

Case Report

Transcranial Magnetic Stimulation (TMS) as a Tool for Early Diagnosis and Prognostication in Cortico-Basal Ganglia Degeneration (CBD) Syndromes: Review of Literature and Case Report

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ABSTRACT

Background: Cortico basal degeneration (CBD) of the brain is a rare progressive neurodegenerative disease which encompasses unique neuropsychiatric manifestations. Early diagnosis is essential for initiating proper treatment and favorable outcome. Transcranial Magnetic Stimulation (TMS), a well-known technique for assessment of cortical excitatory and inhibitory properties. It was suggested that in a degenerative disease like CBD which involves the cortex as well as the subcortical structures, comparing both hemispheres, a differential pattern in TMS can be obtained which would help in early identification, prognostication and early therapeutic intervention. **Case Report:** We describe a case of CBD with corroborative clinical and imaging picture wherein single pulse TMS was used over both the hemispheres measuring the following parameters of interest which included: Motor Threshold (MT), Central Motor Conduction Time (CMCT) and Silent Period (SP). **Results and Conclusion:** Differential patterns of MT, CMCT and SP was obtained by stimulating over both the hemispheres with the affected hemisphere showing significantly reduced MT and prolonged CMCT implying early impairment of cortical and subcortical structures thereby revealing the potential application of TMS being utilized in a novel way for early detection and prognostication in CBD syndromes.

Key words: Cortico-Basal degeneration (CBD), differential hemispheric parameters, transcranial magnetic stimulation(TMS)

INTRODUCTION

Cortico basal degeneration (CBD) of the brain is a progressive neurodegenerative disease and is a rare

entity which encompasses both neurological and Psychiatric manifestations. It is reported in 5% of cases with Parkinsonism as well as has an incidence of 0.62-0.92 per 100,000 population per year and a prevalence of 4.9-7.3 per 100,000 population.^[1] CBD is characterized clinically by features of Apraxia, Neglect, Cortical (parietal) sensory loss, asymmetrical myoclonic jerks, unusual symptoms like alien hand phenomena; insidious and progressive subcortical dementia, gait disturbances and parkinsonian features.^[2] Due to its similarity with diseases like Frontotemporal dementia, Parkinson's disease dementia, Parkinson plus syndromes, Alzheimer's illness as well as vascular

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dementia it is often under diagnosed in the initial stages and treatment initiation is often delayed till overt manifestations are seen in later stages during which period disease becomes severe and less amenable for medications having an apparently poor prognosis. Investigations like magnetic resonance (MR) imaging, positron emission tomography (PET) scanning as well as cerebrospinal fluid (CSF) studies are technically demanding and expensive and often fail to clinch the diagnosis. Thus the need for a relatively simple and efficacious method for early detection and prognostication of CBD is quite pertinent.^[3,4]

Transcranial Magnetic Stimulation (TMS) is a non-invasive, well validated and relatively simple method for determining the excitatory and inhibitory properties of the motor cortex. Its utility for early definite ante mortem diagnosis in cortical dementias has been reported by the authors before.^[5] It has been described that there is reduced Cortical Motor Threshold (MT) in Alzheimer's disease and prolonged Central Motor Conduction Time (CMCT) along with shortened Silent Period (SP) in Alzheimer's disease (AD) and Frontotemporal dementia (FTD). Increased cortical excitability and decreased cortical inhibition in AD suggests defective modulatory inhibition by the Parietal lobe whereas early involvement of motor pathways with apparently normal Motor Threshold is suggestive of Frontal lobe dysregulation seen in FTD as well the potential utility of GABA agonists for treatment in these conditions.^[5,6] On this basis, it was suggested that in a degenerative disease like CBD which involves the cortex as well as the subcortical structures, comparing both hemispheres, a differential pattern in TMS can be obtained which would help in early identification, prognostication and early therapeutic intervention.

CASE REPORT

A 59-years-old accountant came with 3 years history of memory disturbances, calculation difficulty, and way finding difficulty with history of getting lost on the way back home once. He also complained of transient twisting and tingling sensations in the right foot on standing, which used to be intermittent and lasts few seconds and relieved on continual walking and on lifting feet from the ground. While walking he occasionally had a subjective feeling that his foot was getting twisted but no abnormality was noticed by his wife. There is no history suggestive of buckling at knees, wobbling at the ankle, sensory loss, motor weakness, behavioural symptoms, dressing difficulty, visual hallucinations, myoclonic jerks or seizures. No past history of Diabetes mellitus, Hypertension, smoking or alcohol intake. No family history of similar illness was elicited. Examination revealed normal vitals.

His Higher mental function was abnormal in terms of impaired short term memory and learning. His Hindi Mental Status Examination (HMSE), an Indian version of Mini Mental Status Examination (MMSE) score was 16/31.^[7] Detailed Neuropsychological examination using NIMHANS Neuropsychological Battery revealed deficits in Frontal, Parietal and medial Temporal lobe functions. Investigations revealed normal blood parameters, normal liver and renal function tests. MR imaging of the brain showed diffuse atrophy with left hemisphere being more atrophic than the right including the basal ganglia structures suggestive of features consistent with CBD [Figure 1].

