# Searching for neural biomarkers in psychiatry: not a descriptive but a constitutive practice

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*Both authors would like if possible to present this work as a dual presentation.

In neuroscience, non-invasive neuroimaging techniques are widely used with the promise of identifying biomarkers for patients. Classically, researchers compare a patient group with a group of “unaffected” controls to detect differences in brain structure or function (a case-control approach). In recent years, frameworks such as HiTOP and RDoC have conceptualised mental disorders as the extreme ends of continuous dimensions of functioning.

Both approaches rely on an assumption: that there exists a “normal” range of functioning, against which deviation can be quantified. Importantly, “normality” and “deviation” are not clinical ground truths, but statistical constructs that depend on how the reference class is defined. Accordingly, what counts as “normal” is determined through analytical choices. In other words, defining who counts as “healthy” establishes the baseline from which deviation is measured, thereby shaping what can be detected as signal and what is treated as noise.

Drawing on our own research, we illustrate these issues using both case-control type analyses and more advanced machine-based learning techniques applied to neuroimaging data. We demonstrate how the assumptions embedded in common analytical frameworks shape the conclusions that can be drawn. Finally, we offer recommendations for the field and argue that the reference-class problem should be made explicit.