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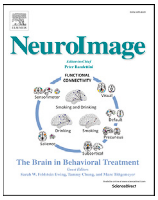

Callosal microstructure affects the timing of electrophysiological left-right differences

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ABSTRACT

The neural architecture of the corpus callosum shows pronounced inter-individual differences. These differences are thought to affect timing of interhemispheric interactions and, in turn, functional hemispheric asymmetries. The present study aimed at elucidating the neuronal mechanisms underlying this relationship. To this end, we used a combined DTI and EEG study design. In 103 right-handed and healthy adult participants, we determined the microstructural integrity of the posterior third of the corpus callosum and examined in how far this microstructural integrity was related to between-hemisphere timing differences in neurophysiological correlates of attentional processes in the dichotic listening task. The results show that microstructural integrity of the posterior callosal third correlated with attentional timing differences in a verbal dichotic listening condition but not in a noise control condition. Hence, this association between callosal microstructure and between-hemisphere timing differences is specific for stimuli, which trigger hemispheric bottom-up processing in an asymmetric fashion. Specifically, higher microstructural integrity was associated with decreased left-right differences in the latency of the N1 event-related potential component and hence more symmetric processing of dichotic stimuli between the two hemispheres. Our data suggest that microstructure of the posterior callosal third affects functional hemispheric asymmetries by modulating the timing of interhemispheric interactions.

1. Introduction

The corpus callosum is thought to be a fundamental factor for the emergence and maintenance of functional hemispheric asymmetries (Bryden and Bulman-Fleming, 1994; Ringo et al., 1994; Bamiou et al., 2007; Luders et al., 2010; Ocklenburg et al., 2016a). It is widely accepted to play an important role in both the integration and modulation of various processes in favor of the dominant hemisphere (Bloom and Hynd, 2005). One of the arguments for this role is the conduction velocity of callosal fibers, which can be estimated from their myelination and diameter. Electron microscopic studies indicate that in monkeys the majority of callosal axons are unmyelinated and have an average diameter of 0.75 μm (Lamantia and Rakic, 1990). In adult humans axon diameter varies between 0.6 and 1.0 μm (Aboitiz et al., 1992) and around 70% of callosal fibers are myelinated (Fields, 2008). The myelination influences the conduction time between the left and right hemispheres. In myelinated callosal fibers the conduction velocity is approximately 30 ms and between 150 and 300 ms in unmyelinated callosal fibers. Importantly, inter-individual variation of the callosal architecture in humans has been linked to the speed of interhemispheric processing (Westerhausen et al., 2006b; Horowitz et al., 2015) and callosal interaction is important for the establishment of functional brain asymmetries (Gazzaniga, 2000; Herve et al., 2013). However, it is virtually unknown to what extent the callosal architecture mediates the speed of hemispheric processing in the context of functional hemispheric asymmetries.

A prominent example of functional hemispheric asymmetries is speech perception (Bethmann et al., 2007; Ocklenburg et al., 2013b; Van der Haegen et al., 2013; Hugdahl and Westerhausen, 2016), which can be demonstrated with the dichotic listening paradigm (DLT). In this simple task, two different consonant-vowel syllables are simultaneously

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presented to the left and the right ear via headphones (Hugdahl, 2011), resulting in a larger number of correct reports from the right ear - the so-called „right ear advantage“ (REA) (Foundas et al., 2006). Since left-hemispheric auditory areas mainly process input from the right ear, the REA is thought to reflect the extent of left-sided dominance for auditory speech perception. Interestingly, the strength of the REA shows large inter-individual variation (Hirnstein et al., 2014). With regards to the role of the corpus callosum for dichotic listening, two theoretical models have been proposed to explain the neural foundation of this inter-individual variance.

According to the “structural model” (Kimura, 1967, 2011), the REA is caused by the anatomy of the ascending auditory pathway. Since contralateral projections are stronger than ipsilateral projections, right ear input is processed in the speech dominant left hemisphere, while input from the left ear primarily arrives in the non-dominant right hemisphere. Therefore, left ear input needs to be transferred to the left hemisphere to be processed. This transfer process is thought to occur via the corpus callosum. According to the “attentional model” (Kinsbourne, 1970; Hiscock and Kinsbourne, 2011), the anticipation of verbal stimuli leads to a preparatory left-hemispheric activation, resulting in an attentional bias towards the right ear. Hence, the right ear input is processed faster, thus producing the REA. In this model, the corpus callosum is thought to equalize the level of activation between the two hemispheres. Importantly, both models make the same prediction about the influence of the corpus callosum on the REA: a higher structural integrity of the corpus callosum is thought to lead to a more symmetric performance, because of better interactive capacities between the two hemispheres.

