Subcortical Vascular Cognitive Impairment, No Dementia: EEG Global Power Independently Predicts Vascular Impairment and Brain Symmetry Index Reflects Severity of Cognitive Decline

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Background and Purpose: Vascular cognitive impairment, no dementia (vCIND) is a prevalent and potentially preventable disorder. Clinical presentation of the small-vessel subcortical subtype may be insidious, and differential difficulties can arise with mild cognitive impairment. We investigated EEG parameters in subcortical vCIND in comparison with amnestic multidomain mild cognitive impairment to determine the additional diagnostic value of quantitative EEG in this setting.

Methods: Fifty-seven community-residing patients with an uneventful central neurologic history and first presentation of cognitive decline without dementia were included. Neuropsychological test results were correlated with EEG parameters. Predictive values for vCIND and amnestic multidomain mild cognitive impairment were calculated using receiver operating characteristic curves and logistic regression modeling.

Results: Vascular cognitive impairment, no dementia and amnestic multidomain mild cognitive impairment differed with regard to the EEG (delta + theta)/(alpha + beta) ratio (DTABR) and pairwise derived brain symmetry index. We found statistically significant correlations between pairwise derived brain symmetry index and immediate verbal memory, immediate global memory, verbal recognition, working memory, and mean memory score in vCIND. Verbal fluency (odds ratio: 1.54, 95% confidence interval: 1.04–2.28, $P = 0.033$) and (delta + theta)/(alpha + beta) ratio (odds ratio: 2.28, 95% confidence interval: 1.06–4.94, $P = 0.036$) emerged as independent diagnostic predictors for vCIND with an overall correct classification rate of 95.0%.

Conclusion: Our data indicate that EEG is of additional value in the differential diagnosis and follow-up of patients presenting with cognitive decline. These findings may have an impact on memory care.

Key Words: Vascular cognitive impairment, Silent stroke, EEG, Brain symmetry index, Mild cognitive impairment.

Vascular cognitive impairment, no dementia (vCIND) is an etiologically and clinically heterogeneous disorder in which the pattern of neurocognitive deficits is often related to the extent and

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location of the vascular lesions. Although executive and visuospatial dysfunctions seem to constitute the core disturbances in vascular cognitive impairment (Galluzzi et al., 2005; Jokinen et al., 2006, 2009*b*; Sachdev et al., 2004), variability is added by lesions in other brain regions (Looi and Sachdev, 1999). Subcortical vCIND caused by small-vessel disease is a more homogeneous subgroup of vascular cognitive impairment and is relatively common in elderly population. Frequently, its presentation is insidious with an unclear temporal relation between cognitive decline and brain imaging findings (O'Brien et al., 2003). Mild cognitive impairment (MCI), especially of the amnestic multidomain MCI (amdMCI), may represent the early symptomatic stage of dementia of the Alzheimer type (Flicker et al., 1993; Palmer et al., 2008; Petersen et al., 1995; Tierney et al., 1996). Vascular risk factors and previous stroke increase the risk of dementia (Di Carlo et al., 2007; Solfrizzi et al., 2004; Viswanathan et al., 2009). In the Canadian Study of Health and Aging, which included more than 10,000 participants, vCIND was the most prevalent form within the group of patients (aged 65 to 84 years) with vascular cognitive impairment (including vascular dementia, mixed dementia, and vascular cognitive impairment without dementia) (Rockwood et al., 2000). Importantly, the rate of institutionalization in patients with vCIND is similar to that in vascular dementia and the mortality rate in vCIND is similar to that in vascular dementia or mixed dementia of the Alzheimer type (Rockwood et al., 2000). Patients with subcortical ischemic vascular disease were found to have a threefold risk of developing dementia independent of age, gender, education, and medial temporal lobe atrophy after 3 years of follow-up (Jokinen et al., 2009*a*). Structural MRI or computerized tomography imaging of the brain is crucial to diagnose vascular cognitive impairment disclosing white matter lesions and/or lacunar infarcts (Erkinjuntti et al., 2000; Roman, 2000). In patients with MCI, deep white matter and periventricular lesions predicted progression to non-Alzheimer dementia, whereas isolated medial temporal lobe atrophy was associated with progression to Alzheimer disease (AD) (Staekenborg et al., 2009; van de Pol et al., 2007). Regardless of their location, subcortical lacunar infarcts and white matter lesions impair frontal lobe function (Reed et al., 2004; Tullberg et al., 2004), resulting in a negative impact on general cognitive status (Kuczynski et al., 2008; Kwan et al., 1999; Reed et al., 2001), which is consistent with the hypothesis of disruption of frontal-subcortical circuits in subcortical vascular cognitive impairment (Cummings, 1994). Electroencephalography allows a noninvasive, inexpensive, and sensitive evaluation of cerebral function. The EEG abnormalities correlated with cognitive function in and discriminated between various types of dementia (Jeong et al., 2004; Gawel et al., 2007, 2009). Some studies investigated the value of EEG in MCI (Jelic et al., 1998, 2000; Liedorp et al., 2009; Moretti

