The cerebellum is believed to play an essential role in a variety of motor and cognitive functions through reciprocal interaction with the cerebral cortex. Recent findings suggest that cerebellar involvement in the network specialized for visual body motion processing may be mediated through interaction with the right superior temporal sulcus (STS). Yet, the underlying pattern of structural connectivity between the STS and the cerebellum remains unidentified. In the present work, diffusion tensor imaging analysis on seeds derived from functional magnetic resonance imaging during a task on point-light biological motion perception uncovers a structural pathway between the right posterior STS and the left cerebellar lobule Crus I. The findings suggest existence of a structural loop underpinning bidirectional communication between the STS and cerebellum. This connection might also be of potential value for other visual social abilities.

Keywords: cerebellum, connectivity, diffusion tensor imaging, point-light biological motion, superior temporal sulcus

Introduction

Recent neuroimaging and lesion studies indicate cerebellar involvement not only in motor but also in a variety of cognitive functions (see Strick et al. 2009 for review). Cerebellar engagement in cognitive processing has been shown to be mediated through bidirectional neuroanatomical connections with the frontal and parietal cortices (Dum and Strick 2003). Corresponding structural pathways are revealed by diffusion tensor imaging (DTI; Salmi et al. 2010). Cerebellar contribution has also been implicated in memory, auditory, and language functions, visual body motion and face perception, emotional processing, and social cognition (e.g., Petersen et al. 1989; Grossman et al. 2000; Vaina et al. 2001; Kils et al. 2003; Ohnishi et al. 2004; Riecker et al. 2005; Gobbini et al. 2007; Stoodley and Schmahmann 2009; Sokolov et al. 2010). These cognitive functions are considered to be primarily hosted in the temporal lobe (e.g., Scoville and Milner 1957; Perrett et al. 1985; Howard et al. 1996; Glover 1997; Allison et al. 2000; Grossman et al. 2000; Vaina et al. 2001; Beauchamp et al. 2004; Ohnishi et al. 2004; Pavlova et al. 2004; Pelphrey et al. 2005; Gobbini et al. 2007; Saygin 2007; Hein and Knight 2008; Da Costa et al. 2011; Herrington et al. 2011; Krakowski et al. 2011), and, in particular, the superior temporal sulcus (STS). Yet, possible connectivity pathways between the cerebellum and temporal cortex remain largely unknown.

Resting-state functional connectivity magnetic resonance imaging (fcMRI) suggests that the cerebellum is connected to the superior temporal cortex (O’Reilly et al. 2010; Habas et al. 2011; Dobromyslin et al. 2012) and to the inferior and anterior temporal cortices (Krienen and Buckner 2009; Buckner et al. 2011). By using dynamic causal modeling (DCM) in language and auditory domains (Booth et al. 2007; Pastor et al. 2008) and psychophysiological interactions (PPI) analysis during imitation of finger movements (Jack et al. 2011), effective connectivity has been revealed between the cerebellum and several functional areas within the superior temporal cortex. The STS, predominantly in the right hemisphere, is considered a major hub within the cortical network underpinning visual social cognition and biological motion processing (e.g., Bonda et al. 1996; Allison et al. 2000; Beauchamp et al. 2002; Grossman and Blake 2002; Pelphrey et al. 2003; Puce and Perrett 2003; Saygin et al. 2004; Pavlova 2012). In accord with neuroanatomical knowledge on contralateral connections between the cerebral cortices and cerebellar hemispheres (e.g., Middleton and Strick 1994), patients with lesions to the left lateral cerebellum exhibit deficient visual perception of body motion (Sokolov et al. 2010). As indicated by DCM, 2-way effective connectivity between the left cerebellar lobule Crus I and the right STS may subserve visual processing of point-light human locomotion (Sokolov et al. 2012). Resting-state and task-dependent fcMRI represent correlation analyses on time courses of activity in different brain regions that are aimed at identifying specific functional networks (Kleinschmidt et al. 1994; Biswal et al. 1995; Raichle et al. 2001; Fox and Raichle 2007). However, resulting correlations may also reflect similar, but not necessarily interconnected activity. Effective connectivity methods, such as PPI and DCM, analyze experimentally induced changes in coupling between regions in task-related imaging data (Friston et al. 1997, 2003). In particular, DCM reveals intrinsic connectivity between brain areas, direction of communication, and task-specific modulation within a network (Friston et al. 2003). Yet, it cannot be excluded that remote brain regions may mediate communication revealed through effective or functional connectivity analyses. The existence of structural pathways between brain areas exhibiting functional or effective connectivity therefore substantially reinforces concepts of direct interaction. Possible structural connections underlying...
communication between the STS and cerebellum have not yet been identified.

