CORTICAL FUNCTION IN ALZHEIMER’S DISEASE AND FRONTOTEMPORAL DEMENTIA

Abstract
Objectives: Alzheimer’s disease (AD) and the behavioral variant of frontotemporal dementia (bvFTD) are the most common causes of dementia; however, their overlapping clinical syndromes and involved brain regions make a differential diagnosis difficult. We aimed to identify the differences in the cognition and motor cortex excitability between AD and bvFTD patients. Methods: Twenty-seven AD patients and 30 bvFTD patients were included in the study. Each participant received a neurological evaluation. Cognitive event-related potentials (P300) were recorded during an auditory oddball task. Next, the excitability of the motor cortex, including the resting, facilitated motor threshold (RMT and FMT) and cortical silent period (CSP), were assessed during transcranial magnetic stimulation (TMS). Results: The bvFTD patients exhibited significantly longer P300 latencies compared with AD patients. There was a significant negative correlation between cognition and P300 latency in the bvFTD group. The AD patients showed significantly reduced RMT and FMT values compared to the bvFTD group; however, no significant correlation was found between AD severity and the excitability of the motor cortex. Conclusions: Cognition and motor cortical functions are different between AD and bvFTD patients. Non-invasive electrophysiological examinations have the potential to identify unique pathophysiological features that can be used to differentially diagnose AD and bvFTD patients.

Keywords
Alzheimer’s disease (AD) • Behavioral variant of frontotemporal dementia (bvFTD) • Cortical function • Event-related potentials (ERP) • Transcranial magnetic stimulation (TMS)
global cognition using the Mini-Mental State Examination (MMSE) and 30 bvFTD patients. We evaluated their cognitive and potential features of AD and bvFTD. We recruited 27 AD patients and 30 bvFTD patients for our study. We used ERPs and TMS to assess the cortical and subcortical functions related to AD and bvFTD. Therefore, the different behavioral and cognitive functions between AD and bvFTD patients that explain the different clinical presentations of these two types of dementia require further verification.

We hypothesized that there are differences in the cognition and motor cortex excitability between AD and bvFTD patients that explain the different behavioral and cognitive features of each type of dementia. Therefore, we used ERPs and TMS to assess the cortical features of AD and bvFTD. We recruited 27 AD and 30 bvFTD patients for our study. We evaluated their global cognition using the Mini-Mental State Examination (MMSE) and Montreal Cognitive Assessment (MoCA) scores. In addition, we assessed their clinical severity using the Clinical Dementia Rating (CDR), determined their cognitive cortical functioning based on the P300 latency and amplitude, and measured their motor cortex excitability using the resting motor threshold (RMT), facilitated motor threshold (FMT) and cortical silent period (CSP).

**Experimental procedures**

**Standard protocol approvals, registration, and patient consent**

This study was approved by the Medical Ethics Committee of Tianjin Huanhu Hospital. Written informed consent was obtained from each enrolled subject or his/her authorized guardian. The participants underwent general physical, psychological and laboratory examinations and biological samples were collected prior to enrollment in the study. At the time of recruitment, none of the subjects were taking cholinomimetic agents, antidepressants, neuroleptics, or sedative-hypnotic drugs for at least one week prior to the assessment, and all patients received professional suggestions for further treatment.

**Subjects**

The subjects were recruited from the outpatients of Tianjin Huanhu Hospital between 2011 and 2014. The recruited AD patients were diagnosed using the National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer's Disease and Related Disorders Association criteria for probable AD [35, 36]. The diagnosis of bvFTD was based on the clinical criteria proposed by McKhann et al. and Neary et al. [37, 38]. The criteria for exclusion in the study included any significant neurological or psychiatric illness that can influence cognitive function and the presence of a significant unstable systemic illness or organ failure. All patients were subjected to evaluation on the severity of their cognitive deterioration and dementia by using the Mini-Mental State Examination (MMSE), Montreal Cognitive Assessment (MoCA), and Clinical Dementia Rating (CDR) scales. The MMSE is a brief measure of cognitive functioning, and it has high test-retest reliability, internal consistency and inter-rater reliability [39]. The MMSE consists of 11 items and has a maximum score of 30 and a cut-off score of 24 with a sensitivity of 87% and specificity of 82% [40]. The MoCA is a 30-point cognitive test consisting of executive function and attention tasks that were designed for individuals who scored 24-30 on the MMSE [41, 42]. Thus, we used the MMSE and MoCA as measures of general cognition. The CDR offers a global characterization of everyday functions that may be affected by the neurodegenerative disease and is a clinical scale developed to assess the presence and severity of dementia [43]. The CDR is a five-point scale in which CDR-0 denotes no cognitive impairment. The remaining four points represent various stages of dementia (0.5 = mild cognitive impairment, 1 = mild dementia, 2 = moderate dementia, 3 = severe dementia). In our study, all of the patients with dementia scored 1-2 on the CDR. In other words, we chose participants with mild- to moderate cognitive impairment. Due to the limited sample size, we did not create subgroups for disease severity.

