Mild Traumatic Brain Injury and qEEG

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Disclosures

• No disclosures.
• This work is in the final stages of approval as a joint ACNS/AAN guideline.
Learning Objective

• Understand the evidence for the use of quantitative EEG (qEEG) to diagnose mild traumatic brain injury (mTBI).

Outline

• qEEG and mTBI Background
• Methodology Description
• Analysis of the Evidence
• Clinical Context
• Conclusions and Recommendations
qEEG and mTBI Background

- Traditional EEG review focuses on visual assessment of brain rhythms.
  - Unable to resolve inter-related brain network oscillations that may relate to cognition.\(^1\)

- Various computer driven algorithms are broadly referred to as “quantitative EEG”.\(^2\)

qEEG and mTBI Background

- qEEG is a promising but controversial tool in the field of mild traumatic brain injury (mTBI).

- TBI is a physical injury to the brain causing compression or tearing of tissue.\(^3\)

- mTBI may lead to chronic cognitive and psychiatric symptoms.\(^3\)

- Rapid and accurate diagnosis of mTBI is an important issue.\(^4\)
  - Military
  - Athletes
  - Medico-legal
qEEG and mTBI Background

• ACNS/AAN Joint qEEG Guideline (1997)\(^5\)

  Special Article
  Neurology 1997-09-277-292
  Assessment of digital EEG, quantitative EEG, and EEG brain mapping:
  Report of the American Academy of Neurology and the
  American Clinical Neurophysiology Society*  
  Marc Nowe, MD, PhD

  – Adjunctive tool in epilepsy/intra-op monitoring - Class I and II evidence
  – Other uses – Class II and III evidence

Methodology

• Primary Aim
  – For patients with or without post-traumatic symptoms (abnormal cognition or behavior), does qEEG either at the time of injury or remote from the injury, as compared to current clinical diagnostic criteria, accurately identify those patients with mild traumatic brain injury (TBI) (i.e., concussion)?

• Secondary Aims
  – Differentiating between mTBI and other diagnoses.
  – Detecting mTBI in the presence of CNS medications.
  – Pertinence of statistical methods.
Methodology

- List of Reviewers
  - Jeffrey R. Tenney, MD, PhD - Department of Pediatrics, University of Cincinnati College of Medicine, Cincinnati, OH; Division of Neurology, Cincinnati Children’s Hospital Medical Center, Cincinnati, OH
  - David Gloss, MD – Department of Neurology, Charleston Area Medical Center, Charleston, WV
  - Ravindra Arya, MD, DM - Department of Pediatrics, University of Cincinnati College of Medicine, Cincinnati, OH; Division of Neurology, Cincinnati Children’s Hospital Medical Center, Cincinnati, OH
  - Peter W. Kaplan, MD – Department of Neurology, Johns Hopkins University School of Medicine, Baltimore, MD
  - Ronald Lesser, MD - Department of Neurology, Johns Hopkins University School of Medicine, Baltimore, MD
  - Vicki Sexton – ASET – The Neurodiagnostic Society
  - Marc Nuwer, MD, PhD – Department of Neurology, David Geffen School of Medicine at UCLA; Department of Clinical Neurophysiology, Ronald Reagan UCLA Medical Center

Abstracts Reviewed (N = 598)
- Retrieved and reviewed from literature search in databases (search completed March 21, 2017)
- Excluded (N = 530)
  - Failed to meet inclusion criteria
- Reviewed Full Text Article (N = 68)
- Excluded (N = 39)
  - Failed to meet inclusion criteria
- Graded (N = 29)
  - Only met Class IV criteria
- Included (N = 9)
### Analysis of Evidence

