

Callosal Transfer Test Performance in Patient with Multiple Sclerosis: A Case Report

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ABSTRACT

Patient (P) female, 23, consistent right-hander was diagnosed as having multiple sclerosis at the onset of clinical symptoms (loss of sensation in the left limb and left part of the face). MRI revealed demyelination in cerebellar region, intratentorial white matter and tissue adjacent to the fourth ventricle, as well as demyelinated plaques localized in the rostrum, truncus and splenium of corpus callosum. One year after, aggravation of clinical symptoms (loss of sensation in the right limb and in the right part of the face, difficulty in holding as well as recognizing things, discoordination of movements and occasional diplopia) was registered. Patient was tested on callosal interhemispheric transfer of information after the spontaneous resolve of most of symptoms. At that period, patient experienced paresthesia in the upper limb when bending the neck. Tests on finger cross-localization, cross-matching of objects, drawing to dictation, simultaneous drawing with both hands, reading words perceived by "non-verbal" right hemisphere and line bisection were administered. Patient was found successful in performing all tests on interhemispheric transfer of information, suggesting the callosal system of study participant efficient in interhemispheric communication.

Keywords

Multiple sclerosis, Corpus callosum, Interhemispheric transfer.

Introduction

Corpus callosum (CC) is a bundle of myelinated commissural fibers, connecting cortices of two brain hemispheres. Anterior part of CC (genu and rostrum) connects frontal and premotor cortex, middle part (body) connects motor, somatic sensory and parietal cortex, and posterior part (splenium) contains fibers connecting temporal and occipital cortex [1,2].

Examination of split-brain patients – subjects with surgically severed CC [3-5] and studies on callosal agenesis, complete or partial [6], as well as experiments with animals [7-9], have demonstrated the significance of callosal connections in integration and transfer of information from both cerebral hemispheres to process sensory, motor, and cognitive signals. At the same time, evidence suggest, that not only callosal agenesis or surgical

dissection, but also degradation of callosal structure can influence the interhemispheric transfer of information [10]. Studies report on the callosal functional insufficiency in patients with callosal degradation due to traumatic brain injury, demyelination of callosal fibers [11], alcoholism, viral infections [12], toxic pathology [13]. We focus here on the consequences of the demyelination of callosal fibers in case of multiple sclerosis (MS) - the common pathology associated with the corpus callosum, with sclerotic plaques mostly localized in the body of the CC of human [14] and animals [15]. Studies, using electrophysiological and imaging methods, report on disrupted callosal connectivity in MS patients [16-19]. Behavioral tests on interhemispheric communication in MS patients mostly focus on higher cognitive functions, such as memory, language, spatial orientation, reasoning and information processing speed, as well as motor coordination and calculation [20-24]. However only few studies address the problem by the use of behavioral tests on callosal interhemispheric transfer of information.

Behavioral tests on callosal interhemispheric transfer of information are based on the assumption as following: Somatic-sensory stimuli from the left vs right body part, reach the contralateral hemisphere, right vs left respectively, via the crossed sensory pathways. Therefore, somatic-sensory information perceived by the one hemisphere from contralateral body part, can be transferred to the opposite hemisphere via callosal axons. As for the control of limb movements, they are mostly controlled by the crossed cortical spinal pathways arising in the contralateral hemisphere. Therefore, hemisphere, ipsilateral to the limb may control it via callosal connections to the opposite hemisphere, contralateral to that limb [25-29]. Visual sensory input from each eye may be artificially lateralized to one hemisphere using the DVF method [30]. Stimuli, presented left vs right of fixation point are perceived by the right vs. left hemisphere respectively. In these case, visual sensory information is perceived by one brain hemisphere and transferred to the opposite hemisphere via callosal fibers. Lateralization of verbal function in the left hemisphere in right-handers suggests, that to read the word, presented right of the fixation point, subject uses the left, verbal hemisphere, while to read the word, presented left of fixation point, information should be transferred from the perceiving “non-verbal” right hemisphere to the left hemisphere via callosal fibers [4,6,25,26,31].

Patients with MS were reported to demonstrate lower scores in interhemispheric transfer tests such as dichotic listening, bimanual finger tapping and crossed finger localization test. At the same time, MS patients show significant atrophy of the CC during 5-year follow-up and concomitant progression of impairment in interhemispheric transfer test performance [32,33]. Authors report on asynchronous tapping in bimanual synchronous finger tapping task performance in patients with MS. Unilateral agraphia when writing to dictation with the left hand was registered in right-handed MS patient, suggesting the disconnection between the auditory-verbal regions of the left hemisphere and executive motor cortex of the right hemisphere. Limited number of studies of interhemispheric exchange of information in MS patients, encourages to extend the research in this direction.

