RELATIONSHIP BETWEEN VASOPRESSIN, NEUROPHYSIN AND ACTH, CORTISOL PLASMA LEVELS IN NON SUPPRESSOR PATIENTS DURING DEXAMETHASONE SUPPRESSION TEST.

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ABSTRACT

In order to test the specificity of the previously described relationship between total immunoreactive neurophysins (IRN) and cortisol plasma levels during Dexamethasone Suppression Test (DST) in Non Suppressor (N.S.) patients, we have replicated our initial study using specific vasopressin-neurophysin (hN_pI), vasopressin (AVP) and ACTH radioimmunoassays during DST in 20 inpatients.
A specific relationship between hN_pI and ACTH ($r : 0.71$, $p < 0.05$) and AVP and cortisol ($r : 0.72$, $p < 0.05$) was found in the post-Dex. 4 p.m. sample in 11 N.S. but not in 9 S patients. Those results further substantiate our working hypothesis of a putative role of vasopressinergic-neurophysinergic function in the early escape to Dex. in some psychiatric patients.

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INTRODUCTION

In a previous work we demonstrated a correlation between IRN and cortisol plasma levels in N.S. but not in S patients during Dexamethasone (Dex) Suppression Test (DST). This led us to postulate that neuropituitary peptides could play a role in the early escape to Dex in N.S. patients (Legros et al., 1982a). Since AVP is known to share a potentiating effect of corticotropin releasing factor (CRF) on ACTH release (Yates et al., 1971; Turkelson et al., 1982; Gilles et al., 1982) and since neurophysin-I (hN_pI) is specifically related to AVP biosynthesis in the human neuropituitary (Legros and Louis, 1972) and released in the blood with it (Dax et al., 1979), we replicated our initial work studying specifically hN_pI and AVP, together with ACTH and cortisol plasma levels in the course of DST in psychiatric patients.

MATERIAL AND METHODS

The samples were composed of 20 patients hospitalized in the Psychopharmacology Unit of the "Hôpital Universitaire de Bavière" (Liege, Belgium): they were 9 males (age 40.3 $\pm$ 17) and 11 females (age 37.2 $\pm$ 13.1). All patients were diagnosed according to the Research Diagnostic Criteria (Spitzer et al., 1978) by 2 independent psychiatrists: 12 patients were suffering from major depressive disorders (10 primary and 2 secondary) 4 from minor depressive disorders, 2 from generalized anxiety disorders, 1 from schizophrenia and 1 from schizo-affective disorders, depressed type. They were free of somatic illness as evidenced by clinical examination and laboratory tests and had not a weight with deviation from ideal weight of more than 25 %. All patients gave informed consent and were kept free of any medication for at least 2 weeks before the test.

DST were realized according to Caroll et al (1981) (Dex. 1 mg at 11 p.m.) and patients were classified according to the plasma cortisol

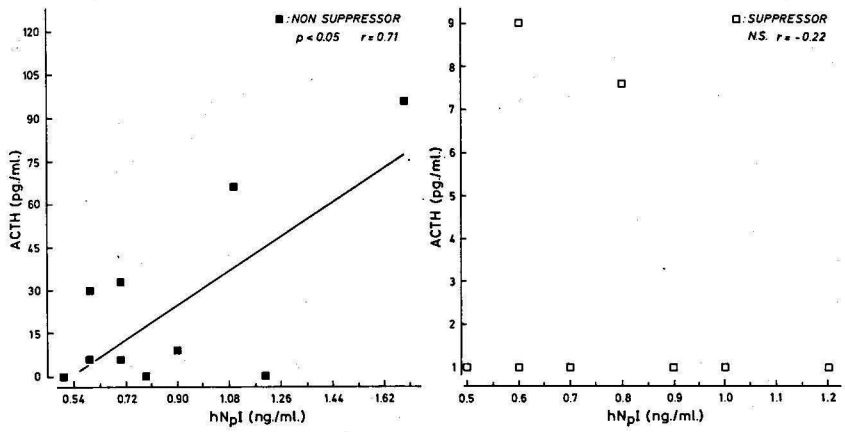

Fig. 1 - Individual plasma levels of ACTH and hN_pI in 10 Non Suppressor (N.S.) and 8 Suppressor (S) patients in the course of Dexamethasone Suppression Test (4 pm values)

