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Outline

1. Mild cognitive impairment (MCI)
2. Event related potentials
3. Conclusions
1. *Mild Cognitive impairment (MCI)*

- The term MCI is used to describe a memory impairment

*MCI patients*

- Face usually memory problems or mild problems in other cognitive function bigger than these expected due to aging
MCI criteria according to Petersen

1. Subjective memory complaint
2. Objective memory impairment
3. Normal general cognitive function
4. Normal IADLs/ADLs
5. No dementia (according to DSM-IV, NINCDS-ADRDA criteria)

Petersen et al. (1999). Arch Neurol. 55:303-308
FIGURE 1. Current diagnostic algorithm for diagnosing and subtyping MCI

MCI=mild cognitive impairment.

1. Progression of MCI

Aging

MCI

AD

Cognitive function

Age

Petersen RC, 2003
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2. Event related potentials

Event-related potentials (ERPs) are very small voltages generated in the brain structures in response to specific events or stimuli

- visual
- auditory
- word
- An action that needs thought e.g. the sum of two numbers
N1: preattentive perceptual processing in primary cortex
N2: stimulus detection
N3: stimulus categorization and memory updating
N400: semantic/conceptual processing
P2: preattentive perceptual processing in primary cortex
P3: stimulus categorization and memory updating
P600: syntactic processing

Potential (μV)
~ -2 to -5

N1 (N100)
N2 (N200)
N400
P2 (P200)
P3 (P300)
P600

Time (ms)
~ 1000
2. Auditory event related potentials

Small electric potentials that are derived from the brain as an answer to the stimulus

Examination procedure:
- Through earphones a repetitive sound of known frequency is heard
- In between there is a sound of different frequency: "oddball"
Auditory event related potentials - 2

- Respondent receives a task that is related to “target” stimulus. This task may be related to motor response - pressing buttons after the target stimuli or by checking the capability of working memory - counting “target” stimuli.
3. AERPs and Alzheimer's disease

Parra et al., 2012
3. P300 wave

P3b: context updating, information delivery, stimulus categorization, and cognitive closure
Suggest the use of P300 wave as a diagnostic marker for Alzheimer’s Disease
N200 latency might serve as a potential useful marker in the early diagnosis of AD.

A cut-off value of 287 ms resulted in a sensitivity of 100% and a specificity of 91% in the prediction of MCI patients that converted to AD.
N200-MMN wave

- MMN latencies were significantly longer in amnestic MCI patients compared to controls
Patients with AD had significantly prolonged N200 latencies compared to the control group (Howe 2014).

N200 latency is an informative indicator of information-processing deterioration in patients with cognitive impairment.
N400 wave

- N400 wave is usually abnormal in AD, typically reduced in amplitude and delayed in latency beyond that seen in normal aging.

- N400 repetition effect is diminished and in MCI patients who later on convert to dementia within the next 3 years.

Olichney et al., 2013; Kutas et al., 1988
Chapter 16

Biomarkers in Alzheimer’s disease with a special emphasis on event-related oscillatory responses

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\begin{table}[h]
\centering
\begin{tabular}{|c|c|c|c|c|c|}
\hline
\textbf{AD markers} & \textbf{For diagnosis} & \textbf{For progression} & \textbf{For drug effects} & \textbf{Noninvasiveness} & \textbf{Low cost} \\
\hline
Amyloid PET & + & - & - & + & - \\
FDG-PET & + & + & + & + & - \\
CSF & + & ± & - & - & - \\
Structural MRI & + & + & - & + & - \\
Electrophysiology & + & + & + & + & + \\
\hline
\end{tabular}
\caption{Biological markers used in AD and/or MCI, and their usage or advantages}
\end{table}

AD: Alzheimer’s disease; FDG-PET: fluorodeoxyglucose positron emission tomography; CSF: cerebrospinal fluid; MRI: magnetic resonance imaging.
• ERPs can be used for the discrimination of MCI subtypes
Combination with CSF proteins
MCI conversion to AD
Correlation between b-amyloid (1-42) and N200L

Papaliagkas et al., 2009
Evaluation of AD treatment


Measures of AD drug treatment efficacy

AD drugs had little impact on ERP biomarkers and their utility in diagnosing and predicting AD in individuals.

May show that AD therapeutic treatments have little positive effect in preventing disease progression
Event-related Potentials and the Diagnosis of Alzheimer’s Disease—
The COGNISION™ System

David A Casey, MD

Associate Professor, Department of Psychiatry and Behavioral Sciences, University of Louisville School of Medicine
TMS- P300 wave
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- ERPs hold promise as an electrophysiological tool for the early and accurate diagnosis of AD and MCI.

- However, certain methodological issues need to be resolved before ERPs enter the arena of clinical practice.
Thank you very much for your attention