Stress and nerve growth factor
Findings in animal models and humans
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Abstract

Stress is elicited by environmental, social or pathological conditions occurring during the life of animals and humans that determine changes in the nervous, endocrine and immune systems. In the present review, we present data supporting the hypothesis that stress-related events both in animal models and humans are characterized by modifications of endogenous nerve growth factor (NGF) synthesis and/or utilization. Stress inducing alteration in NGF synthesis and/or utilization appears to be more severe during neurogenesis and in early postnatal life. However, NGF endogenously released during stress may promote remodeling of damaged tissues following acute and/or chronic stressful events.

Keywords: NGF; Stress; Schizophrenia; Electroconvulsive treatment; Environmental changes; Neurotrophin; Behavior

1. Stress

Stress is triggered by numerous unexpected environmental stimuli occurring during life, such as aggressive behavior, fear, forced physical activity, sudden environmental changes, social isolation or pathological situations (Dennenberg et al., 1964; Greenough and Volkmar, 1973; Hilakivi-Clarke et al., 1991; McEwen and Sapolsky 1995; Mohammed et al., 1990, 1993; Weiner, 1989). Considerable evidence published in the last decades has focused on a constellation of neurochemical, biochemical and molecular effects caused by stress in the central nervous system (CNS) and in the endocrine and immune systems (Ben-Eliyahu et al., 1991; Eichelmann, 1992; Jiang et al., 1990; Levine et al., 1967; Nisipeanu and Korczyn, 1993; Santucci et al., 2000; Smith, 1996; Ueyama et al., 1997; Walsh et al., 1973). Neurohormones, cytokines and catecholamines have been considered as mediators of stress-induced immune and endocrine-related alterations, as well as in relation to the expression and severity of neuroimmunological and immunological disorders. Recent findings indicate that circulating and brain nerve growth factor (NGF) levels undergo significant variations after exposure to stressful events (Alleva et al., 1993; Aloe et al., 1986, 1990; Lakshmanan, 1987). We have shown that intermale aggressive behavior induced in mice by social isolation causes alteration in the NGF levels in the bloodstream (Aloe et al., 1990; Maestri-pieri et al., 1990) and in the CNS (Aloe et al., 1986, 1990, 1994b). We have also provided evidence that anxiety-like behavior induced by fear, alcohol consumption, heroin withdrawal and neuropsychiatric-like disorders is also characterized by an altered basal NGF level in the bloodstream (Aloe et al., 1997b; Bersani et al., 1999; Fiore et al., 1999, 2000, 2001), suggesting a possible NGF implication in the physiopathological response to stress and stress-related events. NGF is also implicated in the activation of the hypothalamic–pituitary–adrenal (HPA) axis (Otten et al., 1979; Scaccianoce et al., 1993; Snider and Johnson, 1989), representing a link between neuroendocrine and immune elements, that translates environmental messages, such as a stressful condition, into physiopathological responses. Chronic stress, depression and glucocorticoids seem to be key factors that lead to loss of brain neurons and reduced size of the hippocampus (Gould et al., 1990; Lane et al., 1997; Meaney et al., 1988).

The aim of this review is to present these and other emerging studies supporting the hypothesis that stress-