MSc Project 2: What can the rodent brain tell us about the human brain?

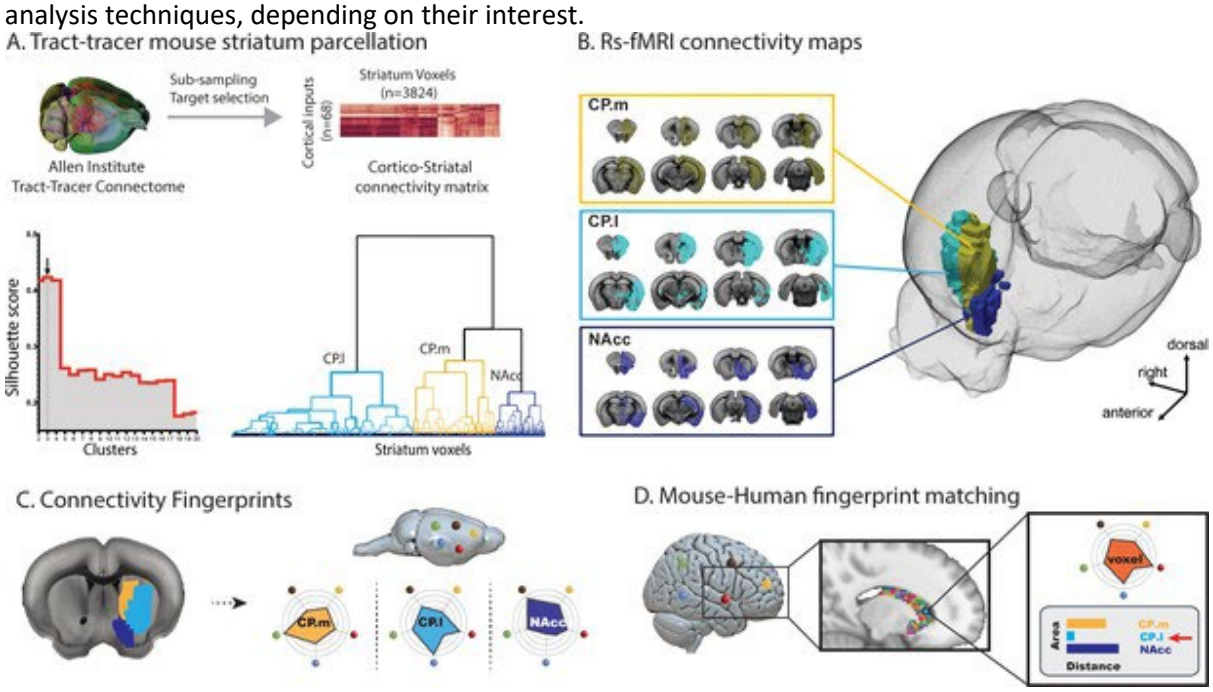
The rodent brain—specially the mouse brain—is the most often-used 'model brain' that we study to understand our own. These days, genetic models of disease are commonly studied in the mouse, but the translation to understand actual human diseases often ends up in failure. This is for a large part due to the fact that we have very little quantitative understanding of how the organization of the mouse and human brains relate. We are the developing the first tools to do make such comparisons explicit, using gene expression, functional MRI, and structural MRI data. This project will allow the student to either develop such tools, to apply them to compare specific parts of the mouse and human brain, or to assess the suitability of the mouse model for a particular human brain disease.

The student can enrol in a number of research projects, depending on their interests. Some ongoing projects are:

1. Creating a whole-brain rodent to human brain atlas

For many areas of the human brain, it is controversial whether they have an equivalent in the mouse brain. Some research groups claim that the mouse has a miniature prefrontal cortex, some claim that this huge structure is unique to humans. The answer to this question is of crucial importance for translational neuroscience. We aim to compare brain organization across species using high-throughput data, such as MRI data and gene expression data. We have a lot of expertise using these techniques comparing the brains of different primates, but the rodent has only recently been a focus of ours. Given that the rodent is becoming increasingly popular in research, this work has very high impact.