Neuroanatomical findings in nonhuman primates suggest the existence of projections from the STS to the pons (Brodal 1978; Glickstein et al. 1985, 1994; Schmahmann and Pandya 1991) and from the pons to the cerebellum (Brodal 1979; Glickstein et al. 1994). DTI, based on detection of more homogeneous diffusion of water molecules along structures such as white matter tracts (e.g., Basser et al. 1994; Mori et al. 2002), is currently the only technique for in vivo studying structural connectivity in humans. Despite DTI data on exist-

Materials and Methods

Participants

Sixteen healthy, right-handed, male volunteers (mean age 26.8 ± 3.5 years) with normal or corrected-to-normal vision, without history of neurological or psychiatric disorders, head injuries, or medication for anxiety or depression participated. Part of the group was involved in a previous study (Sokolov et al. 2012). Informed written consent was obtained in accordance with the requirements of the local ethical committee of the University of Tübingen Medical School.

fMRI Data Processing

Statistical Parametric Mapping (SPM8, Wellcome Institute of Cognitive Neuroscience, London, UK, http://www.fil.ion.ucl.ac.uk/spm) was used for processing of fMRI data to identify seeds for probabilistic tractography. Details on fMRI data preprocessing are described elsewhere (Sokolov et al. 2012). In summary, standard SPM slice timing and realignment corrections, as well as segmentation were conducted prior to normalization of the images to MNI space. Statistical analysis based on a general linear model was run on the resulting individual fMRI data. The individual whole-brain images for the contrast canonical versus scrambled biological motion were included in a second-level random effects whole-brain analysis. Individual activation clusters (threshold P < 0.001, uncorrected) located closest to the corresponding group maxima in the left cerebellar Crus I and the right posterior STS were extracted and served as seeds for subsequent probabilistic tractography. Both regions of interest could be identified in each data set. Neuroanatomical sites of the individual clusters were confirmed by using automated anatomical labeling (Tzourio-Mazoyer et al. 2002) that included a 3-D MRI human cerebellar parcellation (Schmahmann et al. 1999). MNI coordinates were converted into Talairach space by use of the icbm2tal transform (Lancaster et al. 2007).

DTI Data Processing

The processing of DTI data was conducted by using the FMRIB Software Library (FSL4, Oxford Centre for Functional MRI of the Brain, UK, http://www.fmrib.ox.ac.uk/fsl). Initially, to remove voxels located outside the brain, the Brain Extraction Tool (Smith 2002) was applied to the T1-weighted anatomical reference image and a volume without diffusion sensitization. Motion and eddy current correction, coregistration of diffusion-weighted images with the anatomical reference image, and alignment of the diffusion-weighted and anatomical images to the MNI space were performed using the FMRIB Linear Image Registration Tool (FLIRT; Jenkinson et al. 2002). Gradient directions were adjusted accordingly following each FLIRT step. Running Bayesian Estimation of Diffusion Parameters Obtained using Sampling Techniques with modelling of Crossing Fibres (BEDPOSTX; Behrens et al. 2007) on each individual normalized data set provided the diffusion parameters for each voxel.

Probabilistic tractography (step length = 0.5 mm, number of steps = 2000, number of pathways = 5000, curvature threshold = 0.2) with modified Euler integration providing for higher tracking accuracy was performed on the individual BEDPOSTX outputs. Only streamlines passing through both the Crus I and STS seeds were retained. Individual tractography outputs were thresholded at 5% of the robust intensity range (corresponding to a 95% confidence interval). Two participants did not exhibit significant connectivity maps and were excluded from group analysis. To assess overlaps in tract topology and interindividual variability, the individual maps were converted to binary maps (voxel value = 1 for streamlines passing through this voxel) and, subsequently, mathematically averaged to create a group variability map (Ciccarelli et al. 2003).

