Quantifying Brain-Behavior Links: Advances and Current Applications of Morphometricity in Neuroimaging

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Morphometricity (m^2) quantifies the proportion of trait variance explained by structural brain features [6]. This approach was originally inspired by genetics, and was largely made possible by the UK Biobank large MRI collection. In this presentation, we will review a decade of m^2 results and applications encompassing 19 in-depth studies (+38 associated) of independent research groups throughout Australia, France, Norway, USA, and the UK.

Morphometricity revealed strong links between various traits and brain structure [2, 3, 6]. Sabuncu et al. (2016) reported the m^2 of psychiatric and cognitive traits across nine studies, comprising over 3,800 individuals. Their results on Alzheimer's disease were extended by Couvy-Duchesne et al. (2025, N = 9,400), which reported the m^2 of different disease stages and neuropsychological domains. Exploratory analyses have reported the m^2 of hundreds of traits from the UK Biobank (N = 8,500 - 37,000) [1, 4] or of several early life traits from the ABCD cohort (N = 7,760) [3]. These studies have shown that many behavioral and biological characteristics are associated with a measurable structural footprint in brain neuroanatomy.

Yet, morphometricity estimates can vary across studies due to different methodological choices. The choice of image processing (e.g., Region of Interest, [ROI], choice of atlases, vertex-wise or voxel-wise representation) impacts m^2 [4, 5]. So does the choice of kernel (e.g., Gaussian [7], or more traditional linear kernel used in genetics [1]). Lastly, implementations may also contribute to differences in results, from MATLAB scripts to validated and optimised genetic software [1, 2, 8].

Despite these challenges, m^2 has been successfully used to compare MRI processing methods, and narrow down the source of the signal (e.g., ROI-based estimates). Recent developments enable robust estimation for non-normal distributed phenotypes and summary statistics promise to reduce the need to access individual level data and to accelerate computation. Future avenues of research include modeling of interactions (e.g., age $\times$ m^2) and non-linear contributions of brain measurements. Further work is required to clarify the impacts of kernel choice on estimates and standard errors, and investigation of model assumptions.

References

1. B. Couvy-Duchesne. A unified framework for association and prediction from vertex-wise grey-matter structure. *Human Brain Mapping*, 41(14), 2020.
2. B. Couvy-Duchesne. Grey-matter structure markers of alzheimer's disease, alzheimer's conversion, functioning and cognition: A meta-analysis across 11 cohorts. *Human Brain Mapping*, 46(2), 2025.
3. A. Dahl. Genetic and brain similarity independently predict childhood anthropometrics and neighborhood socioeconomic conditions. *Developmental Cognitive Neuroscience*, 65(1), 2024.
4. E. Delzant. Choice of processing pipelines for t1-weighted brain mri impacts association and prediction analyses. *Human Brain Mapping*, 46(16), 2025.
5. A. Furtjes. A quantified comparison of cortical atlases on the basis of trait morphometricity. *Cortex*, 158(1), 2023.
6. M. R. Sabuncu. Morphometricity as a measure of the neuroanatomical signature of a trait. *Proceedings of the National Academy of Sciences of the United States of America*, 113(39), 2016.
7. Z. Wen. Identifying shared neuroanatomic architecture between cognitive traits through multiscale morphometric correlation analysis. *Lecture Notes in Computer Science*, 14394 LNCS(227-240), 2023.
8. Z. Wen. Multiscale estimation of morphometricity for revealing neuroanatomical basis of cognitive traits. *Proceedings - International Symposium on Biomedical Imaging*, 2024.