A total of 80 subjects with cognitive impairment were enrolled in the study. Sixty-five subjects met the criteria for AD or bvFTD, and 15 subjects had other types of dementia. Eight subjects did not complete the ERP experiments. Thus, 27 AD patients and 30 bvFTD patients were included in the final analysis. The demographic and neuropsychological details of the participants are listed in Tables 1 and 2. The participants first underwent the ERP examination, and then completed the TMS examination 30 min later.

**ERP procedure**

The auditory oddball stimuli used were simple and easily gained the attention of the subjects. The oddball P300 is an indicator of memory function, and many studies have investigated the utility of auditory P300 for the assessment of AD [44-46]. A simple auditory two-tone discrimination (oddball paradigm) was used to elicit ERP responses. Five hundred tones (25-millisecond duration with a 1.5-second interstimulus interval) were binaurally presented through headphones in a pseudorandomized order. Targeted (2000 Hz, 100 dB) and non-targeted (1000 Hz, 100 dB)
tones appeared with a probability of 20% and 80%, respectively. The targeted stimulation superposition was 100 times. The stimulus display used was a DanTeC™ KEYPoiNT® G4 Workstation. Electroencephalograms (EEG) were recorded from two scalp derivations (central, Cz, and parietal, Pz) according to the international 10-20 standard. The guidelines written by Picton et al. state that ERPs can be adequately examined for clinical purposes using simple recording channels [13]. In support of a previous study [47], these authors also suggested that analyzing ERPs collected using simple recording channels [13]. In our study, we limited our study to ERPs at the Pz and Cz. Two linked electrodes were attached to the left and right earlobes (A1-A2) as a reference. Other electrodes were placed above and below the left eye to monitor eye movements, and one ground electrode was attached to the middle of the forehead.

Subjects were comfortably seated in an armchair in a sound-attenuated room and asked to relax, close their eyes, and minimize eye and mandibular movements during the recording. Subjects were requested to press a hand-held button when they detected a target stimulus. They were also requested to silently count the target tones, and report the total number of tones at the end of the session. The test was initiated only when the subject demonstrated a complete understanding of the task. All datasets with a 95% concordance between the number of stimuli presented and the total number of tones reported were used for further analysis.

The data were initially band-pass filtered between 0.2 and 20 Hz. The recording was initiated at 100 ms before stimulation to capture a baseline measurement. The recording was maintained for 900 ms thereafter. Next, eye movement components were removed using an algorithm [48]. After their removal, the remaining components were back-projected onto the EEG channels. The P300 amplitude was defined relative to the baseline period, which was set at the 100 ms level prior to stimulus onset. An automated peak-picking procedure was used to determine peak amplitudes and latencies. The P300 wave was defined as the maximum point between 300 and 600 ms after stimulus onset. Reaction times were not recorded for the oddball paradigm.

### TMS procedure
All participants were tested while lying comfortably in order to achieve complete relaxation. The EMG was monitored in the background using acoustic feedback before and during all TMS recordings. Magnetic stimulation was performed with a butterfly-shaped coil (loop diameter of 50 mm) connected with a single MagDuo Pro 30 Stimulator (MagVenture Inc., Alpharetta, GA, USA) through a MC-BT0 that discharged a maximum output of 2.5 T. Motor-evoked potentials (MEP) during the TMS were recorded from the abductor pollicis brevis (APB) via surface electrodes applied in a belly tendon pattern. The coil was placed 6 cm lateral to the Cz along the interlobe line, over the scalp region corresponding to the primary hand motor area and contralateral to the target muscle. In both AD and bvFTD groups, the TMS procedures were performed bilaterally.

