Brain-derived neurotrophic factor in cerebrospinal fluid as a potential biomarker for Huntington’s disease

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Abstract

Brain-derived neurotrophic factor (BDNF), a member of the neurotrophin family that maintains neuronal development, survival, and synaptic plasticity, is synthesized in the cortical neurons and transported to striatal neurons. BDNF synthesis and transport are regulated by huntingtin (HTT) CAG repeats, and HD progression. In HD, it is thought that mutated HTT-induced deficit of BDNF may be involved in early selective striatal neurons vulnerability. BDNF has never been quantified in cerebrospinal fluid (CSF) as a potential biomarker for HD progression. We aimed to investigate BDNF in plasma and CSF and their relative association with clinical and imaging measures.

Methods

• First, we compared several commercially available immunoassays: Human BDNF ELISA Kit (Sigma-Aldrich, Saint Louis, MO, United States), BDNF Emax ImmunoAssay System (Promega, Madison, WI, United States), and SIMOA Human BDNF Discovery Kit (Quanterix™, Lexington, MA, United States).

• Then, we employed SIMOA (single-molecule array) to quantify BDNF concentration in 20 controls, 20 premanifest HD, and 37 manifest HD.

Results: ELISA versus SIMOA

• Blood BDNF was quantifiable and correlated in all three immunoassays.

• CSF BDNF was below the limit of quantification in Promega (2003) and Sigma-Aldrich (4/20) ELISAs.

• SIMOA was able to quantify BDNF in all plasma and CSF samples.

Conclusions

• Unlike the ELISAs, SIMOA is sensitive enough to quantify BDNF in CSF.

• We urge caution in interpreting studies where conventional ELISA was used to quantify CSF BDNF.

• BDNF concentration did not distinguish between the healthy controls and HD mutation carriers at any stage and did not significantly correlate with clinical and imaging measures.

• Based on this data, BDNF does not appear to be a reliable biomarker for Huntington’s disease progression.