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Differentiation of Subjective Cognitive Decline, Mild Cognitive Impairment, and Dementia Using qEEG/ERP-Based Cognitive Testing and Volumetric MRI in an Outpatient Specialty Memory Clinic

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Abstract.

Background: Distinguishing between subjective cognitive decline (SCD), mild cognitive impairment (MCI), and dementia in a scalable, accessible way is important to promote earlier detection and intervention.

Objective: We investigated diagnostic categorization using an FDA-cleared quantitative electroencephalographic/event-related potential (qEEG/ERP)-based cognitive testing system (eVox® by Evoke Neuroscience) combined with an automated volumetric magnetic resonance imaging (vMRI) tool (Neuroreader® by Brainreader).

Methods: Patients who self-presented with memory complaints were assigned to a diagnostic category by dementia specialists based on clinical history, neurologic exam, neuropsychological testing, and laboratory results. In addition, qEEG/ERP ($n = 161$) and quantitative vMRI ($n = 111$) data were obtained. A multinomial logistic regression model was used to determine significant predictors of cognitive diagnostic category (SCD, MCI, or dementia) using all available qEEG/ERP features and MRI volumes as the independent variables and controlling for demographic variables. Area under the Receiver Operating Characteristic curve (AUC) was used to evaluate the diagnostic accuracy of the prediction models.

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Results: The qEEG/ERP measures of Reaction Time, Commission Errors, and P300b Amplitude were significant predictors (AUC = 0.79) of cognitive category. Diagnostic accuracy increased when volumetric MRI measures, specifically left temporal lobe volume, were added to the model (AUC = 0.87).

Conclusion: This study demonstrates the potential of a primarily physiological diagnostic model for differentiating SCD, MCI, and dementia using qEEG/ERP-based cognitive testing, especially when combined with volumetric brain MRI. The accessibility of qEEG/ERP and vMRI means that these tools can be used as adjuncts to clinical assessments to help increase the diagnostic certainty of SCD, MCI, and dementia.

Keywords: Dementia, electroencephalography, magnetic resonance imaging, mild cognitive impairment

INTRODUCTION

As the older adult population in the U.S. continues to grow, the incidence rate of dementia due to Alzheimer's disease (AD) and other causes is expected to increase proportionally. As of 2022, there are approximately 6.5 million older adults aged 65 or older with AD, and that number is expected to rise to 12.7 million in 2050 [1]. Early identification of dementia must be prioritized to implement preventative care and offset future interpersonal and financial stressors for patients and care providers. Simple cognitive tests like the Mini-Mental Status Exam (MMSE) and the Montreal Cognitive Assessment (MoCA) are widely available and easily administered by primary care practitioners but may have relatively low sensitivities and specificities, especially with respect to mild cognitive impairment (MCI) [2, 3]. There is a lack of diagnostically accurate tools for assessing memory loss without specialists, which can lead to delay in diagnoses. Considering the limitations of available diagnostic methods, there exists considerable demand for new tools to distinguish between subjective cognitive decline (SCD), MCI, and dementia in clinical practice.

Early detection of cognitive decline leading to dementia can include magnetic resonance imaging (MRI), positron emission tomography (PET), biomarker analysis drawn from cerebrospinal fluid (CSF), and comprehensive neuropsychological assessment [4–6]. Structural MRI, specifically, has a large body of evidence identifying a signature atrophy pattern in AD, characterized by extensive left-lateralized volume loss in the hippocampus and the broader medial temporal lobe (MTL) compared to healthy, age- and gender-matched controls [7, 8]. Further, models combining MTL atrophy with measures of memory function are more predictive of SCD, MCI, and dementia than either feature alone [9–11]. However, not all patients may receive objective memory testing, as neuropsychological assessments can be expensive or inaccessible in underserved areas [4]. Additional structural markers, such as PET and CSF analysis, can further aid predictive models, but they may not accurately capture the distinction between the various stages of cognitive impairment [12, 13].