Results

We conducted probabilistic DTI tractography between 2 seeds, one in the right STS (Talairach coordinates of the group
cluster: \( x = 52, y = -54, z = 8 \) and another in the left lateral cerebellar lobule Crus I \( (x = -39, y = -56, z = -30) \), that were identified in a whole-brain analysis of fMRI data obtained during biological motion processing (Fig. 1). Regions in the right STS and the left cerebellar lobule Crus I have been previously reported to be active and to effectively communicate with each other during visual processing of point-light biological motion (Sokolov et al. 2012). Individual probabilistic tractography data (at a 95% confidence interval) and the group variability map indicate 2 pathways forming a structural loop between the right STS and the left Crus I (Fig. 1). A representative individual 3D reconstruction is shown in Figure 2.

The 2 fiber tracts pass distinct landmarks between the right STS and left cerebellum, such as the thalamus, pons, and medial or superior cerebellar peduncles. One fiber tract passes more anteriorly through the posterior limb of the right internal capsule and through the pons where the fibers cross to the left medial cerebellar peduncle. The other pathway passes through the left dentate nucleus, the left superior cerebellar peduncle and, having crossed into the right cerebellar peduncle, through the right thalamus, and then through a more posterior portion of the posterior limb of the internal capsule. Both fiber tracts merge further cephaladly and turn to the right posterior superior temporal cortex. In agreement with earlier data (Makris et al. 2005), these white matter tracts correspond to the right superior longitudinal fascicles II and IV. Some fibers also connect the right STS with ipsilateral cerebellum. The group variability map (based on binary individual structural connectivity maps thresholded at 5% of the robust intensity range that corresponds to a 95% confidence

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**Figure 1.** Group variability map of probabilistic tractography on individual seeds in (a) the right superior temporal sulcus (STS; green cluster) and the left lateral cerebellar lobule Crus I (blue cluster); for both seeds, group clusters are displayed. Some fibers connect the right STS with the ipsilateral cerebellum. The fiber tracts leave (b) the right STS cluster (green) along (c) the superior longitudinal fascicles II and IV. (d) They turn caudally and (e) split into an anterior and a posterior portion that further caudally form (f) a more lateral and a more medial pathway. (g) The anterior, caudally more lateral fibers join the corticopontine tract in the posterior crus of the internal capsule, whereas the posterior, caudally more medial pathway passes through the thalamus and, thus, can be attributed to the dentato-rubro-thalamo-cortical tract. (h) The fiber tract passing through the left superior cerebellar peduncle form the cerebello-temporal pathway. (i) Fibers crossing to the left in the pons, passing through the left medial cerebellar peduncle and reaching the left cerebellar lobule Crus I (blue) belong to the temporo-cerebellar pathway. Image orientation according to radiological convention. Slice position indicated in upper right corner. Fiber tracts and seed regions overlaid on the brain-extracted MNI standard space template provided within FSL.
The cerebral cortex and the cerebellum are thought to communicate through closed loops: An area in the cerebral cortex projecting to a cerebellar region receives input from this same region (Kelly and Strick 2003; Salmi et al. 2010). The present findings extend previous data inasmuch as they suggest the existence of 2-way structural connections between the temporal cortex and cerebellum. Previous DTI analysis within the cerebral peduncle primarily aimed at exploring prefrontal inputs to the cerebellum yielded disproportional connections from the temporal lobe (Ramnani et al. 2006). However, because of presumably high tract curvature and various intersections, cerebello-temporal connections may be more difficult to detect than other cerebro-cerebellar pathways. High-resolution DTI sequences and optimized processing methods used in the present study allow for enhanced analysis on intersections and direction changes within and between voxels. Acquisition of 2 data sets per participant further contributes to improving both sensitivity and consistency of diffusion parameter estimation.

Resting-state functional connectivity has been reported between the temporal cortex and cerebellum (Krienen and Buckner 2009; O’Reilly et al. 2010; Buckner et al. 2011; Haber et al. 2011; Dobromyslin et al. 2012). However, due to narrow neuroanatomical evidence in regard to possible underlying structural connectivity and intrinsic limitations of functional connectivity analyses, this communication has been considered to be mediated by the posterior parietal cortex and inferior parietal lobule (Gazzola and Keysers 2009; Krienen and Buckner 2009). The present DTI findings suggest existence of a direct structural pathway that may subserve communication between the STS and cerebellum.