PATIENTS AND METHODS

Transcranial magnetic Stimulation was attempted after informed consent with the patient seated comfortably. The Figure of eight coil was used for stimulation of both cortices at different occasions and first dorsal interossei muscle contraction in both hands was noted consecutively. Motor threshold (MT) estimated on motor cortex by applying 10 stimuli which generated at least 5 complexes >50 mcV and elicited in each cortex. The magnetic field percentage required for the generation was assigned as the MT. Supramaximal stimuli (150% of the MT) was then applied over each cortex and latency calculated which was designated as T1. Second site of stimulation was over *Vertebrae prominence* which is at C7 and designated as T2. CMCT is then equal to T1-T2. Then Silent period (SP) was assessed by calculating the period of EMG arrest from the end of motor evoked potential while First Dorsal Interossei muscle (FDI) is contracted in both the hands.

RESULTS

The MT was lowered over both the hemispheres with the right MT being lower (33%) as compared to the left (37%). This was consistent with the findings of MT in previous studies related to AD showing increased excitability and decreased inhibition.^[5,6] The CMCT

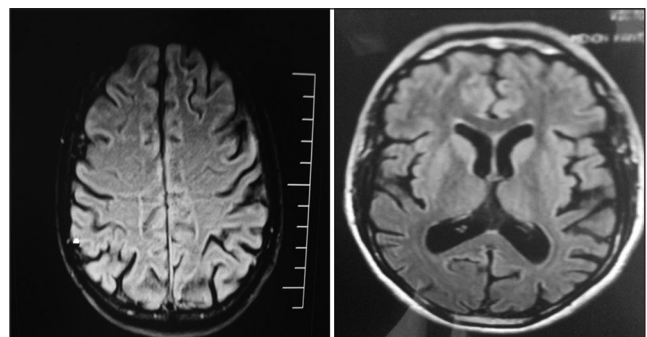


Figure 1: MRI showing asymmetric cortical and subcortical atrophy in CBD

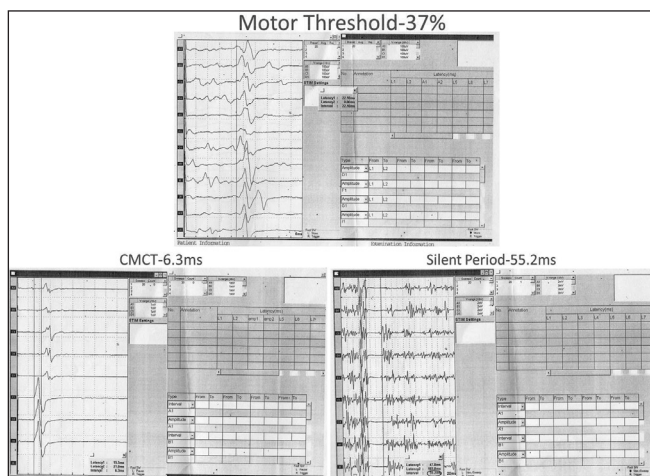


Figure 2: TMS parameters when stimulated over the left (dominant) cortex

values on the other hand showed prolongation when the right cortex was stimulated (9.1 ms) when compared to the stimulation of the left cortex.(6.3 ms). This was corroborative with the previous findings by the authors in FTD patients thereby showing the subcortical involvement of the affected side as well.^[5] The silent period was decreased in both the right FDI (was 55.2 ms) and in the left (was 46.4 ms) which was also consistent with the previous work done by the authors where the common factor of reduced silent period was observed in both AD and FTD^[5] [Figures 2 and 3].

DISCUSSION AND CONCLUSION

As hypothesized, differential patterns were obtained from both cortices using the same parameters which were quite interesting. It is important to note that both decreased MT as well as prolonged CMCT while stimulating the affected cortex can indicate the underlying pathology in the cortex as well as in the sub cortex. TMS thus can become a valuable non-invasive tool for early detection of integrity of both cortical and subcortical structures as well. This can be hopefully used in centers with limited facilities catering to economically weaker patients especially in developing countries where trained manpower and resources are scarce. As TMS machine can be easily transported also, portability and technical issues would not become a hindrance. The duration of the entire test is also very less (<20 minutes per patient). The potential application also involves testing, validating and even improving the accuracy of animal models established for

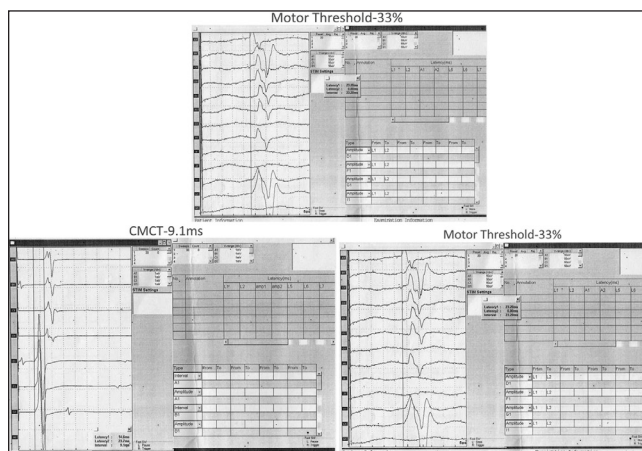


Figure 3: TMS parameters when stimulated over the right cortex

various neurodegenerative illnesses which can be more effective in drug development and testing strategies without any harm to the animal models as well as to the Human counterparts. Recognition of the novel but unexplored technique can help in augmenting research in dementia and movement disorders in the long run.

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