For these reasons, quantitative electroencephalography (qEEG) has become a promising diagnostic adjunct. Mobile, noninvasive, and relatively inexpensive, qEEG is a cortical mapping tool that is being implemented for the early detection and ongoing clinical management of dementia. There is significant evidence that qEEG-based biomarkers can be used to classify MCI and dementia, especially using event-related potentials (ERPs), which are time-sensitive brain responses to specific motor, cognitive, or sensory events [14–18]. The study of cognitive processes using P300, an ERP component that surfaces specifically around 250–500 ms, is commonly done using an oddball paradigm, in which high frequency "non-target" stimuli and low frequency "target" stimuli are presented in a random order [19]. This design requires sustained attention and precise task execution and thus is highly effective in examining cognitive deficits over time [20]. Notably, dementia severity and early-stage neuropathology have been correlated with trackable changes in P300 amplitude and latency [21]. Recent research has also found that P300 latency increases in the progression from normal cognition to MCI to dementia, while P300 amplitude decreases significantly during the progression from MCI to dementia [22–24]. In addition, ERP studies collected during an oddball task have been shown to reflect increasing degrees of SCD, with lower P300 amplitudes correlating with more self-reported symptoms and lower cognitive performance measures [25].

Although there has been extensive recent research into the individual use of qEEG/ERP and volumetric MRI (vMRI) neuroimaging to assess SCD, MCI, and

dementia, there is little existing study of the diagnostic utility of combining them. The current study seeks to address this gap by analyzing both qEEG/ERP and volumetric MRI data within a real-world clinical sample to determine whether they can accurately classify patients into their cognitive diagnostic category (SCD, MCI, or dementia). The objective of this study is to investigate whether these tools can be used as adjuncts to simple cognitive tests already available to practitioners in primary care settings.

METHODS

Participants

With approval from the St. John's Cancer Institute Institutional Review Board (Protocol JWCI-19-1101) and in accord with the Helsinki Declaration of 1975, retrospective chart review was done on patients aged 55 and older seen at the Pacific Brain Health Center in Santa Monica, CA between July 2018 and February 2021. Authors ASG, RMG, THB, SM, and DAM read and reviewed patient medical records through an Electronic Medical Record (EMR) system and manually compiled relevant data into a de-identified database for analysis. As part of presenting to a specialty memory clinic with memory complaints, patients were evaluated by a dementia specialist and assigned to a diagnostic category (see the *Diagnoses of SCD, MCI, and dementia* section below). In addition, patients underwent testing with an FDA-cleared quantitative electroencephalographic/event-related potential (qEEG/ERP)-based cognitive testing system (eVox® by Evoke Neuroscience). Of 161 patients with qEEG/ERP data, 69 were categorized with SCD, 53 with MCI, and 39 with dementia due to AD with or without other contributing factors (e.g., vascular disease; see Table 1). A subset ($n = 111$) of the 161 patients had brain MRI scans with automated quantification of regional brain volumes using Neuroreader® by Brainreader, an FDA-cleared tool validated for use in dementia populations [26]. Forty-two of these patients had diagnoses of SCD, 39 had diagnoses of MCI, and 30 had diagnoses of dementia (see Table 1).

Additional demographic characteristics and clinical data were abstracted from the patient medical charts, including age at testing, sex, years of education, and MMSE scores. If patients did not complete an MMSE at the time of assessment or did not have an MMSE score on file ($n = 40$), MoCA scores were used and converted to an MMSE equivalent score using a validated conversion table [27]. We used the MMSE or MoCA scores on file closest to the date of qEEG/ERP testing. Because depression can affect memory and cognition, the presence or absence of current or prior depression was recorded for all patients at the time of qEEG/ERP testing and presented as a clinical characteristic (see Table 1). *APOE* test results were only available for 81 of the 161 participants (and 63 of the 111 subset with vMRI data) for reasons ranging from cost, lack of insurance coverage, and privacy concerns.

Diagnosis of SCD, MCI, and dementia

Board-certified dementia specialists (VRP and DAM) used standard clinical methods, including clinical history (e.g., hypertension, diabetes, head injury, and depression), neurological examination, cognitive testing (i.e., MMSE or MoCA), and laboratory results (e.g., vitamin B-12, thyroid stimulating hormone, and rapid plasma regain testing) to rule out