The resting motor threshold (RMT) was defined as the minimal intensity required to elicit MEP with a 50 μV peak-to-peak amplitude in five out of ten consecutive trials. The facilitated motor threshold (FMT) was determined using the same method while subjects made their strongest muscle contraction. FMT was defined as the minimal intensity eliciting an MEP larger than 50 μV in five out of ten consecutive trials. All subjects were asked to perform approximately 100% of their maximal contraction while the electromyographic activity was recorded. Ten magnetic stimuli were applied at an intensity of

| Table 1. Demographic and clinical information of the study subjects. |
| --- | --- | --- | --- |
| AD (27) | bvFTD (30) | t value | P value |
| Sex, M/F (n) | 12/15 | 13/17 | 0.933 |
| Age (years) | 72.07 ± 1.62 | 68.13 ± 1.43 | 1.83 | 0.073 |
| Education (years) | 10.96 ± 0.77 | 11.10 ± 0.62 | -0.14 | 0.887 |
| MMSE | 19.85 ± 0.73 | 21.70 ± 0.87 | -0.16 | 0.113 |
| MoCA | 13.93 ± 0.90 | 14.47 ± 1.03 | -0.39 | 0.697 |

AD, Alzheimer’s disease; bvFTD, behavioral variant of frontotemporal dementia; M/F, male/female; MMSE, Mini-Mental State Examination; MoCA, Montreal Cognitive Assessment.

| Table 2. Normality of demographic, clinical and electrophysiological data for the AD and bvFTD groups. |
| --- | --- | --- | --- |
| AD | bvFTD | Kolmogorov-Smirnov | P value |
| Age (years) | 72.07 ± 1.62 | 68.13 ± 1.43 | 0.254 | 0.616 |
| Education (years) | 10.96 ± 0.77 | 11.10 ± 0.62 | 0.770 | 0.384 |
| MMSE | 19.85 ± 0.73 | 21.70 ± 0.87 | 1.290 | 0.261 |
| MoCA | 13.93 ± 0.90 | 14.47 ± 1.03 | 0.419 | 0.520 |
| P300-Pz Latency (ms) | 377.44 ± 7.35 | 400.97 ± 6.33 | 0.383 | 0.538 |
| Amplitude (μV) | 9.66 ± 1.71 | 8.86 ± 1.24 | 0.859 | 0.358 |
| P300-Cz Latency (ms) | 378.63 ± 7.65 | 398.90 ± 6.33 | 0.804 | 0.374 |
| Amplitude (μV) | 9.87 ± 1.79 | 7.68 ± 1.25 | 0.832 | 0.366 |
| RMT (%) | 44.37 ± 1.27 | 49.83 ± 1.43 | 3.521 | 0.066 |
| FMT (%) | 30.89 ± 0.95 | 34.71 ± 0.97 | 1.177 | 0.283 |
| CSP (ms) | 157.10 ± 8.17 | 155.14 ± 4.93 | 3.103 | 0.084 |

AD, Alzheimer’s disease; bvFTD, behavioral variant of frontotemporal dementia; MMSE, Mini-Mental State Examination; MoCA, Montreal Cognitive Assessment; Cz, central; Pz, parietal; RMT, resting motor threshold; FMT, facilitated motor threshold; CSP, cortical silent period.
140% FMT. The cortical silent period (CSP) was defined as the time between the end of the MEP and the return of voluntary electromyographic activity, and ten consecutive responses were averaged.

Statistical analysis
Statistical analysis was performed using SPSS (version 18.0, released 2009, SPSS Inc., Chicago, IL, USA). For RMT, FMT, CSP, and P300 amplitude and latency, the Kolmogorov test was performed to evaluate continuity. Afterwards, t-tests were conducted to evaluate differences between the AD and bvFTD groups. P-values less than 0.05 were considered significant. To evaluate the relationship between cognitive performance (MMSE and MoCA) and electrophysiological parameters, Pearson’s correlation coefficients were calculated.

Results
Subject characteristics
The AD and bvFTD groups did not statistically differ in age (t = 1.83, p = 0.073), the number of years of education (t = -0.14, p = 0.887) or cognitive ability (MMSE: t = -1.61, p = 0.113; MoCA: t = -0.39, p = 0.697). The clinical data are provided in Table 1.