et al., 2007*a*) and the influence of vascular lesions in MCI on the EEG (Babiloni et al., 2008*a*, 2008*b*; Moretti et al., 2007*b*, 2008*a*, 2008*b*). Previously, we reported that the cortical sources of abnormal EEG activity in regions implicated in the default mode network are revealed by standardized low-resolution brain electromagnetic tomography at an early stage in vascular cognitive impairment (Sheorajpanday et al., 2013). Earlier, we investigated the reproducibility and clinical relevance of the (delta + theta)/(alpha + beta) ratio (DTABR) and the pairwise derived brain symmetry index (pdBSI) as quantitative EEG spectral power parameters in ischemic cerebrovascular disease (Finnigan and van Putten, 2013; Sheorajpanday et al., 2009, 2010, 2011*a*, 2011*b*).

Early and specific secondary prevention of cognitive decline might be beneficial. The earliest stage potentially amenable to specific therapeutic intervention is when the patient presents with cognitive complaints. The primary aim of this study was to investigate the DTABR and the pdBSI as global EEG parameters in community-residing patients with an uneventful central neurologic history presenting with cognitive complaints for discriminatory features between amdMCI and subcortical vCIND. We furthermore investigated if these EEG parameters correlate with the level of cognitive decline in vCIND.

PATIENTS AND METHODS

Study Population

The EEG was recorded in 57 patients from our memory clinic with a clinical diagnosis of amdMCI (n = 22) or vCIND (n = 35). These patients presented with cognitive complaints confirmed by an informant. Inclusion criteria were (1) first presentation of cognitive decline, (2) age ≥ 55 years, (3) intact activities of daily living, and (4) able and willing to undergo full cognitive assessment. Exclusion criteria were (1) reversible cause for cognitive dysfunction, (2) dementia as defined by the NINCDS-ADRDA and NINDS-AIREN criteria (McKhann et al., 1984; Roman et al., 1993), (3) mass (effect) lesion on neuroimaging, (4) history of cerebrovascular event, (5) large vessel disease and imaging findings showing cortical infarction, and (6) axis I *DSM-IV* disorder (American Psychiatric Association, 1994). All patients underwent physical, neurologic, radiologic (brain computed tomography or MRI), and biochemical (including thyroid function, vitamin B12, folic acid, and syphilis serology) evaluation as part of the diagnostic routine. The study was conducted according to the revised Declaration of Helsinki (1998) and was approved by the central Institutional Review Board of Ziekenhuis Netwerk Antwerpen.

Neuropsychological Assessment

The neuropsychological test battery for all study participants consisted of: the Mini-Mental State Examination (MMSE) (Folstein et al., 1975), the Wechsler Memory Scale III (WMS-III; Wechsler, 1997*b*), matrix reasoning from the Wechsler Adult Intelligence Scale III (Wechsler, 1997*a*), the Trail Making Test (Reitan and Wolfson, 1992), the Rey-Osterrieth Figure (Osterrieth, 1944), the Boston Naming Test (Kaplan et al., 1983; Mariën et al., 1998), a semantic and phonological verbal fluency task (1-minute generation of names of animals, means of transport, vegetables, clothes, and words starting with phoneme F, A, and S) (unpublished norms), Raven Progressive Matrices (Raven et al., 2003), and Hierarchic Dementia Scale (Rönnberg and Ericsson, 1994). To account for individual age and education effects and to allow comparisons, neuropsychological test results were

