**Exploring the Genetic Architecture of the Human Neurological Proteome using Whole Genome Sequencing**

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The human proteome has a stronger genetic component compared to many complex diseases, making it a valuable resource of potential disease biomarkers and drug targets. This is especially so for highly polygenic neurological disorders whose mechanisms remain elusive. Here, we present the first sequence-based protein quantitative trait loci (pQTL) analysis of 92 neurological proteins. We perform a meta-analysis using deep whole-genome sequencing (WGS) data from two isolated Greek cohorts, MANOLIS (22.5x WGS; N=1,356) and Pomak (18.4x WGS; N=1,537). A total of 123 independently-associated variants in 84 loci reach study-wide significance (*P*<1.14x10-10) for 63 proteins, all of which are at least nominally significant (*P*<3.78x10-4) and have the same direction of effect in both cohorts. To further elucidate the genetic architecture, independent variants were classified into 89 (72%) *cis-* and 34 (28%) *trans-*acting pQTLs. Ten variants have consequences equal to or more severe than missense, and 33 overlap regulatory regions. We also discover variants that have previously been linked to psychiatric disorders. For example, an intronic *trans-*pQTL in the *ITIH4* gene is associated with increased NEP levels (*rs2239547; P=*1.19x10-129; BETA=0.637983; SE=0.026328), and is an established risk variant for schizophrenia and bipolar disorder. This analysis represents the largest and only WGS-based pQTL study of neurological proteins to date, delivering insight into the rare and common genetic variant landscape underlying the human neurological proteome and its connection to neurological diseases.