Abstracts

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Whole-exome sequencing associates novel CSMD1 gene mutations with familial Parkinson disease

**Objective** Despite the enormous advances made in deciphering the genetic architecture of Parkinson disease (PD), the majority of PD is idiopathic, with single gene mutations explaining only a small proportion of the cases.

**Methods** In this study, we clinically evaluated 2 unrelated Spanish families diagnosed with PD, in which known PD genes were previously excluded, and performed whole-exome sequencing analyses in affected individuals for disease gene identification.

**Results** Patients were diagnosed with typical PD without relevant distinctive symptoms. Two different novel mutations were identified in the CSMD1 gene. The CSMD1 gene, which encodes a complement control protein that is known to participate in the complement activation and inflammation in the developing CNS, was previously shown to be associated with the risk of PD in a genome-wide association study.

**Conclusions** The CSMD1 mutations identified in this study might be responsible for the PD phenotype observed in our examined patients. This, along with previous reported studies, may suggest the complement pathway as an important therapeutic target for PD and other neurodegenerative diseases.

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Moderate blast exposure alters gene expression and levels of amyloid precursor protein

**Objective** To explore gene expression after moderate blast exposure (vs baseline) and proteomic changes after moderate (vs low) blast exposure.

**Methods** Military personnel (n = 69) donated blood for quantification of protein level, and peak pressure exposures were detected by helmet sensors before and during a blast training program (10 days total). On day 7, some participants (n = 29) sustained a moderate blast (mean peak pressure = 7.9 psi) and were matched to participants with no/low-blast exposure during the training (n = 40). PAXgene tubes were collected from 1 training site at baseline and day 10; RNA sequencing day 10 expression was compared with each participant’s own baseline samples to identify genes and pathways differentially expressed in moderate blast-exposed participants. Changes in amyloid precursor protein (APP) from baseline to the day of blast and following 2 days were evaluated. Symptoms were assessed using a self-reported form.

**Results** We identified 1,803 differentially expressed genes after moderate blast exposure; the most altered network was APP. Significantly reduced levels of peripheral APP were detected the day after the moderate blast exposure and the following day. Protein concentrations correlated with the magnitude of the moderate blast exposure on days 8 and 9. APP concentrations returned to baseline levels 3 days following the blast, likely due to increases in the genetic expression of APP. Onset of concentration problems and headaches occurred after moderate blast.

**Conclusions** Moderate blast exposure results in a signature biological profile that includes acute APP reductions, followed by genetic expression increases and normalization of APP levels; these changes likely influence neuronal recovery.

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