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Cognitive impairment in Chinese IIDDs revealed by MoCA and P300

Qiuming Zeng[a], Xiaohua Dong[a], Chunyun Ruan[b], Bo Hu[a], Binting Zhou[a], Yuanyuan Xue[a], Yu Liu[a], Huan Yang[a,*]

[a] Department of Neurology, Xiangya Hospital, Central South University, PR China
[b] Department of Neurology, Luoyang Central Hospital Affiliated to Zhengzhou University, PR China

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ABSTRACT

To investigate the value of MoCA and auditory P300 as a cognitive assessment tool in chinese idiopathic inflammatory-demyelinating diseases (IIDDs), eighty three consecutive patients with IIDDs and thirteen sex- and age-matched healthy controls were recruited in the study. MMSE, MoCA and auditory P300 potential were administrated to each participant. The percentage of cognitive impairment in IIDDs patients was 24.1% by using MMSE, while the percentage was 81.9% by using MoCA. The majority of IIDDs participants had MMSE scores in the normal range. In contrast, few IIDDs participants scored in the normal range on the MoCA. Age, EDSS and depression correlated negatively with the total score of MoCA and MMSE. Years of education correlated positively with MoCA and MMSE. ADEM patients scored lower on all MoCA subtests. Prolonged latency P300 which negatively correlated with MoCA and reduced P300 amplitude which positively correlated with MoCA were detected in IIDDs patients. Thus MoCA is superior to the MMSE as a cognitive impairment scan tool and P300 is useful for detecting cogntive deficiency in chinese IIDDs.

1. Introduction

Idiopathic inflammatory-demyelinating diseases (IIDDs) are monophasic or relapsing disorders characterized by attacks of inflammatory demyelination affecting different sites of the central nervous system (CNS) (Canellas et al., 2007). IIDDs represent a broad spectrum of CNS disorders, mainly including multiple sclerosis (MS), neuromyelitis spectrum disorders (NMOSD), clinically isolated syndrome (CIS), acute disseminated encephalomyelitis (ADEM), acute transverse myelitis (ATM), idiopathic demyelinating optic neuritis (IDON), Balo concentric sclerosis (BCS), pseudotumor demyelinating disease of the CNS, brain stem inflammatory demyelinating syndrome and so on (Canellas et al., 2007).

As the most common form of IIDDs, the cognitive impairment of MS has been demonstrated for a long time by several of studies, with prevalence rates ranging from 43% to 70% (Benedict et al., 2006; Chiaravalloti and DeLuca, 2008; Rao et al., 1991), especially referred to attention, recent memory, information processing speed, executive functions, verbal intellectual ability, and visuospatial perception (De Sonneville et al., 2002; Kujala et al., 1996; Wishart and Sharpe, 1997). More than that, the presence of cognitive impairment in NMOSD (Blanc et al., 2008; He et al., 2011; Kim et al., 2016; Saji et al., 2013), CIS (Anhoque et al., 2010; Feuillet et al., 2007; Potagas et al., 2008) and ADEM (Hahn et al., 2003; Suppiej et al., 2014) is also recognized recent year. But there were few studies about the cognitive impairment in IIDDs patient, especially in chinese IIDDs patients.

Cognitive impairment can be assessed by neuropsychological tests, which depending on patient compliance, can last 3–5 h. Therefore, there is an important need for reliable and costeffective screening tests in clinical practice. A brief screening tool would be a more practical approach for frontline clinicians to detect cognitive deficiency. The most common cognitive screening assessment tool used in neurosurgical clinics is the Mini-Mental State Examination (MMSE) (Folstein et al., 1983), which is quick (5–10 min) and easy to administer in a clinic setting. Conversely, the MMSE appears to be less sensitive to mild cognitive impairment (MCI), and thus does not encompass all of the cognitive deficits that might occur following IIDDs. It is particularly weak in its ability to measure executive functions, such as abstract thinking, judgment, problem solving and perception, all of which are relevant to the type of dementia associated with MS (Beatty and Goodkin, 1990; Scherer, 2007). However, the Montreal Cognitive Assessment (MoCA) places greater emphasis on frontal executive function and attention tasks, and it may be more sensitive for the detection of non-Alzheimer's disease dementia (Nasreddine et al., 2005). Thus, whereas the MoCA seems to be a promising avenue as a cognitive screening measure in IIDDs, it remains to be examined.

The main limitation of neuropsychological testing including cognitive screening tool in patients with IIDDs is a physical disability, which

* Correspondence to: Department of Neurology, Xiangya Hospital, Central South University, 87 XiangYa Road, Changsha, Hunan 410008, PR China.
E-mail address: yangh69@126.com (H. Yang).

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includes the reduction of visual acuity and fine motor limit. In this case, cognitive electrophysiology plays an important role because it is not limited by existence of a physical disability. The P300 is an endogenous potential, which belongs to the event-related potential, which allows the study of the aural cortex in the central nervous system. It represents the cortical activity comprising the discriminative, the integrative and the attention skills, being an excellent indicator of the cortical processing speed. The P300 which reflects cognitive processes as attention, recognizing, and working memory is frequently abnormal in cognitive impaired patients (Kraus and McGee, 1994). The numerous clinical P300 studies (Bennys et al., 2007; Golob et al., 2007; Katsarou et al., 2004) strongly suggest that this ERP component, elicited by auditory, visual or somatosensory stimuli, may be clinically useful as an index of cognitive function.