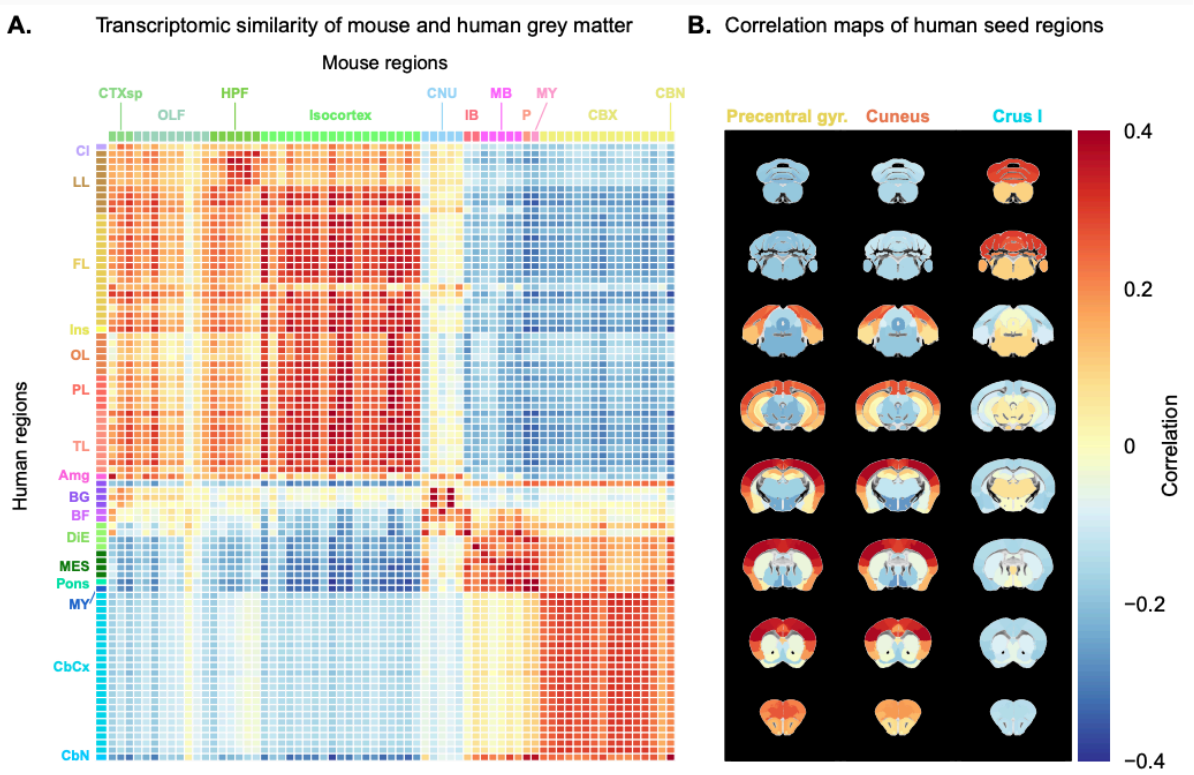
Students working on this project can choose to focus more on anatomy or more on advanced analysis techniques, depending on their interest.



Relevant literature: (1) Balsters et al., 2020, eLife 9:e53680, doi: 10.7554/eLife.53680; (2) Beauchamp et al., 2022, bioRxiv, doi:10.1101/2022.03.18.484766

2. Testing the validity of the mouse model for disease

Using our comparative techniques, we can validate disease models of the human brain. We can do this in two ways. First, we can build a ‘difference map’, describing exactly which parts of the human brain are too different from the mouse brain to study in that animal. We can then investigate which diseases target those areas—meaning that the mouse model will be a poor model to study for these patients. Second, we can use our comparative techniques to predict how disease manipulations in the rodent would look like in the human brain, providing the first ever quantitative mouse-to-human quantitative translational neuroscience.



Relevant literature: (1) Mars et al., 2021, Annu Rev Neurosci 44:69-86, doi:10.1146/annurev-neuro-10220-025942; (2) Van den Heuvel et al., 2019, Brain 142:3991-4002, doi:10.1093/brain/awz330

Potential students are welcome to contact the primary supervisor (rogier.mars@donders.ru.nl) to see further work ongoing in the lab.