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Short Communication

Corpus callosum function in verbal dichotic listening: Inferences from a longitudinal follow-up of Relapsing-Remitting Multiple Sclerosis patients

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ABSTRACT

This study conducted a follow-up of 13 early-onset slightly disabled Relapsing-Remitting Multiple Sclerosis (RRMS) patients within an year, evaluating both CC area measurements in a midsagittal Magnetic Resonance (MR) image, and Dichotic Listening (DL) testing with stop consonant vowel (C-V) syllables. Patients showed a significant progressive loss of posterior CC areas (isthmus and splenium) related to increasing EDSS scores and an enhancing right ear advantage (REA) over time. A significant correlation between posterior CC areas and DL scores emerged in both evaluations, being negative for the right and positive for the left ear. The pattern of correlations suggests that the CC can serve an inhibitory and also excitatory influence on the contralateral hemisphere when studying the phonological processing of language.

Statement of significance to the neuroscience of language: The scope of the manuscript is language lateralization. The task used in the experiment is a verbal dichotic listening task, tapping the most basic phonological aspects of language. Finally, the available research is scarce when focusing on the interhemispheric excitation or inhibition of the corpus callosum in linguistic functioning.

1. Introduction

The corpus callosum (CC) is the major fiber bundle in the human brain, with more than 200 million axons providing a large connection mainly between homologous cortical areas in mirror-image sites (Huang et al., 2005). The CC permits interhemispheric transfer of information but it is largely unknown how this manifests at a functional level, whether in an excitatory or inhibitory manner (Bloom & Hynd, 2005). The CC would have an excitatory role if the engagement of a specific region in one hemisphere tended to activate – via CC paths – the homotopic regions of the other hemisphere. The CC would have an inhibitory role if the processing of those homotopic regions were suppressed (Hellige, 1993). An example of the excitatory function is the callosal propagation of an epileptic focus, which acts as a facilitatory mechanism for the spreading of the seizure to the ipsilateral territory in both hemispheres (Brown, Day, Rothwell, Thompson, & Marsden, 1991). An example of inhibitory function is the deactivation of the ipsilateral primary motor (M1) areas during motor tasks, due to transcallosal inhibitory inputs from the contralateral M1 (Lenzi et al., 2007).

In this study our interest was to elucidate the functioning of the corpus callosum regarding excitation and/or inhibition but concerning specifically the phonological processing of language, involving concretely the speech/listening performance.

Multiple Sclerosis (MS) patients offer a reliable way to study the function of the CC since the pathological landmark of their disease, the demyeliniating plaques, tend to be located at periventricular brain areas, therefore affecting the corpus callosum. In addition, there is increasing evidence to consider MS as a neurodegenerative as well as inflammatory disease (Casanova et al., 2003), which should imply the loss of axons traveling through the CC, possibly due to Wallerian degeneration (Evangelou et al., 2000), and the subsequent callosal loss evolving over time (Juha et al., 2007).

In MS patients it seems worthwhile to apply a behavioral paradigm presenting lateralized stimuli, as the dichotic listening (DL) task, to study functional aspects of the CC. In DL, two different and competitive auditory stimuli are presented to both ears and, if they are verbal, a right ear advantage (REA, superior reporting of right ear stimuli) usually emerges (Hugdahl, 2003). The REA is classically interpreted as the result of stronger contralateral than ipsilateral auditory projections (so the right ear would be better connected with the left hemisphere and vice-versa) and a critical role for the CC in transmitting verbal information from the left ear via the acoustic cortex of the right hemisphere to

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language-processing areas of the left hemisphere. Reinforcing this, a number of studies (Gadea et al., 2002; Pelletier et al., 2001; Rao et al., 1989; Reinvang, Bakke, Hugdahl, Karlsen, & Sundet, 1994) have found significant correlations between DL scores and midsaggital CC area of MS patients, measured through Magnetic Resonance (MR) images. All these studies found a reduced left ear performance in DL for the patients compared with controls and also an inverse correlation between the REA and total callosal area. Thus, the thinning of the CC (especially at the posterior regions) was correlated with the highest REA. At first glance this would imply that the CC plays an excitatory role in interhemispheric communication: as it becomes smaller the observed behavioral laterality increases while that function is subsumed mainly by a unique hemisphere. However, the REA index is a combined measure that is calculated from the difference in raw scores inter-ears. Following the above model for the REA, one might expect only a positive correlation between the CC and the left ear, with no right-ear correlation, whose score does not depend on callosal transfer. Instead of this, when correlations by ear were performed in a sample of MS patients, the right ear score was inversely correlated (and the left positively) with the middle and posterior callosal sectors (Reinvang et al., 1994). This same finding was observed in a study performed in a sample of 25 Relapsing-Remitting MS (RRMS) patients with minimal physical disability and a disease of short temporal evolution (Gadea et al., 2002). Other authors have found the same pattern of correlations in normal subjects (Clarke, Lufkin, & Zaidel, 1993; Westerhausen, Woerner, et al., 2006).

