Deficits of visuospatial working memory and executive function in single- versus multiple-domain amnestic mild cognitive impairment: A combined ERP and sLORETA study

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HIGHLIGHTS

- Md-aMCI showed reduced P300 amplitudes, compared to sd-aMCI during VSWM task.
- Md-aMCI showed reduced N200 amplitudes, compared to sd-aMCI during Go/Nogo task.
- ERP and sLORETA during VSWM and Go/Nogo enabled distinguishing md-aMCI from sd-aMCI.

ABSTRACT

Objective: According to recent criteria of classification, amnestic mild cognitive impairment (aMCI) could be divided into two categories: single-domain aMCI (sd-aMCI) and multiple-domain aMCI (md-aMCI). The difference between sd-aMCI and md-aMCI needs further exploration. The present study aimed to compare deficits in visuospatial working memory (VSWM) and executive function between sd-aMCI versus md-aMCI patients by use of event-related potentials (ERP) and standardized low-resolution brain electromagnetic tomography analysis (sLORETA).
Methods: The ERP data were measured and analyzed in 26 sd-aMCI, 13 md-aMCI patients and 46 healthy elderly controls (HEC) during VSWM and Go/Nogo processes.
Results: During VSWM task, md-aMCI patients showed decreased P300 amplitude compared to HEC and sd-aMCI patients (All $p < 0.05$). As compared to sd-aMCI, md-aMCI showed a hypoactivation in the right middle frontal gyrus in 1-back task during the P300 time range. During the Go/Nogo task, sd-aMCI and md-aMCI patients showed reduced N200 amplitude, compared to HEC (All $p < 0.05$). However, md-aMCI patients had decreased N200 amplitude, with respect to sd-aMCI patients. Further, as compared to sd-aMCI patients, md-aMCI patients showed a hypoactivation in the right superior frontal gyrus during the N200 time range.
Conclusions: These findings with a combined ERP and sLORETA study showed more severe deficits in updating operations of WM, detections of the target stimulus and conflict processes in md-aMCI, compared to sd-aMCI patients.
Significance: The present study showed that a combined ERP and sLORETA study during the VSWM and Go/Nogo tasks could distinguish md-aMCI from sd-aMCI.

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1. Introduction

Amnestic mild cognitive impairment (aMCI) represents a prodromal stage of Alzheimer's disease (AD). According to criteria of classification, aMCI was divided into two categories: single-domain aMCI (sd-aMCI) and multiple-domain aMCI (md-aMCI) for individuals with the only deficit of episodic memory or deficits

of additional other cognitive domains, respectively (Winblad et al., 2004). Epidemiological evidence showed that aMCI patients progress to AD with a 4–10 times higher risk in comparison with healthy elderly (Petersen et al., 2001, Bischkopf et al., 2002, Grundman et al., 2004). Early diagnosis of aMCI is essential for an early intervention to slow down its progression to AD.

According to previous studies, the conversion from aMCI to AD shows sequential deficits of cognitive domains with the beginning of deficits of episodic and semantic memory deficits, followed by executive function, attention deficits, visuospatial memory, verbal recall deficits, and finally all cognitive domains affected in AD (Bäckman et al., 2005, Bondi et al., 2008, Webster et al., 2014). These studies supported a hypothesis that sd-aMCI might be a prodromal stage of md-aMCI. A 4-year follow-up study indicated that individuals with sd-aMCI convert to AD at a 24% rate in comparison with md-aMCI patients at a 77% conversion rate (Bozoki et al., 2001). However, the difference between sd-aMCI and md-aMCI needs further exploration.

In recent years, AD researchers have made advances in the detection of biomarkers for AD, such as tau levels in cerebrospinal fluid (CSF) and Aβ positron emission tomography (PET) imaging and structural magnetic resonance imaging (MRI), functional MRI (fMRI). However, due to the invasive and extraordinarily expensive characteristics of these detection assays, a clinical diagnosis of AD still relies more on the clinical manifestation and neuropsychological tests. Event-related potentials (ERPs) with high temporal resolution instantly reflect summated excitatory postsynaptic potentials (EPSP) and inhibitory postsynaptic potentials (IPSP). It addresses the high speed of cognitive processing and exploring the potential mechanism of neural deficits in aMCI (Nunez and Srinivasan, 2006). ERP alterations might onset at a very early stage of AD. Investigations indicated that young asymptomatic individuals who carry mutations in the amyloid precursor protein (APP) and presenilin-1 (PSEN1) genes show significant changes in ERP components years prior to the appearance of deficits in cognitive functions assessed with neuropsychological tests (Golob et al., 2009, Quiroz et al., 2011). In addition, previous investigations have demonstrated that specific ERP components, such as P50, N200 and P300, might be early biomarkers for aMCI diagnosis (Golob et al., 2002, Golob et al., 2007, Howe, 2014, Howe et al., 2014, Cecchi et al., 2015). However, these investigations did not evaluate ERP components in different aMCI subtypes (sd-aMCI and md-aMCI) separately. In the recent years, some investigations detected significantly increased P50 amplitude during an auditory odd-ball paradigm (Golob et al., 2007), delayed N2cc latency during a Simon task (Cespon et al., 2013, 2015a, Cespon et al., 2015b), decreased N250r amplitude during a delayed match-to-sample tasks (Deiber et al., 2011), delayed P300 latency during an attentional network test (Missonnier et al., 2013) in md-aMCI, compared to sd-aMCI patients. However, previous ERP studies in aMCI patients mainly concentrated on a single cognitive domain. This study aimed to evaluate multiple cognitive domains in the same individuals with two cognitive tasks (visuospatial N-back working memory and Go/Nogo tasks).

Working memory (WM) works as a cognitive system for temporary holding, processing and manipulation of information. Previous studies have demonstrated that WM impairment might be a sensitive biomarker for aMCI diagnosis (Economou et al., 2007, Saunders and Summers, 2011, Zheng et al., 2012). Visuospatial WM (VSWM) is more susceptible to AD-like pathology compared to visual WM (VWM) (Alescio-Lautier et al., 2007). In addition, recent three ERP studies revealed aMCI-related deterioration in response inhibition (Cid-Fernandez et al., 2014, Mudar et al., 2015, Lopez Zunini et al., 2016). Standardized low-resolution brain electromagnetic tomography analysis (sLORETA) is an efficient and widely used functional image method for source localization in ERP studies (Pandey et al., 2012). Additionally, sLORETA is implemented widely in ERP studies with VSWM and Go/Nogo tasks (Bokura et al., 2002, Fallgatter et al., 2002, Suchan et al., 2005, Yin and Liu, 2010, Keeser et al., 2011, Pandey et al., 2012). The present study aimed to explore whether the md-aMCI showed more serious deficits in VSWM-related ERP component (P300) at the parietal electrodes and executive function-related ERP components (N200 and P300) at midline frontal, central and parietal electrodes compared to sd-aMCI patients via a combined ERP and sLORETA study.

2. Methods

2.1. Participants

Initially 98 participants were recruited through community health screening, newspaper advertisements and hospital outpatient services. All participants were Chinese Han, right-handed and between 55 and 80 years old. Our study was approved by Human Participants Ethics Committee of the Affiliated ZhongDa Hospital, Southeast University. Written informed consents were attained from these participants. All these participants went through three-step cognitive evaluation. Initially, two experienced clinicians (Dr. Gu and Dr. Gao) got the demographics, history of cognitive impairment, history of other neurological and psychiatric diseases, history of drug use, physical evaluation for nervous system from participants. Secondly, all participants were evaluated for general cognitive, behavioral, functional and specific cognitive domains impairments using neuropsychological scales. Additionally, blood tests and MRI were performed to exclude other neurological and major medical diseases.

2.2. Neuropsychological tests

Neuropsychological tests included the Mini-Mental State Examination (MMSE) (Folstein et al., 1975), the Clinical Dementia Rating (CDR) (Hughes et al., 1982), the Mattis Dementia Rating Scale-2 (MDRS-2) (Matteau et al., 2011), the Activities of Daily Living (ADL) scale (Nouri and Lincoln, 1987), the Auditory Verbal Learning Test-20-min Delayed Recall (AVLT-20-min DR) (Taylor, 1960), the Rey-Osterrieth Complex Figure Test (ROCFT), the ROCFT-Delayed-20-min Recall (ROCFT-20-min DR) (Osterrieth, 1944), Logical Memory Test-20-min delayed recall (LMT-20-min DR) (Wechsler, 1955), the Digit Symbol Substitution Test (DSST) (Lewandowski, 1984), the Trail Making Tests (TMT) (Strauss et al., 2006), the Stroop Color and Word Test A, B, and C (Golden and Freshwater, 1978), the Digital Span Test (DST) (Lezak, 2004), the Semantic Similarity Test (Similarity) (Wechsler, 1955), Verbal Fluency Test (VFT) (Lezak, 2004) and the Clock Drawing Test (CDT) (Kaplan, 1983), the Picture Naming Test (PNT) (DeLeon et al., 2007). These tests covered general cognitive functions, behavioral function, memory, executive function, attention, visuospatial function and language domains.