Cognitive cortical function
All subjects responded to the target tones of the auditory ERPs with greater than 95% accuracy. Among the ERP parameters measured in this study, the P300 latency in the bvFTD group was significantly longer than in the AD group at the Pz site (AD: 377.44 ± 7.35, bvFTD: 400.97 ± 6.33, t = -2.439, p = 0.018) and Cz site (AD: 378.63 ± 7.65, bvFTD: 398.90 ± 6.33, t = -2.057, p = 0.044). The AD group did not significantly differ from the bvFTD group in P300 amplitude at either site (Pz: t = 0.385, p = 0.701 and Cz: t = 1.102, p = 0.313). The data are shown in Table 3 and Fig. 1. Furthermore, we correlated the ERP parameters with the cognition scores (Supplementary Table 2, and Figs. 2 and 3). A negative correlation was found between the MoCA score and P300 latency within the bvFTD group (Pz: r = -0.371, p = 0.043 and Cz: r = -0.353, p = 0.056) but not the AD group. No correlation was found between the MMSE score

Table 3. Event-related potential latencies and amplitudes at Pz and Cz for the AD and bvFTD groups.

|                | AD (n = 27) | bvFTD (n = 30) | t value (two-tailed) | P value |
|----------------|------------|---------------|---------------------|---------|
| P300-Pz Latency (ms) | 377.44 ± 7.35 | 400.97 ± 6.33 | -2.439              | 0.018*  |
| Amplitude (μV)       | 9.66 ± 1.71 | 8.86 ± 1.24   | 0.385               | 0.701   |
| P300-Cz Latency (ms) | 378.63 ± 7.65 | 398.90 ± 6.33 | -2.057              | 0.044*  |
| Amplitude (μV)       | 9.87 ± 1.79 | 7.68 ± 1.25   | 1.102               | 0.313   |

AD, Alzheimer’s disease; bvFTD, the behavioral variant of frontotemporal dementia; Cz, central; Pz, parietal; *P, significant group differences (P < 0.05).

Figure 1. The latency and amplitude of P300. A. A bar chart of the latency of P300 between the AD and bvFTD groups. The latency of the bvFTD group is significantly different from that of the AD group at both Pz and Cz (P < 0.05). B. A bar chart of the amplitude of P300 between the AD and bvFTD groups. The amplitude of the bvFTD group is not different from that of the AD group at both Pz and Cz (P > 0.05). Abbreviations: AD, Alzheimer’s disease; bvFTD, behavioral variant of frontotemporal dementia.

Figure 2. Correlation between the P300 parameters and MMSE in both AD and bvFTD patients (P < 0.05). A. P300 P latency. B. P300 P amplitude. C. P300 C latency. D. P300 C amplitude. The AD patients are indicated by the blue circles and the bvFTD patients by the red circles. Abbreviations: AD, Alzheimer’s disease; bvFTD, behavioral variant of frontotemporal dementia; MMSE, Mini-Mental State Examination.
and P300 latency. No correlations between the P300 amplitude and cognitive scores were found.

Motor cortical function
There were no significant differences between the right and left hemispheres in any of the motor cortical excitability parameters (Table 4 and Fig. 4). Thus, the average of both hemispheres was used for the AD and bvFTD groups. The RMT and FMT were significantly lower in the AD group than the bvFTD group (RMT: 44.37 vs 49.83, t = -2.818, p = 0.007 and FMT: 30.84 vs 34.71, t = -3.548, p = 0.001) (Table 5). The CSP was not significantly different between groups (t = 0.212, p = 0.833). There was no correlation between MMSE/MoCA scores and the RMT and FMT in either group (Table 6, and Figs. 4 and 5).

Discussion
This study investigated two aspects of brain function involving the association cortex and motor cortex. The results showed that ERPs were decreased in bvFTD patients, as indicated by the longer P300 latency in the oddball task. In addition, the P300 latency may be useful to assess the severity of bvFTD. Our study confirmed that the excitability of the motor cortex during TMS was increased in AD patients, as demonstrated by the reduction in RMT and FMT. We suggest that the combination of ERP and TMS techniques may provide the key to understanding the pathophysiological mechanisms of AD and bvFTD.

The P300 wave is the most frequently recorded potential. The P300 latency is considered a measure of stimulus classification speed and is sensitive to task processing demands and cognitive abilities. The amplitude of the P300 is considered to be the manifestation of brain activity that reflects attention to incoming stimulus information [12]. Previous studies have shown decreased P300 amplitudes and increased P300 latencies in AD patients [3, 18, 23, 49, 50]. In recent years, the utility of P300 in bvFTD patients has been studied. Chen and colleagues found decreased P300 amplitudes and increased P300 latencies in bvFTD patients [5]. In this study, no significant differences were found in P300 latencies between AD and bvFTD groups (t = -0.171, p = 0.865).

Figure 3. Correlation between the P300 parameters and MoCA in both AD and bvFTD patients (P < 0.05). A. P300 Pz latency, B. P300 Pz amplitude, C. P300 Cz latency, D. P300 Cz amplitude. The AD patients are indicated by the blue circles and the bvFTD patients by the red circles. Abbreviations: AD, Alzheimer’s disease; bvFTD, behavioral variant of frontotemporal dementia; MoCA, Montreal Cognitive Assessment.

