Lack of ACTH/cortisol and GH responses to intravenously-infused substance P in Parkinson’s disease

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Accepted March 22, 1993

Summary. In order to test possible changes in the stimulating effect of intravenously-infused substance P (SP) on ACTH/cortisol and GH secretion in Parkinson’s disease, 10 male parkinsonian patients and 10 age-matched normal controls were infused intravenously for 60 min with SP (1.0 or 1.5 pmol/kg⁻¹/min⁻¹ SP) or normal saline. The circulating levels of ACTH, cortisol and GH were measured during and for 20 min after SP or saline infusion. No untoward side effects or changes in blood pressure were observed during SP infusion in any subjects. In basal conditions and during saline infusion, plasma ACTH and cortisol levels were similar in normal and parkinsonian patients. During SP infusions, ACTH/cortisol concentrations in normal controls rose significantly vs baseline and saline test in a dose-dependent fashion. In contrast, at both SP infused amounts, parkinsonian patients showed ACTH/cortisol levels similar to those observed in the saline test. All subjects showed similar basal concentrations of GH. GH levels rose significantly in the normal controls when the higher dose of SP was infused, but they were not modified by the infusion of the lower dose of SP or saline. At both tested amounts of SP and during saline infusion, GH levels remained unchanged in the parkinsonian subjects. In agreement with previous observations in the literature showing SP abnormalities in the parkinsonian brain, these data fail to show significant effects of plasma SP on the ACTH/cortisol and GH secretory systems in Parkinson’s disease.

Keywords: Parkinson’s disease, substance P, ACTH, cortisol, GH

Introduction

The loss of dopaminergic neurotransmission in the nigrostriatal pathway is known to represent the major pathological change in Parkinson’s disease. However, in the parkinsonian brain there are various other neurotransmitter
alterations, which might play a role in the pathophysiology of Parkinson’s disease. Particularly, substance P (SP) is supposed to be in some way involved in the disease process, because of its interactions with dopaminergic neurotransmission (Glowinski et al., 1980; Sivam, 1991). In agreement with this hypothesis, reduction of immunoreactive SP has been reported in the basal ganglia, substantia nigra (Mauborgne et al., 1983; Rinne et al., 1984; Tenuovo et al., 1984; Grafe et al., 1985), cerebrovascular fluid (Pezzoli et al., 1984; Cramer et al., 1991) and adrenal medulla (Stoddard et al., 1991) of patients with Parkinson’s disease. Diminution of SPergic neurotransmission in parkinsonian patients has been confirmed by receptor studies (Tenuovo et al., 1990), whereas immunohistochemical analyses have shown degeneration of SP containing neurones in the brainstem but not in the basal ganglia and substantia nigra of parkinsonian patients (Waters et al., 1988; Halliday et al., 1990; Gai et al., 1991). At present, the reason of this discrepancy is unknown.

The study of alterations in pituitary hormone secretory patterns is considered an useful tool for a better understanding of neurotransmission disorders in cerebral structures, assuming that hypothalamic-pituitary neuroendocrine changes may represent a window of situations in extra-hypothalamic structures (Caraceni and Giovannini, 1988). In the recent past, we have tested the effects of intravenously-infused SP on the secretion of various pituitary hormones in normal human subjects (Coiro et al., 1992a,b). In these studies SP has been infused in a range of doses unable to produce stressful side effects and/or variations in blood pressure. In these experimental conditions, SP has been found capable of stimulating the pituitary secretion of ACTH/cortisol (Coiro et al., 1992a) and GH (Coiro et al., 1992b). These findings prompted us to investigate the effects of a systemic infusion of SP on ACTH/cortisol and GH secretion in parkinsonian patients in order to test in vivo possible abnormalities of SP activity in humans.

Materials and methods

Ten men (56–64 years old; mean ± SE: 59.1 ± 0.78) affected by de novo Parkinson’s disease were randomly chosen to participate in this study. All of them gave their informed consent. The study was in accordance with the Helsinki II declaration. The diagnosis of Parkinson’s disease had been established by the presence of clinical features (resting tremor, bradykinesia and rigidity). The mean (±SE) duration of the disease was 12.3 ± 2 months. The mean (±SE) severity of the clinical stage, assessed with the Hoehn-Yahr scale (1967), was 1.42 ± 0.18. Patients with secondary parkinsonism or with clinical evidence of other major neuroanatomical system involvements were excluded. All patients were assessed with the Hospital Anxiety and Depression Scale (Zigmond and Snaith, 1983), the Research Diagnostic Criteria (Spitzer et al., 1978) and with the Hamilton depression rating scale (Hamilton, 1960). None of the subjects resulted affected by depression. None of them was addicted to an excessive alcohol consumption (<300 ml/week). All subjects were within 10% of their ideal body weight. They were fully ambulatory, well nourished and without clinical or laboratory evidence of renal, hepatic, neoplastic or endocrine-metabolic diseases. Particularly, subjects were screened for the presence of occult thyroid diseases or hyperprolactinemia. For this purpose, the basal levels of T₃, T₄, TSH and PRL and the PRL and TSH responses