transformed to z-score. The z-scores of the WMS-III subtests were averaged to create the mean WMS-III score as a composite measure of global memory function. Hachinski Ischemic Score (Hachinski et al., 1975) was determined as well. Mild cognitive impairment was defined clinically as an impairment in one or more cognitive domains larger than expected for age or education, typically below −1.5 SD, but insufficient to interfere with social and occupational functioning (Petersen, 2004). Patients with clinically significant memory impairment that did not meet the criteria for dementia, and at least one other non–memory-related dysfunction were diagnosed with amdMCI. Patients were diagnosed with vCIND if: (1) the cognitive impairment did not meet the NINDS-AIREN criteria (Roman and Goldstein, 1993) for vascular dementia, (2) the cognitive impairment was presumed to have a vascular cause (e.g., by evidence of sudden onset, stepwise progression, patchy deficits on cognitive testing, other evidence of atherosclerosis, focal neurologic findings), and (3) evidence of subcortical lacunes and/or white matter lesions, excluding patients with cortical or nonvascular lesions, on neuroimaging, according to previously suggested criteria (Erkinjuntti et al., 2000; Ingles et al., 2002).

EEG Analysis

EEG was recorded during at least 10 minutes in an eyes-closed state with the patient awake and alert using a Brainlab Measure Station (OSG, Belgium) as previously described (Sheorajpanday et al., 2009). Nineteen Ag/AgCl electrodes were positioned in accordance to the international 10-20 system, with impedances <5 kΩ. Analog to digital conversion rate was 250 Hz for all channels using a 16-bit AD convertor. Visual artifact rejection and data analysis were performed in EEGLAB (Delorme and Makeig, 2004) with supplementary scripts operating in the MATLAB environment. After data filtering (high pass 0.3 Hz, low pass 30 Hz) and visual artifact rejection, 128 seconds of EEG were analyzed. We have shown that 128 seconds of artifact-free EEG serves as a reliable sample of a particular EEG recording for classic spectral parameters with excellent intrarecord, intrarater and interrater reproducibility (Sheorajpanday et al., 2009). Spectral power was calculated by fast Fourier transform for each electrode over the 1 to 30 Hz range. Power spectral density was calculated using Welch averaged, modified periodogram spectral estimation method with a 2-second Hamming window and 50% overlap. The power of the delta (1–3 Hz), theta (4–7 Hz), alpha (8–13 Hz), and beta 1 (14–20 Hz) frequency bands was used to calculate the DTABR. EEG spectral asymmetry was quantified by the pdBSI, which evaluates asymmetry along homologous channel pairs. The pdBSI is defined as:

$$\text{pdBSI} = \frac{1}{NM} \sum_{j=1}^{M} \sum_{i=1}^{N} \left| \frac{R_{ij} - L_{ij}}{R_{ij} + L_{ij}} \right|,$$

with R_{ij} and L_{ij} being the fast Fourier transformation–based power spectral density of the signal obtained from a right and left channel, respectively, of a homologous channel pair i (with $i = 1, 2, …, M$), for example, C3 and C4, P3 and P4, etc, at frequency j (or Fourier coefficient, with index $j = 1, 2, …, N$). For this specific setting, $M = 8$. The pdBSI was calculated for frequency range (N) 1 to 25 Hz (Sheorajpanday et al., 2009).

Statistical Analysis

Sample size was calculated based on the previously reported difference ± standard error of the difference in pdBSI of 0.0666 ± 0.0135 between stroke patients and control subjects from an

independent cohort with a two-tailed alpha level for between-group comparisons set at $P = 0.05$ and for correlation analysis at a multiple comparison adjusted level of $P = 0.0033$ with an estimated clinico-encephalographic correlation of no less than 0.64 (Sheorajpanday et al., 2009). For the comparison between vCIND and amdMCI, this resulted in a sample power of almost 100% and for the correlation analysis between pdBSI and neuropsychological tests, a power of at least 97% (SamplePower 2.0; SPSS Inc, Chicago, IL). Data were analyzed using the Statistical Product and Service Solution 16.0 software package for Windows (SPSS Inc). Results of neuropsychological tests were transformed to z-scores. Comparisons between z-scores of neuropsychological tests were made by the paired *t*-test. Between-group comparisons were made by independent sample *t*-test and Mann–Whitney test according to distribution. Spearman correlation coefficient was used to calculate correlations between neuropsychological scores and quantitative EEG measures. Independent predictive value of parameters for diagnosis as dichotomized state was assessed using binary forward stepwise regression. To avoid overfitting of the model, only variables that were significantly correlated to the outcome parameter in univariate nonparametric analysis were selected. Significance level was set at $P < 0.05$ with adjustment for multiple comparisons as indicated.

