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Alzheimer disease versus mixed dementias: An EEG perspective

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ABSTRACT

Objective: To examine differences between patients with AD ($n = 54$) and mixed (vascular Alzheimer) dementia ($n = 24$), and controls ($n = 66$), with respect to clinic, neuropsychology, neuroradiology and quantitative EEG (QEEG).
Methods: We used CAMDEX, CT and QEEG.
Results: Patients with mixed dementia had more subcortical lesions. Increased slow frequency EEG power was observed in mixed dementia compared to AD, whereas the level of high frequency power was nearly normal in mixed dementia, but decreased in pure AD. Topography of slow band power was unaltered in both groups, but was changed for fast bands. The Hachinski score and neuropsychological tests showed small differences between mixed dementia and pure AD.
Conclusion: Neuroimaging and QEEG made a greater differential diagnostic contribution than clinical symptoms and neuropsychology. An alteration of slow frequency power with nearly normal high frequency power in mixed dementia may reflect subcortical pathology, whereas cortical pathology in pure AD may relate to decreased fast frequency power. With vascular pathology, less AD pathology is needed for a similar severity of dementia.
Significance: In dementia of the Alzheimer type a vascular component is often found – especially at an older age. The quantitative EEG can contribute to a better understanding of the interaction of the two components.

1. Introduction

Alzheimer disease (AD) has dominated research on dementia, but there is a growing awareness of heterogeneity and in particular of the role of vascular factors (Snowdon et al., 1997; Ince et al., 2001; Lopez et al., 2005).

We compared 24 patients with mixed AD-vascular dementia, with 54 "pure" AD patients and 66 controls with respect to clinical characteristics, neuropsychology, neuroradiology and the quantitative EEG (QEEG). Neuropsychological functions were investigated in some detail, and we expected a priori a worse performance for AD-VAD patients in executive functions, in motor performance and mood. More subcortical damage was expected for patients with mixed etiology, as well as a higher Hachinski score. For the QEEG we looked for differences between AD patients, mixed patients and controls in terms of frequency bands and topography. While AD patients can be well distinguished from controls by their higher low frequency power and lower high frequency power (Jeong, 2004; Schreiter Gasser et al., 1993), differences between AD and vascular dementia (VAD) were controversial, and a comparison of mixed and AD patients is lacking. Thus, for the QEEG this is rather a fact finding investigation.

The role of vascular lesions for developing a dementia of the Alzheimer type has been increasingly recognized in the recent years, in particular for an older age. There seems to be almost a continuum between "pure" AD (typical in presenile cases) and "pure" VAD (typical in some older patients), with mixed cases (estimated to be 35% of cases) having a substantial contribution from both. This makes a categorical diagnosis per se difficult. Imaging is done often for stroke patients only, and dementia of vascular or mixed type may have been overlooked due to not recognizing subcortical damage in general and silent infarcts in particular (Lopez et al., 2005; Kuller et al., 2005; Vermeer et al., 2003; Knopman et al., 2003). However, VAD is itself heterogeneous, can occur with and without clinical strokes, and can be gradual or abrupt (Knopman et al., 2003; Erkinjuntti et al., 2000). As a consequence the Hachinski score is often of limited value in these cases.

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The differentiation of AD and VAD by neuropsychological assessments is also hampered by the heterogeneity of VAD (Storey et al., 2001). When concentrating on small vessel VAD, deficits in executive functions were prominent (Storey et al., 2001), but not always significant (Lopez et al., 2005). Mixed cases were considered particularly problematic. For the QEEG, differences between AD and VD were not conclusive (Jeong, 2004). An interesting recent study found a higher power for VAD patients in the theta-band and in the slow alpha band, compared to AD patients (Babiloni et al., 2004). Nothing has been reported for mixed cases. Our goal was to study the impact of subcortical vascular lesions on neuropsychological performance and on the QEEG in mixed cases, in comparison with "pure" AD patients and controls.

2. Methods

2.1. Subjects

Patients were enrolled at the Central Institute of Mental Health in Mannheim, and controls were recruited from the community or were spouses of patients. Informed consent was obtained, in severely demented patients from relatives, and the study was approved by the local ethics committee. Patients ($n = 138$) had to fulfill the NINCDS-ADRDA criteria for probable or possible AD (McKhann et al., 1984). Control subjects ($n = 66$) had to be non-demented and free of past or present neurological or psychiatric disease. Due to heterogeneity in the patient group, further analysis was based on the CAMDEX diagnosis: this identified 24 patients as of the mixed AD-vascular type and 108 of the AD type. Since the patients with mixed dementia were older, a group of 54 AD patients was selected for an age-matched comparison. (see Table 1 for details).