2.3. Inclusion criteria and exclusion criteria

Included aMCI patients met the diagnostic inclusion criteria proposed by Petersen et al (Petersen et al., 1999) and the International Working Group (Winblad et al., 2004). These included: subjective memory impairment confirmed by subject and his caregiver; MMSE score ≥24; CDR of 0.5; objective memory function documented according to an AVLT-DR score ≤1.5 standard deviation (SD) of age- and education-adjusted norms (cut-off was ≤4 correct responses on 12 items for patients with ≥8 years of education); no or minimal impairment in daily activities; absence

of dementia, symptoms that were not sufficient to meet the criteria of National Institute of Neurological and Communicative Disorders and Stroke or the AD and Related Disorders Association (NINCDS-ADRDA) for AD. In addition, healthy elderly controls (HEC) had a CDR of 0, an MMSE score of ≥ 26 and an AVLT-DR score of >4 for subjects with ≥ 8 years of education.

According to disease histories, blood tests and MRI tests, participants were excluded when they had a history of stroke, epilepsy, alcoholism, Parkinson's disease, major depression, head injury and other neurological or psychiatric disorders; major medical illness, such as cancer, anemia and thyroid dysfunction; severe visual or hearing loss.

Eventually, 85 participants (46 HEC and 39 aMCI patients) were included in the study.

2.4. Classification of aMCI

We classified aMCI patients according to the five cognitive domains: memory, executive function, attention, visuospatial function and language domains. Participants were considered as md-aMCI if they fulfilled the inclusion, exclusion criteria of aMCI and showed impairment in at least one cognitive domain in addition to memory (≤ 1.5 SD from the age- and education-adjusted norms). Other aMCI patients were identified as sd-aMCI. Based on these criteria, 39 aMCI patients were divided into two sub-groups (26 sd-aMCI and 13 md-aMCI patients).

2.5. Procedure and stimuli

All participants performed these tasks in a quiet, sound-proofed, dimly-lit room and sat in front of a 17 inch computer (refresh rate 75 Hz) placed at a distance of 70 cm from their eyes. These participants underwent ERP recordings while performing two tasks involving VSWM and execution function. The two tasks were performed in a sequence with E-Prime 2.0 software (Psychology Software Tools Inc., Pittsburgh, USA). The order of the tasks is not counterbalanced between participants. In addition, participants were asked to minimize head and body movements and to focus on the screen throughout the stimulus presentation. We instructed these participants to respond with the dominant hand. Before each task, participants were asked to practice briefly to confirm that all participants understood these tasks correctly. Procedures are shown in Fig. 1 (Gu et al., 2017) and Fig. 2.

2.5.1. Visuospatial working memory

A visuospatial N-back working memory task was performed. In the task, white blocks (size: 2.6×2.6 deg) were presented in a continuous stream on a black background. Each white block was randomly placed in one of 8 possible locations (horizontal X axis, vertical Y axis and the lower and upper position of both diagonals). The duration was 300 ms for each block and inter stimulus interval (ISI) was 2000 ms. The task included 0-back and 1-back task. In 0-back task, participants should judge whether the presented white block placed on the upper left side of the screen. In 1-back task, participants had to recognize whether the current white block presented in the same location of the previous one. Participants had to distinguish between targets and non-targets by pressing the left or right mouse button with their right index or middle finger. After pressing the button, error rate (ER) for target stimuli, ER for non-target stimuli (false alarm rate, FAR) and mean correct reaction times (RTs) were recorded. Our study included two practice blocks and eight experimental blocks; each block represented either the 0-back or 1-back task. Each block was composed of 20 trials with a 3:7 target/no target relation (Gevins and Cutillo, 1993). Totally, each task included 80 trials (24 targets and 56 non-targets).

2.5.2. Go/Nogo task

A visual Go/Nogo task was performed by the participants. During this task, a continuous stream of stimuli (white single and double triangular figures; size: 2.8×3.8 deg) was randomly presented on a black background. Stimuli displayed with 100 ms and 800 ms as duration and ISI, respectively. Participants had to press the left mouse button with right index finger for each Go stimulus (double triangular), but control their response while confronting Nogo stimuli (single triangle). The Go/Nogo task contained one practice block (composed of 60 Go-stimuli and 40 Nogo-stimuli) and six experimental blocks (totally composed of 360 Go-stimuli and 240 Nogo-stimuli). In this task, we recorded ER for Go stimuli, ER for Nogo stimuli (FAR) and RTs.

2.6. EEG recording and ERP analysis

Electroencephalograms (EEG) were recorded from 64 scalp electrodes positioned on the basis of the international extended 10–20 system using a BrainAmp MR portable ERP system (Brain Products GmbH; Munich, Germany). During online recording, we used the FCz electrode site as an internal reference. Impedances were kept below 10 kΩ.

We performed data analysis with BrainVision Analyzer software 2.0 (Brain Products GmbH; Munich, Germany). For data off-line analysis, all electrodes were re-referenced to the average reference. Two pairs of electrodes were respectively positioned at outer canthi of both eyes as horizontal electrooculogram (HEOG) and above and below the right eye as vertical EOG (VEOG). An independent component analysis (ICA) was performed to eliminate artifacts from eye movements and eye blinks. The EEG signal was digitally filtered with a low cut-off frequency and high cut-off frequency respectively set at 0.01 Hz and 30 Hz. After semiautomatic raw data inspection (rejection levels > +100 µV and < −100 µV), data were segmented. Epochs were created from 100 ms pre- stimulus to 700 ms post-stimulus to calculate the ERP. Baseline correction was done with the mean activity in the 100 ms prior to stimulus. Epochs of EEG were averaged for each condition of interest to create grand averages for each participant.

During VSWM task, on the basis of previous studies (Sokhadze et al., 2008, Shishkin et al., 2011, Yu and Zhang, 2014), our visual inspections of the waveforms and brain topographic maps (supplementary Fig. 1), the peak amplitude and latency of P300 was measured at the parietal (P1, Pz and P2) electrodes. In addition, the latency ranges were 300–500 ms for P300. In Go/Nogo task, according to previous investigations (Cid-Fernandez et al., 2014, Zhang et al., 2016), our visual inspections of the waveforms and brain topographic maps (supplementary Fig. 2), the peak amplitudes and latencies of N200 (time window: 150–250 ms) and P300 (time window: 250–450 ms) were measured across the three midline frontal, central and parietal (Fz, Cz, Pz) electrodes. ERP components were quantified using semiautomatic peak detection processing by Brain Vision Analyzer software (Brain Products, Munich, Germany), which allows the user to adjust the peak on a case by case basis. The peak amplitudes and latencies of all components were acquired with peak detection process.

2.7. Statistical analysis

SPSS 21.0 software was implemented for statistical analysis. The statistical threshold was set at $p < 0.05$.

On the basis of previous studies (Shu et al., 2016, Su et al., 2017), for each cognitive domain (memory, executive function, attention, visuospatial function and language domains), we conducted a composite Z score analysis. For each participant, the Z score was calculated as followed: $Z = (x-\mu)/ SD$ (x represents individual raw scores for each test of each participant, the reciprocal of
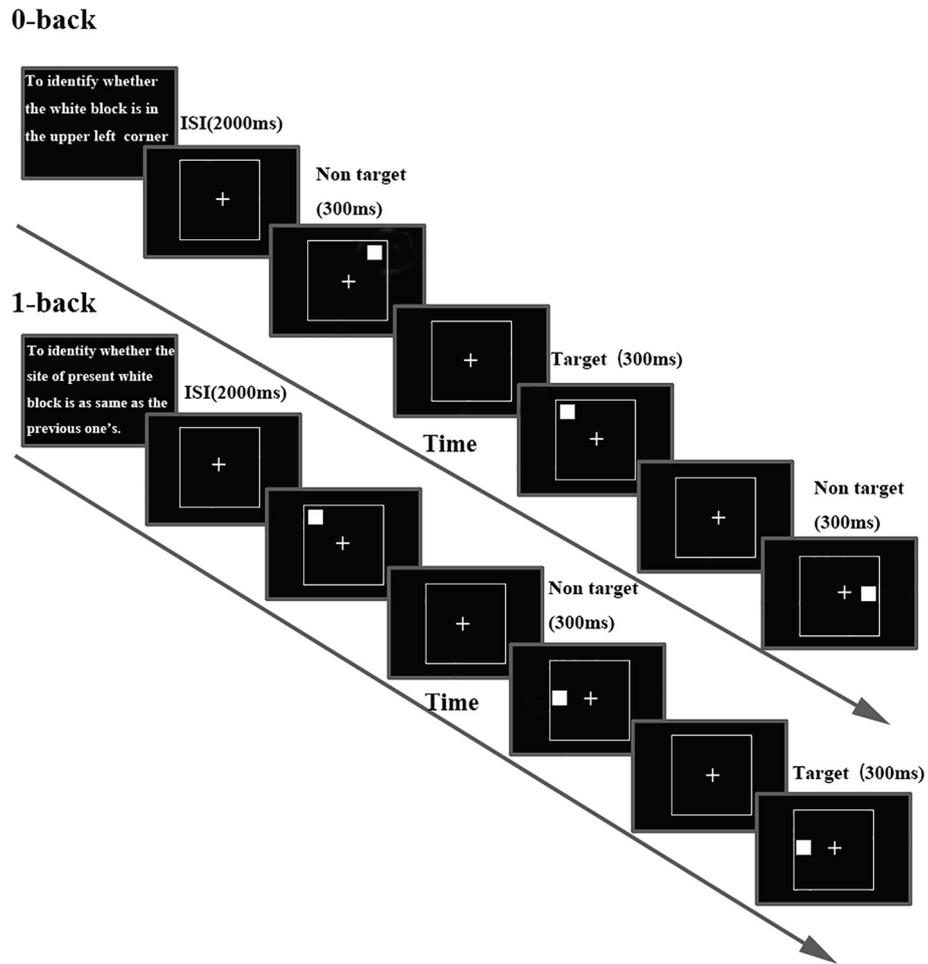
0-back