Table 1
Demographic and clinical characteristics*

	qEEG/ERP Sample ($n = 161$)			qEEG/ERP+vMRI Sample ($n = 111$)		
	Dementia ($n = 39$)	MCI ($n = 53$)	SCI ($n = 69$)	Dementia ($n = 30$)	MCI ($n = 39$)	SCI ($n = 42$)
Age	74.3 (8.0)	72.8 (6.7)	70.6 (6.5)	73.4 (7.8)	72.5 (6.5)	70.6 (6.1)
Female	28 (71.8%)	22 (41.5%)	40 (58.0%)	24 (80.0%)	14 (35.9%)	25 (59.5%)
Caucasian	36 (92.3%)	47 (88.7%)	65 (94.2%)	27 (90.0%)	36 (92.3%)	38 (90.5%)
Education	16.4 (2.7)	16.5 (2.5)	16.8 (2.3)	15.7 (2.5)	16.6 (2.5)	17.3 (2.0)
MMSE	22.3 (4.4)	27.2 (2.0)	28.7 (1.2)	22.0 (4.9)	27.3 (1.7)	28.8 (1.1)
Depressed^	24 (61.5%)	33 (62.3%)	40 (58.0%)	20 (66.7%)	22 (56.4%)	22 (52.4%)
BMI	22.5 (3.4)	25.5 (5.0)	24.5 (3.8)	22.5 (3.3)	25.6 (5.4)	24.2 (3.1)

*Numbers indicate mean with standard deviation (SD) or percentage of subjects (%). MCI, mild cognitive impairment; SCD, subjective cognitive decline; MMSE, Mini-Mental Status Exam; BMI, body mass index. ^Current or past diagnosis of depression at the time of qEEG/ERP testing.

reversible causes of memory loss and for diagnosing SCD, MCI, and dementia in all patients. We used MMSE (or MMSE scores converted from MoCA) to determine evidence of cognitive impairment. In addition, the criteria provided by Langa and Levine [2] (see Box 1) were used to diagnose MCI. The key criteria used to distinguish MCI from dementia were preservation of independence in functional abilities and lack of significant impairment in social or occupational functioning. Finally, SCD was diagnosed as those participants with subjective cognitive complaints but without evidence of MCI as defined above. Diagnostic category was based on the consensus diagnosis between VRP and DAM. For diagnostic categorization of participants in the current analysis, neither quantitative MRI nor qEEG/ERP data were considered. Diagnostic categorization was based on staging of the clinical syndrome of each patient (as found in Langa and Levine), not etiology or subtypes within each stage.

qEEG/ERP data acquisition

All qEEG/ERP data were recorded and collected using the eVox® System (see Supplementary Table 1). Participants were fitted with a qEEG cap with 19 electrodes (FP1, FP2, F7, F3, FZ, F4, F8, T7, C3, CZ, C4, T8, P7, P3, PZ, P4, P8, O1, and O2) positioned on the scalp in line with the International 10-20 system. The qEEG assessment consisted of a 5-min "Eyes Open" resting-state condition, a 5-min "Eyes Closed" resting-state condition, and a 15-min Go-No Go button-press task to generate ERP data. This task delivered four types of stimuli: visual deviant oddball stimulus (a large blue circle); visual standard stimulus (a small blue circle); visual deviant stimulus (a black and white checkboard); auditory deviant stimulus (a static noise). Each stimulus was presented in the same randomized order for 100 ms and followed by a 2100 ms break, and qEEG/ERP data calculated from the resultant waveforms.

MRI data acquisition

MRI scans were conducted using a GE 3.0 Tesla scanner for each subject to obtain a comprehensive volumetric report. MRI data were processed using the Neuroreader® neuroimaging software, which is clinically used to extract regional brain volumes and compare them to healthy age- and gender-matched controls [28]. Amongst the volumes provided by Neuroreader®, we used left and right hippocampal, amygdala, temporal lobe, frontal lobe, and lateral ventricle volumes in our analyses [29, 30], and all volumes were normalized for total intracranial volume (TIV).

Statistical analysis

Data were inspected for outliers, normality, homogeneity of variance and other assumptions to ensure their appropriateness for parametric statistical tests. All qEEG/ERP variables were log-transformed prior to analyses. Cognitive groups (SCD, MCI, and dementia) were compared using ANOVAs (continuous variables) or chi-squared tests (categorical variables) on all demographic measures.

To determine whether qEEG/ERP and vMRI measures differentiated cognitive groups, we first estimated a series of univariate multinomial logistic regression models, with cognitive group (SCD, MCI, and dementia) as the dependent variable and each of the predictors (demographic, clinical, qEEG/ERP, vMRI) as the independent variable. The aim of these preliminary analyses was only to select relevant variables for further multivariable analyses; thus, all variables found to be significant at a level of $p < 0.1$ were retained. We then used the stepwise variable selection method (with an inclusion cut-off of α=0.05) as a second exploratory way to identify possible predictors, since some variables may affect the outcome differently when included in the model simultaneously. Lastly, we estimated a multivariable logistic regression model including all the predictor variables identified using the two methods above. Subsequently, nonsignificant predictors were pruned, and model fit was compared using the Akaike information criterion. Inferences are made only from this final model, with significance set at $p < 0.05$. The predictive ability of the final model was quantified with calculated area under the Receiver Operating Characteristic (ROC) curve (AUC). Due to the relatively small size of our sample, we used leave-one-out cross-validation to provide an unbiased assessment of the model without splitting the available data into training and validation data sets.

