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CROTOXIN DO NOT ALTER THE PLASMATIC CONCENTRATION OF CORTICOSTERONE

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CTX is the major component of the venom of the South American rattlesnake, *Crotalus durissus terrificus*. We have demonstrated that this toxin induces behavioral alterations in the open-field, holaboard and social interaction tests, that are consistent with an anxiogenic effect (*Braz. J. Med. Biol. Res.*, 29: 629-32 and 30: 245-49). Moreover, we have also demonstratad that the gabaergic-benzodiazepine system can be involved in the crotoxin-induced behavioral alterations, since these alterations were antagonized by diazepam and flumazenil. Considering that anxiogenic drugs can activata the hypothalamic-pituitary-adrenocortical exis, our objective was to investigate if this axis was also involved in the crotoxin-induced anxiogenic effect. Adult male Wistar rats (180-220 g) were used. Crotoxin (250 and 500 µg/kg) or saline ware administered intraperitoneally and, after 2 h, blood samples were collected. Blood was centrifuged at 2300 rpm and the plasma separated. Plasma concentrations of corticosterona were determined using a radioimmunoassay. Crotoxin did not alter the plasmatic concentration of corticosterone (ANAVA, P>0.05). The means (ng/ml) + SD were for crotoxin at the dose of 250 µg/kg: 273 ± 29; 500 µg/kg: 325 ± 45, and for saline: 218 ± 25.
Conclusion: Since crotoxin did not alter the plasmatic concentration of corticosterone, we may suggest that the anxiogenic effect of this toxin is not related to an hiperactivity of the hypothalamic-pituitary-adrenocortical axis.
Financial support: FAPESP (95/8804-1)

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REDUCING CHOLINERGIC SIDE EFFECTS: A COMPARISON OF ANTIEMETIC THERAPIES IN ALZHEIMER PATIENTS RECEIVING RIVASTIGMINE

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Dose-related nausea and vomiting are frequent side effects of cholinomimetic anti-dementia compounds. This prospective, randomized, open-label pilot study was designed to evaluate the efficacy of four antiemetic treatments during a four-week forced dose escalation of the cholinesterase inhibitor rivastigmine in patients with Alzheimer's disease (AD). Eighty-two patients were enrolled to receive rivastigmine 3mg/d, with weekly dose increases of 3mg/d up to a maximum dose of 12mg/d. Twenty-six subjects (32%) experienced nausea and/or vomiting requiring antiemetic treatment and were randomized to receive glycopyrrolate 1mg, ondansetron 4mg, trimethobenzamide 250mg, or trihexyphenidyl 2mg. Patients receiving antiemetics were rated on the Emetic Process Rating Scale (EPRS) every 4h and the Clinical Global Impression (CGI) scale at 72h for severity of nausea and vomiting. Treatment success was defined as a CGI rating of 1 (very much improved) or 2 (much improved). In the course of the study it became apparent that only two of the four therapies, trimethobenzamide and trihexphenidyl, drugs which act centrally, were effective (see table below); therefore the glycopyrrolate and ondansetron treatment arms were discontinued. In conclusion, centrally acting antidopaminergic and anticholinergic compounds were effective in reducing nausea and vomiting in AD patients receiving rivastigmine. Thus it appears that nausea and vamiting in patients receiving rivastigmine are centrally mediated.

Antiemetic	Dose	N	% Success (CGI ≤ 2)	Mean (± SD) EPRS* 0 h	72 h
glycopyrrolate	1mg	3	33%	6.0 ± 0.8	5.3 ± 2.9
ondansetron	4mg	4	50%	6.8 ± 2.9	5.3 ± 3.4
trimethobenzamide	250mg	9	89%	5.9 ± 2.4	2.3 ± 1.0
trihexyphenidyl	2mg	10	90%	6.7 ± 1.7	2.1 ± 1.2

*EPRS scale ranges from 2 - 15

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Title: INTRODUCING AN EFFICIENT BIPHASIC METHOD FOR INDUCING STRESS IN RAT (BCWSR method)

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Stress induction in rat is one of the valuable techniques in biological studies. There are a diversity of procedures for induction the stress with some advantages and disadvantages. In this study we have investigated a biphasic technique for induction stress by combination of restraint and cold/room temperature water immersion. MATERIALS & METHODS: Male rats were fasted for 24 hours in metabolic cages (water ad libidum). The rats were kept in supine position with fastened hands and paws by metal thread in an aluminium plate. Then the rats were hung in cold water (4-6° C or 8-10° C) for 15,20,25,30, and 35 minutes. Then the rats were brought out of cold water and were kept in room temperature water for 1,2,3, or 4 hours. Then they were killed and their gastric mucosa were studied with standard techniqes in order to study effect of stress on gastric mucosa, as a standard indicator for stress. RESULTS: The best water temperature in the first phase was obtained 4-6 C, with the best tolerated period of 25 minutes. The best restraint duration in second phase was 3 hours. Average produced ulcer index was 10±0.8 mm. DISCUSSION: In Biphasic Cold Water Supine Restraint (BCWSR) method there were apparent and large gastric ulcers without rat mortality, in a relatively short periode of time. Severe stress with restraint and cold water had injured the gastric mucosa, but short duration (25 minutes) was not sufficient to produce apparent gastric ulcer, so stress continued in restraint and room temperature water, in order to produce gastric ulcer.

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NOCICEPTION AND BRAIN SEROTONIN FOLLOWING SINGLE INTRAPERITONEAL INJECTION AND LONG LASTING PERORAL GLUCOSE INTAKE IN RATS

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The influence of elevated glucose intake on nociception has been investigated mostly in hyperglycemic, diabetic rats or in healthy rats few hours following a single glucose application. We have investigated the time (up to 4 weeks) and the dose (0.1-1M) response of a single intraperitoneal /i.p./ injection of glucose and the influence of 1 week lasting peroral /p.o./ 0.2M glucose on nociception in healthy rats. Pain threshold has been determined as the tail flick latency in tail immersion test at the 55°C. Brain serotonin (5-HT) and its metabolite, 5-hydroxyindoleacetic acid (5-HIAA) have been measured spectrophotofluorimetrically. Following a single i.p. injection of 0.2M glucose pain threshold rises and remains elevated up to 3 weeks posttreatment (20-70%), with an increase being dose dependent at the 2nd and 7th days following 0.2, 0.5 and 1M glucose i.p. injection (32-83%), respectively. Increased pain threshold has also been found at the 1st (79%) and the 7th day (43%) following the continuous p.o. intake of 0.2M glucose. In rats kept on 0.2M glucose p.o. intake for 7 days the content of brain 5-HT, possible modulator of nociception is decreased (-33%), while the 5-HIAA content is increased (20%). 7 days following single i.p. injection of 0.2M glucose the content of brain 5-HIAA is inereased(19%), as well. Unchanged or mildly decreased blood glucose levels in glucose treated animals suggest that altered nociception may be related to glucose-induced insulin secretion and/or altered brain 5-HT transmission, at least in long lasting glucose p.o. treated rats.

Supported by the Ministry of Science of Republic of Croatia.

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