Brain-derived neurotrophic factor (BDNF) as a predictor of response of depressed patients to flouxitine therapy

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Abstract:

Background/ purpose: *Despite the significant progress in the management of major depressive disorder, little is known about biological alterations that underlie the pathophysiology or treatment of depression. Previous studies show that the brain-derived neurotrophic factor (BDNF) may play a role in the pathophysiology of major depressive disorders. Assuming that BDNF may be implicated in the etiology of depression, we examined BDNF concentrations in patients with major depressive disorder, and its correlation with therapeutic response to flouxitine therapy.*

Subjects and methods: *the study included forty depressed patients (25 females and 15 males) and 20 healthy subjects (11 females and 9 males) as a control selected to match the study group in age and gender. All patients were subjected to diagnosis of major depressive disorder using semi-structured clinical interview of DSM-IV-TR, assessment of severity of depression using the 16- item Hamilton Rating Scale of Depression (HRSD) before treatment and 8 weeks after flouxitine treatment, and estimation of the level of Brain Derived Neurotrophic Factor (BDNF) before treatment and 8 weeks after antidepressant treatment.*

Results: *Before treatment, concentrations of BDNF were significantly lower in depressed patients than in control. After treatment, significant rise of BDNF concentration occurred with no significant difference from control. Serum BDNF levels in patients with poor response (17.58 ng/ml [S.D. 4.99]) were significantly lower than those of the patients with good response (28.88 ng/ml [S.D. 7.81], t=5.48, p=0.001). However, there were no significant differences in both groups of the patients, compared to the normal controls (21.60 ± 8.04).*

Introduction:

Significant progress has been made in our ability to treat depression, but not all depressed patients respond to available antidepressants, and the therapeutic response requires several weeks or months of treatment (Duman et al, 2000; Wong & Licinio, 2001). In addition, there is still very little known about the neurobiological alterations that underlie the pathophysiology or treatment of depression. In recent years, research has been directed at sites beyond the level of monoamines and receptors to examine potential postreceptor mechanisms in the action of antidepressant treatment. These studies have identified adaptations of intracellular signaling proteins and target genes that could contribute to the action of antidepressant treatment (Altar C, 1999; Manji et al, 2000). One target gene of antidepressant treatment is brain-derived neurotrophic factor (BDNF). Neurotrophins, and in particular BDNF, play important roles in proliferation, differentiation and survival of neurons during development, as well as in the synaptic activity and plasticity in many groups of mature neurons (Lebrun et al, 2006). Furthermore, BDNF protects against stress-induced neuronal damage, and it might affect neurogenesis in the hippocampus, which is thought to be involved in the pathogenesis of mood disorders (Hashimoto et al, 2004). The possibility that BDNF is also involved in the pathophysiology of stress-related mood disorders is supported by reports that BDNF expression is decreased by exposure to stress (Smith et al, 1995; Nibuya et al, 1999). Clinical brain-imaging studies demonstrate that the volume of the hippocampus is decreased in depressed patients, consistent with the possibility of reduced neurotrophic factor support or synaptic remodeling in depression (Sheline et al, 1996; Sheline et al, 1999; Bremner, 2000). Antidepressant treatment increases the expression of BDNF in limbic structures, most notably the hippocampus (Nibuya et al, 1996; Rosello-Neustadt & Cotman, 1999). Upregulation of BDNF occurs in response to chronic but not acute antidepressant treatment, consistent with