1-back

Fig. 1. Schematic diagram of visuospatial N-back working memory task, separately for each task load. Details about timing for stimulus and inter stimulus interval (ISI) are included.
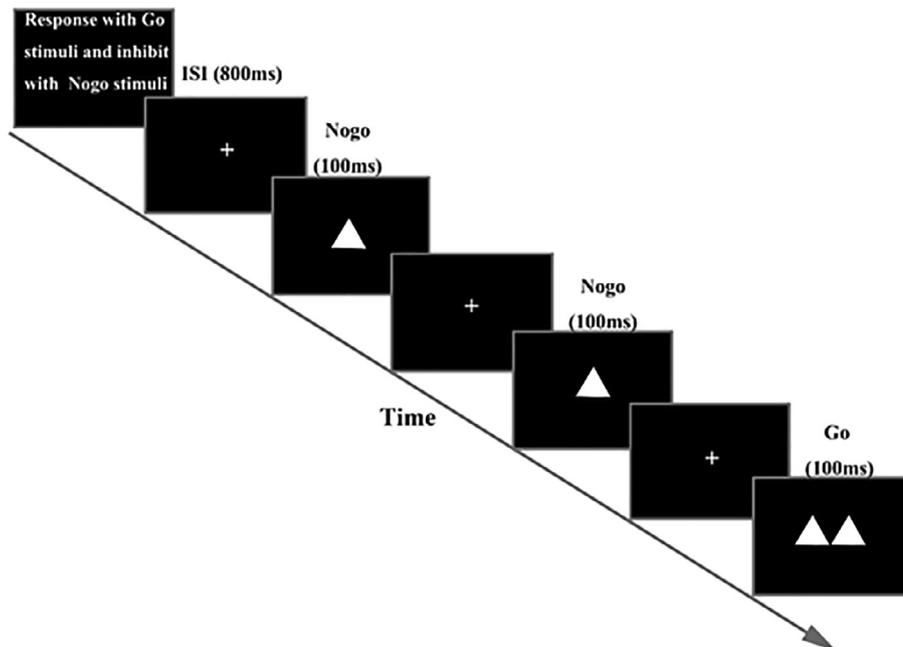
Fig. 2. Schematic diagram of the Go/Nogo task. Details about timing for stimulus and inter stimulus interval (ISI) are included.

the raw time was used in the subtractions for tests that were measured by time), and then the composite Z scores for each cognitive domain were acquired from the mean values of the relevant tests.

One-way analysis of variance (ANOVA) and Fisher's exact probability tests (gender comparison for the sample size of female <5 in a group) were performed for demographic and neuropsychological data between aMCI patients and HEC. In addition, repeated measures ANOVAs (RMANOVAs) were performed for behavioral data, with appropriate Greenhouse-Geisser corrections. For ER and RTs in VSWM task, RMANOVA with post hoc simple main effect analysis was performed with trial-types (0-back vs. 1-back) and stimulus-types (target vs. non-target stimuli) as within-subject factors and groups (HEC, sd-aMCI and md-aMCI) as between-subject factors. For ER in Go/Nogo task, the RMANOVA with post-hoc one-way ANOVA was conducted with trial-types (Go vs. Nogo) as within-subject factors, groups as between-subject factors. For RTs in Go/Nogo task, we performed one-way ANOVA with a post-hoc Bonferroni test. For ERP data, we performed RMANOVA with trial-types and electrodes as within-subject factors, groups as between-subject factors during both VSWM and Go/Nogo tasks.

Our sLORETA version (v20151222) is available at: http://www.uzh.ch/keyinst/loreta.htm. Based on published procedures (Pascual-Marqui, 2002, Pandey et al., 2012), we carried out source localization for P300 in the time frame 300–500 ms post-stimulus during VSWM task. In addition, during Go/Nogo task, we made source localization in the time frame 150–250 ms post-stimulus for N200 and 250–450 ms post-stimulus for P300. The cortex was modeled as a collection of volume elements (voxels) in the digitized Montreal Neurological Institute (MNI) coordinates corrected to the Talairach coordinates (Pascual-Marqui, 2002). Electrode coordinates were generated from the 61 electrode locations. A transformation matrix was created using electrode coordinates. The averaged waveforms (for all 400 time samples, from 100 ms pre stimulus to 700 ms post stimulus) for each participant were converted and saved into ASCII values. Source localization was composed of two key parts: ERP analysis and LORETA analysis. During ERPs analysis in VSWM task, we detected 1-back relative to 0-back difference between groups with t-statistics analysis. During Go/Nogo task, difference between groups in Go and Nogo conditions were acquired with t-statistics analysis. After view of the combined ERP (which is not an actual ERP), latency where maximum t-value occurred were attained for LORETA analysis. The *p*-value of latency where maximum t-value occurred <0.05, is the threshold for deciding significant brain activation difference. The sLORETA values for each participant were computed with ASCII values, electrode coordinates and transformation matrix, separately. For each comparison, a test (Log of ratio of averages) was calculated for time-samples in ERP components with 5000 random permutations. Finally, the result values were shown with a three dimensional (3-D) brain model and evaluated for the level of significances. Additionally, study reported the maximum differences between groups at respective Montreal Neurological Institute (MNI) coordinates and Brodmann areas (BA).

Receiver operating characteristic (ROC) curves for discrimination between individuals with deficits in both episodic memory and additional other cognitive domains (md-aMCI patients) and individuals with no cognitive deficits or only with deficits in episodic memory (HEC and sd-aMCI patients) were calculated for all neurophysiological, behavioral and ERP parameters. Before making ROC curves, the Condition Index (CI) was checked to be lower than and equal to 10 to verify the absence of significant multicollinearity between these predictor variables. As the electrode x group interaction did not affect these ERP parameters (P300 during VSWM tasks and N200 during Go/Nogo tasks), these ERP parameters at different electrodes (P1, Pz, P2 during VSWM tasks and Fz,

Cz, Pz during Go/Nogo tasks) were averaged to calculate the area under curve (AUC) for each parameter.

3. Results

3.1. Demographic and neuropsychological results

Table 1 showed demographic and neuropsychological characteristics of participants. One-way ANOVA indicated no significant main effects of group in age and education. Mann-Fisher's exact probability tests detected no significant group effect on gender. In addition, our study revealed significant group effects on MMSE, MDRS-2, memory function, attention, executive function, visuospatial function and language. Post-hoc Bonferroni tests indicated reduced memory function in both sd-aMCI and md-aMCI patients, compared to HEC. In addition, post-hoc Bonferroni tests detected that as compared to both HEC and sd-aMCI patients, md-aMCI patients showed decreased attention, executive function and language. Moreover, md-aMCI showed lower scores in general cognitive function (MMSE and MDRS-2) and visuospatial function, compared to HEC.

3.2. Behavioral results

3.2.1. Visuospatial working memory

Supplementary table 1 showed the overall statistic for RMANOVA. RMANOVA indicated significant main effects of trial-type, stimulus-type and group on ER [trial-type: F (1, 82) = 45.938, $p < 0.001$, stimulus-type: F (1, 82) = 21.669, $p < 0.001$, group: F (2, 82) = 6.645, $p = 0.003$] in VSWM task. Post-hoc simple main effect analysis with Bonferroni correction indicated elevated FAR in both 0- and 1-back conditions in md-aMCI and sd-aMCI patients, compared to HEC [0-back task: md-aMCI: (33.00 ± 18.38) % vs. HEC: (14.30 ± 9.23) %, $p = 0.004$; sd-aMCI: (26.16 ± 14.98) % vs. HEC: (14.30 ± 9.23) %, $p = 0.010$; 1-back task: md-aMCI: (40.43 ± 22.17) % vs. HEC: (19.67 ± 8.81) %, $p = 0.007$; sd-aMCI: (32.53 ± 19.21) % vs. HEC: (19.67 ± 8.81) %, $p = 0.021$]. However, it revealed no significant differences in these indices between sd-aMCI and md-aMCI patients.