RESULTS

Clinical characteristics of the patients are listed in Table 1. We did not find significant correlations between DTABR and any of the evaluated neuropsychological tests (MMSE, WMS-III subtests, Wechsler Adult Intelligence Scale III matrix reasoning, Trail Making Test, Rey-Osterrieth Figure, Boston Naming Test, semantic and phonological verbal fluency, Raven Matrices, and Hierarchic Dementia

Scale) in vCIND ($P > 0.05$) and between neuropsychological tests and pdBSI or DTABR in amdMCI ($P > 0.05$).

In vCIND, we found significant Spearman correlations after multiple comparison adjustment with significance level set at $P = 0.0033$ between immediate verbal memory, immediate global memory, verbal recognition, working memory, mean verbal WMS-III, mean global WMS-III, and pdBSI (Table 2). The correlation between mean WMS-III z-score and pdBSI is illustrated in Fig. 1.

There was a significant difference between patients with vCIND and amdMCI in DTABR (mean ± SEM: 2.71 ± 0.46 vs. 1.09 ± 0.15, Mann–Whitney test, $P = 0.002$) and in pdBSI (mean ± SEM: 0.14 ± 0.006 vs. 0.12 ± 0.004, Mann–Whitney test, $P = 0.023$).

As shown in Table 3, Hachinski Ischemic Score, matrix reasoning, working memory, verbal fluency, pdBSI, and DTABR displayed significant predictive value for vCIND in receiver operating characteristic analysis. Diagnostic accuracy for vCIND was not improved by basic Boolean operators.

In forward stepwise binary logistic regression entering gender, Hachinski Ischemic Score, mean WMS z-score, z-scores of working memory, verbal fluency, matrix reasoning, pdBSI, and DTABR as parameters, which correlated significantly in univariate nonparametric analysis, verbal fluency z-score, and DTABR emerged as independent predictors for vCIND with an odds ratio of 1.54 (95% confidence interval: 1.04–2.28, $P = 0.033$) for the verbal fluency z-score and an odds ratio of 2.28 (95% confidence interval: 1.06–4.94, $P = 0.036$) for DTABR, with a Hosmer–Lemeshow statistic of 0.98 indicating a good model fit of the data. This model had an overall correct classification rate of 95.0% compared with an overall correct classification rate of 82.5% when DTABR was omitted from the model.

DISCUSSION

In this study, community-residing patients with complaints of cognitive decline were evaluated in a clinical setting with a diagnosis of subcortical vCIND based on a standardized protocol consisting of neuropsychological assessments, clinical, biochemical, and neuroradiological evaluations. We selected patients with amdMCI, instead of cognitive healthy persons, as control subjects to allow more clinically relevant comparisons. Patients with amdMCI did have vascular risk factors as indicated in Table 1 and small, presumably nonsignificant, vascular microlesions were allowed, to allow extrapolation of our findings to routine clinical practice in which vascular risk factors are more prevalent as the "hyperhealthy" subject from a normative database might not be frequently encountered in general

TABLE 1. Group Characteristics of Patients Presenting With Cognitive Decline

	vCIND (n = 35)	amdMCI (n = 22)
Demographics		
Age, mean ± SD (range), years	75 ± 6.3 (55–85)	73 ± 7.7 (57–87)
Male gender	24 (69)	9 (26)
Risk factors		
Arterial hypertension	29 (83)	11 (31)
Carotid stenosis ≥50%	2 (6)	0
Cardiac arrhythmia	8 (23)	2 (6)
Congestive heart failure	13 (37)	1 (3)
Coronary disease	17 (49)	2 (6)
Diabetes mellitus	6 (17)	0
Dyslipidemia	16 (46)	5 (14)
Regular alcohol consumption	3 (9)	0
Current smoking	2 (6)	2 (6)
Hachinski Score, mean ± SEM	5.1 ± 0.14	4.5 ± 0.14
Prior treatment		
Antiplatelets	25 (71)	7 (20)
Anticoagulants	7 (20)	2 (6)
Neuropsychological performance, significant differences at $P < 0.0033$		
Working memory	−1.53 ± 0.11	−0.95 ± 0.15
Verbal fluency	−2.43 ± 0.27	−0.61 ± 0.17
Matrix reasoning	−1.55 ± 0.19	−0.69 ± 0.19

Values are given as n (%) unless otherwise stated.
amdMCI, amnestic multidomain mild cognitive impairment; pdBSI, pairwise derived brain symmetry index.

