

The Value of Quantitative EEG Measures in the Early Diagnosis of Alzheimer's Disease

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ABSTRACT

There is growing interest in the discovery of clinically useful, robust biomarkers for Alzheimer's disease (AD) and pre-AD; the ability to accurately diagnose AD or to predict conversion from a preclinical state to AD would aid in both prevention and early intervention. This study aimed to evaluate the usefulness of a statistical assessment of cortical activity using electroencephalograms (EEGs) with normative data and the ability of such an assessment to contribute to the diagnosis of AD. 15 patients with AD and 8 patients with mild cognitive impairment (MCI) were studied. Eyes-closed resting EEGs were digitally recorded at 200 Hz from 20 electrodes placed according to the international 10/20 system on the scalp, and 20 artifact-free EEG epochs lasting 2.56 ms were selected. Each EEG epoch was down-sampled to 100 Hz and matched to the normal data sets. The selected EEGs from each subject were analyzed by standardized Low Resolution Electromagnetic Tomography (sLORETA) and statistically compared with the age-matched normal data sets at all frequencies. This procedure resulted in cortical z values for each EEG frequency with 0.39 Hz frequency resolution for each subject. Some of the AD and MCI patients presented a peak of negative z value around 20 Hz, revealing hypoactivity of the parahippocampal gyrus and the insula in the sLORETA cortical image. In addition, severe cases of AD showed decreased parietal activation. These results were in agreement with evidence from statistical neuroimaging using MRI/SPECT. Submission of normal EEG data sets to sLORETA might be useful for the detection of diagnostic and predictive markers of AD and MCI in individual patients.

Keywords: Alzheimer's Disease, EEG Source Localization, Electroencephalogram (EEG), Global Field Power (GFP), Mild Cognitive Impairment, Standardized Low Resolution Electromagnetic Tomography (sLORETA)

INTRODUCTION

Alzheimer's disease (AD) is usually preceded by a period of cognitive decline, and this preclinical or prodromal AD state has been conceptualized as mild cognitive impairment (MCI) by Petersen et al. (Petersen et al., 1999). However, MCI

remains an unsettled prognosis; some people with MCI will not develop dementia, others may "revert" to normal, and many go on to develop dementia (especially AD). It is clear that the discovery of clinically useful and robust biomarkers for AD and pre-AD are necessary for clinicians to accurately diagnose AD and

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predict the conversion of a preclinical state of AD. Such markers would be ideal means of prevention and early intervention.

Since the proposal of MCI by Petersen et al. in 1999 (Petersen et al., 1999), predictive validation of the MCI condition using spontaneous EEGs and various quantitative methods has been accumulating. The neurophysiological changes recorded by EEG activity reflect the pathological cortical dysfunction of dementing disorders and may precede any pathological changes that are detectable by neuroimaging techniques (such as MRI, SPECT, and PET). Therefore, EEG recordings might catch the subtle changes involved in MCI in a preclinical stage of dementia. However, there is still insufficient evidence for the diagnostic utility of resting EEGs in dementia, and MCI is still not a sufficient diagnostic tool to establish dementia in the initial evaluation of subjects with cognitive impairment in routine clinical practice. It is necessary to develop optimized methods for establishing the diagnostic value of EEGs in a dementia diagnosis and the predictive utility of EEGs in MCI and questionable dementia. Our study aimed to determine whether automated EEG source localization with z-transformed age-appropriate population norms could identify AD and MCI individuals with a high degree of accuracy.

METHOD

Subjects

We studied 15 patients with AD based on the diagnostic criteria of the National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer's Disease and Related Disorders Association (NINDS-ADRDA) (McKhann et al., 1984) and 8 patients with MCI based on the guidelines of Petersen et al. (Petersen et al., 1999). All patients underwent general medical, neurological, neuropsychological, and brain MRI assessments as part of the standard diagnostic work-up for dementia. All subjects were assessed for general cognitive function using the Mini-Mental State Examination (MMSE) (see Table 1).

Procedure

EEG Recording

The EEGs were recorded from the 20 electrodes (Fp1/2, Fz, F3/4, F7/8, T3/4, C3/4, Cz, P3/4, Pz, T5/6, O1/2, Oz) of the international 10/20 system using a Neurofax EEG-1518 (Nihon-Khoden, Japan). Eyes-closed resting EEGs were digitally sampled at 200 Hz and 20 artifact-free EEG epochs lasting 2.56 ms were selected.

Table 1. Subject's information

	AD	MCI
Number	15	8
Gender (male/female)	6 / 9	6 / 2
Age (years; median, range)	75, 50-89	65.5, 49-79
MMSE (score; median, range)	18, 0-24	28, 25-30
Slightly impaired (number) MMSE 21-30	4	-
Moderately impaired (number) MMSE 11-20	6	-
Severely impaired (number) MMSE 0-10	5	-

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