Animal models play an indispensable role in neuroscience research, both in the context of understanding disease and developing treatment and in the context of obtaining data that cannot be obtained in the human. While numerous species have been used to model the human brain, the mouse has emerged as the most prominent of these, due to its rapid life cycle, straightforward husbandry, and amenability to genetic engineering (Hedrich, Mossmann, and Nicklas 2004; Houdebine 2004; Dietrich, Ankeny, and Chen 2014; Ellenbroek and Youn 2016). Mouse models have proven to be extremely useful for understanding diverse features of the brain, from its molecular neurobiological properties to its large-scale network properties (REFS). However, translation from the mouse brain to the human has not been straight-forward. XXX WE NEED EXAMPLE OF THIS, SUCH AS HELEN’S PHASE III FAILURE EXAMPLE

Successful translations require an understanding of how effects on one brain (the model species) are likely to manifest in the other (the actual species of interest, i.e., the human). This is not trivial, as the mouse and the human diverged from a common ancestor about 80 million years ago (Kaas, 2012). Although there are common themes apparent in all mammalian brain studied to date (Krubitzer, 2007), large differences between the mouse and human brain are apparent. These differences manifest themselves in the obvious size differences, but also in the potential absence of homolog of large parts of the human cortex in the mouse (Preuss, 2005). Direct comparisons across brains are further complicated by the fact that researchers in the different traditions use different nomenclature to refer to similar anatomical areas (Laubach, 2011; Van Heukelum et al., 2020).

Ideally, the field of translational neuroscience would develop anatomical atlases that would make the similarities and differences between brains explicit. This approach would describe brains in a common dimension that is directly comparable between the two species and quantify how similar each part of one brain is to each part of the other. Such a ‘common space approach’ allows one to evaluate similarity across regions in a quantitative fashion (Mars et al., 2021). This way, potential homologs can be formally tested and parts of the brain that do not allow straight-forward translation can be identified (Mars et al., 2018). Establishing such a formal translation between the mouse and the human brain would have the potential to XXX A FEW WORDS THAT REFLECT THE POTENTIAL OF MOUSE TRANSLATIONAL WORK

One approach towards building such common spaces has been to exploit connectivity. The connections of a brain region tend to be unique and can therefore be seen as a diagnostic of an area (Passingham et al., 2002; Mars, Passingham, Jbabdi, 2018). The approach of building a common connectivity space relied on defining agreed upon homologies and then expressing the connectivity fingerprint of regions under investigating with those established homologies in the two brains (Mars et al., 2016). The established homologies then form a ‘common space’ across the two brains. Helped by advances in MRI, a series of early studies compared the connectivity of the macaque and human brain, showing identifying homologies as well as specializations across association cortex (Mars 2013; Sallet 2013; Neubert 2014). The same approach has recently been applied to mouse-human comparisons for the first time, demonstrating conserved organization between mouse and human striatum, but some specialization is human caudate related to prefrontal connectivity (Balsters et al., 2020). A similar study recently compared connectivity of the medial frontal cortex across rats, marmosets, and humans (Schaeffer et al., 2021). However, the lack of established homologs limit the use of connectivity to compare rodents to humans.

A more promising approach to mouse-human comparisons could be to exploit the spatial patterns of gene expression. Advances in transcriptomic mapping allow one to characterise the differential expression of many thousands of genes across the brain and compare the pattern between regions (Ortiz et al., 2021). Whole-brain maps are now available for multiple species Such maps for the human cortex show topographic patterns that mimic those observed in other modalities, such as a gradient between primary and heteromodal areas of the neocortex (Burt et al., 2018). Importantly, such patterns seems to be conserved across mammalian species (Fulcher et al., 2019), which opens us the possibility of using the expression of homologous genes as a common space across species.

Here we examine the patterns of similarity between the mouse and human brain using a common space constructed from spatial transcriptomic data sets. We begin with an initial set of 2624 homologous genes. Subsequently, we present and evaluate a novel method for improving the resolution of mouse-human neu- roanatomical correspondences using a supervised machine learning approach. Using the novel representation of the gene expression common space, we analyse the similarity of mouse and human isocortical subdivisions and demonstrate that sensorimotor regions exhibit a higher degree of similarity than supramodal regions. Finally, we demonstrate that the correspondence between mouse and human striatal regions is more nuanced than suggested by standard neuroanatomical nomenclature.