University of Groningen

Comparison of the Effects of Chlordiazepoxide and Buspirone on Plasma Catecholamine and Corticosterone Levels in Rats under Basal and Stress Conditions

Boer, S.F. de; Gugten, J. van der

Published in:
Pharmaceutisch Weekblad Scientific Edition

IMPORTANT NOTE: You are advised to consult the publisher's version (publisher's PDF) if you wish to cite from it. Please check the document version below.

Document Version
Publisher's PDF, also known as Version of record

Publication date:
1989

Link to publication in University of Groningen/UMCG research database

Citation for published version (APA):
Boer, S. F. D., & Gugten, J. V. D. (1989). Comparison of the Effects of Chlordiazepoxide and Buspirone on Plasma Catecholamine and Corticosterone Levels in Rats under Basal and Stress Conditions. *Pharmaceutisch Weekblad Scientific Edition*, *11*(6), J4-J4.

Copyright
Other than for strictly personal use, it is not permitted to download or to forward/distribute the text or part of it without the consent of the author(s) and/or copyright holder(s), unless the work is under an open content license (like Creative Commons).

The publication may also be distributed here under the terms of Article 25fa of the Dutch Copyright Act, indicated by the “Taverne” license. More information can be found on the University of Groningen website: https://www.rug.nl/library/open-access/self-archiving-pure/taverne-amendment.

Take-down policy
If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.

Downloaded from the University of Groningen/UMCG research database (Pure): http://www.rug.nl/research/portal. For technical reasons the number of authors shown on this cover page is limited to 10 maximum.

COMPARISON OF THE EFFECTS OF CHLORDIAZEPOXIDE AND BUSPIRONE ON PLASMA CATECHOLAMINE AND CORTICOSTERONE LEVELS IN RATS UNDER BASAL AND STRESS CONDITIONS.

S.F.de Boer and J.van der Gugten.

The effects of the classical benzodiazepine (BDZ) anxiolytic drug chlordiazepoxide (CDP; BDZ-receptor agonist) and the non-BDZ anxiolytic agent buspirone (BUSP; 5-HT1A receptor agonist) on basal and stress-induced plasma noradrenaline (NA), adrenaline (A) and corticosterone (CS) release were investigated. Male Wistar rats, provided with a permanent heart catheter and a permanent stomach catheter, were used. These catheters allow frequent blood sampling and intragastric drug infusions, respectively, in the freely behaving animal. The stress consisted of placing the animal either into an unfamiliar cage (novel environment stress; NES) or into shallow water of 35° C (water immersion stress; WIS). BDZ receptor activity in blood was measured by use of a radioreceptor assay.

Acute administration of CDP (1-27 mg/kg) produced dose-dependent increases in basal plasma CS secretion but was without effect on basal NA and A levels. Dose-dependent increases in plasma NA, A and CS contents were observed after acute treatment with BUSP (0.2-20 mg/kg). A medium dose of CDP (9 mg/kg) attenuated the NES- and WIS-induced CS and CA elevations. High doses of CDP, that elevated basal CS release, prevented a further CS increase by NES and inhibited the NA and A response to NES. The CDP effects on basal and stress-induced CS and catecholamine (CA) secretion were completely blocked after pretreatment with the BDZ receptor antagonist flumazenil (Ro 15-1788). BUSP (2 and 20 mg/kg) was not effective in attenuating the NES- or WIS-elicited rise of CS, NA and A. However, the 20 mg/kg dose of BUSP actually enhanced the NES-induced plasma A response. Six daily CDP (9 mg/kg) pretreatments produced tolerance to the slight elevation in basal CS triggered by acute administration of CDP on day 7, but increased the efficacy of the drug's CS and CA attenuating action in stressed rats, Six daily BUSP (2 mg/kg) pretreatments also produced tolerance to the acute BUSP-induced effect on basal CS and CA release, but did not affect the stress-induced CS and CA response.

In conclusion, BUSP does not have the BDZ-like property to inhibit stress-induced elevations in CS, NA and A.

Netherlands Institute for Drugs and Doping Research, Faculty of Pharmacy, Sorbonnelaan 16, 3584 CA Utrecht, The Netherlands.

EFFECTS OF DEPRIVATION FROM ATRIAL NATRIURETIC FACTOR ON CENTRAL HEMODYNAMIC REGULATION IN WKY, WKY WITH 5 WEEKS OLD MYOCARDIAL INFARCTION (IWKY) AND SPONTANEOUSLY HYPERTENSIVE RATS (SHR)

