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Editorial

Should You be Genotyped for the BDNF Val66Met Polymorphism?

Michael J Chen*

Department of Biological Sciences, California State University, Los Angeles, CA, USA

***Corresponding Author**: Michael J Chen, Department of Biological Sciences, California State University, Los Angeles, CA, USA.

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There is growing body of strong and compelling evidence that the Val66Met polymorphism of the gene for brain-derived neurotrophic factor (*bdnf*) could serve as a reliable predictor for genetic predisposition to depression [1-3], geriatric depression [4], rumination [5], bipolar depression [6,7], anxiety [8,9], reduced cognition and memory [10,11], suicide [6,12-14] and lack of coping strategies for stress in humans [15,16], which are supported by rodent studies [8,9,17]. The pathology manifests itself in the form of reduced cortical [18], medial pre-frontal cortical [19] and striatal [20] plasticity, hippocampal volume [7,15], and white matter connectivity [21], impaired intracellular survival signaling [17] and spike-timing synaptic plasticity [19] and higher BDNF levels in the serum [22]. Note, that regarding findings of higher serum BDNF levels [22,23], if reliably replicated in other studies, could serve as a strong indicator of the presence of the Val66Met allele, inasmuch as it would suggest lower BDNF levels in the brain. Obviously, however, such human correlational studies, aimed at determining whether a relationship exists between BDNF levels in the central nervous system (CNS) and in the blood [24] cannot be conducted.

On the other hand, whereas one meta-analytic study found a significant relationship between episodic stress and depression, moderated by the Val66met allele [25], other meta-analyses found no significant genotype effect of this single nucleotide polymorphism in predicting depression [26] and hippocampal volume [27-29]; indeed, meta-analysis failed to find a significant association even between serum BDNF levels and suicidal behaviors [30]. Moreover, and contrary to the above, in single studies, the Val66Met allele was not associated with childhood depression [31], autism spectrum disorders [23] or memory impairment [29,32]. Besides mood disorders, and consistent with the role of BDNF in putative neuronal survival and neuroprotective effects [33], the met allele of *bdnf* is associated with decreased recovery following several forms of brain damage, such as subarachnoid hemorrhage [34] and stroke [35].

The world-wide distribution of this polymorphism seems to hover, on average, at about 20% for most of the European continent, higher for the African continent and lower in Asia [36]. If 20% were taken as a rough estimate, then this means that each person has a one-in-five chance that they are at least heterozygous for this allele. This represents a significant risk factor for those whose lifestyle, such as diet and nutrition [37,38] and lack of exercise [39], might precipitate the emergence of depression, suicide ideation, slower recovery from CNS trauma and neurodegenerative diseases, all of which, at least to some degree, depend on BDNF. Indeed, this allele has been shown to nullify the otherwise beneficial effects of physical exercise on cognition [40]. Thus, despite the glaring discrepancies in the literature as to whether the BDNF Val66Met allele is detrimental, it would still behoove families or individuals whose lifestyles may make them more vulnerable to these medical problems be genotyped for the *bdnf* Val66Met allele.

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