**POLYGENIC RISK FOR DEPRESSION INCREASES RISK FOR ISCHEMIC STROKE**: **FROM THE STROKE GENETICS NETWORK (SIGN) STUDY**

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**Background and Purpose:**Depression has been elevated by the American Heart Association to the status of a risk factor for poor prognosis in patients with acute coronary syndrome. While depression is a risk factor for stroke in large prospective studies, it is unknown whether these conditions have a shared genetic basis.

**Methods**: We applied a polygenic risk score (PRS) for major depressive disorder (MDD) derived from European ancestry analyses by the Psychiatric Genomics Consortium (PGC) to a GWAS of ischemic stroke in the NINDS Stroke Genetics Network (SiGN). Included in separate analyses were 12,577 stroke cases and 25,643 controls of European ancestry and 1,353 cases and 2,383 controls of African ancestry. We examined the association between depression PRS and ischemic stroke overall and with etiologic subtypes using logistic regression analyses.

**Results:** The depression PRS was associated with higher risk of ischemic stroke overall in both European (p=.025) and African ancestry (p=.011) samples from SiGN. Ischemic stroke risk increased by 3.0% (OR=1.03, 95%CI: 1.00 -1.05) for every one standard deviation increase in PRS for those of European ancestry and by 8% (OR=1.08, 95%CI: 1.04-1.13) for those of African ancestry. Among stroke subtypes, elevated risk of small artery occlusion was observed in both European and African ancestry samples. Depression PRS was also associated with higher risk of cardioembolic stroke in European ancestry and large artery atherosclerosis in African ancestry persons.

**Conclusions:** Higher polygenic risk for MDD is associated with increased risk of ischemic stroke overall and with small artery occlusion. Additional associations with ischemic stroke subtypes differed by ancestry.