The cortico-cortical structural connectivity of the human insula

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Introduction

The insula, the fifth lobe of the brain, is a complex structure involved in numerous functions including the processing of somatosensory, viscerosensory, auditory, language, and vestibular stimuli among other things. Tracing studies on non-human primates reveal a wide array of cortical connections in the frontal (orbitofrontal cortex, prefrontal cortex, cingulate areas, and supplementary motor area), parietal (primary and secondary somatosensory cortices) and temporal (temporal pole, superior temporal sulcus, auditory cortex, prorhinal and entorhinal cortices) lobes (Mesulam et al., 1982; Mufson et al., 1982). The human insula is 30% larger and more complex and its structural connectivity is still poorly established. Until now, only three groups have attempted to unravel the connectivity of the human insula using tractography, albeit with a low number of subjects and with varying results (Cloutman et al., 2012; Cerliani et al., 2012; Jakab et al., 2012). We report here our findings of the trajectory of white matter fibers between the human insula and other cortical structures, benefiting from a high number of subjects and latest advances in tractography.

Methodology

We scanned 46 healthy human subjects on a 3T Philips MRI with high angular resolution diffusion imaging using deterministic tractography diffusion weighted images with 60 directions. We used Advanced Normalization Tools to create a representative template resampled to 1mm, from which a gray matter probabilistic map was extracted in order to create 200 randomly parcellated regions in each hemisphere. As for the insula, it was divided into 19 regions in each hemisphere based on sulco-gyral delimitations. We then used the FMRIB’s software library for preprocessing and MRtrix for processing the data. Tractography algorithm was performed on a 1mm dilated white matter probabilistic mask with a 35^{o} curvature degree, a length limit of

500mm, 10 000 streamlines from each ROI and by estimating the fiber orientation distribution function for a greater fiber crossing discrimination. We computed the number of fibers between the insula and each parcellated region of the cortex for each subject. Finally, we normalized the number of fibers from each ROI of the insula by the volume of each ROI, and extracted the connected cortical regions with a mean of at least 25 fibers.

Results

We found fibers connecting the insula with the frontal, temporal and parietal lobes. Within the frontal lobe, the insula has connections to the orbitofrontal cortex, the superior/middle/inferior frontal gyri, the cingulate gyrus, and the pre- and post-central gyri). Within the temporal lobe, the insula has connections with the superior/middle/inferior temporal gyri, temporal pole, and amygdala and parahippocampal gyrus. Within the parietal lobe, the insula has connections with the post-central gyrus, superior parietal lobule and supramarginal gyrus. We found no insular connections to occipital areas. There was a clear differential connectivity pattern from the anterior to the posterior insula.

Conclusions

Our study reveals a wide array of connections between the insula and the frontal, temporal and parietal lobes with a clear differential connectivity pattern moving from the anterior to the posterior insula, in line with macaques tracing studies. Notably, we were able to reveal for the first time in humans clear structural connectivity between the insular cortex and cingulate cortex as well as the parahippocampal gyrus by overcoming known methodological limitations such as crossing fibers (i.e. corona radiata) and false negatives (i.e. probabilistic approach). Lack of insular connections to the occipital lobe suggests that such previous reports were false positives due to the proximity of the claustrum.

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