We used the above procedure to estimate a model with only the qEEG/ERP variables as predictors for the larger cohort ($n = 161$) as well as the cohort with vMRI data ($n = 111$). We then determined the effect of adding volumetric measures as predictors to the model with qEEG/ERP predictors in the $n = 111$ cohort. All analyses were performed using SAS v 9.4 (SAS Institute, Cary, N.C.).

RESULTS

Subject characteristics

Demographic characteristics of the sample are summarized in Table 1. Patients with dementia (mean age 74.3 (SD 8.0) years) were significantly older than those with SCD (70.6 (6.5), $p = 0.01$). There were significantly more females in the dementia group (71.8%) compared to MCI (41.5%; $p = 0.004$). The groups did not differ in mean years of education, but each group differed significantly from the other in MMSE scores (Dementia: 22.3 (4.4); MCI 27.2 (2.0); SCD: 28.7 (1.2), $p < 0.0001$). BMI was significantly lower in the dementia group (22.5 (3.4)) compared to both MCI and SCI (25.5 (5.0) and 24.5 (3.8) respectively, $p = 0.002$). These characteristics were consistent across the full sample, as well as the subset of 111 patients with volumetric MRI data (Table 1).

Model with only qEEG/ERP variables

Among the qEEG/ERP variables evaluated for model inclusion (see Supplementary Table 1), P300b amplitude, Reaction Time, and Commission Errors were found to significantly differentiate participants with SCD, MCI, and dementia (AUC = 0.79). Participants with dementia and MCI had significantly lower P300b amplitude than participants with SCD (Table 2). Participants with dementia exhibited significantly greater reaction time than participants with MCI and SCD. All three groups differed from each other significantly in Commission Errors (Table 2).

The same three qEEG/ERP predictors (P300b amplitude, Reaction Time, and Commission Errors) were obtained for the $n = 111$ subset of participants who had vMRI data available, with a very similar AUC of 0.78. AUCs (and their 95% confidence intervals) for pairwise differentiation of diagnostic categories are presented in Table 3 (see also Supplementary Figure 1 for the ROC curves).

Model with qEEG/ERP and vMRI variables

Amongst all the regional volumes tested for model inclusion, using only the left temporal lobe (normalized by intracranial volume) was sufficient to differentiate cognitive diagnostic category with an accuracy of 0.77. Left temporal lobe volume differed significantly between all 3 groups (Table 2). Pairwise differentiation of cognitive categories using this volume measure yielded AUCs that are very similar to those using only qEEG/ERP measures (Table 3).

Using both the qEEG/ERP and vMRI variables yielded a diagnostic accuracy of 0.87 in the multinomial logistic regression model. We present the odds ratios and their associated confidence intervals for all the predictors in the two single modality models as well as the combined qEEG/ERP and vMRI model

Table 2
Quantitative EEG and volumetric MRI measures* by study groups

	qEEG/ERP Sample ($n = 161$)				
	Dementia ($n = 39$)	MCI ($n = 53$)	SCD ($n = 69$)	Group comparisons F(2,156), p	Post-hoc tests
P300b Amplitude	10.6 (5.3)	11.2 (4.9)	14.2 (7.3)	5.19, $p = 0.007$	dementia<SCD, $p < 0.003$; MCI < SCD, $p < 0.03$
Reaction Time	618.2 (201.7)	554.6 (97.4)	529.8 (57.0)	6.08, $p = 0.003$	dementia>MCI, $p < 0.05$; dementia > SCD, $p < 0.0007$
Commission Errors	18.6 (19.8)	6.6 (9.7)	2.3 (2.6)	31.71, $p < 0.0001$	all $p < 0.0001$
	qEEG/ERP+vMRI Sample ($n = 111$)				
	Dementia ($n = 30$)	MCI ($n = 39$)	SCD ($n = 42$)	Group comparisons F(2,106), p	Post-hoc tests
P300b Amplitude	10.3 (5.3)	11.0 (4.8)	13.8 (7.6)	3.34, $p = 0.04$	dementia<SCD, $p < 0.02$
Reaction Time	634.4 (217.3)	535.9 (68.9)	530.7 (55.1)	6.88, $p = 0.002$	dementia>MCI, $p < 0.003$; dementia > SCD, $p < 0.0006$
Commission Errors	16.5 (16.1)	5.6 (7.8)	2.5 (3.1)	22.13, $p < 0.0001$	dementia>MCI, SCD, $p < 0.0001$; MCI > SCD, $p < 0.04$
Left Temporal Lobe Volume^	78.5 (11.1)	91.4 (16.7)	99.1 (10.9)	19.02, $p < 0.0001$	dementia<SCD, $p < 0.0001$; dementia < MCI, $p < 0.009$; MCI < SCD, $p < 0.0004$