The primary aim of the present study was to test the hypothesis that MoCA is more sensitive than MMSE for detecting cognitive impairment in IIDDs paitents. Then we also investigate the relationship of P300 and MoCA and the value of auditory P300 as a cognitive assessment tool in IIDDs.

2. Method

2.1. Participants

Eighty three consecutive patients with IIDDs were recruited from the Department of Neurology, Xiangya Hospital, Central South University between June 2014 and May 2016. The recruited patients consisted of 24 patients with MS, 11 with clinically isolated syndromes (CIS) according to 2010 revised McDonald criteria (Polman et al., 2011), 37 with NMO spectrum disorders (NMOSD) according to 2015 criteria of the International Panel for NMO Diagnosis (IPND) (Wingerchuk et al., 2015), and 11 with acute disseminated encephalomyelitis (ADEM) according to the criteria of the International Advisory Committee on Clinical Trials in MS of the US National MS Society (Miller et al., 2008). All participants were free of other neurological conditions. Patients were not preselected on the basis of cognitive complaints, and all patients were evaluated more than 1 month from any recent relapse.

Thirteen sex- and age-matched healthy controls (HC) (three males, 10 females; mean age 31.62 years, SD 11.42 years) with no previous history of neurological dysfunction and with normal findings on neurological examination were recruited in the same hospital. All procedures performed in the study involving human participants were in accordance with the ethical standards of Xiangya Hospital medical ethics committee. Informed consent was obtained from all individual participants included in the study.

2.2. Clinical data

The main demographic and clinical characteristics including age, gender, education, age at onset of IIDD, EDSS, Serum AQP4 antibody (commercial tissue-based immunofluorescence assays) and disease duration of the patients studied are reported in Table 1.

2.3. Cognitive testing

MMSE and MoCA were administrated to each participant by a trained investigator who was blind to the subject's clinical conditions. All of these exams are completed in a relaxed, quiet environment. MMSE and MoCA scores have a one hour interval for reducing the bias. A cutoff of ≥ 27 on the MMSE was chosen to indicate normal cognitive function (Crum et al., 1993). For MoCA, one point is added if the subject has < 12 years of education (Hoops et al., 2009). The accepted cutoff of < 26 on the MoCA was taken to indicate cognitive impairment (Nasreddine et al., 2005). The Hospital Anxiety and Depression Scale (HADS) was also administered to all patients, in order to evaluate their mood.

2.4. Electrophysiologic recordings

Professional electromyography physicians performed the P300 potential for all the subjects. The auditory stimuli were presented in a random sequence with target tones of 2000 Hz occurring 20% of the time and standard tones of 1000 Hz occurring 80% of the time (Katsarou et al., 2004). Tones were presented binaurally through headphones at an interstimulus interval of 1.1 s. The subject is required to distinguish between the two tones by responding to the target (moving the index finger of their right hand) and not responding to the standard (Squires et al., 1976). Twelve Ag/AgCl recording electrodes were placed on the scalp according to the 10/20 system (Fz, Cz, Pz, Oz, A1, A2, F3, C3, P3, F4, C4, and P4 sites; impedance < 5 kOhm). Electrodes were placed above and below the left eye to monitor eye movements, and 1 electrode on the forehead was the ground. A1 and A2 are the reference electrode sites. The EEG and EOG were amplified and collected continuously, with additional offline analysis. Eyeblink artifacts were corrected using an algorithm, and sweeps were then averaged according to stimulus type (standard or target). Sweeps to targets were visually inspected for artifacts before being accepted into the average. Sweeps to nontargets were automatically rejected if the voltage on any electrode site exceeded $\pm$ 75 μV (Golob et al., 2009). ERPs were digitally filtered. Peak latencies of components were calculated relative to stimulus onset. Amplitudes of stimulus-evoked potentials were defined relative to a 100-msec baseline period immediately before stimulus presentation. The P50 was defined as the maximum positivity between 40 and 70 msec poststimulus, the N100 was the maximum negativity between 70 and 160 msec, and the P200 was the maximum positivity between 150 and 250 msec. The N200 was the maximum negativity between the P200 and P300, and the P300 was identified as the largest positive peak between 280 and 450 ms. The P50, N100, P200, and N200 components were measured from the Cz site; the P300 was measured from the Pz site.

2.5. Statistical analysis

Results were presented as mean $\pm$ S.D. Statistical analyses were performed using SPSS® 17.0 software and $P < 0.05$ (two-tailed) was considered statistically significant. Differences between groups were analyzed by one-way ANOVA, non-parametric Mann-Whitney tests (data were not normally distributed) and Pearson χ^2 tests(gender distribution). P- value is corrected for multiple comparisons using Bonferroni's correction. Pearson correlations (for continuous variables) and Spearman rank order correlations were calculated to examine the relations between clinical characteristics, P300 and task performance. The graphs were performed by Graphpad Prism version 5.0 for Windows (GraphPad Software, San Diego, CA).

3. Results

3.1. Demographic and clinical data

The demographic, clinical characteristics and laboratory findings of patients and controls are summarized in (Table 1). No significant differences were found between IIDDs patients and HC by gender, age, years of education. There were also no significant EDSS or onset age differences between the subgroups of IIDDs. Disease duration was shorter for the CIS subgroup, compared to the MS and NMOSD groups.

3.2. Cognitive function in IIDDs patients

3.2.1. MMSE and MoCA scores of patients with IIDDs

The percentage of cognitive impairment in IIDDs patients was 24.1% by using MMSE, while the percentage was 81.9% by using