Regarding RTs, RMANOVA indicated significant main effects of trial-type, stimulus-type and group on RTs [trial-type: F (1, 82) = 38.089, $p < 0.001$, stimulus-type: F (1, 82) = 34.869, $p < 0.001$, group: F (2, 82) = 6.365, $p = 0.003$]. Post-hoc simple main effect analysis with Bonferroni correction showed prolonged RTs with non-target and target stimuli in 1-back task in both md-aMCI and sd-aMCI patients, compared to HEC [non-target stimuli: md-aMCI: (825.60 ± 147.68) ms vs. HEC: (662.41 ± 86.00) ms, $p = 0.006$; sd-aMCI: (819.80 ± 209.98) ms vs. HEC: (662.41 ± 86.00) ms, $p = 0.019$; target stimuli: md-aMCI: (974.46 ± 141.62) ms vs. HEC: (800.40 ± 124.08) ms, $p = 0.003$; sd-aMCI: (973.08 ± 202.65) ms vs. HEC: (800.40 ± 124.08) ms, $p = 0.015$]. However, no significant difference in this index was revealed between sd-aMCI and md-aMCI patients.

3.2.2. Go/Nogo task

RMANOVA indicated significant main effects of trial-type, group [trial-type: F (1, 82) = 290.56, $p < 0.001$; group: F (2, 82) = 226.99, $p < 0.001$] and a significant interaction effect of the two factors [F (2, 82) = 3.765, $p = 0.028$] on ER. Post-hoc simple main effect analysis with Bonferroni correction indicated elevated FAR in both md-aMCI and sd-aMCI patients, compared to HEC [FAR: md-aMCI: (10.35 ± 0.98) % vs. HEC: (6.90 ± 1.59) %, $p = 0.005$; sd-aMCI: (9.85 ± 1.68) % vs. HEC: (6.90 ± 1.59) %, $p = 0.004$; ER: md-aMCI: (5.31 ± 2.81) % vs. HEC: (0.50 ± 1.67) %, $p = 0.006$; sd-aMCI: (3.65 ± 0.98) % vs. HEC: (0.50 ± 1.67) %, $p = 0.005$], whereas no significant difference was revealed between sd-aMCI and md-aMCI patients.

Table 1

Demographic data, neuropsychological performance and behavioral data for all subjects. Significant difference was indicated between three groups.

	HEC (n = 46)	sd-aMCI (n = 26)	md-aMCI (n = 13)	F or probability	p-value
Age (years)	70.17 (5.623)	71.15 (5.662)	71.54 (6.802)	0.401	0.671
Gender (Male/Female)	21/25	16/10	9/4	3.100	0.212
Education level (years)	12.22 (2.956)	10.81 (2.825)	10.81 (3.250)	2.390	0.098
MMSE scores	28.43 (1.294)	27.31 (1.934)	26.62 (2.434)	7.360	0.001[*, b]
MDRS-2 scores	137.54 (3.111)	135.81 (4.391)	132.92 (6.677)	6.371	0.003[*, b]
CDR	0	0.5	0.5	–	–
Memory function					
AVLT-20 min DR	6.02 (1.844)	1.96 (1.536)	1.85 (2.075)	55.159	< 0.001[*, a, b]
ROCFT-20 min DR	17.80 (6.691)	12.79 (6.650)	11.46 (6.276)	7.349	0.001[*, a, b]
LMT-20 min DR	6.71 (2.382)	4.12 (3.244)	4.19 (2.905)	9.194	< 0.001[*, a, b]
Memory (Z score)	0.47 (0.541)	−0.49 (0.611)	−0.64 (0.631)	33.016	< 0.001[*, a, b]
Attention					
DSST	36.11 (10.067)	33.83 (8.432)	27.77 (8.064)	4.081	0.020[*, b, c]
TMT Part A time (second)	64.74 (16.879)	77.38 (31.765)	99.46 (35.032)	10.319	< 0.001[*, b, c]
Stroop A (second)	26.48 (5.726) 64.74 (16.879)	29.88 (6.421)	31.38 (5.516)	4.877	0.010[*, b]
Stroop B (second)	44.02 (12.755)	44.72 (9.190)	53.75 (9.411)	3.607	0.032[*, b]
Attention (Z score)(z score)score)	0.19 (0.832)	−0.04 (0.621)	−0.56 (0.542)	5.248	0.007[*, b, c]
Executive function					
DST-backward	4.98 (1.856)	4.19 (1.856)	3.85 (1.144)	3.378	0.039[*, b]
Stroop C (second)	81.57 (32.362)	85.84 (17.813)	115.92 (45.282)	5.884	0.004[*, b, c]
TMT Part B time (second)	166.39 (52.021)	187.46 (59.955)	237.77 (72.305)	7.793	0.001[*, b, c]
Similarity	19.67 (4.908)	17.23 (3.362)	14.38 (2.959)	8.720	< 0.001[*, b]
VFT	43.41 (8.350)	40.12 (6.872)	37.23 (7.907)	3.705	0.029[*, b]
Executive function (Z score)	0.22 (0.651)	−0.09 (0.422)	−0.53 (0.531)	9.350	< 0.001[*, b, c]
Visuospatial function					
ROCFT	35.52 (0.937)	34.77 (1.608)	33.85 (2.193)	8.209	0.001[*, b]
CDT	27.85 (2.357)	26.37 (2.744)	24.27 (2.743)	8.028	0.001[*, b]
Visuospatial function (Z score)	0.23 (0.477)	−0.01 (0.392)	−0.50 (0.821)	9.313	0.001[*, b]
Language					
PNT	9.30 (0.840)	9.08 (1.017)	8.15 (1.908)	5.436	0.006[*, b, c]
Language (Z score)	0.21 (0.719)	0.02 (0.870)	−0.77 (1.633)	5.436	0.006[*, b, c]
Behavioral profiles in 0-back task					
Target-ER (%)	13.41 (12.190)	17.77 (21.500)	19.12 (17.370)	1.241	0.295
Target-RTs (ms)	694.96 (100.840)	736.49 (186.010)	765.10 (147.830)	1.849	0.165
Non-target -FAR (%)	6.72 (6.692)	10.62 (10.830)	15.31 (16.250)	4.146	0.019[*, b]
Non-target-RTs (ms)	653.38 (89.282)	731.10 (165.730)	736.55 (202.330)	2.627	0.080
Behavioral profiles in 1-back task					
Target-ER (%)	22.77 (11.927)	32.53 (19.205)	40.43 (22.170)	4.511	0.015[*, b]
Target-RTs (ms)	875.50 (149.150)	937.60 (189.840)	973.08 (202.650)	2.315	0.106
Non-target -FAR (%)	17.20 (13.010)	25.12 (18.917)	31.77 (22.046)	4.673	0.012[*, b]
Non-target-RTs (ms)	691.78 (106.786)	792.24 (185.633)	819.80 (209.982)	3.925	0.025[*, b]
Behavioral profiles in Go/Nogo task					
Go-ER (%)	2.70 (14.520)	3.65 (0.982)	5.31 (2.810)	0.294	0.746
FAR (%)	6.90 (1.590)	9.85 (1.676)	10.35 (0.982)	49.284	< 0.001[*, b]
RTs (ms)	334.06 (50.703)	366.97 (50.703)	378.32 (38.755)	7.011	0.002[*, b]

Data are presented as mean ± SD.

Notes: *p* value of gender was obtained by Fisher's exact probability tests; *p* values for comparison in other demographic data, neuropsychological performance and behavioral data were acquired by one-way ANOVA with post-hoc Bonferroni tests; *indicates statistical difference between groups, *p* < 0.05. Post hoc Bonferroni tests showed significant group differences between [a]HEC and sd-aMCI patients, [b]HEC and md-aMCI patients, [c]sd-aMCI and md-aMCI patients. Abbreviations: ANOVA, analysis of variance; AVLT-20-min DR, Auditory Verbal Learning Test-20-min Delayed Recall; CDR, clinical dementia rating; CDT, Clock Drawing Test; DSST, Digit Symbol Substitution Test; DST, Digital Span Test; ER, error rate; FAR, false alarm rate; HEC, healthy elderly controls; LMT-20-min DR, Logical Memory Test-20-min delayed recall; MDRS-2, Mattis dementia rating scale-2; md-aMCI, multiple-domain amnestic mild cognitive impairment; MMSE, Mini-Mental State Exam; PNT, Picture Naming Test; ROCFT, Rey-Osterrieth Complex Figure Test; ROCFT-20-min DR, ROCFT-Delayed-20-min Recall; RTs, reaction times; SD, standard deviation; sd-aMCI, single-domain amnestic mild cognitive impairment; Similarity, Semantic Similarity Test; TMT, Trail Making Tests; VFT, Verbal Fluency Test.