Indeed, this relation has been examined in clinical studies and studies in healthy individuals on different anatomical levels. First, clinical studies support the role of the corpus callosum in dichotic listening, as partial or complete callosotomy leads to increased REA in favor of the left hemisphere, based on a suppression of left ear reports (Clarke et al., 1993; Pollmann et al., 2002; Peru et al., 2003; Musiek and Weihing, 2011). Hence, the absence of the corpus callosum leads to stronger functional hemispheric asymmetries. Second, macroscopic anatomical properties of the corpus callosum, like the size of the midsagittal area, are positively correlated with the percentage of correct left ear reports and negatively correlated with the percentage of correct right ear reports (Westerhausen et al., 2006c). Thus, callosal macrostructure is associated with less functional asymmetry between the two hemispheres. Yet, more recent imaging methods such as diffusion tensor imaging (DTI) allow in-vivo tractography of specific fiber tracts (Catani et al., 2002; Behrens et al., 2007) as well as the microstructural quantification via means of fractional anisotropy (FA) (Basser and Pierpaoli, 1996). FA in white matter is thought to reflect myelin, axon diameter and packing density, axon permeability and fiber geometry (Wedeen et al., 2005; Mori and Zhang, 2006; Madler et al., 2008; Beaulieu, 2009; Zatorre et al., 2012) and is thus seen as a measure of microstructural integrity (Schulte et al., 2005; Genc et al., 2011a; Van Schependom et al., 2017), which in turn is associated with conduction velocity. DTI examinations in humans show that fiber connections within the corpus callosum are arranged in a topographic manner (Hofer and Frahm, 2006; Zarei et al., 2006). Especially the posterior third of the corpus callosum consists of interhemispheric fibers connecting the temporal cortices with each other. The posterior callosal third is important for transmitting both syntactic and prosodic information (Sammler et al., 2010). Accordingly, Westerhausen et al. (2009) identified transcallosal fibers in the posterior parts of the corpus callosum, which interconnect the superior temporal regions of both hemispheres. They found that the mid-sagittal tract size of superior temporal projections was positively correlated with the percentage of correct left ear reports. However a link between correct left ear reports and callosal microstructure was not found. Similarly, the neurophysiological basis of this effect in relation to the callosal microstructure is elusive.

There is clear evidence that the N1 event-related potential (ERP) component for dichotic stimuli, reflecting bottom-up attentional processes (Herrmann and Knight, 2001; Beste et al., 2010; Ocklenburg et al., 2012), is faster in the left than right the hemisphere; i.e. there is a strong latency difference between the hemispheres (Eichele et al., 2005). Since the important link between electrophysiological timing differences and callosal microstructure has not been shown so far, the current study examines this aspect by means of a dichotic listening task. The study is the first that interrelates electrophysiology and callosal microstructure. Given the evidence of a link between callosal microstructure and conduction velocity, we hypothesized that hemispheric latency difference is decreased in participants with higher microstructural integrity of the posterior callosal third.

2. Methods

2.1. Subjects

145 German-speaking volunteers (68 males and 77 females) with a mean age of 23.5 years (range 18–33) participated in the present study. We used the Edinburgh Handedness Inventory (EHI) to examine the handedness for each participant (Oldfield, 1971). This questionnaire yields a laterality quotient with a range between +100 and −100, with positive values indicating right- and negative values indicating left-handedness. The sample consisted of 106 right-handed (mean laterality quotient: 85.88, SD: 20.32) and 39 left-handed participants (mean laterality quotient: −73.39, SD: 24.89). All participants were healthy with no history of psychiatric or neurological disorders. Before the experiment, all participants underwent audiometric screening. None of the participants included in our final sample had interaural differences above 15 dB for any of the tested frequencies (6000 Hz, 3000 Hz, 1500 Hz and 750 Hz). Participants were given written informed consent and were either paid or compensated with course credit. Due to difficulties with the EEG acquisition, four participants (2 males and 2 females, 1 left-handed and 3 right-handed) were excluded from the study. Thus the final sample consisted of 141 participants (67 males, 38 left-handed). The right-handed subsample ($n = 103$; 48 males) showed a mean age of 23.7 years (range 19–33) and the averaged EHI laterality quotient was 85.99 ($SD = 20.15$). The left-handed subsample ($n = 38$; 19 males) had a mean age of 22.84 ($SD = 3.03$) and an averaged EHI laterality quotient of −72.69 ($SD = 24.83$). The ethics committee of the psychological faculty at Ruhr-University Bochum approved the study. All participants gave written informed consent and were treated in accordance with the declaration of Helsinki. Subjects were tested in two sessions. The first session included the handedness questionnaire and the EEG dichotic listening task. The second session consisted of the MRI imaging.

2.2. Dichotic listening paradigm

At the beginning of the experiment participants were seated in a chair in front of the presentation monitor, while EEG electrodes were already attached to the participant's scalp. The experiment was a passive dichotic listening task, which was conducted in accordance with a previous study (Beste et al., 2015). The stimuli consisted of six different consonant-vowel syllable pairs (e.g., “BA, “DA”, “GA”, “KA”, “PA”, and “TA”) that were digitally recorded and spoken by an adult German male. These stimuli were pretested and validated in previous studies (Ocklenburg et al., 2013a). Stimulus presentation was conducted using Presentation software (Neurobehavioural Systems, Inc., Albany, USA) at 30 dB via earphones. Participants were instructed to passively listen to the presented sounds. Differences between the voice onset times of voiceless (“KA”, “PA”, and “TA”) and voiced consonants (“BA”, “DA” and “GA”) were controlled for, thus the temporal envelopes of the syllables were matched. In the “dichotic condition” two different syllables were presented simultaneously to the two ears. All possible syllable pairs were presented counterbalanced to both ears, to avoid possible confounding effects of syllable-type. A “noise condition” was included as a control measure, in which the participants were confronted with white noise on