Material and Methods

Patient, I.H. (initials are changed), female, 23, was diagnosed by treating neurologist as having MS. Diagnosis was put in the June 2020, after the onset of clinical symptoms (loss of sensation in the left limb and left part of the face). MRI (T2Flair, T2tse, T1ffe, T2fs, DW1, epw-b500, MIPVEN 3D PCA) was performed in axial and sagittal sections, with and without contrast (omiscan). Neocortical layer was found preserved, demyelinated plaques found in the parenchymatous tissue of brain hemispheres, periventricular white matter, and CC (Figure 1), with diffusion restriction and intact contrasting, common in the acute phase of the MS. At the same time, multiple demyelinated plaques were fixed without diffusion restriction in cerebellar region, intratentorial white matter and tissue adjacent to the fourth ventricle.

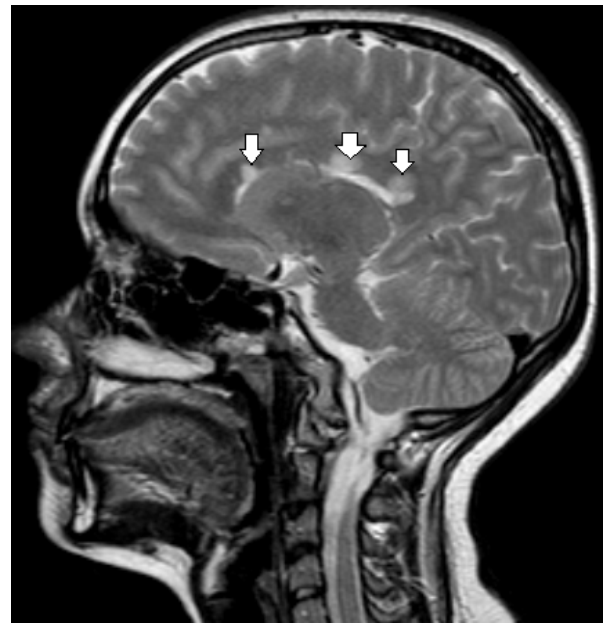


Figure 1: Demyelinated parts of the CC (indicated by the arrows) in I.H.

Demyelinated plaques are localized in the rostrum, truncus and splenium of CC. Patient scored 28 in Mini Mental State Examination. I.H. made mistakes when counting backward from 100 by sevens, but corrected it immediately, and substituted word “Flower” with “House” when requested to remember 3 words (Hammer, Flower, Car) told earlier by instructor.

Aggravation of clinical symptoms (loss of sensation in the right limb and right part of the face, difficulty in holding as well as recognizing things, discoordination of movements and occasional diplopia) was registered in September 2020. Most of symptoms resolved spontaneously in 2-3 weeks. Tests on callosal interhemispheric transfer of information were administered in September 2021. At that period, patient experienced paresthesia in the upper limb when bending the neck. I.H. was informed about the aim of the study and character of experimental approach. Patient was familiarized with the content of the article before it’s submission for publication and a written consent was obtained from patient concerning participation in the study and publication of the data obtained.

Procedure

Handedness questionnaire, modified from [34], was used and laterality index calculated. Patient was requested to decide, which hand is preferable for drawing, using scissors, knife, spoon, toothbrush, holding computer mouse, a hammer, a comb and a key when unlocking a door. Handedness index was calculated as $R-L/R+L$, where R and L stand for the total number of movements, performed by the proffered right and left hand respectively. Handedness index range is -1 (consistent left-hander) +1 (consistent right-hander).