Figure 4. Bar graphs of TMS parameters in the left and right hemispheres. The bar graphs show no differences between the hemispheres within the AD and bvFTD groups (P > 0.05). A. RMT, B. FMT, C. CSP. Abbreviations: AD, Alzheimer’s disease; bvFTD, behavioral variant of frontotemporal dementia; CSP, cortical silent period; FMT, facilitated motor threshold; RMT, resting motor threshold; TMS, transcranial magnetic stimulation.
in FTD patients when compared with age-matched controls [23]. The abnormal P300 components may be due to changes in the brain regions associated with the P300. P300 generation involves a widespread network of cortical structures that overlap in AD and FTD, including parietal, temporal, and prefrontal cortices [51, 52].

Furthermore, recent studies analyzed the P300 component in FTD and AD patients. Jimenez-Escrig and colleagues found that the P300 latency of FTD patients was significantly longer compared with the AD group [22]. However, another study showed no difference between AD and bvFTD patients [23]. Interestingly, our study found that bvFTD patients had a longer P300 latency compared with AD patients. One reason for this discrepancy may be due to subject selection. FTD is rather heterogeneous clinical entity and shows variable clinical and neuropathological manifestations. We assessed only bvFTD patients. In contrast, patients with primary progressive aphasia and semantic dementia were included in the study by Jimenez-Escrig. The specific molecular pathologies and involved brain regions of different dementia subtypes may affect ERP parameters to some extent. Another explanation is that clinically diagnosed FTD can involve a mixed pathology of both FTD and AD or turn out to be another FTD subtype based on postmortem neuropathological analysis. Thus, the results of these studies are not sufficiently robust to firmly support the use of the P300 paradigm to distinguish between AD and bvFTD patients. Longitudinal studies are needed to clarify this point.

Our study identified increased excitability of the motor cortex in AD patients when compared with bvFTD patients. These findings are consistent with previous studies [29, 53-56]. Recent neuropathological studies showed that the density of neurofibrillary tangles and senile plaques in the motor cortex was approximately equivalent to other areas considered to be

Table 4. Differences in TMS parameters in the left and right hemispheres within the AD and bvFTD groups.

|         | Left hemisphere | Right hemisphere | t value | P value |
|---------|----------------|------------------|---------|---------|
| AD      |               |                  |         |         |
| RMT (%) | 43.96 ± 1.34  | 44.77 ± 1.44     | -0.728  | 0.473   |
| FMT (%) | 29.70 ± 1.00  | 31.26 ± 1.19     | -1.435  | 0.165   |
| CSP (ms)| 158.23 ± 8.47 | 155.97 ± 8.48    | 0.501   | 0.621   |
| FTD     |               |                  |         |         |
| RMT (%) | 49.57 ± 1.54  | 50.10 ± 1.44     | -0.638  | 0.528   |
| FMT (%) | 35.33 ± 1.12  | 35.22 ± 1.08     | 0.102   | 0.920   |
| CSP (ms)| 154.55 ± 4.88 | 155.75 ± 5.26    | -0.481  | 0.634   |

AD, Alzheimer’s disease; bvFTD, the behavioral variant of frontotemporal dementia; CSP, cortical silent period; FMT, facilitated motor threshold; RMT, resting motor threshold; TMS, transcranial magnetic stimulation.

Table 5. Excitability of the motor cortex in AD and bvFTD patients.

|         | AD (n = 27) | FTD (n = 30) | t value | P value |
|---------|-------------|--------------|---------|---------|
| RMT (%) | 44.37 ± 1.27| 49.83 ± 1.43 | -2.818  | 0.007   |
| FMT (%) | 30.89 ± 0.95| 34.71 ± 0.97 | -3.548  | 0.001   |
| CSP (ms)| 157.10 ± 8.17| 155.14 ± 4.93| 0.212   | 0.833   |

AD, Alzheimer’s disease; bvFTD, the behavioral variant of frontotemporal dementia; CSP, cortical silent period; FMT, facilitated motor threshold; RMT, resting motor threshold; *, P < 0.05.

