
<td>• Comparative differences in absolute alpha and theta powers, alpha and theta reactivity, and alpha/theta index between ADG and CG; • Sensitivity, specificity, and AUC of ROC curve to discriminate between ADG and CG.</td>
</tr>
<tr>
<td>Ommundsen, 11 Norway 2011</td>
<td>Retrospective study</td>
<td>104 patients with various degrees of dementia, or cognitive impairment. The mean age was 67.5 ± 9.9 years, and the mean MMSE score was 26.5 ± 3.6 points.</td>
<td>qEEG</td>
<td>Clinical neurological assessment incorporating the MMSE</td>
<td>• qEEG statistical pattern to diagnose AD and discriminate it from other subtypes of dementia; • Sensitivity, specificity and AUC of ROC curve of qEEG to discriminate subtypes of dementia.</td>
</tr>
</tbody>
</table>

AD = Alzheimer’s Disease; ADG = AD group; CG = control group; AUC = area under the curve; MMSE = Mini Mental State Examination; NRS = non-randomized studies; EEG = electroencephalograph; qEEG = quantitative electroencephalograph, ROC = receiver operating characteristic.
### Appendix 3: Summary of Critical Appraisal of Included Studies

<table>
<thead>
<tr>
<th>First Author, Publication year</th>
<th>Strengths</th>
<th>Limitations</th>
</tr>
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<tbody>
<tr>
<td>Fonseca, 2011</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Both parametric and non-parametric statistics were used to compare the ADG and CG where applicable giving suggesting robustness of the analysis.</td>
<td>• AD group was compared to a healthy group. Therefore it is unknown whether AD could be differentially diagnosed from other psychiatric conditions.</td>
</tr>
<tr>
<td></td>
<td>• Clinical diagnosis was done using recognized methods and tools.</td>
<td>• The increment in accuracy provided by the qEEG was small when faced with the clinical criteria.</td>
</tr>
<tr>
<td></td>
<td>• Details of EEG procedure and determination of qEEG parameters were provided to enable reproducibility.</td>
<td>• It is unknown whether the number of patients involved provided enough power to detect clinically meaningful differences between the groups because the authors did not indicate that a power calculation was done.</td>
</tr>
<tr>
<td>Ommundsen, 2011</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• EEG analysis was carried out by individuals without access to any clinical data.</td>
<td>• The study was not a RCT and the included patients were not recruited consecutively. Rather, the qEEG test was performed on referred patients for whom the clinician found it suitable. This may have introduced selection bias.</td>
</tr>
<tr>
<td></td>
<td>• Two experienced physicians independently made diagnosis of dementia or MCI using approved standards and resolved their differences by consensus, and the consensus diagnosis was used in all analysis.</td>
<td>• It is unknown whether the less stringent exclusion criteria introduced patient with other conditions which could have influenced the outcomes.</td>
</tr>
<tr>
<td></td>
<td>• The study involved patients in everyday practice at a memory clinic without any strict exclusion criteria except patients with extensive substance abuse or serious psychiatric symptoms who are rarely referred to memory clinics. Therefore, its findings are likely to be generalizable to patients with dementia and MCI.</td>
<td>• The authors did not report calculation of sample size to detect clinically meaningful difference between the tests. Thus it is unclear if a type II error was present in this study.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Diagnosis was based on opinion of two experts. Since there is no existing gold standard test for dementia diagnosis, their conclusions may differ from other experts.</td>
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</tbody>
</table>

AD = Alzheimer's Disease; ADG = AD group; CG = control group; MCI = mild cognitive impairment; RCT = randomized controlled trial; EEG = electroencephalograph; qEEG = quantitative electroencephalograph.
### Appendix 4: Main Study Findings and Authors’ Conclusions

<table>
<thead>
<tr>
<th>First Author, Publication year</th>
<th>Main Study Findings</th>
<th>Authors’ Conclusions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fonseca, 2011</td>
<td>• A combination of the MMSE and the left hemisphere alpha/theta index of the qEEG resulted in improvement of in accuracy of AD diagnosis over MMSE alone (95.3% versus 92.2%).&lt;br&gt;• The specificity, sensitivity and the AUC of the ROC curve resulting from a combination of the MMSE and the left hemisphere alpha/theta index were higher than MMSE alone (96.6% versus 93.3%; 94.1% versus 91.2%; and 0.983 versus 0.956, respectively).&lt;br&gt;• The accuracy of left hemisphere alpha/theta index was lower than MMSE alone (75.0% versus 92.2%).&lt;br&gt;• The specificity, sensitivity and the AUC of the ROC curve achieved with the left hemisphere alpha/theta index were lower than MMSE alone (70.0% versus 96.6%; 79.4% versus 94.1%; and 0.771 versus 0.965, respectively).&lt;br&gt;• There was significantly less alpha power in both ADG and CG suggesting that the alpha power alone could not be a diagnostic parameter.&lt;br&gt;• The theta indices were lower in the ADG compared with CG but the difference was not statistically significant, suggesting that the theta power alone could not be a diagnostic parameter.</td>
<td>“Although the MMSE has been the instrument used to evaluate the patients, from a practical point of view it would appear important to investigate the possibility that EEG variables could increase the accuracy when combined with the traditional evaluation instruments. On studying this aspect, it was shown that the left hemisphere alpha/theta index was the only EEG parameter allowing for an increment in the accuracy in relation to MMSE, reaching 95.3%. The other qEEG parameters showed inferior discrimination in comparison with that obtained using the mini-mental state examination, which was 92.4%.” 10 page 188</td>
</tr>
<tr>
<td>Ommundsen, 2011</td>
<td>• A statistically significant association between the clinical AD diagnosis and the qEEG AD diagnosis was not achieved for three models tested:&lt;br&gt; 1) comparing pure AD patients with the remaining patients $\chi^2 = 2.543$ ($p = 0.111$),&lt;br&gt; 2) AD/VaD + Pure AD patients versus remaining patients $\chi^2 = 3.655$ ($p=0.056$); and&lt;br&gt; 3) AD + AD/VaD + progressive MCI patients $\chi^2 = 3.293$ ($p = 0.70$).&lt;br&gt;• Both models 1) and 2) had sensitivity of 73% with specificity of 46% and 48%, respectively. Model3) had sensitivity of 68% and specificity of 51%.&lt;br&gt;• The AUC of the ROC curve for the three models was 0.36, 0.36, and 0.38, respectively, each falling below the 0.5 mark attributed to chance.</td>
<td>“The qEEG was poor at diagnosing AD, as it produced many false-positive results.”11 page 195</td>
</tr>
</tbody>
</table>

AD = Alzheimer’s Disease; ADG = AD group; CG = control group; AD/VaD = mixed AD and vascular; AUC = area under the curve; MCI = mild cognitive impairment; MMSE = Mini Mental State Examination; EEG = electroencephalograph; qEEG = quantitative electroencephalograph; ROC = receiver operating characteristic; $\chi^2 = Chi – square$