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Is neurotrophin-3 involved in bipolar disorder? Data from animal and human studies

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Background: Previous findings indicate that neurotrophic signaling systems may play a role in the pathophysiology of bipolar disorder (BD). We have recently found that serum neurotrophin-3 (NT-3) levels are increased during manic and depressive episodes (Walz *et al.* Neurosci Lett, in press). In the present study, we correlated such findings with results from an animal model of mania.

Methods: The present animal model was designed to mimic the management of acute mania. Adult male Wistar rats received d-amphetamine (AMPH) 2 mg/kg IP or saline for 14 days. Between days 8–14 rats received either lithium 47.5 mg/kg IP b.i.d. or valproate 200 mg IP b.i.d. (n = 15 animals per group). Serum and hippocampal NT-3 levels were measured using an enzyme-linked immunosorbent assay (sandwich-ELISA).

Results: AMPH and lithium increased serum and hippocampal NT-3 levels in saline pretreated rats (One-way ANOVA; $P < 0.05$). Valproate had no effects on serum or hippocampal NT-3 in saline pretreated rats. In AMPH pretreated rats, serum NT-3 levels was increased ($P < 0.05$) but hippocampal NT-3 levels were not different than control (saline) rats after lithium treatment. After valproate treatment, hippocampal NT-3 levels was increased ($P < 0.05$) and serum NT-3 levels were not different than control animals.

Conclusions: We demonstrated that serum NT-3 levels are increased during manic and depressive episodes (humans) and in AMPH-treated (manic) rats, indicating that AMPH might model neurotrophic changes observed in human studies. In addition, this study suggests that the mood stabilizers lithium and valproate exert distinct effects on central (hippocampal) and peripheral (serum) NT-3 levels. Whether such effects are related to their mechanisms of action it remains to be determined.

Keywords: bipolar disorder, neurotrophin-3, mania, neurotrophic factors