International Journal of Psychophysiology 93 (2014) 390–397

Contents lists available at ScienceDirect

International Journal of Psychophysiology

journal homepage: www.elsevier.com/locate/ijpsycho

Quantitative EEG in Alzheimer's disease: Cognitive state, resting state and association with disease severity

Heinrich Garn [a,1], Markus Waser [a], Manfred Deistler [b], Reinhold Schmidt [f], Peter Dal-Bianco [d], Gerhard Ransmayr [e], Josef Zeitlhofer [d], Helena Schmidt [f], Stephan Seiler [f], Guenter Sanin [c], Georg Caravias [e], Peter Santer [d], Dieter Grossegger [g], Wolfgang Fruehwirt [g], Thomas Benke [c,*]

[a] AIT Austrian Institute of Technology GmbH, A-1220 Vienna, Austria
[b] Vienna University of Technology, A-1220 Vienna, Austria
[c] Department of Neurology, Innsbruck Medical University, A-6020 Innsbruck, Austria
[d] Department of Neurology, Vienna Medical University, A-1090 Vienna, Austria
[e] Department of Neurology, Linz General Hospital, A-4020 Linz, Austria
[f] Department of Neurology, Graz Medical University, A-8036 Graz, Austria
[g] Dr. Grossegger & Drbal GmbH, A-1190 Vienna, Austria

ARTICLE INFO

Article history:
Received 22 March 2014
Received in revised form 3 June 2014
Accepted 6 June 2014
Available online 14 June 2014

Keywords:
Alzheimer's disease
Quantitative EEG
Cognitive state
Resting state

ABSTRACT

Background: Quantitative electroencephalogram (qEEG) recorded during cognitive tasks has been shown to differentiate between patients with Alzheimer's disease (AD) and healthy individuals. However, the association between various qEEG markers recorded during mnestic paradigms and clinical measures of AD has not been studied in detail.
Objective: To evaluate if 'cognitive' qEEG is a useful diagnostic option, particularly if memory paradigms are used as cognitive stimulators.
Methods: This study is part of the Prospective Registry on Dementia in Austria (PRODEM), a multicenter dementia research project. A cohort of 79 probable AD patients was included in a cross-sectional analysis. qEEG recordings performed in resting states were compared with recordings during cognitively active states. Cognition was evoked with a face–name paradigm and a paired-associate word list task, respectively. Relative band powers, coherence and auto-mutual information were computed as functions of MMSE scores for the memory paradigms and during rest. Analyses were adjusted for the co-variables age, sex, duration of dementia and educational level.
Results: MMSE scores explained 36–51% of the variances of qEEG-markers. Face–name encoding with eyes open was superior to resting state with eyes closed in relative theta and beta1 power as well as coherence, whereas relative alpha power and auto-mutual information yielded more significant results during resting state with eyes closed. The face–name task yielded stronger correlations with MMSE scores than the verbal memory task.
Conclusion: qEEG alterations recorded during mnestic activity, particularly face–name encoding showed the highest association with the MMSE and may serve as a clinically valuable marker for disease severity.

1. Introduction

Alzheimer's disease (AD) is a progressive neurological disorder which can be diagnosed in advanced disease stages with high diagnostic accuracy. However, early AD is more difficult to detect and currently requires the use of costly technical diagnostic facilities, such as MRI, FDG-PET or laboratory based investigations (Dubois et al., 2007). Alternatively, several previous studies have employed quantitative electroencephalogram (qEEG) as an economical, noninvasive tool to differentiate normal controls (NC) or subjects with preclinical disease stages from patients with manifest AD (for reviews, see: Drago et al., 2011; Sakkalis, 2011; Platt and Riedel, 2001; Leiser et al., 2001; Santos et al., 2010; Dauwels et al., 2010; Giannakopoulos et al., 2009; Rossini et al., 2007; Uhlhaas and Singer, 2006; Menendez,

* Corresponding author at: Klinik für Neurologie, Anichstr. 35, A-6020 Innsbruck, Austria. Fax: +43 51250423852.
E-mail addresses: heinrich.garn@ait.ac.at (H. Garn), markus.waser@ait.ac.at (M. Waser), manfred.deistler@tuwien.ac.at (M. Deistler), reinhold.schmidt@medunigraz.at (R. Schmidt), peter.dal-bianco@meduniwien.ac.at (P. Dal-Bianco), gerhard.ransmayr@akh.linz.at (G. Ransmayr), josef.zeitlhofer@meduniwien.ac.at (J. Zeitlhofer), helena.schmidt@medunigraz.at (H. Schmidt), stephan.seiler@medunigraz.at (S. Seiler), guenther.sanin@i-med.ac.at (G. Sanin), georg.caravias@akh.linz.at (G. Caravias), peter.santer@meduniwien.ac.at (P. Santer), office@alphatrace.at (D. Grossegger), w.fruehwirt@alphatrace.at (W. Fruehwirt), thomas.benke@i-med.ac.at (T. Benke).
[1] Tel.: +43 505504103; fax: +43 505504125.

http://dx.doi.org/10.1016/j.ijpsycho.2014.06.003
0167-8760/

2005; Jeong, 2004). It has been shown that the essential qEEG hallmarks of AD are (i) slowing of the frequency spectrum, (ii) changing synchrony between sites across the cortex, particularly with disease progression, and (iii) reduced signal complexity. Thus, AD was found to be associated with an increase of spectral power at low frequencies (delta and theta waves) and a decrease of power at higher frequencies (alpha and beta waves). Furthermore, synchrony between EEG channels as measured by coherence increases during the first years of AD and decreases in later disease stages. Signal complexity generally decreases with disease progression, as evident from an increase of auto mutual information.

