Brain Derived Neurotrophic Factor Gene Polymorphism Associated with Language Acquisition

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The influence of the val66met polymorphism of the Brain Derived Neurotrophic Factor (BDNF) coding gene was examined in language acquisition at 18 to 20 months. Children homozygous for the met allele had significantly larger productive vocabularies, linking BDNF to early language and supplementing associations between met and positive childhood outcomes.

INTRODUCTION

BRAIN DERIVED NEUROTROPHIC FACTOR (BDNF)
Activity-dependent secretion of the BDNF protein...
- mediates long-term potentiation of neurons in the hippocampus and amygdala (Agassandian, Gedney & Cassell, 2006; Lu, 2003)
- contributes to memory formation (Tyler et al., 2002).

VAL66MET ALLELE
- Functional single nucleotide polymorphism of the BDNF coding gene
- Associated with variation in memory and attention.
- Adults homozygous for the more common valine (val) allele of val66met display better episodic memory than those homozygous for methionine (met) (Egan et al., 2003)
- But in children, val is associated with increased risk of attention deficit hyperactive disorder (Kent et al., 2006)

PRESENT STUDY
Language acquisition requires memory formation, so BDNF may also be associated with language acquisition. The current study examined how variations in BDNF might influence language acquisition in 18 to 20 month olds.

METHOD: LANGUAGE ASSESSMENT

Assessed from caregiver completion of the MacArthur Communicative Development Inventory Short Form (Fenson et al., 2000), a parental report inventory of children's production of selected vocabulary items.

The CDI is both valid, correlating highly with laboratory assessments of vocabulary (Dale, 1991), and internally reliable, correlating across 18 to 24 months of age (Corkum & Dunham, 1996).

CDI productive vocabulary scores at 1 and 2 years of age correlate strongly with assessments of vocabulary and grammar on other measures at 3 years and represent a negative predictor for later language problems (Feldman et al., 2005).

METHOD – GENOTYPING

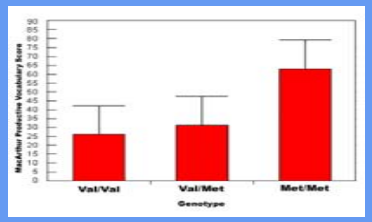
Following parental permission, BDNF was genotyped from DNA extracts prepared from buccal swabs using QuickExtract (Epicentre).

The BDNF locus was PCR amplified with the following conditions: 2 mM MgCl2, 0.2 mM dNTPs, 0.05 U/ul Taq polymerase (Fermentas), 0.2 uM of the primers 5'-ACTCTGGAGAGCGTGAAT-3' and 5'-ATACTGTCACACACGCTC-3' and cycled 40 times at 94°, 55°, and 72° for 30 second intervals using a PTC-200 or -225 thermocycler (MJ Research).

The Val66Met allele was determined by digesting the amplification products with NlaIII (NEB) and separating the fragments with 3% high resolution agarose (Sigma) gel electrophoresis. The valine versus methionine alleles were distinguished by the presence of a 243 bp or 168 bp DNA fragment, respectively.

RESULTS

Analysis of variance: val66met had a significant effect on productive vocabulary, $F = 3.87$, $p = .03$, omega squared = .10.



MacArthur Productive Vocab

	Mean	Std. Deviation
Val/Val	26.18	21.801
Val/Met	31.23	24.407
Met/Met	63.00	15.716
Total	29.44	23.412

Pairwise comparisons: Tukey's HSD tests found that...
- met-homozygous children had larger productive vocabularies than val-homozygous children, $q(3;54) = 3.90$, $p = .02$
- met-homozygous children had a greater mean vocabulary size than heterozygous children; this difference approached significance, $q(3;54) = 3.15$, $p = .07$
- heterozygous children and val-homozygous children did not significantly differ in their vocabulary size, $q(3;54) = 1.00$, $p = .76$

Polynomial contrasts:
- The number of met alleles had a significant linear effect on vocabulary, $F(1,51) = 5.566$, $p = .022$.
- The quadratic term was not significant, $F(1,51) = 2.163$, $p = .147$

Sex differences: No significant differences were found between boys and girls in productive vocabulary, $F(1,44) = .047$, p = .830.

CONCLUSIONS

These data display links between early language acquisition and functional polymorphisms in BDNF and suggest that met-homozygous children may show advantages in language acquisition. This finding is consistent with prior findings linking the met allele to positive outcomes in childhood attention and learning.

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REFERENCES

Agassandian, K., Gedney, M., & Cassell, M.D. (2006). Neurotrophic factors in the central nucelus of amygdala may be organized to provide substrates for associative learning. *Brain Research*, 10, 78-86.

Corkum, V., & Dunham, P. (1996). The Communicativ Development Inventory-WORDS Short Form as an index of language production. *Journal of Child Language*, *23*, 515-528.

Dale, P.S. (1991). The validity of a parent report measure on vocabulary and syntax at 24 months. *Journal of Speech and Hearing Research*, *34*, 565-571.

Egan, MF, Kojima, M, Callicott, JH, Goldberg, TE, Kolachana, BS, Bettolino, A, et al. (2003). The BDNF val66met polymorphism affects activity-dependent secretion of BDNF and human memory and hippocampal function. *Cell*, 112, 257-269.

Fenson, L., Pethick, S., Renda, C., Cox, J.L., Dale, P.S., & Reznick, J.S. (2000). Short-form versions of the MacArthur Communicative Development Inventories. *Applied Psycholinguistics*, 21, 95-116.

Kent, L., Green, E., Hawi, Z., Kirley, A., Dudbridge, F., Lowe, N., et al. (2005). Association of the paternally transmitted copy of common Valine allele of the Val66Met polymorphism of the brain-derived neurotrophic factor (BDNF) gene with susceptibility to ADHD. *Molecular Psychiatry*, 10, 939-943.

Tyler, W.J., Alonso, M., Bramham, C.R., & Pozzo-Miller I.D. (2002). From acquisition to consolidation: on the role of brain-derived neurotrophic factor signaling in hippocampal dependent learning. *Learning & Memory*, 9, 224-237.

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