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MEANINGFUL PSYCHIATRIC PHENOTYPES EMERGE FROM A BAYESIAN TAXONOMY OF EYE MOVEMENTS

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Use of DSM and ICD nosology to stratify adult psychiatric illnesses poses significant practical challenges for biomarker discovery. Illness categories and subtypes have not been validated by objective tests. The epistemology and language of diagnostic psychiatric tools prevails during 2013-2014 while continuing to say nothing about the biological underpinnings of mental disorders. Assays mapped onto the current nomenclature remain contentious because empirical analyses and clinical intuition are often in conflict, producing 'misclassifications' that are difficult to interpret. DSM-5 revisions are obliged to incorporate empirical psycho-bio-physiological measurements supporting graduated dimensional descriptions of mental health disorders that properly reflect both quanta and spectra of variation extant in the population. Eye movements elicited by simple cognitive tasks are an endophenotypic bridge between the genetics, neuropathology, cognition, and ethno-socio-cultural factors of the major neurodevelopmental psychiatric disorders. We have shown that multivariate measures of oculomotor dysfunction are capable of differentiating schizophrenia, bipolar disorder and endogenous major depression cases with exceptional specificity (Benson et al (2012) *Eur Psychiatry* 27(Supp1):1; Benson et al (2013) *Eur Arch Psychiatry Clin Neurosci* 263(Supp1): S19). Here we used unsupervised Bayesian clustering to stratify cases and controls using only their eye movement data. Performance measures from smooth pursuit, free-viewing and steady fixation tasks were used. Twelve clusters described a continuum of phenotypes, associated with schizophrenia, bipolar, mixed affective cases, and undiagnosed controls. Composite clusters evinced cases with shared and/or comorbid symptoms and subclinical groups. Eye movement abnormalities through their task-related substrates represent an objective bottom-up approach to diagnosis outside current categorical systems.

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