*Numbers indicate mean with standard deviation (SD). Note that while raw values are presented in the Table, log-transformed qEEG/ERP measures were used for all analyses. Group comparisons (ANOVAs) controlled for age and gender for qEEG/ERP measures and total intracranial volume additionally for vMRI measures. ^F(2,105) for Left Temporal Lobe Volume, due to additional covariate.

Table 3
Diagnostic accuracy of models with qEEG/ERP and vMRI predictors*

	AUC (95% CI)	Sensitivity	Specificity
qEEG/ERP only			
Dementia versus MCI	0.82 (0.72, 0.93)	80.0	79.5
Dementia versus SCI	0.87 (0.78, 0.96)	80.0	85.7
MCI versus SCI	0.72 (0.63, 0.82)	76.9	69.5
vMRI only			
Dementia versus MCI	0.79 (0.70, 0.90))	83.3	71.7
Dementia versus SCI	0.89 (0.81, 0.97)	76.7	92.9
MCI versus SCI	0.74 (0.63, 0.85)	71.8	71.4
qEEG/ERP+vMRI			
Dementia versus MCI	0.86 (0.78, 0.94)	83.3	76.9
Dementia versus SCI	0.96 (0.91, 1.00)	96.7	95.7
MCI versus SCI	0.79 (0.69, 0.90)	79.5	71.4

*Results presented are for $n = 111$; qEEG/ERP variables are log-transformed before all analyses. AUC, Area under Receiver Operating Characteristic curve.

Table 4
Significant quantitative EEG* and volumetric predictors of cognitive diagnoses: dementia, MCI, and SCD

	OR[$] (95% CI)	β	SE (β)	Wald's χ^2 (1)	*p*
qEEG/ERP predictors only					
P300b Amplitude	0.36 (0.15, 0.89)	–1.03	0.46	4.91	0.03
Commission Errors	3.28 (2.12, 5.08)	1.19	0.22	28.24	<0.0001
Reaction Time	26.00 (1.29, 526.12)	3.26	1.53	4.51	0.03
vMRI predictors only					
Left Temporal Lobe Volume	0.36 (0.24, 0.54)	–0.1	0.02	25.22	<0.0001
qEEG/ERP+vMRI combined					
P300b Amplitude	0.25 (0.09, 0.69)	–1.41	0.53	7.04	0.008
Commission Errors	2.96 (1.82, 4.82)	1.09	0.25	19.04	<0.0001
Reaction Time[#]	5.67 (0.18, 178.30)	1.73	1.76	0.97	0.2
Left Temporal Lobe Volume	0.37 (0.23, 0.57)	–0.1	0.02	19.89	<0.0001

*qEEG/ERP variables are log-transformed before all analyses. [$]Odds ratio per unit increase in predictor, except for left temporal lobe volume where OR presented is for an increase of 10 units. [#]Not significant in the combined model.

(Table 4). While P300b amplitude and Commission Errors as well as left temporal lobe volume remained significant predictors, Reaction Time was no longer associated with cognitive category in the combined model. Examining the pairwise AUCs, the predictive performance of this combined qEEG/ERP and vMRI model was superior to either of the two alone in all cases (Table 3; Supplementary Figure).

DISCUSSION

We examined the potential use of a quantitative electroencephalographic/event-related potential-based cognitive testing system combined with an automated volumetric magnetic resonance imaging tool to detect various stages of cognitive impairment. Together, these two methods differentiate SCD, MCI, and dementia to a high degree of accuracy in this 'real world' clinical sample. Specifically, just using P300b amplitude and Commission Errors from qEEG/ERP, in combination with left temporal lobe volume from vMRI, is sufficient to predict SCD, MCI, and dementia diagnoses accurately. Using just the qEEG/ERP measures or the vMRI measures alone also lead to reasonably accurate predictions; however, the combined qEEG/ERP and volumetric MRI model was shown to be superior. The accuracy of this combined model is comparable to that of neuropsychological assessments for differentiating diagnostic category [31].