One-way ANOVA indicated significant main effect of group on RTs during Go/Nogo task [F (2, 82) = 7.011, p = 0.002]. Additionally, post-hoc Bonferroni tests revealed prolonged RTs in md-aMCI patients, compared to HEC (All p < 0.05). However, no significant difference was detected between sd-aMCI and md-aMCI patients.

3.3. ERP results

3.3.1. VSWM task

Fig. 3 A showed grand-average ERP waveforms for HEC, sd-aMCI and md-aMCI groups, in the 0- and 1-back task, at P1 (a), Pz (b) and P2 (c) electrodes.

RMANOVA detected significant main effects of trial-type and group on P300 amplitude during VSWM task [trial-type: F (2, 82) = 9.104, p = 0.003; group: F (2, 82) = 6.393, p = 0.003]. No significant interaction effects were indicated in our study. Post-hoc simple main effect analysis with Bonferroni correction indicated that md-aMCI patients showed decreased P300 amplitude at P1, P2 electrodes in 0-back task and P1, Pz and P2 electrodes in 1-back task, compared to HEC (All p < 0.05, see Table 2 and Fig. 3B). Additionally, post-hoc simple main effect analysis with Bonferroni correction detected decreased P300 amplitude in md-aMCI at P2 electrode in 1-back task, with respect to sd-aMCI patients (p < 0.05, see Table 2 and Fig. 3B). However, no significant difference was detected between sd-aMCI and HEC. Moreover, no main
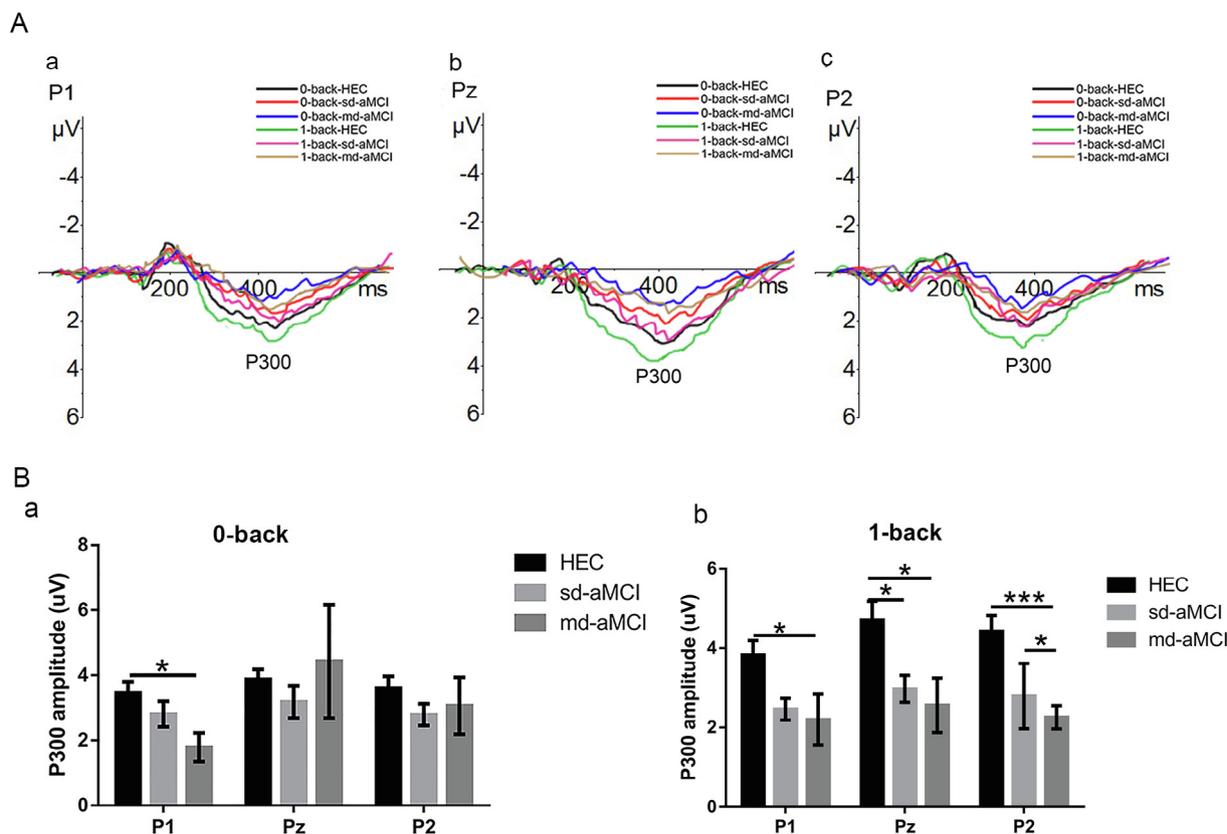
Fig. 3. A. Grand-average ERP waveforms for HEC, sd-aMCI and md-aMCI groups, in the 0- and 1-back task, at P1 (a), Pz (b) and P2 (c) electrodes. Group differences in P300 amplitude could be clearly seen in both 0- and 1-back tasks (decreased P300 amplitude in md-aMCI group, compared to HEC). B. P300 amplitude comparison at P1, Pz and P2 electrodes in the 0-back (a) and the 1-back (b) conditions between HEC, sd-aMCI and md-aMCI patients. It revealed that md-aMCI patients showed significantly decreased P300 amplitudes at P1 electrode in 0-back task and at P1, Pz and P2 electrodes in 1-back task, compared to HEC. In addition, sd-aMCI showed decreased P300 amplitude at Pz electrode in 1-back task, compared to HEC. Values were shown as the mean ± SE, $^*p < 0.05$, $^{***}p < 0.001$. Abbreviations: ERP, event-related potential; HEC, healthy elderly controls; md-aMCI, multiple-domain amnestic mild cognitive impairment; sd-aMCI, single-domain amnestic mild cognitive impairment; SE, standard error.

effects or interaction effects on P300 latency reached the significant level.

Table 3 showed comparison of source localization between HEC, sd-aMCI and md-aMCI during VSWM tasks with sLORETA. The sLORETA indicated that md-aMCI patients showed a hypoactivation in the right superior frontal gyrus (SFG, BA 8) compared to HEC in both 0-back and 1-back tasks during P300 time range (see Fig. 4A and B). In addition, it revealed a hypoactivation in

the right middle frontal gyrus (MFG, BA 8) in md-aMCI patients compared to sd-aMCI patients in this comparison (see Fig. 4C).

3.3.2. Go/Nogo task

Fig. 5A showed grand-average ERP waveforms for HEC, sd-aMCI and md-aMCI groups, in the Nogo and the Go conditions, at Fz (a), Cz (b) and Pz (c) electrodes.

Table 2
ERP data (N200 and P300 amplitude) for HEC, sd-aMCI and md-aMCI patients during VSWM and Go/Nogo tasks.

Condition	Electrode	HEC (n = 46)	sd-aMCI (n = 26)	md-aMCI (n = 13)
0-back	P1	3.47 (2.19)	2.81 (2.01)	1.79 (1.52)[b]
	Pz	3.99 (2.12)	3.26 (2.97)	2.47 (2.64)
	P2	4.02 (2.47)	3.17 (1.69)	2.05 (1.61)[b]
1-back	P1	3.96 (2.27)	3.15 (1.00)	2.19 (1.64)[b]
	Pz	4.42 (2.25)	3.45 (1.97)	2.19 (1.39)[b]
	P2	4.23 (2.71)	3.99 (1.05)	2.26 (1.28)[b,c]
Nogo	Fz	−4.37 (2.21)	−3.83 (1.88)	−2.49 (1.54)[b]
	Cz	−4.20 (1.92)	−3.34 (2.26)[a]	−2.61 (1.28)[b]
	Pz	−3.99 (1.32)	−3.32 (1.27)	−2.28 (0.93)[b]
Go	Fz	−3.41 (1.57)	−2.82 (1.11)	−2.05 (0.92)[b]
	Cz	−3.07 (1.56)	−2.43 (0.64)	−1.84 (0.59)[b,c]
	Pz	−2.67 (0.91)	−2.31 (0.56)	−1.87 (0.73)[b]

Data are presented as mean ± SD.
Note: ERP data were analysed by RMANOVA with post hoc simple main effect analysis; Post hoc simple main effect analysis with Bonferroni correction showed significant group differences between [a]HEC and sd-aMCI patients, [b]HEC and md-aMCI patients.
Abbreviations: aMCI, amnestic mild cognitive impairment; ERP, event-related potential; HEC, healthy elderly controls; md-aMCI, multiple-domain amnestic mild cognitive impairment; RMANOVA, repeated measures analysis of variance; SD, standard deviation; sd-aMCI, single-domain amnestic mild cognitive impairment; VSWM, visuospatial working memory.

Table 3
Comparison of source localization between HEC, sd-aMCI and md-aMCI in VSWM tasks with sLORETA.