In Finger Localization Test (FLT), patient was sitting at the table,

blindfolded, with hands put on the table face up. Observer touched with a pencil fingertip on one palm, one by one, in random order, and patient had to bend the corresponding finger of opposite palm. Test was performed in 2 series, first with right hand touched by observer, second – the left hand touched by observer. In Object Matching test (FMT), patient was sitting at the table, blindfolded. Observer put the objects, one by one, in I.H.'s hand and patient had to palpate it and to find the same object in the row of objects with the opposite hand. Test was performed in 2 series, first with right hand palpating the object, second – the left hand palpating the object. The total number of objects for matching was 5 (bottle lid, chewing gum, small silicon toy, pencil, pen lid). The number of objects in the row was 10. In Line bisection test (LBT), paper and pencil version, 5 lines of different length, drawn on the paper were presented to patient with request to find and mark a midpoint of each line. Divided visual field method (DVF) was used in Figure drawing test (FDT) and Word reading test (WRD) as well. Patient was sitting in front of the computer screen at a distance of 45 cm. Chin rest was used to fix the head stable. Patient was asked to look at fixation point (red spot in the center of the screen) and respond to visual stimuli immediately after their exposition. We observed patients eye movements and presented the stimuli only when patient was judged to look at fixation point. In each trial, visual stimulus was exposed for 140 ms followed by masking stimulus (black stripes on the white background) for 1 second. After this, fixation point was exposed again. In WRD visual stimuli, a total of 10 vertically written words were presented one by one, in a random manner either on the right (5 words), or on the left (5 words) of fixation point. Patient was requested to read words aloud. In the first trial of FDT geometrical figures (triangle and circle) were exposed one by one, triangle on the left of the fixation point, circle – on the right, and patient was requested to draw these figures without eye control with one hand: triangle with the left hand, circle with a right hand. In the second trial, figures were exposed simultaneously, and patient was requested to draw them without eye control simultaneously with both hands. In another trial, I.H. blindfolded, was instructed to draw figures (Cross and rectangle) to dictation with one hand.

Results and Discussion

Patient's handedness index was +100 – consistent right-hander. Patient performed FLT without mistakes, at the first attempt, irrespective of which hand, right or left, was touched by the observer and which hand, left or right respectively, responded to the touch. Responses were immediate, without delay. No mistakes were recorded in the OMT as well. However, finding 5 objects with the right hand (First trial) took longer (70 s in total) than finding objects with the left hand in the second trial (20 s in total). Faster performance in the second trial, in our opinion, should be ascribed to the adaptation to the task procedure. I.H. was successful in drawing figures to dictation. In test of simultaneous drawing, patient displayed the same quality of drawing, as in case of drawing with a single hand. Bimanual coordination of finger opposition movements was found impaired in MS patients with callosal demyelination, suggesting insufficient communication

between the hemispheres [35]. Contrary to the hemispheric coordination in finger opposition movements, independent action of hemispheres is necessary to perform simultaneous drawing in FDT. Simultaneous drawing does not make problem for split-brain patients as long as CC is severed and there is no conflict between hemispheres, realizing different drawing programs. Therefore, patient's performance could suggest independent functioning of brain hemispheres in simultaneous FDT. However, when drawing circle and triangle simultaneously, left limb of I.H. was left behind the right one, the delay, which is necessary to cope with conflicting drawing program for the right vs left limb, usual for subjects with efficient interhemispheric communication. Unilateral agraphia of the left hand is considered a symptom of callosal disconnection [36] between the right hemisphere motor areas that control movement of the left limb and “verbal” left hemisphere in right-handers. In contrary to finding of unilateral agraphia in MS patient, successful performance in drawing to dictation, suggests corpus callosum efficient in connecting these cortical areas in I.H.

I.H. was successful in reading all words (100%), presented either to the left of fixation point (i.e. perceived by the right hemisphere) or to the right side of fixation point (i.e. perceived by the left hemisphere). I.H. is consistent right-hander with handedness index 100. This suggests lateralization of speech function in patient's left hemisphere and normal functioning of callosal fibers in the transfer of information from the right to the left hemisphere in performance. Resection of the posterior CC is suggested to produce consistent bias in LBT performance [37]. However, no significant bias (more than 1-2 mm from the midpoint in bisecting 2 lines out of 5) was registered in LBT performance.

Authors report on progression of impairment in interhemispheric transfer test performance in 5 years follow up of MS patients [38]. In the current study, patient was found successful in interhemispheric transfer test performance one year after the MS diagnosis. This suggests callosal system of I.H. 1 year after the onset of clinical symptoms still efficient in providing functional interconnection between the visual, as well as somatic-sensory neocortical regions of brain hemispheres.

The limitations of the current study are such as following: Further study is necessary to provide more precise description of callosal lesion. Some studies suggest women to have less lateralized verbal function on individual level [39] and we cannot be completely sure, that I.H. does not fall in the group of individuals, with bilateral representation of language. time, there are individual cases when information, lateralized to the one hemisphere of split-brain patient, is still available to the other half-brain [5] and, presumably, extra callosal connectivity of brain hemispheres is expected in particular cases of the sclerotic damage to the CC. With this respect, compensatory role of the anterior commissure [40] as well as involvement of ipsilateral cortical-motor pathways [41] in case of I.H. should be taken into account. Tests on interhemispheric transfer of information have some limitations as well. Using DVF method, observer should be sure, that eyes of the subject are fixed on the fixation point. We controlled patient's gaze by observing

her eye movements, however, only use of eye tracking apparatus or electro-oculography can completely assure, that gaze does not shift to the right/left of the screen [30].

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