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Letter to the Editor

Variance in Facial Recognition Performance Associated With BDNF in Schizophrenia

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Deficits in memory are among the most severe cognitive impairments in schizophrenia [Heinrichs and Zakzanis, 1998], and show evidence of familiality [Goldberg et al., 1990; Cannon et al., 2000]. Brain derived neurotrophic factor (BDNF) is a critical element in modulating synaptic changes, such as hippocampal long-term potentiation (LTP), associated with learning and adaptive behaviors in adult animals [Poo, 2001; Tyler et al., 2002]. In the gene coding for BDNF, a frequent polymorphism (VAL66MET; dbSNP: rs6265) has previously been associated with variance in verbal memory recall in schizophrenia [Egan et al., 2003; Dempster et al., 2005; Tan et al., 2005]. Whether this effect for the VAL66MET polymorphism is specific to verbal memory functioning or may also be associated with variance in visual and spatial memory in schizophrenia is unclear. Based on a control sample, Hariri et al. [2003] reported that the VAL66MET polymorphism was also associated with changes in cortical activation during a visual recognition task using fMRI.

We investigated whether the BDNF VAL66MET polymorphism was associated with visuo-spatial memory function in schizophrenia. After receiving ethics approval we conducted memory assessments of a subset of our total sample (comprised of 359 cases and 745 controls, all of Irish nationality and ancestry). Inclusion was dependent on patients' continuing availability and consent, as well as their being clinically stable, aged between 18 and 60 years, and free from confounding factors such as epilepsy, substance abuse, or acquired brain injury. This subgroup ($n = 91$), comprised of 4 MET/MET, 20 MET/VAL, and 67 VAL/VAL carriers, had a mean age of 46.2 years (SD9.3), was comprised primarily of males (75%), and had a predominantly chronic illness history (duration in years 22.3 ± 10.4; range 4–42). Visual spatial memory recall was measured using the paired associate learning task from the Cambridge Automated Test Battery (CANTAB). Recognition memory was measured using the facial recognition memory test from the Wechsler Memory Scale (3rd Edition; WMS-III). Pre-morbid IQ was also ascertained using the Wechsler Test of Adult Reading (WTAR). Controls in our study were obtained through the Irish blood transfusion service and neuropsychological data was not obtainable for these.

Consistent with previous reports, BDNF VAL66MET was not associated with risk for schizophrenia in our total case control sample (BDNF MET allele frequency in 359 cases vs. 745 controls (16.7% vs. 16.7%)). When patients were classified on the basis of BDNF genotype (carriers of 1 or 2 copies of the MET alleles vs. homozygous VAL carriers), no differences between genotype groups were observed on demographic variables, pre-morbid IQ or prescribed antipsychotic medication type (typical vs. atypical). MET carriers did not differ from homozygous VAL carriers in visuo-spatial memory performance ($F(2,87) = 0.08$; $P > 0.05$). However, carriers of the MET allele showed significantly poorer performance in immediate facial recognition ($F(2,87) = 6.78$; $P < 0.05$) (Fig. 1). In a regression equation, when the effects of age and pre-morbid IQ (both of which influence memory performance) were partialled out, BDNF genotype explained 7% of the variance in immediate facial recognition in the present sample.

Our investigation of BDNF VAL66MET extends previous research by suggesting a role for this polymorphism in mediating facial recognition in schizophrenia. This polymorphism has previously been associated with visual recognition memory in healthy controls [Hariri et al., 2003], and explained in terms of the deleterious effects of the MET allele on hippocampal function, which is in turn behaviorally expressed by poorer memory tasks performance. Facial recognition deficits are widely reported in schizophrenia, along with evidence of their familiality [Goldberg et al., 1995; Conklin

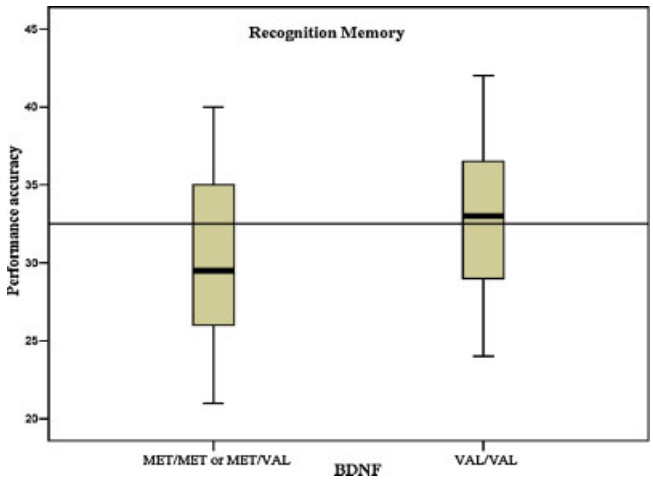

Fig. 1. Differences in performance accuracy associated with BDNF genotype as measured using the WMS-III immediate facial recognition subtest.

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et al., 2002]. Our findings suggest that BDNF may be one of the genes explaining variance in these deficits, and that its effects are not specific to either verbal or visual modalities.

The association of the BDNF MET allele with reduced memory function in the absence of an association with the broader schizophrenia phenotype is consistent with previous reports [Dempster et al., 2005; Tan et al., 2005]. Also, BDNF explains variance in memory performance in controls [Egan et al., 2003; Dempster et al., 2005], and memory performance in other psychiatric disorders [e.g., bipolar; Rybakowski et al., 2003]. Instead of specifically increasing risk for schizophrenia, therefore, the BDNF Met allele is acting to further reduce cognitive ability in patients with schizophrenia who are already liable to poorer cognitive functioning.

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