TABLE 2. Statistically Significant Spearman Correlations Between Neuropsychological Tests and Pairwise Derived Brain Symmetry Index in Vascular Cognitive Impairment, No Dementia

Test	Spearman rho	*P*
Immediate verbal memory	−0.66	0.0004
Immediate global memory	−0.57	0.0027
Verbal recognition	−0.75	<0.0001
Working memory	−0.59	0.0026
Mean verbal WMS-III	−0.72	<0.0001
Mean global WMS-III	−0.67	<0.0001

WMS-III, Wechsler Memory Scale III.
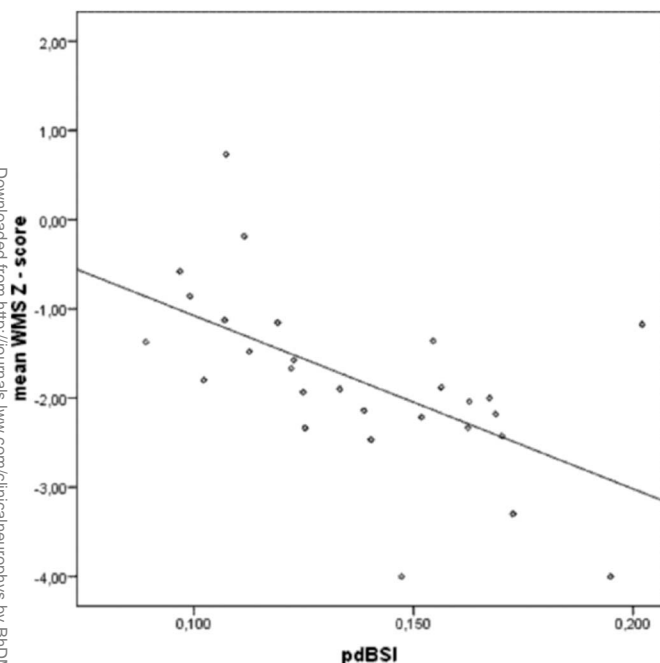
FIG. 1. Correlation between global memory decline as measured by the mean Wechsler Memory Scale z-score and pairwise derived brain symmetry index. There is a satisfactory relation with mean WMS z-score = -0.50 − pdBSI × 20.

clinical practice (Coburn et al., 2006). Patients were diagnosed with amdMCI based on operationally defined clinical and psychometric criteria without etiopathogenetic certainty. The -1.5 SD cut point might be of limited value in routine clinical practice to determine cognitive impairment in highly educated individuals, where impairment might reflect a decline from a superior to an average cognitive performance (Luis et al., 2003). To account for individual age and education effects in this study, neuropsychological test results were transformed to z-score. However, we cannot exclude the possibility of including more severely affected highly educated individuals in the vCIND and/or amdMCI groups. Vascular cognitive impairment, no dementia and amdMCI groups were balanced in terms of age and MMSE score. Homogeneity in global memory functioning between the two groups in our study was *post hoc* confirmed by the absence of a significant difference in mean global WMS-III score.