Our finding that P300b amplitude is a significant predictor of cognitive impairment is consistent with several earlier studies. P300b amplitude is known to decrease with cognitive dysfunction [32] and increase with better memory abilities in healthy controls. High rates of commission errors, especially paired with a slow reaction time, may indicate impaired attention [33], which is common as cognition worsens in an older population. We also found that left temporal

volume atrophy is an important predictor of cognitive function. MTL atrophy has been associated with decreased performance on memory, language, and orientation [34] and has been found to predict dementia, particularly AD [9, 35, 36]. Although many other regional volumes (including the right temporal volume) were significantly different between our cognitive categories, they did not add further explanatory power to the prediction model, beyond what was provided by the left temporal lobe volume. Many authors have focused on the hippocampus, when studying MCI and onset of AD [37–39]. Our study includes participants with dementia, not only AD. Since the hippocampus is specifically related to new memory formation, but cognitive impairment involves more than just memory formation, it is not surprising that our approach did not identify the hippocampus as the primary predictor of cognitive diagnosis.

Patients in the study were categorized into diagnostic categories, namely SCD, MCI, and dementia, by the study clinicians as part of their clinical workup. However, it is well-known that cognition exists across a continuum and these cognitive categories are based on approximate cut-offs along this continuum [40–42]. Consequently, it may be possible to employ Item Response Theory (IRT) and associated methods for the refinement and scoring of the measures to arrive at a model of cognition. The premise of IRT models is that a 'causal' common latent variable (in this case, cognition) underlies the observed responses (items) and as such, these responses are diagnostic of an individual's position on the underlying continuous latent variable. Notwithstanding the challenges of applying IRT [43], such models hold promise and have been used to model the progression of cognitive decline [44, 45].

Considering the importance of early detection of cognitive impairment, these findings may also provide insight into a novel method of identifying patients at increased risk of dementia. The EEG measures in this predictive tool could, with or without vMRI added to the model, be particularly useful in certain clinical settings, such as rural areas, which often lack economical, accessible, and comprehensive neuropsychological assessments; it could also be beneficial in situations in which patient tolerability to lengthy diagnostic testing is low [46, 47]. The EEG assessment used in the current study is a portable system, and thus can be delivered to where the patient is located for testing. Importantly, given that online cognitive assessments are becoming better and more accessible, combined use of online memory testing with portable EEG assessment and telehealth services may allow for entirely remote-based early detection of cognitive decline. In addition, this study demonstrates the advantage of combining data from qEEG and volumetric imaging to aid the clinician in determining a diagnosis. Initial stages of cognitive impairment are heterogeneous and complex [48, 49] and finding tools and assessments to specifically differentiate SCD and MCI has proven difficult. However, the combined qEEG/ERP and vMRI model was able to distinguish between the two stages with a relatively high degree of accuracy. In routine clinical care, this model may be an important adjunct to traditional assessments in distinguishing between SCD and MCI, thus allowing clinicians to implement preventative care sooner. Earlier intervention is crucial to limit the rate of disease progression and provide patients with greater autonomy and quality of life.

Strengths of the current study include the relatively large real-world clinical sample, and the use of two physiological tools, both with easy access, to differentiate SCD, MCI, and dementia. It is also notable that we found the same three qEEG/ERP predictors in the larger cohort as well as the subset which had quantitative volumetric data available, indicating the robustness of the model. However, future studies should replicate these findings in a larger, more racially and ethnically diverse sample, when other qEEG features and regional volumes may become important. As this study utilized a convenience sample of the patients who presented to Pacific Brain Health Center (PBHC) in Santa Monica, CA with memory and/or other cognitive complaints, it does not include a healthy control group, and there was a significant age difference between participants with dementia and SCD. Incorporating genetic testing results in a predictive model, either in the form of a polygenic risk score or as specific genetic risk variants, is desirable as well, if such results are available. Further, it would be informative to subtype the MCI patients into amnestic and non-amnestic, to determine if amnestic MCI had similar patterns on qEEG/ERP and vMRI as patients with dementia. Additionally, future research should examine longitudinal cohorts to track changes in qEEG/ERP and vMRI features over time and how these may impact cognitive classification. Nevertheless, this study represents an important first step in using easily accessible, mobile functional mapping tools to help increase the diagnostic certainty of SCD, MCI, and dementia and to improve the early and correct identification of patients who might otherwise go untreated.

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SUPPLEMENTARY MATERIAL

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