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Authors
Cramer, Steven C
Warren, Michael
Enney, Lori
et al.

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BDNF Polymorphism and Clinical Outcome in the GAIN Trials.

Steven C Cramer, Michael Warren, Univ of California, Irvine, Irvine, CA; Lori Enney, GlaxoSmithKline, Rsch Triangle Park, NC; Natalie Sanaee, Saege Hancock, Vincent Procaccio; Univ of California, Irvine, Irvine, CA

Objective: The growth factor brain derived neurotrophic factor (BDNF) is the most abundant neurotrophin in the brain. BDNF is important to a number of plasticity-related functions including long term potentiation, activity-dependent synaptic competition, and recovery from stroke. A single nucleotide polymorphism (val66met) is present in one or both BDNF alleles in approximately 30% of people, and is associated with brain changes including reduced plasticity. The current study addressed the hypothesis that presence of this BDNF polymorphism is associated with poorer behavioral recovery from stroke. **Methods:** Among 255 consenting subjects from the GAIN Americas and GAIN International trials, we extracted [1] stored DNA, examined for the presence of the BDNF polymorphism; [2] clinical history; and [3] scores on NIH Stroke Scale (NIHSS), Barthel Index, and modified Rankin Scale at baseline, 1 month post-stroke, and 3 months post-stroke. Presence of the polymorphism was correlated with change in the three scores from baseline to 1 month and from baseline to 3 months. **Results:** The 12 subjects with the val66met genotype in both alleles had significantly more

lacunes and milder strokes, and were excluded from further analysis, leaving 158 subjects (65%) without the polymorphism and 85 subjects (35%) with one copy. These two groups were well matched at baseline except [1] those with the polymorphism were more likely to be Asian than those without, as previously reported (26% vs. 5%, $p<0.0001$), and [2] fewer subjects with the polymorphism had a history of myocardial infarction than those without (8% vs 20%, $p<0.03$). Of the planned six comparisons, one was significant: subjects with the polymorphism had a smaller change in NIHSS score from baseline to 1 month, as compared to those without the polymorphism (2.5 +/− 1.0 vs. 4.0 +/− 0.6 points, mean +/− SEM, $p<0.04$ without correction for multiple comparisons). **Conclusions:** The data provide little or no support for the hypothesis that the BDNF val66met polymorphism is associated with poorer behavioral recovery from stroke. Possible reasons are that this polymorphism does not influence brain events underlying recovery after stroke, or that any polymorphism-related effect is only one of many major influences. Most published studies regarding polymorphism effects on plasticity pertain to short-term changes. Further studies on the effect of the BDNF val66met polymorphism on long-term forms of plasticity are needed.