The goal of this study was to accomplish a follow-up of RRMS patients with a year interval, evaluating both CC area measurements and DL testing. We expected a decrease in midsaggital CC area together with an increase in behavioral laterality (thus, greater REA in DL). In addition, we explored the correlations of each ear separately with the CC area measurements, to help elucidate the excitatory versus inhibitory role of the CC in dichotic listening performance and interhemispheric communication.

2. Method

2.1. Subjects

A total of 13 right-handed subjects with clinically definite or probable Relapsing-Remitting Multiple Sclerosis disease (eight men and five women) underwent two evaluations with a year interval. Their mean age was 26.3 years (SD 4.3, range 19–32) with mean years of education of 13.1 (SD 3.4, range 8–17). At baseline, eight of them met the criteria of Poser et al. (1983) for clinically definite RRMS. Five were probable MS at baseline, according to MRI Barkhof's criteria (1997), and two of them developed definite MS within the year of follow-up. Their mean months of disease duration at the first evaluation was 22.15 (SD 12.11, range 10–48), and the mean score for the Kurtzke (1983) disability scale (EDSS) was 1.3 (SD 0.63, range 0–2.5). All patients were in clinical remission at the time of testing, met the audiometric criterion for inclusion (less than 10 dB ear difference at 500, 1000, 2000, 3000 and 6000 Hz), and had the same MR examination protocol at both time-points of the study. Although six patients were receiving at the second evaluation a specific treatment for MS (interferon B) as part of a clinical trial, there were not significant differences between treated and non-treated patients in any moment with regard to EDSS scores or disease evolution time.

2.2. Materials

2.2.1. Magnetic Resonance measurements

MR was performed on a 1.5-Tesla Gyroscan (Philips Medical Systems, The Netherlands). A sagittal acquisition was obtained with a T1-weighted echo-gradient sequence with prepulse inversion (repetition time = 20 ms, echo time = 5 ms). The images had 6 mm slice thickness, with 256 × 256 pixels acquisition matrix and 250 mm field of view.

The quantification of the CC area was performed in the midsagittal image and the measurements were done by a radiologist (E. A.) who was unaware of the hypothesis tested. On the digital image, the maximum distance between the anterior and posterior CC limits was bisected and the resulting halves bisected again. Perpendicular lines erected on the points of division intersected with the CC and defined four areas in mm^2 (A1, A2, A3 and A4). The sector A1 included the rostrum and the genu of the CC; A2 referred to the main body; A3 the posterior body and anterior isthmus; and A4 approximately the posterior isthmus and the splenium (Fig. 1).

2.2.2. Dichotic Listening test

The dichotic stimuli consisted of the six stop consonants paired with the vowel /a/ to form six consonant vowel (C-V) syllables (ba, da, ga, ka, pa and ta). The syllables were paired with each other in all possible combinations to form 36 different syllable pairs. From these, the homonymic pairs (e.g., ba–ba) were included in the test as a perceptual control, but they were not considered in the statistical analyses. The other 30 syllables were duplicated and randomly recorded, giving 60 test trials, with a maximum correct score of 60. This DL test has achieved a test–retest reliability of .86 (Gadea, Gomez, & Espert, 2000). The subjects were informed that different syllables would be presented to each ear simultaneously, and were asked to report only one syllable (the one perceived most clearly).

2.2.3. Design and statistical analyses

Normality of all tested variables was confirmed by the Kolmogorov–Smirnov test ($p > .05$). To assess reliability of the morphometric procedure over time, an intraclass correlation (two-way mixed effects model, absolute agreement) for total CC and each subregional area was calculated.

To analyze callosal MR imaging measures (total area and four regions), a paired t test was applied between the two measures taken at the first and second moment. Regarding DL testing, an Analysis of Variance (ANOVA) was performed on the raw scores (correctly reported items) according to design 2 (ear input – RE versus LE) × 2 (moment – first versus second) with repeated measurements on both factors. Preliminary analyses showed that sex had no effect on the results so this variable was removed. Post-hoc paired t tests were also applied. Finally, Spearman rank

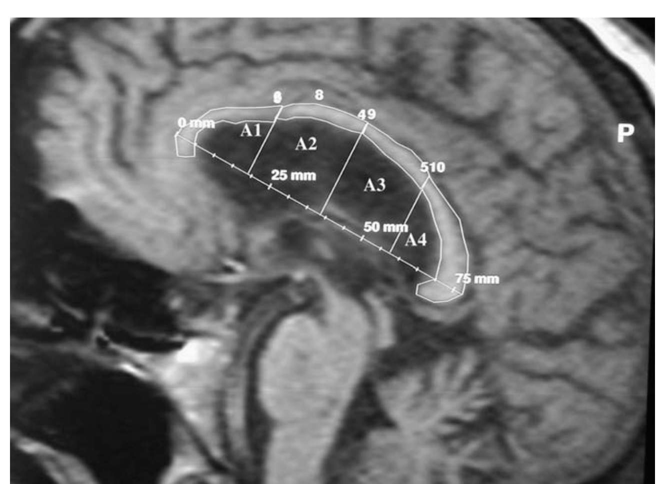

Fig. 1. Measurement of the corpus callosum.