Journal of Autism and Developmental Disorders, Vol. 21, No. 1, 1991

Brief Report: Plasma β-Endorphin and Cortisol Levels in Autistic Patients[1]

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Several studies (Herman et al., 1987; Richardson and Zaleski, 1983; Sandman, Barron, & Colman, 1990a; Sandman et al., 1983) reported success with opiate blockers in the treatment of self-injurious behavior (SIB). In direct studies of the possible influence of β-endorphin (BE) in autism, Campbell, Adams, Small, Tesch, and Currens (1988; Campbell et al., 1989, 1990) reported that the majority of autistic children given naltrexone responded favorably. However, measures of various opiates in plasma or cerebrospinal fluid (CSF) of autistic patients have been inconclusive. (Gillberg, Terenius, & Lonnerholm, 1985; Sandman, Barron, Chicz-DeMet, & DeMet, 1990b; Weizman, Weizman, Tyano, Szekely, & Sarne, 1984). In the current study, plasma levels of BE in autistic patients were compared with healthy and patient controls.

[1]The support of Francis M. Crinella, Director, SDRI, is appreciated. The assistance of Lou Sarrao, Hugh Kohler, Carol Bitcon, Nadia Atie, Pat Donnelly, and the staff of Program V is sincerely appreciated. Supported in part by grant MH41446 NIMH.
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0162-3257/91/0300-0083$06.50 © 1991 Plenum Publishing Corporation

METHODS

Subjects

Patients diagnosed as autistic (n = 8; 26 ± 3 years of age) were compared with an institutionalized patient control group (n = 13; 24 ± 6 years of age) and a normal healthy control group (n = 17; 29 ± 11 years of age). Each of patients had been diagnosed as autistic on admission to Fairview (AAMD).

Materials and Methods

Blood samples were collected for BE measurements at 8 a.m. and 8 p.m. Plasma levels of BE were determined by a solid phase two-site immunoradiometric assay (IRMA) using the Allegro Immunoassay System (Nichols Institute Diagnostics; San Juan Capistrano, CA; see Sandman et al., 1990b). The antiserum employed has 1.6% cross-reactivity for β-lipotropin at 500 pg/ml and has less than 0.01% cross-reactivity with related opiates at 5 μg/ml. Results were quantified by the four-parameter logistic method using the "two plus two" iterative procedure with reweighing developed by Rodbard at NIH (Program RIA004; Biomedical Computing Technology Information Center, Nashville, TN). The Allegro Beta-Endorphin Immunoassay system has a minimum detectable dose (MDD) = 10 pg/ml (95.0% confidence limit) with a coefficient of variance CV = 4.1% (intraassay) and CV = 9.0% (interassay) at the highest concentration measured in the present study.

Cortisol Assay

Plasma cortisol levels were assayed by immunofluorescence using an automated procedure on an Abbott TDx Analyzer (Abbott Laboratories; Abbott Park, IL, Sandman, et al., 1990b). The sensitivity of the TDx cortisol assay is MDD = 0.45 μg/dl with a CV = 8.42% (intraassay), CV = 7.23% (interassay) at 4 μg/dl and CV = 2.65% (intraassay), CV = 2.7% +interassay) at 40 μg/ml.

RESULTS

Plasma BE concentrations were significantly lower for developmentally disabled patient (DD) controls than normal controls for both morning,

$t(28) = 4.13, p < .001$, and evening, $t(28) = 3.45$, $p < .001$, samples. Cortisol concentrations were not significantly different for the groups at either sampling period.

Plasma BE levels of autistic patients were significantly lower than normal control subjects for both morning, $t(21) = 2.90, p < .01$ and evening measures, $t(21) = 3.40, p < .01$. Autistic patients (35.4 pg/ml) had higher morning BE levels than the DD patient control group (27.7 pg/ml) but the difference failed to achieve acceptable levels of statistical significance, $t(11) = 1.80, p < .10$. There was no difference between patient controls (24.1 pg/ml) and autistic patients (23.6 pg/ml) for evening BE levels. There were no significant differences in cortisol levels between autistic patients and control groups for either the morning or evening measurements.

DISCUSSION

Plasma BE concentration was significantly lower in patients with autism than in normal healthy controls for both morning and evening measurements. Autistic patients had higher morning BE plasma concentration than an institutionalized DD control group, although this difference was not statistically significant. These findings partially confirm an earlier report of lower plasma opiates (humoral endorphin) in autistic patients compared with healthy controls (Wiezman et al., 1984). Neither Wiezman et al. in plasma nor Gillberg et al. (1985) in CSF found that levels of endogenous opiates distinguished autistic patients from patient controls, although Gillberg et al. reported that autistic patients with SIB had higher levels of CSF BE fractions than patient controls.

BE and cortisol levels are normally related through a common link at the level of a large precursor molecule, pro-opiomelanocortin (POMC). Cortisol is not a direct POMC product, but release is stimulated by adrenocorticotropin (ACTH), which is contained in the POMC molecule. Therefore, a dissociation of BE and cortisol measures implies either the presence of a hypothalamic/adrenal dysfunction and/or an altered rate of endorphin degradation by inactivating peptidase(s). The effectiveness of small doses of naloxone and naltrexone in autistic behavior (Campbell et al., 1989, 1990; Herman et al., 1987; Richardson & Zaleski, 1983; Sandman et al., 1990a; Sandman et al., 1983) is consistent with opiate receptor supersensitivity that may result from decreased availability of BE.

However, if forms of autism are related to "addiction" to neonatal levels of BE (Panksepp, 1979; Sahley & Panksepp, 1987), long-term changes in brain receptors may result. For example, perinatal exposure of rats to high levels of BE produced lasting changes in the density of opiate (Zadina,

Kastin, Manasco, Pignatiello, & Nastiuk, 1987) and dopamine receptors (Sandman & Yessaian, 1986). Thus, exposure to a high concentration of BE that accompanies perinatal distress and hypoxia (Davidson, Til-Ad, Rogovin, Laron, & Reisner, 1987) may result in permanent changes of opioid and perhaps dopamine receptors.

The findings of similar plasma cortisol levels among patient controls, normal controls, and autistic patients are consistent with previous reports of normal diurnal patterns of salivary cortisol in 9 of 12 autistic patients (Hoshino et al., 1987). Two studies (Hoshino et al., 1987; Jensen, Realmuto, & Garfinkel, 1985) have reported that autistic children commonly show abnormal cortisol response to the dexamethasone suppression test (DST). Therefore, it is possible that some of our subjects may have had a hypothalamic–pituitary–adrenal (HPA) axis abnormality. This abnormality, if present in our study, did not influence physiological steroid levels.

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