P.J.F. de Vries, C.M. Tyssen, H.A.J. Struyker Boudier, and J.F.M. Smits

The effects of exogenously applied ANP on central hemodynamics have been well documented. Deprivation from circulating ANP can elucidate its physiological hemodynamic role. Therefore, we investigated the effects of monoclonal antibody administration on central hemodynamics under normal and pathophysiological conditions. Wistar Kyoto (WKY), WKY with 5 weeks old myocardial infarction (32±2% of the left ventricle; IWKY) and SHR were instrumented with an electromagnetic flowprobe around the ascending aorta and catheters in the abdominal artery, thoracic vena cava and abdominal vena cava for measurement of mean arterial pressure (MAP), central venous pressure (CVP) and for administration of drugs respectively. The animals were slowly injected with a bolus of 150 µl mouse serum (MS) as control on the first day and 150 µl mouse ascites, containing monoclonal antibodies (MA) raised against APII, on the second day. Hemodynamics were recorded continuously during 60 min. As control for deprivation, increasing doses of rANP (0.25, 0.50, 1.0 and 2.0 µg/kg.min increased stepwise every 15 min) were infused intravenously. Deprivation was concluded after MA administration because hemodynamics did not change significantly on rANP infusion. After MS administration, MAP increased during 60 min for WKY (6±3 mmHg). No other changes occurred in either model. After MA, cardiac output (CO) (11±2 ml/min) and stroke volume (SV) (26±6 µl) increased significantly and total peripheral resistance (TPR) (-0.20±0.05 mmHg.min/ml) decreased significantly for WKY. CO was elevated in SHR and IWKY (6±2 ml/min and 7±3 ml/min, respectively), whereas SV and TPR remained constant.
These studies suggest a physiological role of ANP in the regulation of CO rather than MAP under normal and pathophysiological conditions.

Dept. of Pharmacology, University of Limburg, P.O. Box 616, 6200 MD Maastricht

1

MACROPHAGE DEPLETION ABROGATES PITUITARY-ADRENAL ACTIVATION IN RESPONSE TO LIPOPOLYSACCHARIDE(LPS) IN RATS.

R.H. de Rijk, N. van Rooyen, F.J.H. Tilders, F. Berkenbosch

There is growing evidence for bidirectional communication between the immune and the neuroendocrine system. Recently, we have shown that interleukin-1 activates pituitary-adrenal activity in rats. Similar effects have been demonstrated for interleukin-6 and tumor necrosis factor-α. These cytokines are produced by mononuclear cells such as macrophages (Mø), endothelial cells and others and play a key role in the regulation of the acute phase respons response. The present study analyses the role of Mø in the activation of the hypothalamus-pituitary-adrenal (HPA)-axis.
Intraperitoneal injection of LPS, a standard stimulus to induce inflammation, induced an increase in plasma ACTH and glucocorticoids (GC). The rise in GC was dependent on the dose of LPS administered with an ED50 of 1.5 µg/kg. When dichloromethylene diphosphate (DMDP)-liposomes are injected in vivo, Mø are selectively depleted for a period of 5 days after administration (1). When these animals were injected with LPS on day 4, the rise in ACTH and GC was largely inhibited.
These results indicate that the activation of the HPA-axis during inflammation is dependent on functionally intact Mø.

1 N. van Rooyen, E. Claassen (1988) In: Liposomes as drug carriers. Edited by G. Gregoriades; John Wiley & Sons Ltd., pp. 131.

Department of Pharmacology, Free University Medical Faculty; Van der Boechorststraat 7, 1081 BT Amsterdam, The Netherlands

1

ONTOGENY OF FUNCTIONAL OPIOID RECEPTORS IN THE RAT BRAIN.

T.J. de Vries, F. Hogenboom, A.H. Mulder and A.N.M. Schoffelmeer.

Endogenous opioid peptides are thought to play a role in the development of the brain. In addition, there are several indications that opiates, e.g. administered during pregnancy, disturb normal brain development. Therefore, we examined the ontogeny of functional opioid receptors in the rat brain, in casu those receptors mediating presynaptic inhibition of neurotransmitter release and inhibition of dopamine (DA)-sensitive adenylate cyclase, with highly selective agonists for μ-, δ- and κ-receptors. On gestational day 17 (E17) strong inhibitory effects of the selective μ-agonist D-Ala^2, MePhe^4, Gly-ol^5-enkephalin (DAGO) on the electrically-evoked release of [^{3}H]NA from cortical slices and of the selective κ-agonist U-50,488 on the electrically-evoked release of [^{3}H]DA from striatal slices were found. Electrically-evoked release of [^{3}H]ACh from striatal slices was not detectable before postnatal day 7 (P7), but on that day it was already strongly inhibited by the selective δ-agonist D-Pen^2, D-Pen^5-enkephalin (DPDPE). The μ- and δ-opioid receptors coupled to DA-sensitive adenylate cyclase in the striatum were found to develop asynchronously. Selective activation of μ-receptors with DAGO resulted in an inhibition of D-1 dopamine receptor-stimulated adenylate cyclase activity on E17, whereas activation of δ-receptors with DPDPE was not effective until P14.
These data confirm the early appearance of μ- and κ-opioid receptors and the relatively late development of δ-opioid receptors in the rat brain. Most importantly, they show that already in an early stage of development opioids are able to mediate modulation of noradrenergic (via activation of μ receptors) and dopaminergic (via activation of μ and κ receptors) neurotransmission processes. Therefore, these opioid receptor types could play a role in brain development and/or developmental disturbances.

Department of Pharmacology, Medical Faculty, Free University, Van der Boechorststraat 7, 1081 BT Amsterdam, The Netherlands.