2.2. Clinical and neuropsychological assessment

This was done with the Cambridge Mental disorders of the Elderly Examination (CAMDEX, Roth et al., 1986). This instrument includes e.g. the MMSE, part one of the Blessed Dementia Scale, and the Hachinski ischaemic score. The Cambridge Cognitive Examination (CAMCOG) served as neuropsychological assessment.

2.3. Neuroradiology

Patients (40 of 54 AD patients and 18 of 24 mixed patients) and controls (50 of 66) underwent unenhanced CT scans with a Siemens Somaton DR2. A maximum of 15 slices, 8 mm thick, were taken parallel to the orbitomeatal line. Regions of interest were outlined, and computerized planimetry of CSF areas was performed. The total intracranial volume and the ventricular and fissure volumes were calculated according to Cavalieri's principle. (The CSF volumes are presented as proportion of the total intracranial volume, and allowed the calculation of ventricular brain ratio (VBR)). The score for leukoariosis (0–3) reflects periventricular and white matter hypodensities. Lacunar infarcts defined as sharply delineated hypodense lesions with a maximum diameter of 2 cm were counted on each slice in the basal ganglia, thalamus, brain stem, cerebellum and subcortical white matter. Small lacunas were assigned a score one and larger ones a score two. A so-called subcortical index was formed post-hoc by summing up the lacunar scores over all localizations.

2.4. EEG techniques

The EEG eyes closed was recorded monopolarly against shunted earlobes as references at F_7, F_3, F_z, F_4, F_8, T_3, C_3, C_z, C_4, T_4, T_5, P_3, P_z, P_4, T_6, O_1, O_2. EOG artefacts were monitored bipolarly in the vertical and horizontal direction. Of the 120 s of activity digitized, an epoch of 20 s was selected for quantitative analysis following Möcks and Gasser (1984), and a visual check (This selection criterion was established in normal children, but subsequently validated in adults and patient groups). Occular artefacts were corrected (Möcks et al., 1989), as well as muscular artefacts (Gasser et al., 2005). Spectral power was computed in the bands (Hz) delta (1.5–3.5), theta (3.5–7.5), alpha1 (7.5–9.5), alpha2 (9.5–12.5), beta1 (12.5–18.5), beta2 (18.5–25.0).

2.5. Statistical methods

Results are presented as mean and standard deviation $\bar{x}(s)$ and box plots. Band power was log-transformed to obtain an approximate normal distribution (Gasser et al., 1982). The QEEG was analyzed via repeated measures ANOVA with the between factor "group" (controls, AD, mixed patients), and the within factor "sagittal line" (frontal, central, parietal) and "horizontal line" (outer left, left, middle, right, outer right). A Greenhouse–Geisser correction led to conservative p-values.

3. Results

3.1. Clinical characteristics

All parameters were comparable for the two patient groups (Table 1). Controls had a much higher MMSE (to be expected), and on average a younger age. The younger age has to be considered in comparisons involving the control group, by making an age adjustment when age is a significant factor.

The Hachinski score was 4.83 (2.85) for the mixed group and 3.74 (2.36) for the AD group but the difference was not significantly different ($p = 0.12$).

3.2. Neuropsychology

Overall neuropsychological functions showed little differences between the two groups (see Fig. 1). A significant difference was found for visuo-constructive praxis (copying and drawing), where Alzheimer patients performed worse ($p = 0.050$, two-tailed t-test). The difference in ideomotor praxis was in the same direction ($p = 0.086$), whereas ideational praxis was almost identical ($p = 0.99$). No differences were found with respect to motor functions and mood.

3.3. Neuroradiology

Lacunar infarcts expressed as subcortical index (see Section 2) were significantly more pronounced in the mixed group (Table

Table 1
Mean and standard deviation of demographic and clinical parameters

Samples	n	m	f	Age		Age at onset		Duration $\bar{x}$, s		MMSE $\bar{x}$, s	
				$\bar{x}$	s	$\bar{x}$	s				
Controls	66	35	31	66.7	6.9	–	–	–	–	29.0	1.0
AD	54	17	37	75.5	6.2	71.0	6.8	4.5	3.2	13.9	7.4
Mixed	24	8	16	75.2	7.1	70.6	7.3	4.7	4.4	14.5	7.5