Items	MNI coordinates			Brodmann area	Brain region	Log of ratio of average	p-Value
	x	y	z				
md-aMCI vs. HEC (0-back)	15	30	55	8	Superior Frontal Gyrus	−2.81	0.04160
md-aMCI vs. HEC (1-back)	40	20	55	8	Superior Frontal Gyrus	−2.91	0.03560
md-aMCI vs. sd-aMCI (1-back)	35	30	50	8	Middle Frontal Gyrus	−2.62	0.04780

Abbreviations: HEC, healthy elderly controls; md-aMCI, multiple-domain amnestic mild cognitive impairment; MNI, Montreal Neurological Institute; sd-aMCI, single-domain amnestic mild cognitive impairment; sLORETA, standardized low-resolution brain electromagnetic tomography analysis; VSWM, visuospatial working memory.

RMANOVA indicated significant main effects of trial-type, electrode and group on N200 amplitude in Go/Nogo task [trial-type: F (1, 82) = 46.703, $p < 0.001$; electrode: F (2, 82) = 4.212, $p = 0.022$; group: F (2, 82) = 9.341, $p < 0.001$]. No interaction effects reached the level of significance. Post hoc simple main effect analysis with Bonferroni correction indicated that md-aMCI patients showed deceased Nogo-N200 amplitudes at Fz and Pz electrodes and Go-N200 amplitude at Fz, Cz and Pz electrodes, compared to HEC (All $p < 0.05$; see Table 2 and Fig. 5B). As compared to sd-aMCI patients, md-aMCI patients showed reduced Go-N200 amplitude at Cz electrode. In addition, it indicated reduced Nogo-N200 amplitude at Pz electrode in sd-aMCI, with respect to HEC. Moreover, our study detected no significant main effects or interaction effects on N200 latency.

Regarding P300 amplitude, RMANOVA indicated that significant main effects of trial-type and electrode in Go/Nogo task [trial-type: F (1, 82) = 6.684, $p = 0.019$; electrode: F (2, 82) = 4.272, $p = 0.046$]. However, no main effect of group and interaction effects reached level of significance. In addition, not any significant main or interaction effects were detected in P300 latency.

Table 4 showed comparison of source localization between HEC, sd-aMCI and md-aMCI in Go/Nogo tasks with sLORETA. sLORETA indicated that md-aMCI showed a hypoactivation in the right medial frontal gyrus (MFG, BA 9) relative to HEC in both Nogo and Go task during N200 time range (see Fig. 6A and C). Md-aMCI showed a hypoactivation in the right superior frontal gyrus (SFG, BA 10) compared to sd-aMCI in both Nogo and Go task during N200 time range (see Fig. 6B and D). In addition, md-aMCI showed a hypoactivation in the right SFG (BA 8) compared to sd-aMCI in Go task during P300 time range (see Fig. 6E).

3.4. ROC curves to discriminate between md-aMCI patient from HEC and sd-aMCI patients

Fig. 7 illustrated ROC curves to discriminate between md-aMCI patient from HEC and sd-aMCI patients with largest AUC for the different types of data (neurophysiological data, behavioral data and ERP data), respectively. For the model, the maximal CI was <10, which indicated the absence of significant multi-collinearity between these predictor variables. For executive function and combination of visuospatial executive function, episodic memory, information processing speed and executive function, AUC was 0.803 and 0.834 (negative cases: HEC, sd-aMCI; positive cases: md-aMCI), respectively. AUC was 0.811 and 0.871 respectively for ER for Go stimuli and combination of ER for Go stimuli and ER for target stimuli in 1-back task. In addition, for P300 amplitude in 1-back task and combination of P300 amplitude in 1-back task and Go-N200 amplitude, AUC was 0.837 and 0.927, respectively. It indicated that ROC curves for combination of P300 amplitude in 1-back task and Go-N200 amplitude showed the largest AUC. For the parameter, considering 0.39 as the predicted probability cut-off point, the indexes of sensitivity and specificity were 0.97 and 0.89, respectively.

4. Discussion

The present investigation detected decreased P300 amplitude in md-aMCI patients during VSWM task, compared to HEC and sd-aMCI patients. In addition, sLORETA models showed that md-aMCI showed a hypoactivation in the right SFG (BA 8) during the P300 time range in 0-back and 1-back tasks, compared to HEC. Moreover, md-aMCI patients showed a hypoactivation in the right MFG (BA 8) during the P300 time range in 1-back task, compared to sd-aMCI patients. During the Go/Nogo task, both sd-aMCI and md-aMCI patients showed reduced N200 amplitude, compared to HEC. As compared to sd-aMCI patients, md-aMCI patients showed reduced Go-N200 amplitude at Cz electrode. Additionally, md-aMCI presented a hypoactivation respectively in the right MFG (BA 9) compared to HEC and in the right SFG (BA 10) compared to sd-aMCI patients during the N200 time range in both Nogo and Go tasks.

It was reported that md-aMCI patients showed reduced P300 amplitude compared to HEC during VSWM task. According to previous studies, P300 originates from attention-driven WM changes and updating operation of WM (Papageorgiou et al., 2002, Polich, 2007). Corresponding to our investigation, previous studies revealed reduced P300 amplitude during WM task in aMCI patients, compared to HEC (Newsome et al., 2013, Li et al., 2016). In addition, sLORETA indicated that md-aMCI patients showed a hypoactivation in the right SFG (BA 8), compared to HEC. Frontal activation is associated with WM maintenance (Wager and Smith, 2003). In addition, a voxel-based morphometry (VBM) study indicated that md-aMCI patients showed gray matter (GM) atrophy in the parietal association cortex (Li and Zhang, 2015). Moreover, Shu et al. (Shu et al., 2012) revealed connectivity impairment in the frontal cortices in md-aMCI with diffusion tensor imaging (DTI). However, previous studies indicated no GM atrophy or white matter abnormality or abnormal resting-state brain activation in frontal cortex in sd-aMCI patients (Whitwell et al., 2007, Shu et al., 2012, Li et al., 2014). The present sLORETA study showed no significant differences in brain activation between sd-aMCI patients and HEC during P300 time range. However, the present study indicated that md-aMCI patients showed decreased P300 amplitude, compared to sd-aMCI patients. Moreover, md-aMCI patients showed a hypoactivation in the right MFG (BA 8) during P300 time range, compared to sd-aMCI patients. These results supported that md-aMCI showed more severe deficits in updating operation of WM, compared to sd-aMCI patients.