(Delta + Theta)/(Alpha + Beta) Ratio

Cognitive impairment secondary to subcortical infarcts is often accompanied by generalized cortical blood flow and metabolic changes (De Reuck et al., 1998; Sabri et al., 1998; Sultzer et al., 1995). Subcortical lesions in mixed dementia induce an increase of slow frequency EEG power (Schreiter Gasser et al., 2008). Increased delta and decreased alpha power was associated with the severity of vascular damage in MCI (Moretti et al., 2007b). In our previous study in the same cohort of patients on EEG source activity using standardized low-resolution brain electromagnetic tomography, we found a statistically significant decrease in parieto-occipital alpha 1 relative power current density in vCIND compared with patients with transient ischemic attack (TIA) and MCI. There was a significant decrease in frontal and parieto-occipital beta 1 relative power current density in vCIND compared with patients with TIA, and a significant increase in (pre)frontal delta activity in vCIND compared with amdMCI (Sheorajpanday et al., 2013). Concordantly, we found a significant higher global DTABR in vCIND compared with amdMCI. Moreover, DTABR emerged as an independent diagnostic predictor for vCIND. In subcortical vascular dementia (SVD) and AD, Gawel et al. (2007) and Gawel et al. (2009) found that patients with mild, moderate, and severe AD as a whole group showed significantly decreased alpha/(delta + theta) power ratio compared with the whole group of patients with mild and moderate SVD. In the comparison based on the severity of cognitive decline (determined by MMSE score), global alpha/delta power ratio was found to be a differentiating parameter between AD and SVD only in moderate dementia. The mean frequency at one of three selected derivations (T3-T4) was found to differentiate between AD and SVD in mild and moderate dementia (Gawel et al., 2009). Besides differences in patient selection according to the level of cognitive decline, the incorporation of power spectral density in the beta 1 frequency range may have contributed to this discrepancy. Beta activity is related to cognitive processes (Ray and Cole, 1985). Significantly less resting state power was observed in MCI exclusively, and in AD primarily in the beta frequency (12–22 Hz) range (Baker et al., 2008). In a simultaneous functional MRI and EEG study during resting wakefulness, power in the 17 to 23 Hz beta activity range was positively correlated with Blood-Oxygen-Level-Dependent functional MRI activity in posterior cingulate cortex, precuneus, temporo-parietal junction, dorsomedial prefrontal cortex, suggesting that spontaneous cognitive operations during conscious rest, that is, in the default mode of brain function is mediated by 17 to 23 Hz beta activity (Laufs et al., 2003). Early in AD, changes occur in the beta frequency range (Kwak, 2006; Wada et al., 1997). Therefore, we chose to use the ratio of relative power in alpha and beta to theta and delta band as global EEG measure to cover a more extended pathophysiological frequency range of interest. We

TABLE 3. Predictive Values of Clinical, Neuropsychological, and EEG Parameters for Vascular Cognitive Impairment, No Dementia in Receiver Operating Characteristic Analysis

	AUC	SE	95% CI	*P*	Value	SNS	SPC	PPV	NPV	FPR	FNR	ACR
Hachinski	0.70	0.07	0.57–0.84	0.010	5	0.77	0.46	0.69	0.56	0.55	0.23	0.65
Matrix reasoning	0.82	0.07	0.69–0.95	0.001	−1.15	0.67	0.82	0.73	0.62	0.32	0.33	0.67
Working memory	0.80	0.07	0.66–0.94	0.002	−1.15	0.71	0.77	0.67	0.64	0.36	0.33	0.65
Verbal fluency	0.89	0.05	0.79–1.00	<0.001	−1.15	0.81	0.82	0.82	0.72	0.28	0.18	0.78
pdBSI	0.68	0.07	0.54–0.82	0.023	0.13	0.71	0.46	0.70	0.48	0.41	0.40	0.60
DTABR	0.75	0.06	0.63–0.88	0.002	1.00	0.77	0.60	0.74	0.59	0.41	0.26	0.68

ACR, accuracy; AUC, area under the curve; CI, confidence interval; DTABR, (delta + theta)/(alpha + beta) ratio; FNR, false-negative rate; FPR, false-positive rate; pdBSI, pairwise derived brain symmetry index; PPV, positive predictive value; NPV, negative predictive value; SE, standard error; SNS, sensitivity; SPC, specificity.

have shown that this range is of interest in ischemic cerebrovascular disease (Sheorajpanday et al., 2010, 2011a, 2011b, 2009) and in vascular cognitive decline (Sheorajpanday et al., 2013).

A significant correlation between alpha/(delta + theta) ratio and mean wave frequency and mental impairment according to total MMSE score was found in SVD (Gawel et al., 2007). The absence of such a correlation in our study of a less severely affected patient population might be explained by the transformation of the total MMSE scores to age and educational level–adjusted z-score (Crum et al., 1993) in our population. Moreover, the MMSE is not a sensitive test for subcortical cognitive decline as it may overlook executive dysfunction (Jefferson et al., 2002; Mamikonyan et al., 2009; Price et al., 2005; Roman et al., 2002). In SVD, no significant association was found between white matter lesions and MMSE score (Price et al., 2005). In Parkinson disease, another prototypical fronto-subcortical disorder, almost one third of patients with intact global cognition as defined by a normal score on the MMSE met the criteria for MCI (Mamikonyan et al., 2009), which suggests that the severity of subcortical cognitive impairment may be underestimated by the MMSE. Severity matching based on MMSE scores should also be recognized as a relative, but practically inevitable, shortcoming in our study.

