

Effect of electroconvulsive therapy on biopterin and large neutral amino acids in severe, medication-resistant depression

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Abstract

Biopterin, neopterin and the large neutral amino acids (LNAA), i.e. phenylalanine, tyrosine, tryptophan, isoleucine, leucine and valine were measured in plasma of 20 severely depressed inpatients before and after a course of electroconvulsive therapy (ECT). These patients showed a significantly lower plasma biopterin concentration at baseline in comparison with healthy controls. After treatment an increase in biopterin was found, which was statistically significant in the depressed patients with psychotic features. The plasma phenylalanine–tyrosine ratio, which previously increased, normalised after ECT. Mean tryptophan concentration was lower in depressed patients than in normal controls. The patients who responded to ECT showed an increase in the tryptophan concentration and its ratio (tryptophan/LNAA) after treatment. Our results suggest that ECT increases biopterin, which probably results in synthesis of amino acids, especially tyrosine. Furthermore, ECT seems to increase cerebral tryptophan availability because of less tryptophan catabolism parallel with biopterin activation. More research is required to see if biopterin could be useful as a biological marker for the depressive state in this subgroup of patients, because this compound seems to play an important role in the etiology and treatment of depression. © 2001 Elsevier Science Ireland Ltd. All rights reserved.

Keywords: Affective disorder; ECT; Neopterin; Phenylalanine; Tyrosine; Tryptophan

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1. Introduction

The metabolism of biogenic amines has been hypothesised to play a key role in the pathophysiology of affective disorders. A functional deficiency of cerebral norepinephrine and serotonin is still the most widely accepted model for understanding the biology of depression and the therapeutic action of antidepressant treatments (Van Praag, 1982). Tetrahydrobiopterin (BH4) is the essential co-factor for the hydroxylation of phenylalanine, tyrosine and tryptophan, which is the rate-limiting step in the formation of dopamine, norepinephrine and serotonin, respectively (Kapatos et al., 1993; Levine, 1988). Independent from its function as co-factor for the hydroxylation,

BH4 also enhances the release of these neurotransmitters from nerve terminals (Mataga et al., 1991; Wolf et al., 1991). A link between BH4 and both nitric oxide, a neuroendocrine modulator of the HPA axis, and the immune system has been hypothesised (van Amsterdam and Opperhuizen, 1999)

BH4 is synthesised *de novo* from guanosine triphosphate (GTP), which is converted to dihydroneopterin triphosphate (NHPT3). The latter is converted by a series of tetrahydro intermediates to BH4. The concentration of cellular BH4 is dependent on this pathway and a salvage mechanism that converts quinonoid dihydrobiopterin to BH4 by the enzyme dihydropteridine reductase. Hydrolysis of NHPT3 yields dihydroneopterin,

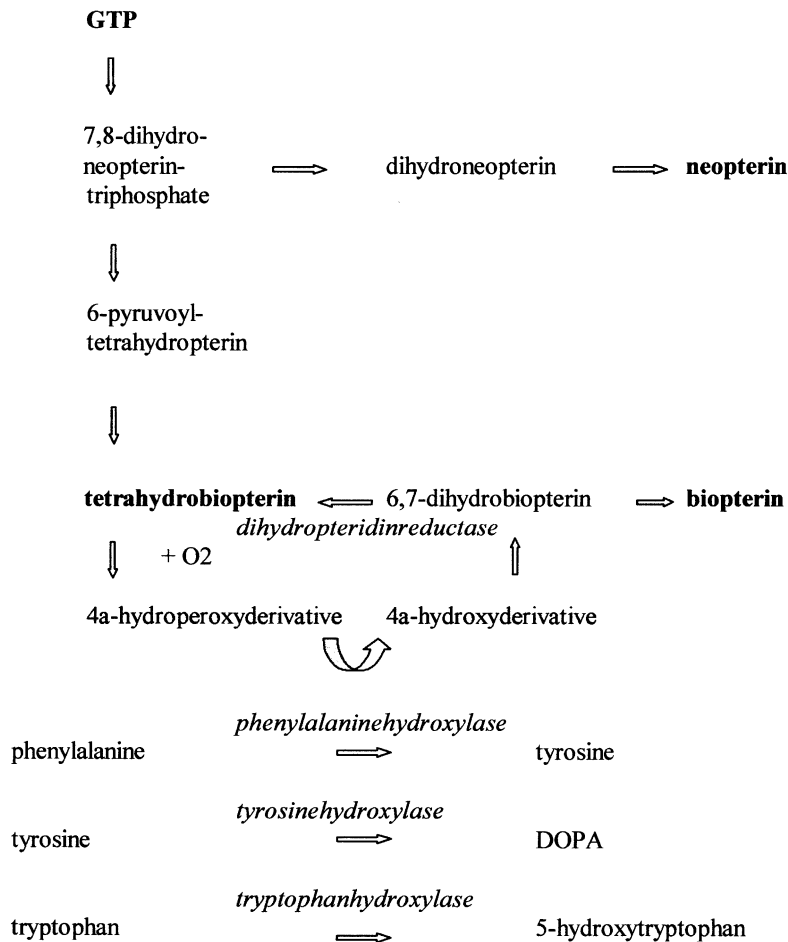


Fig. 1. Biosynthesis of tetrahydrobiopterin and its effect on the hydroxylation of phenylalanine, tyrosine and tryptophan.

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