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>Class</th>
<th>Blind</th>
<th>Cohort Size</th>
<th>Controls Type</th>
<th>qEEG Method</th>
<th>Results</th>
<th>Notes</th>
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<tbody>
<tr>
<td>Arbour</td>
<td>2015</td>
<td>III</td>
<td>No</td>
<td>34</td>
<td>Yes</td>
<td>Previous database</td>
<td>Higher beta power for mTBI in O1 in NREM sleep</td>
<td>1) No diagnostic study design 2) No awake qEEG</td>
</tr>
<tr>
<td>Corradini</td>
<td>2014</td>
<td>III</td>
<td>No</td>
<td>26</td>
<td>Yes</td>
<td>Newly acquired</td>
<td>Lower alpha power in mTBI with mild-severe impairment</td>
<td>1) Not controlled 2) No diagnostic study design</td>
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<tr>
<td>O'Neil</td>
<td>2012</td>
<td>III</td>
<td>No</td>
<td>119</td>
<td>No</td>
<td>Brainscope (handheld frontal recording)</td>
<td>TBI-index with improved specificity than New Orleans Criteria (NOC) to predict positive head CT</td>
<td>1) Not controlled 2) Excludes lowest risk mTBI group (without head CT ordered)</td>
</tr>
<tr>
<td>Khoury</td>
<td>2013</td>
<td>III</td>
<td>No</td>
<td>24</td>
<td>Yes</td>
<td>Newly acquired</td>
<td>Lower delta power for mTBI</td>
<td>1) No diagnostic study design 2) No awake qEEG</td>
</tr>
<tr>
<td>McCrea</td>
<td>2010</td>
<td>III</td>
<td>No</td>
<td>28</td>
<td>Yes</td>
<td>Brainscope (handheld frontal recording)</td>
<td>Multivariate analysis of 7 qEEG features were abnormal for mTBI at days 0 and 5 but not at day 45</td>
<td>1) Narrow spectrum of persons with and without disease</td>
</tr>
<tr>
<td>Moore</td>
<td>2010</td>
<td>III</td>
<td>Yes</td>
<td>52</td>
<td>Yes</td>
<td>Spectral Power (High density EEG)</td>
<td>Decreased alpha and increased beta frontal asymmetry for mTBI</td>
<td>1) No correction for multiple comparisons</td>
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<tr>
<td>Subovicova</td>
<td>2009</td>
<td>III</td>
<td>No</td>
<td>21</td>
<td>No</td>
<td>Wavelet entropy</td>
<td>Entropy was reduced at 7 days post-mTBI</td>
<td>1) No diagnostic study design 2) Comparison to baseline but not controls</td>
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<tr>
<td>Tomkins</td>
<td>2011</td>
<td>III</td>
<td>Yes</td>
<td>22</td>
<td>Yes</td>
<td>Spectral Power</td>
<td>Increase in delta power for mTBI</td>
<td>1) Diagnostic study for PTE</td>
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<tr>
<td>Virji-Babul</td>
<td>2014</td>
<td>III</td>
<td>No</td>
<td>9</td>
<td>Yes</td>
<td>Newly acquired</td>
<td>No small world topology differences</td>
<td>1) No diagnostic study design 2) Group level but not individual analyses</td>
</tr>
</tbody>
</table>

### Analysis of Evidence

#### mTBI Diagnosis

- All studies graded as Class III.
- No standard qEEG analysis method.
  - Spectral power (5,6,7,9,11,13)
  - Proprietary “TBI-index” (2,8,10)
  - EEG microstates, sLORETA, wavelet entropy, graph theory (3,7,12,14)

- The evidence does not support the use of qEEG to accurately identify patients with mTBI either at the time of injury or remote from the injury.
Analysis of Evidence

Differentiation of mTBI from related diagnoses

• Some studies compared mTBI to healthy controls, +/- pain, +/- post-traumatic epilepsy.\(^9,13\)
• None compared to other related disorders (depression, ADHD, autism, migraine).

• The evidence does not support the use of qEEG to correctly differentiate mTBI from other disorders.

Analysis of Evidence

Presence of medications

• No studies used a medication wash out period or included medication use as a confounder.
• One study specifically excluded participants for “use of psychotropic medication or other drugs known to influence sleep or motor behavior”.\(^9\)

• The evidence does not support the use of qEEG to reliably identify patients with mTBI in the presence of CNS medications.
Analysis of Evidence
Differentiation between mTBI and state (drowsiness)

- 6 studies – controlled for wakefulness
- 4 studies – completed awake with eyes closed\textsuperscript{8,10,11,14}
- 2 studies – completed during sleep\textsuperscript{6,9}
- No studies compared qEEG measures while awake and drowsy/asleep

- The evidence does not support the use of qEEG to differentiate between drowsiness and mTBI.

Analysis of Evidence
Statistical considerations

- No agreement related to statistical measures for qEEG analyses.
- Correction for multiple comparisons is necessary
  – Two studies discussed use of multiple comparison corrections\textsuperscript{11,14}

- The evidence does not demonstrate that suitable statistical measures exist when using qEEG to identify patients with mTBI.
Clinical Context

• Identification of individuals with mTBI is an important goal.
• Altered brain rhythms following mTBI has been reported and their use as a biomarker requires further exploration.
• Lack of standardization
  – Acquisition
  – Analysis
  – Misinterpretation of artifact

Conclusions and Recommendations

• Current evidence does not support the clinical use of qEEG either at the time of the injury or remote from the injury to diagnose mTBI (Level U).

• qEEG remains an investigational tool for mTBI diagnosis (Class III evidence).
Suggestions for Further Research

• Important issues to be addressed
  
  – Definition of a gold-standard against which diagnostic performance of any qEEG modality could be measured
  
  – Consensus on methods for data acquisition
  
  – Analysis of multiple qEEG measures representing different neurophysiological aspects
  
  – Use of appropriate statistical methods to develop a predictive model
  
  – Blinding to clinical status
  
  – Effect of potential confounders
  
  – Careful statistical considerations

References


Thank You

• Authorship Group
  – Marc Nuwer, MD, PhD
  – Ravindra Arya, MD
  – David Gloss, MD
  – Peter Kaplan, MD
  – Ronald Lesser, MD
  – Vicki Sexton (ASET)

• ACNS Guidelines Committee Chairs
  – Tammy Tsuchida, MD, PhD
  – Jun Park, MD