Although previous research has found AD-specific markers in qEEG, this technique is presently not among the recommended standard diagnostic tools of AD. Since impairments of cognitive functions (e.g. amnesia) are typical and early symptoms of AD, qEEG recorded during active cognitive performance may contain more and better diagnostic markers than recordings during rest. We investigated a large cohort of patients with early and moderate AD using a comprehensive analysis of qEEG and cognitive parameters. In particular, we aimed to evaluate a) whether recording of qEEG during or immediately after cognitive effort reveals more significant findings than during the unengaged resting state, b) how well brain dynamics of qEEG can serve as surrogate markers of AD, and c) which of the cognitive tasks administered evokes the most prominent qEEG changes. Based on previous studies our tentative hypotheses were that early and moderate AD is associated with several pathological qEEG markers, that cognitive activity related to a memory task is accompanied by abnormal qEEG, and that active cognition provides more diagnostic clues in qEEG than resting states (Klimesch, 1999).

2. Materials and methods

2.1. Study and participants

The Prospective Registry on Dementia in Austria (PRODEM Austria) is a longitudinal multicenter study of AD and other dementias in a routine clinical setting (Seiler et al., 2012; Benke et al., 2013). Participants were recruited prospectively in 4 tertiary-referral memory clinics. The study was approved by the Ethic Committees of the individual research sites, and patients gave their written informed consent to participate in the study. AD was diagnosed according to the NINCDS-ADRDA criteria (McKhann et al., 1984). Additional inclusion criteria were non-institutionalization, no need for 24-hour care, and availability of a caregiver who agreed to provide information on the patient. Duration of disease (in months) was estimated by the caregiver who also gave information regarding the patient's education, disease stage as assessed by Clinical Dementia Rating (CDR, Berg, 1988), and basic and instrumental activities of daily living (Gelinas et al., 1999). The MMSE (Folstein et al., 1975) was used as a global measure of cognition and staging of dementia. In the present study, 79 patients (50 females) with a diagnosis of probable AD were included. Important demographic and disease variables of the study population are summarized in Tables 1 and 2. As evident from their CDR and MMSE scores the cohort was in an early to moderate disease stage of AD. About 49% of the patients were treated with cholinergic substitution treatment. Five patients received antipsychotics.

2.2. Experimental procedure

The rationale for the current study was to record, analyze and compare qEEG during periods of rest and cognitive activity, and to explore which period and qEEG markers best predict the concurrent MMSE score. With regard to the earliest and most frequent cognitive impairment of AD, two episodic memory paradigms were chosen as disease-relevant tasks, one visual–verbal and one strictly verbal. Details of the test procedure and qEEG recording are shown in Table 3.

2.2.1. Tests and administration

A memory test was designed to compare mnestic activity with the resting state. Test materials contained verbal and figural information and were adapted to patients with dementia. Details of the testing procedure are summarized in Table 3. The face–name task was started after a rest interval (360 s, rest 1 with eyes closed and rest 2 with eyes open); then, 3 face–name pairs were presented (encoding 1). Next, the three faces were shown alone, and the corresponding names had to be reported (name recall 1), followed by a second presentation of the three face–name pairs (encoding 2). After a 90 s consolidation interval, during which participants were asked to close their eyes and keep faces and names in mind, the three encoded faces had to be recognized and distinguished from 6 distracter faces (recognition). Next, the names of the three target faces had to be retrieved again (name recall 2). The word-pair task consisted of an encoding period (encoding 3) during which 3 word pairs were visually presented twice, and a recall trial (word recall, completion of the paired associate as response to a given single word). Maximum possible scores were 18 for the face–name test, and 3 for the word-pair test. qEEG was recorded both during resting states and during cognitive activity when patients learned and recalled new information. qEEG markers were calculated separately for the eleven periods of the test. Intervals of rest and cognitive activity were compared as to their corresponding qEEG activity.

2.3. EEG recordings

Patients sat in upright position on a comfortable chair with neck rest. A 21 inch computer screen was placed in convenient distance to the patient's head. The room was normally illuminated with no dazzling light and disturbances were held off during the recordings. EEG data were collected from 19 monopolar electrode sites of the international 10/20 system. Data acquisition was performed on an AlphaEEG amplifier with NeuroSpeed software (Alpha Trace Medical systems, Vienna, Austria). Electrodes for the horizontal electrooculogram (H-EOG) were placed on the right side of the right eye and on the left side of the left eye. Electrodes for the vertical electrooculogram (V-EOG) were placed vertically above and below the left eye. The ground electrode was placed at FCz. Connected mastoid electrodes were used as reference. Electrode contacts were arranged to achieve impedances below 10 kΩ.

Table 1
Group characteristics for the whole group of 79 patients.

	Median	Median absolute deviation	Range
Age (years)	75	6	52–88
Level of education (scale 1–6)	2	1	1–6
Duration of illness (months)	23	13	2–120
MMSE (max. 30)	22	2	26–15
CDR (max. 3)	0.5	0.5	0–2
DAD (max. 100)	90	10	30–100

Table 2
Group characteristics for 40 medication-free patients.

	Median	Median absolute deviation	Range
Age (years)	74	7	54–87
Level of education (scale 1–6)	2	1	1–4
Duration of illness (months)	14	8.5	2–60
MMSE (max. 30)	23	2	26–15
CDR (max. 3)	0.5	0	0–2
DAD (max. 100)	92.5	7.5	45–100