The present study showed reduced N200 amplitude in md-aMCI patients and sd-aMCI patients compared to HEC during Go/Nogo task. Nogo-N200 is related to pre-motor inhibition processes (Falkenstein et al., 1999) or conflict processes (Nieuwenhuis et al., 2003), whereas Go-N200 is associated with detection of the target stimulus and reflects selective attention processes com-
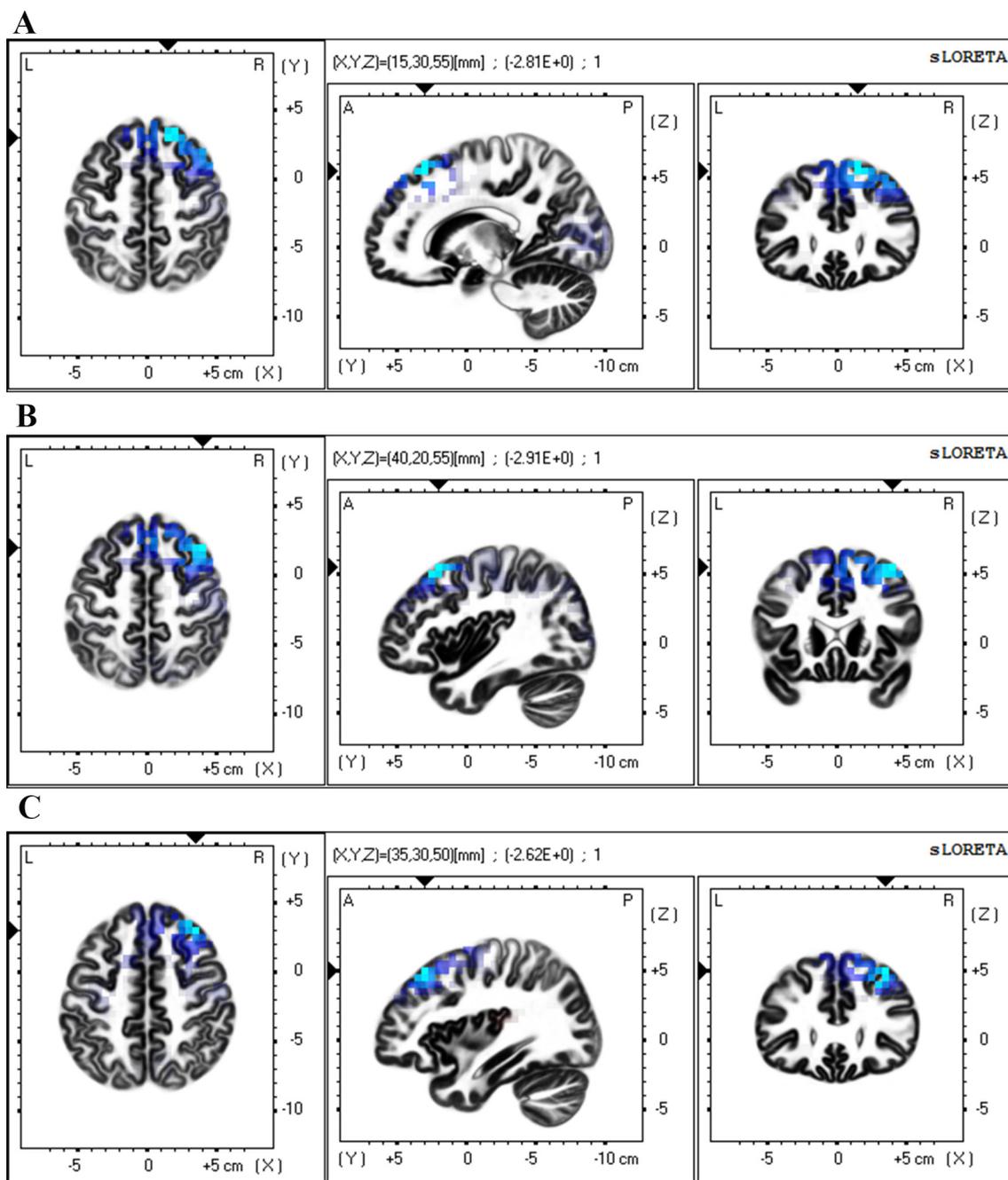
Fig. 4. The sLORETA images showing statistical differences in P300 in the 0-back and 1-back tasks between different groups during VSWM task (3D-view and slice-view). A. The three slice-view images located the maximal difference in P300 between md-aMCI and HEC (MNI coordinates x, y, z = 15, 30, 55) in 0-back task. Negative difference was in blue color with reference of P300 in HEC in 0-back task. B. The three slice-view images located the maximal difference in P300 between md-aMCI and HEC (MNI coordinates x, y, z = 40, 20, 55) in 1-back task. Negative difference was in blue color with reference of P300 in HEC in 1-back task. C. The three slice-view images located the maximal difference in P300 between md-aMCI and sd-aMCI (MNI coordinates x, y, z = 35, 30, 50) in 1-back task. Negative difference was in blue color with reference of P300 in sd-aMCI in 1-back task. Abbreviations: HEC, healthy elderly controls; md-aMCI, multiple-domain amnestic mild cognitive impairment; MNI, Montreal Neurological Institute; sd-aMCI, single-domain amnestic mild cognitive impairment; sLORETA, standardized low-resolution brain electromagnetic tomography analysis; VSWM, visuospatial working memory; 3D, three dimensional.

ing into action (Bennys et al., 2007). Recently, Cid-Fernandez et al. (Cid-Fernandez et al., 2014) detected a consistent result with our result that aMCI patients showed decreased N200 amplitude during the Go/Nogo task, compared to HEC. Our study indicated that sd-aMCI showed decreased Go-N200 amplitude at the Cz electrode, compared to HEC. It revealed early N200 alteration prior to deficits in task performance (reflected by ER, FAR and RTs) in sd-aMCI patients, which is quite different from another ERP study with a

Simon task (Cespon et al., 2013). Up to now, no study explored ERP component alterations in both sd-aMCI and md-aMCI during Go/Nogo task. We believe this finding still demanded further investigations to clarify the ERP alterations during the Go/Nogo task. The present study indicated a hypoactivation in the right MFG (BA 9), a source region of Go-N200 and Nogo-N200 (Tian and Yao, 2008), in md-aMCI patients compared to HEC in both Nogo and Go task during N200 time range. It revealed that defi-
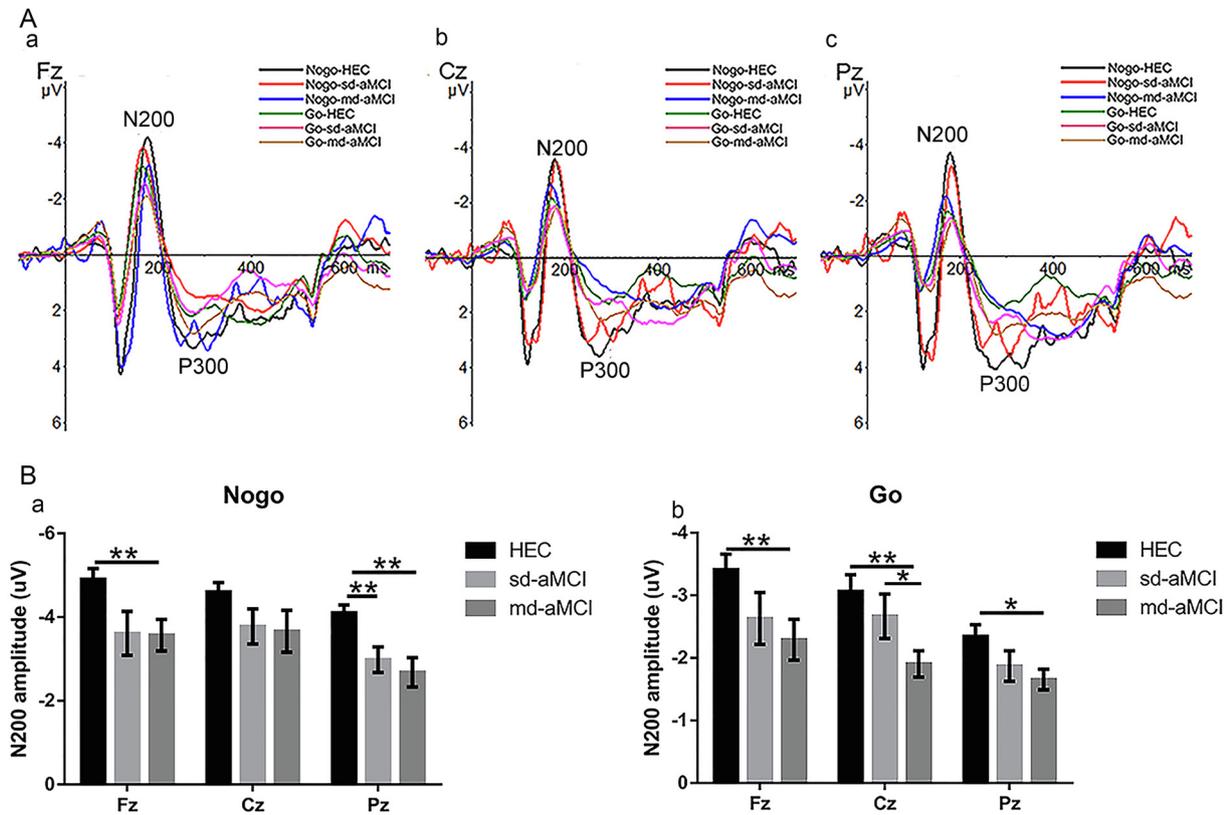
Fig. 5. A. Grand-average ERP waveforms for HEC, sd-aMCI and md-aMCI groups, in the Nogo and the Go conditions, at Fz (a), Cz (b) and Pz (c) electrodes. Group differences could be clearly seen for both Nogo-N200 and Go-N200 (decreased P300 amplitude in md-aMCI group, compared to HEC). B. N200 amplitude comparison at Fz, Cz and Pz electrodes in the Nogo (a) and the Go (b) conditions between HEC, sd-aMCI and md-aMCI patients. It showed deceased Nogo-N200 amplitudes at Fz, Pz electrodes and Go-N200 amplitudes at Fz, Cz, Pz electrodes in md-aMCI patients, compared to HEC. In addition, it showed decreased Nogo-N200 amplitudes at Pz electrode in sd-aMCI, compared to HEC. Values were shown as the mean ± SE, $^*p < 0.05$, $^{**}p < 0.01$. Abbreviations: ERP, event-related potential; HEC, healthy elderly controls; md-aMCI, multiple-domain amnestic mild cognitive impairment; sd-aMCI, single-domain amnestic mild cognitive impairment; SE, standard error.

Table 4
Comparison of source localization between HEC, sd-aMCI and md-aMCI in Go/Nogo tasks with sLORETA.