Table 6. Relationships between cognition and electrophysiological parameters in the AD and bvFTD groups.

|         | AD (p = 27) | FTD (n = 30) | t value | P value |
|---------|-------------|--------------|---------|---------|
| P300-Pz |             |              |         |         |
| Latency (ms) | -0.301 | -0.281 | -0.346 | -0.371* |
| Amplitude (μV) | 0.107 | 0.060 | -0.005 | 0.015   |
| P300-Cz |             |              |         |         |
| Latency (ms) | -0.308 | -0.316 | -0.275 | -0.353   |
| Amplitude (μV) | 0.099 | 0.017 | 0.151 | 0.105   |
| RMT (%) | -0.227 | -0.063 | 0.091 | 0.128   |
| FMT (%) | 0.426* | -0.301 | 0.047 | 0.307   |
| CSP (ms) | 0.193 | 0.346 | -0.287 | -0.019  |

AD: Alzheimer’s disease; bvFTD, behavioral variant of frontotemporal dementia; CSP: cortical silent period; Cz, central; FMT, facilitated motor threshold; MMSE, Mini-Mental State Examination; MoCA, Montreal Cognitive Assessment; Pz, parietal; RMT, resting motor threshold; *, P < 0.05.
specific targets for AD abnormalities [57, 58]. Secondly, the primary motor cortex expresses muscarinic receptors and receives widespread inputs from cholinergic pathways. Therefore, some researchers have suggested that the cholinergic deficits in AD modify the excitability and function of the motor system [59-61]. Clinically, the excitability changes occur long before clinical signs of motor deficits are detected [62]. We speculate that the observed hyperexcitability is a compensatory mechanism to execute voluntary movements. In contrast, the excitability of the motor cortex was preserved in the bvFTD group. Thus, TMS has the potential to be used as a noninvasive tool for reaching an early differential diagnosis between cholinergic (AD) and non-cholinergic forms of dementia (FTD). FTD includes a wide spectrum of heterogeneous clinical and anatomical conditions. Alberici and colleagues found that TMS might help in distinguishing differences among the FTD clinical spectrum [33].

Furthermore, we found a lack of correlation between AD severity and cortical excitability parameters. These findings are consistent with the study by Ferreri et al. [54]. In contrast, Alagona et al. [63] found a significant correlation between RMT and MMSE, indicating that the lower the MMSE score, the lower the RMT (cortical hyperexcitability). However, this may be ascribed partly to the clinical homogeneity of their patients (all of them had mild dementia). In contrast, our participants showed different levels of disease severity. In the early stages of AD, a decrease in RMT (cortical hyperexcitability) may be a compensatory mechanism for the loss of cortical neurons involved in motor functions. However, in the advanced stages of AD, the excitability is decreased owing to cortical atrophy. Although TMS does not represent a specific diagnostic tool for AD, it may provide the key to understanding the pathophysiological mechanisms of AD.

We recognize the overall limitations of our work. First, all of the AD and bvFTD diagnoses were made clinically without neuropathological confirmation. Based on postmortem neuropathological analyses, some studies suggested that clinically

Figure 5. Correlation between the TMS parameters and MMSE in both AD and bvFTD patients (P < 0.05). A. RMT, B. FMT, C. CSP. The AD patients are indicated by the blue circles and the bvFTD patients by the red circles. Abbreviations: AD, Alzheimer’s disease; bvFTD, behavioral variant of frontotemporal dementia; CSP, cortical silent period; FMT, facilitated motor threshold; RMT, resting motor threshold; TMS, transcranial magnetic stimulation.

Figure 6. Correlation between the TMS parameters and MoCA in both AD and bvFTD patients (P < 0.05). A. RMT, B. FMT, C. CSP. The AD patients are indicated by the blue circles and the bvFTD patients by the red circles. Abbreviations: AD, Alzheimer’s disease; bvFTD, behavioral variant of frontotemporal dementia; CSP, cortical silent period; FMT, facilitated motor threshold; RMT, resting motor threshold; TMS, transcranial magnetic stimulation.
diagnosed AD or bvFTD involves a mixed pathology of other degenerative diseases. Secondly, we chose simple and easily available parameters, such as RMT and FMT, to assess motor cortex excitability. Further study of the pathophysiology should include additional parameters such as short-latency afferent inhibition, intracortical facilitation, and intracortical inhibition.

Conclusions

The novel findings of the present study concern the differences in cortical functioning between patients with AD and bvFTD. The results showed that bvFTD patients displayed a significantly longer P300 latency compared with AD patients. Simultaneously, AD patients displayed a hyperexcitability of the motor cortex, which may be a compensatory mechanism for the execution of voluntary movements. We suggest that combining different electrophysiological tools will help determine the unique pathophysiological mechanisms in AD and bvFTD.

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