The right temporal cortex, and, in particular, the right STS is engaged in visual body motion processing (e.g., Perrett et al. 1985; Bonda et al. 1996; Beauchamp et al. 2002; Grossman and Blake 2002; Pelphrey et al. 2003; Puce and Perrett 2003; Saygin et al. 2004). The present DTI findings based on task-specific seeds derived from analysis of fMRI data during observation of human locomotion may not only provide a possible structural correlate for interaction between the left cerebellum and the right STS during biological motion processing (Sokolov et al. 2012), but also for functional crosstalk between the cerebellum and STS in audiovisual integration (Baumann and Greenlee 2007; Baumann and Mattingley 2010; Petrini et al. 2011), imitation of body motion (Jack et al. 2011), observation of goal-directed hand movements (Gazzola and Keysers 2009; Turella et al. 2012), and visual social cognition (Ohnishi et al. 2004; Gobbini et al. 2007). Both biological motion and Heider-and-Simmel animations, consisting of moving geometric shapes that convey the impression of social interaction, elicit overlapping activations in the STS and lateral cerebellum (Gobbini et al. 2007). Another fMRI study also showed activation in the right STS and the left lateral cerebellum related to Heider-and-Simmel animations (Ohnishi et al. 2004). A similar contralateral structural connectivity pattern with a loop between the right cerebellum and the left temporal cortex could underpin cerebellar engagement in language processing (Petersen et al. 1989; Raichle et al. 1994; Riecker et al. 2005, 2006; Ackermann et al. 2007). Effective connectivity has already been reported between the right medial cerebellum and left middle and superior temporal cortices during a rhyming judgment task (Booth et al. 2007).

Social impairment and alterations in biological motion perception are intertwined in patients with autistic spectrum disorders and schizophrenia (Blake et al. 2003; Kim et al. 2005; Klin et al. 2009; Koldewyn et al. 2010, 2011; Nackaerts et al. 2012; Pavlova 2012). Moreover, in these conditions, abnormal structural connectivity parameters have been reported in the cerebellar tracts (Kanaan et al. 2009; Sivaswamy et al. 2010).

Discussion

By combining DTI with fMRI analysis, the present work reveals structural connections between the STS and cerebellum, offering novel insights into understanding of cerebro-cerebellar connectivity. Originating in the STS and Crus I seeds, the pathways pass along midbrain and diencephalic landmarks for cerebro-cerebellar connections known from previous neuroanatomical and DTI studies (e.g., Brodal 1975, 1979; Glickstein et al. 1985, 1994; Schmahmann and Pandya 1991; Dum and Strick 2003; Evrard and Craig 2008; Salmi et al. 2010). This suggests anatomical plausibility of the DTI findings and, in conjunction with previous neuroanatomical knowledge on connectivity patterns between the cerebellum and cerebral cortex (e.g. Brodal 1975; Nieuwenhuys et al. 1991; Strick et al. 2009), allows for repartition of the structural connection into a cortico-cerebellar pathway (those fibers passing the pons and medial cerebellar peduncle) and a cerebello-cortical tract (those fibers passing the superior cerebellar peduncle and thalamus). Although previous work points to a high degree of correspondence between DTI and neuroanatomical data (Johansen-Berg et al. 2005), future neuroanatomical studies are required to confirm this outcome.

The cerebral cortex and the cerebellum are thought to communicate through closed loops: An area in the cerebral cortex projecting to a cerebellar region receives input from this same region (Kelly and Strick 2003; Salmi et al. 2010). Figure 2. 3-D reconstruction of the structural loop between the right superior temporal sulcus (STS) and the left lateral cerebellar lobule Crus I in a representative individual. SCP: superior cerebellar peduncle; MCP: medial cerebellar peduncle.
and the temporal white matter (Barnea-Goraly et al. 2004; Lee et al. 2007; Schlösser et al. 2007). The only significant interaction in a correlation analysis between diffusion anisotropy (as a parameter for fiber pathway integrity) and social impairment in children with Asperger syndrome was found for the left superior cerebellar peduncle (Catani et al. 2008), which is the main conduit for information flow from the left cerebellum to the right cerebral cortex. As suggested by the present data, the left superior cerebellar peduncle might also contain fibers reaching the right STS. This study thereby promotes further investigation of associations between disintegration of cerebro-cerebellar networks and social cognition. Taken together, the evidence for a structural loop between the left cerebellum and the right STS may stimulate future research on the role of temporocerebello-temporal interactions for higher cognitive processing in typical and atypical development.

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Notes
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