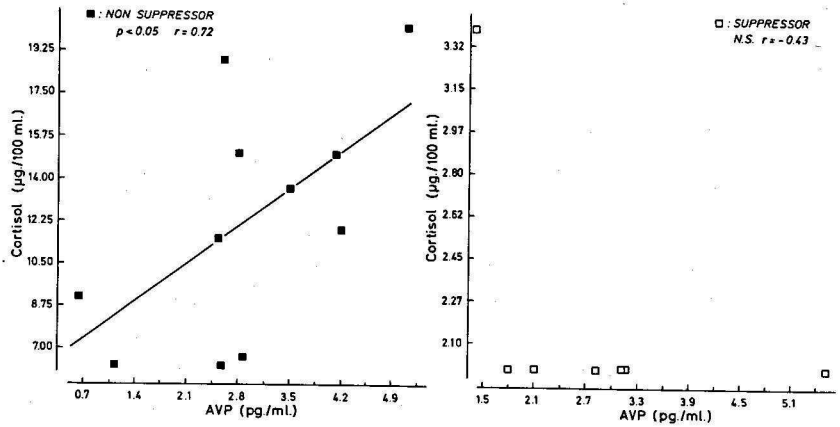

Fig. 2 - Individual plasma levels of cortisol and AVP in 11 Non Suppressor (N.S.) and 7 Suppressor (S) patients in the course of Dexamethasone Suppression Test (4 pm values)

levels at 4 p.m. the day after (S < 5µg %, N.S. > 5µg %). Techniques for hN_pI, plasma cortisol and ACTH assays has been given in one previous paper (Legros et al., 1982b), plasma AVP were assayed by RIA (Mens et al., 1980). AVP and ACTH assays were realized on 18 samples only. Additional blood samples were taken and other hormonal analysis were realized in this study; they will be discussed together with the complete clinical results in a future report.

RESULTS

Among the 20 patients tested, 11 were classified as N.S. and 9 as S. Mean ACTH was 17.9 $\pm$ 8.5 pg/ml in the N.S. and 2.5 $\pm$ 1.2 pg/ml in the S group (ns, $p < 0.09$); mean hN_pI was 0.89 $\pm$ 0.13 ng/ml in the N.S. and 0.71 $\pm$ 0.06 ng/ml in the S group (ns); mean AVP was 2.9 $\pm$ 0.5 pg/ml in the N.S. and 2.5 $\pm$ 0.6 pg/ml in the S group (ns). There was no relationship between the 4 variables studied in the S group whereas there was a significant relationship between hN_pI and ACTH ($r : 0.71$, $p < 0.05$) (Fig. 1) and AVP and cortisol ($r : 0.72$, $p < 0.05$) (Fig. 2) in the N.S. group.

DISCUSSION

A highly significant relationship between immunoreactive hN_pI and ACTH release has been described previously in 1 male volunteer presumably under the influence of "psychological stress" (Legros et al., 1982b) whereas a correlation between plasma AVP and cortisol has been demonstrated during experimental ethanol intoxication in some male volunteers (Linkola et al., 1979). De Wied's group demonstrated that the inhibitory action of Dex. on stress induced ACTH release was independent of the hypothalamic system (De Kloet et al., 1974). In the rat, Smelik et al. (1982) demonstrated that Dex. can suppress stress -as well as metabolic- induced ACTH release and Kneppels et al. (1982)

demonstrated that Dex. can inhibit AVP release in some but not in all types of neuropituitary activation.

On the other hand, Gann and Carlson (1982) demonstrated a double regulatory mechanism for ACTH release: a metabolic one, steroid suppressible, independent of AVP release, and a neurogenic one, inhibited by anti-AVP antibodies. Those authors postulated that the vasopressinergic bundle involved in this ACTH modulation originate in the Para-Ventricular Nucleus (PVN); we have recently demonstrated an increase of circulating IRN in rats submitted to mild stress condition (Crine et al., 1982).

Our present results further substantiate our working hypothesis of a relationship between vasopressinergic and neurophysinergic functions and corticotrop release during DST in N.S. but not in S patients. This relation could be due either to a neuromediator dysfunction leading to an independent hyperactivity of the two hormonal systems (in that case hN_pI and AVP levels would be higher in the N.S. than in the S group which is not the case) either to a more specific interaction between AVP, hN_pI and the corticotrop system. This interaction could be due either to the known facilitatory action of AVP (and presumably other neuropituitary peptide) on CRF activity (see introduction) either to the biosynthesis of a "neurointermediate" ACTH through the biosynthesis of a precursor common to ACTH, beta-endorphin, AVP and neurophysin as suggested in the fifties by Mialhe-Voloss (1958) and described recently by the Cohen's group (coenophorin) (Lauber et al., 1981).

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