Pairwise Derived Brain Symmetry Index

The pdBSI was recently introduced as a sensitive measure of ischemic damage in patients with acute ischemic stroke. This index is an extension of the (global hemispheric) Brain Symmetry Index, introduced by van Putten et al. (2004), revised in 2007, and was shown to correlate significantly with hemispheric damage in patients with acute stroke (van Putten, 2007; van Putten and Tavy, 2004; van Putten et al., 2004). In acute ischemic stroke, the change in EEG brain symmetry during intravenous thrombolysis correlated significantly with the change in the National Institute for Health Stroke Scale score (de Vos et al., 2008). The pdBSI displayed high intra-recording, intrarater and interrater reproducibility, reliably discriminated between patients with stroke and TIA or control subjects and correlated significantly with clinical status and volume of recent ischemia among different levels of stroke probability (Sheorajpanday et al., 2009). The pdBSI was an independent predictor of early neurologic deterioration, mortality, and small-vessel stroke etiology in acute anterior circulation syndrome of presumed ischemic origin (Sheorajpanday et al., 2010). In lacunar and posterior circulation syndromes of presumed ischemic origin, pdBSI emerged as an independent predictor for radiologically confirmed stroke, even after resolution of symptoms at the time of EEG recording (Sheorajpanday et al., 2011a). In patients with persistent neurologic deficits at EEG recording, pdBSI was correlated with functional outcome and was independently associated with disability 6 months after ischemic stroke (Sheorajpanday et al., 2011b).

In this study, the additional diagnostic value of pdBSI in silent small-vessel stroke presenting as subcortical vascular impairment without dementia was evaluated. We found a significant difference in pdBSI between patients with vCIND and amdMCI and significant correlations between pdBSI and immediate verbal memory, immediate global memory, verbal recognition, and working memory in vCIND. Our findings also demonstrate that pdBSI correlates with global memory decline as defined by mean WMS-III z-score in vCIND.

Concluding Remarks

This study performed in a cohort of 57 community-residing residents with an uneventful neurologic history and first presentation of cognitive declince without dementia demonstrates that cortical deafferentation by subcortical lesions in subcortical vCIND is accompanied by changes in the EEG. Importantly, these changes were shown to discriminate between disease states and parallel disease severity as determined by clinical indicators of disease state and severity.

White matter lesions in vascular cognitive impairment induce a widespread increase of delta and theta power (D'Onofrio et al., 1996; Moretti et al., 2004, 2007b; Szelies et al., 1999), whereas cholinergic deafferentation and corticocortical disconnection induce a significant reduction in alpha and beta power (Babiloni et al., 2009; Baker et al., 2008; Kwak, 2006; Moretti et al., 2004; Wada et al., 1997). In full concordance to this, DTABR was an independent predictor of disease state in this cohort of cognitively impaired non-demented patients.

The pdBSI was significantly higher in subcortical vCIND compared with amdMCI but did not show independent predictive value for disease state. The lack of discriminatory power can be explained by its very nature: pdBSI as a symmetry-based marker evaluates power spectral density asymmetries along homologous channel pairs in the 1 to 25 Hz frequency range without weighing the relative contributions of slow over fast EEG power characterizing the disease states as mentioned above. The pdBSI did correlate highly and significantly with memory indices, especially with verbal memory, in vCIND. Because memory impairment is not an exclusive feature of any of the two disease states under investigation (Jokinen et al., 2006; Looi and Sachdev, 1999; Price et al., 2005; Reed et al., 2007), a parameter reflecting the severity of memory impairment cannot differentiate between the two states. The highly significant and strong correlation observed between pdBSI and global memory impairment, however, may allow a sensitive and cost-effective follow-up of patients with subcortical vCIND to monitor preventive and symptomatic treatment response.

In many memory clinics, EEG is part of the diagnostic workup as memory disturbances, confusion, and even dementia may be the sole clinical manifestation of a complex focal status or a protracted postictal state in elderly patients (Sheorajpanday and De Deyn, 2007).

Our findings extend the applicability of EEG in memory care, as it may allow an easy, inexpensive, and reliable evaluation of cognitive dysfunction. The results from this exploratory study should be confirmed in a larger population.

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