Stroke

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Abstract 23: BDNF val^{66}met Genotype is Associated With Greater Brain Atrophy After Stroke

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Abstract

Background: Genetic factors may be useful to understand differences in outcomes post-stroke. We studied an imaging measure of brain atrophy in relation to two genotypes that may be associated with differences in stroke recovery, the val^{66}met genotype for brain-derived neurotrophic factor (BDNF) and the ApoE e4 genotype. Each genotype has been associated with brain atrophy in non-stroke populations. The current study hypothesized that each genotype is associated with brain atrophy after stroke.

Methods: The ICARE Study examined behavioral outcomes after stroke in relation to motor therapies. Of 361 ICARE enrollees, genetic and neuroimaging data were available in 127. The volume of the ventricles and the brain were measured, and brain atrophy expressed as the Ventricle-Brain Ratio (VBR). For MRI scans, VBR was first extracted from the scans using ALVIN then manually refined. For CT scans, VBR was extracted manually. All VBR measurements were verified by a neuroimaging expert. VBR was examined in relation to the two genotypes of interest, BDNF val^{66}met and ApoE e4, controlling for the 3 covariates employed in ICARE: motor deficits, enrollment site, and time post-stroke at study entry.

Results: There were 61 MRI and 66 CT scans. These were acquired 5±11 days post-stroke, which did not vary according to either genotype. Median ventricle volume=26.1 cc; brain volume=1,163 cc; and VBR=0.024. The BDNF val^{66}met genotype was present in 23 subjects; ApoE e4, in 41; both were in HW equilibrium. Presence of the BDNF val^{66}met genotype was associated with greater atrophy: median VBR increased 1.97-fold when this genotype was present vs. absent (p=0.01), controlling for above covariates; and remained significant (p=0.04) when also controlling for age. This BDNF gene-imaging correlate did not extend to gene-behavioral findings. The ApoE e4 genotype was not related to VBR (p=0.88).

Conclusions: Median degree of brain atrophy is 97% greater in patients with stroke when the BDNF val^{66}met genotype is present, at least for the mild-moderately impaired subjects enrolled in ICARE. Understanding the biology of inter-subject differences in brain anatomy after stroke can provide insights into patient heterogeneity and inform efforts to individualize stroke recovery therapies.

Footnotes

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