Structural Connectivity Mapping of the Central Amygdala

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Introduction

The central amygdala (CeA) is a key hub for integrating emotion, interoception, and autonomic responses, yet its structural connectivity remains largely unmapped. To address this, we investigated the structural connectivity of the CeA in both humans (using high-resolution diffusion MRI) and mice (using the Allen Mouse Connectivity Atlas), aiming to reveal its subcortical and cortical projection patterns and functional integration across domains.

Methods

Diffusion MRI data from 730 subjects in the Human Connectome Project (Van Essen et al., 2012) were processed using multi-shell modeling via BEDPOST (Jbabdi et al., 2012; Jenkinson et al., 2012) and probabilistic tractography with PROBTRACKX (Behrens et al., 2007). The central amygdala (CeA) was defined using the CIT168 Subcortical Atlas (Pauli et al., 2018) and used as the seed region. Group-level connectivity probability maps were anatomically assigned using the HCP XTRACT Atlas, Harvard–Oxford Atlas, and Brainstem Navigator Atlas.
The Allen Mouse Connectivity Atlas provides voxel-wise efferent projections from the CeA using anterograde tracers (Kuan et al., 2015). The analysis combines the top 10 experiments (by injection volume) to delineate 3D projection density maps from the CeA to different brain regions.

Results

The CeA exhibited widespread structural connectivity across cortical, subcortical, brainstem, and cerebellar regions, supporting its integrative role in emotion, memory, and autonomic regulation. Key pathways included the fornix, optic radiation, and fronto-occipital fasciculus. The strongest cortical associations were found in the subcallosal, cingulate, and parahippocampal areas, while subcortical targets included the thalamus, hippocampus, and amygdala. Brainstem nuclei such as the PCRtA, LPB, DR, and PAG showed high connectivity, highlighting roles in arousal and visceral control. The structural connectivity maps in the mouse also show widespread projection patterns to different cortical and subcortical areas.

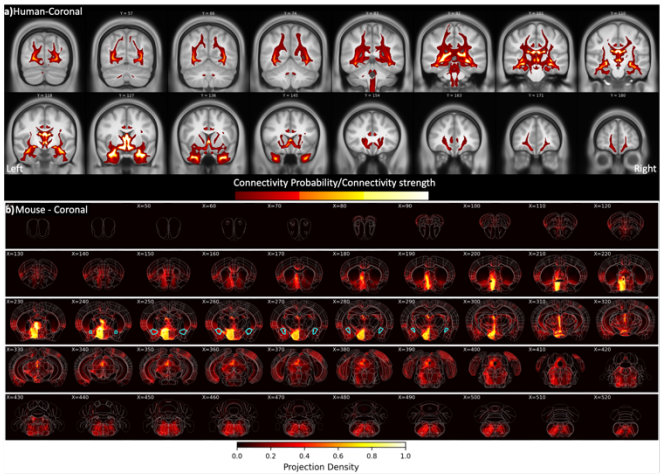

Fig 1: Structural Connectivity of the Central Amygdala (CeA): a) Probabilistic tractography results showing group-level structural connectivity maps of the left and right CeA to the ipsilateral hemisphere in 730 subjects. b) Coronal slice view showing projection density from the central amygdala (CeA), highlighting efferent connectivity patterns across brain regions.

Conclusion

Our findings demonstrate that the CeA exhibits widespread structural connectivity with cortical, subcortical, and brainstem regions, consistent with its role as an integrative hub for emotion, interoception, and autonomic regulation. Robust connections to the PAG, PBN, NTS, DMV, and LC highlight its involvement in visceral pain and gut–brain communication. In the mouse brain, anterograde tracer data similarly reveal broad projection patterns, underscoring the CeA's engagement in diverse brain–body functions. While diffusion tractography provides valuable macroscale insights, it remains an indirect measure of water diffusion along fiber pathways, which does not reflect actual axonal projections with the accuracy of tracer studies and is therefore susceptible to false positives and anatomical misinterpretation.