Items	MNI coordinates			Brodmann area	Brain region	Log of ratio of average	*p*-Value
	x	y	z				
N200							
Nogo (HEC vs. md-aMCI)	20	40	20	9	Medial Frontal Gyrus	2.67	0.04860
Nogo (sd-aMCI vs. md-aMCI)	25	45	25	10	Superior Frontal Gyrus	2.96	0.04380
Go (HEC vs. md-aMCI)	20	35	25	9	Medial Frontal Gyrus	3.18	0.02080
Go (sd-aMCI vs. md-aMCI)	25	45	25	10	Superior Frontal Gyrus	3.25	0.01400
P300							
Go (sd-aMCI vs. md-aMCI)	20	35	45	8	Superior Frontal Gyrus	2.76	0.03120

Abbreviations: HEC, healthy elderly controls; md-aMCI, multiple-domain amnestic mild cognitive impairment; MNI, Montreal Neurological Institute; sd-aMCI, single-domain amnestic mild cognitive impairment; sLORETA, standardized low-resolution brain electromagnetic tomography analysis.

cient Go-N200 and Nogo-N200 in md-aMCI might be derived from hypoactivation in the right MFG. Neuroimaging studies supported our results that GM atrophy is detected in the MFG in individuals with MCI compared to HEC (Twamley et al., 2006). In addition, our result revealed that md-aMCI patients showed decreased Nogo-N200, Go-N200 and a hypoactivation in the right SFG (BA 10) compared to sd-aMCI in both Nogo and Go task during N200 time rage and in Go task during P300 time range. Zhang et al. (2012) supported our result that their study indicates GM atrophy in the bilateral frontal lobes in md-aMCI compared to sd-aMCI patients with a VBM study. Moreover, the present study detected that ROC curves for combination of P300 amplitude in 1-back task and Go-N200 amplitude showed the largest AUC (0.927), which

supported that P300 amplitude during VSWM task and N200 amplitude during Go/Nogo task could work as a sensitive and specific biomarker for identifying sd-aMCI and md-aMCI patients.

There are some limitations to our study. Firstly, the small sample size might limit the generalization of our findings. Secondly, the present study was a cross-sectional study; longitudinal studies are needed to predict progression of aMCI subtypes to AD. Thirdly, source localization with sLORETA lacks high spatial resolution, simultaneous ERP-fMRI might solve the problem. Lastly, further investigations were needed to explore ERP and sLORETA alterations in sd-aMCI and md-aMCI in other cognitive domains to support our results.
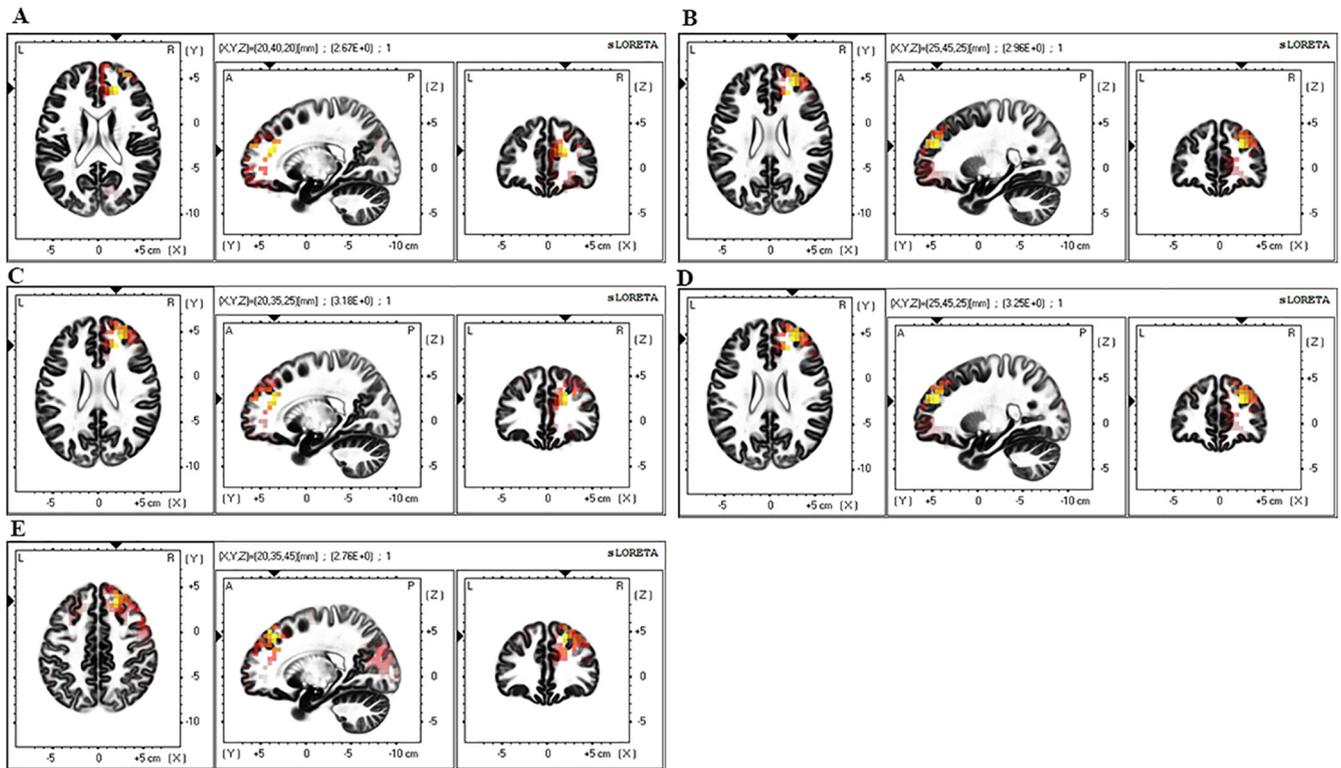
Fig. 6. The sLORETA images showing statistical differences in Nogo-N200, Go-N200 and Go-P300 between different groups during Go/Nogo task (3D-view and slice-view). A. The three slice-view images located the maximal difference in Nogo-N200 between HEC and md-aMCI (MNI coordinates x, y, z = 20, 40, 20). Positive difference was in yellow color with reference of Nogo-N200 in md-aMCI. B. The three slice-view images located the maximal difference in Nogo-N200 between sd-aMCI and md-aMCI (MNI coordinates x, y, z = 25, 45, 25). Positive difference was in yellow color with reference of Nogo-N200 in md-aMCI. C. The three slice-view images located the maximal difference in Go-N200 between HEC and md-aMCI (MNI coordinates x, y, z = 20, 35, 25). Positive difference was in yellow color with reference of Go-N200 in md-aMCI. D. The three slice-view images located the maximal difference in Go-N200 between sd-aMCI and md-aMCI (MNI coordinates x, y, z = 25, 45, 25). Positive difference was in yellow color with reference of Go-N200 in md-aMCI. E. The three slice-view images located the maximal difference in Go-P300 between sd-aMCI and md-aMCI (MNI coordinates x, y, z = 20, 35, 45). Positive difference was in yellow color with reference of Go-P300 in md-aMCI. Abbreviations: md-aMCI, multiple-domain amnestic mild cognitive impairment; MNI, Montreal Neurological Institute; sd-aMCI, single-domain amnestic mild cognitive impairment; sLORETA, standardized low-resolution brain electromagnetic tomography analysis; 3D, three dimensional.
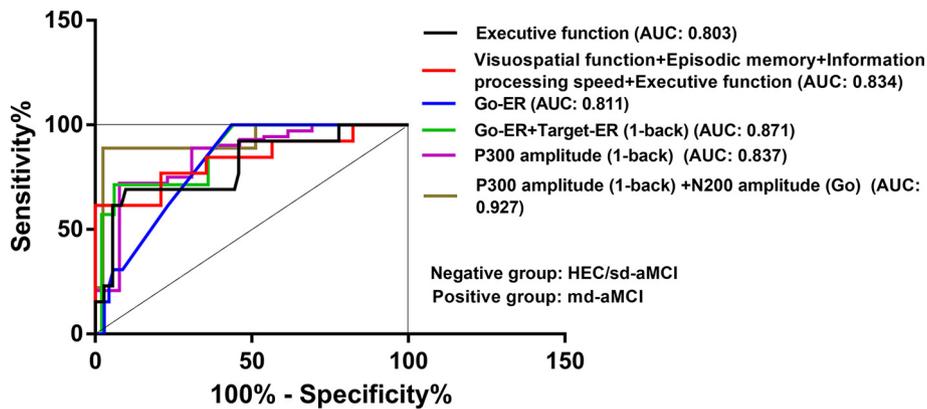
Fig. 7. ROC curves are represented for executive function (black line), combination of visuospatial working memory, episodic memory, information processing speed and executive function (red line), ER for Go stimuli during Go/Nogo task (blue line), combination of ER for Go stimuli and ER for target stimuli in 1-back task (green line), P300 amplitude in 1-back task (purple line) and combination of P300 amplitude in 1-back task and Go-N200 amplitude (brown line). For each curve and parameter, ROC analyses included those groups showing significant differences between them. In the ROC analyses, negative groups include the HEC and sd-aMCI patients. Positive groups include md-aMCI patients. Abbreviations: ER, error rate; HEC, healthy elderly controls; ROC, receiver operating characteristics. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

5. Conclusion

The present study with a combined ERP and sLORETA study revealed more serious deficits in updating operations of WM, detections of the target stimulus and conflict processes in md-aMCI, compared to sd-aMCI patients.

Acknowledgements

Conflict of interest

None of the authors have potential conflicts of interest to be disclosed.

Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.clinph.2019.01.025.

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