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## Using BigBrain to establish a histologically-informed MRI reference of the human claustrum

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**Background.** The claustrum is a “sheet-like” telencephalic grey matter structure, wrapped by the capsulae extrema and externa, and tucked between the putamen and insula. Anatomical studies have revealed that the claustrum is one of the most connected of any brain structure (by volume), and demonstrates reciprocal connections across the entire cortical mantle. Though this remarkable connectivity has given rise to a gamut of hypotheses, very little is known about claustral function due to its complex shape, thinness and location, hampering in vivo investigation with conventional MRI. Specifically, typical imaging resolution at 3 Tesla is insufficient to differentiate the claustrum from the insula and putamen, and all but precluded automated segmentation methods.

**Objective.** We are seeking to clarify claustral structure and function using MRI at ultra-high field, with a spatial resolution sufficient, in principle, to disambiguate the claustrum from its surrounding structures. However, these efforts have been limited by the lack of a ‘ground truth’ claustral reference. Our objective is to provide this reference by segmenting the claustrum in the BigBrain dataset. By making our segmentation publicly available, we will provide a shared benchmark to quantify the promise, and pitfalls, of claustral investigation at ultra-high fields.

**Methods.** We have segmented the right claustrum on the 100 micron isotropic BigBrain in MNI ICBM-152 space. We found that ITK-SNAP’s semi-automatic segmentation methods gave rise to both false positives (inclusion) and negatives (exclusion), so opted to delineate the structure manually. Our manual segmentation was informed by simultaneous visualization on all three planes; in cases of ambiguous inclusion/exclusion, we consistently deferred to the axial plane. To quantify the integrity of claustral reconstruction at ultra-high field, we followed the same manual segmentation procedure using a 0.7mm isotropic MP2RAGE dataset on healthy human subjects (N=6) collected on a Siemens 7 Tesla at Maastricht University, Netherlands.

**Results.** The unparalleled resolution afforded by BigBrain has underscored the claustrum’s challenging anatomy. Generally, our reference segmentation is consonant with claustral descriptions in histological literature, though one unanticipated finding is that the right claustrum appears larger than reported (spanning approximately 40mm rostrocaudally and 25mm dorsoventrally, vs. 38mm and 22mm, respectively). Our comparative evaluation of the claustrum in the Maastricht dataset suggests that the claustrum is only partially captured at 7 Tesla; notably, its extreme extents evade detection. We are presently working to quantify the spatial overlap between the BigBrain reference and Maastricht datasets, and estimate heterogeneity between participants in the latter (results forthcoming for presentation).

**Discussion.** We anticipate that our ‘ground truth’ BigBrain segmentation will be of interest to researchers in its own right. Further, we anticipate our work will delineate exactly how (native) ultra-high field MRI falls short of adequately capturing the claustrum in vivo. We hope that our BigBrain reference may inform guided segmentation efforts, which we believe may be necessary for claustral research at ultra-high field. Excitingly, the claustrum’s span appears sufficient to seed connectivity, opening the prospect of moving from microstructure to functional connectomics, and in so doing, unraveling enduring mysteries of claustral function.

**Primary authors:** CALARCO, Navona (University of Toronto; University Health Network); Dr KASHYAP, Sriranga (University Health Network); Dr ULUDAG, Kamil (University Health Network)

**Presenter:** CALARCO, Navona (University of Toronto; University Health Network)

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