P-103

Phagocytic activity of monocytes of panic disorder patients during benzodiazepine receptor activation

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Benzodiazepines, which are widely prescribed for their anxiolytic effects, have been shown to be a potent stimulator of human monocyte chemotaxis (Ruff et al, 1985). The demonstration of functional benzodiazepine receptors on human monocytes, together with recent evidence of receptor-mediated monocyte chemotaxis by other psychoactive peptides, e.g. opiate peptides, suggests a biochemical mediator for psychosomatic effects. Studies by O'Neil and Leonard (1990) have shown a reduction in neutrophil phagocytic activity in Panic Disorder and depressed patients and phagocytic activity returned to normal in response to effective therapy, suggesting the change in neutrophil phagocytic activity to be a potential state-dependent marker for panic and depression.

This study was aimed at determining whether the peripheral benzodiazepine receptors (PBDR), which are abundantly present on mononuclear phagocytes, are involved in phagocytic activity and if there is any difference in response of Panic patients compared to control subjects.

The phagocytic activity of monocytes was measured using a chemiluminescence method (Janah and Das, 1988). Blood samples from drug free patients (mean age 40 yrs) meeting DSMIIIR criteria for Panic Disorder with or without agoraphobia and healthy volunteers (mean age 38 yrs) were used for monocyte preparations. Purified monocytes were obtained using NycoPrep gradient (Nycomed, UK). Diazepam and clonazepam were used as ligand for peripheral and central type of benzodiazepine receptors. Cells were pretreated with the ligands for 10 min before activation with formyl-methionyl-leucyl-phenylalanine (fMLP) and luminol. Results showed that diazepam can activate monocyte PBDR at nanomolar concentrations, but at high concentrations it inhibited the activation. Monocytes from Panic patients showed significantly increased sensitivity to diazepam activation (10^{-7} M). Clonazepam was inactive at all concentrations in its ability to modulate fMLP induced activation of monocytes.

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P-104

P300 in posttraumatic stress disorder: preliminary results

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Posttraumatic Stress Disorder (PTSD) gains acceptance as a psychiatric entity. Biologic and cognitive consequences of trauma have been largely studied. However, in a forensic context, diagnosis and prognosis of PTSD are sometimes difficult to achieve. The recording of the P300, a long latency brain potential, has been proposed as a measure of cognitive functions

in psychiatric patients but has never been recorded in PTSD patients.

In the present study, P300 (recorded at Cz; after a oddball paradigm) has been recorded in 26 subjects (16 females; mean age: 25.6 ± 9.9) one month (Time 1) after an aggression without organic complications. Among our sample, 16 subjects (PTSD+) fulfilled DSM-III-R criteria for PTSD and 10 did not. The mean amplitude of P300 was significantly lower in the PTSD+ group (8.7 ± 2.3 vs 13.7 ± 0.9 microvolts; $p < 0.001$).

Thirteen of the 16 subjects underwent, six months (Time 2) after the trauma, a second SADS procedure, and 8 of them exhibited a major depressive disorder. The mean P300 amplitude recorded at time 1 in those 8 PTSD+ subjects who became depressed was significantly lower than the mean amplitude of the 5 PTSD subjects who did not reach DSM-III-R criteria for major depression at time 2 (7.1 ± 1.9 vs 10.8 ± 1.2 microvolts, $p = 0.003$).

Diagnosis and prognosis of PTSD were thus enlightened by our results.

P-105

Responses to cumulative doses of clonidine in healthy volunteers: cardiovascular, noradrenergic and subjective parameters

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Administration of the selective alpha2-receptor agonist clonidine (CLO) is frequently used as challenge test in psychiatric disorders such as panic disorder or depression in order to investigate central noradrenergic function (Charney and Heninger, 1986; Checkley et al, 1981). After a single dose of 2.0 μg/kg i.v., CLO induces hypotension, bradycardia, sedation and a reduction in plasma noradrenaline (NOR) and MHPG. Reduced or increased responses versus controls have been described following administration of CLO, suggesting an abnormal regulation of noradrenergic function in some patients. The lack of correlation between different responses suggests different mechanisms, originating from differential effects of CLO on peripheral or central, as well as pre- or post-synaptic alpha2-adrenergic receptors. Dose-response-patterns of the different parameters may help to clarify differences in these mechanisms. We therefore studied effects of four doses of CLO i.v. (0.25, 0.5, 1.0 and 2.0 μg/kg) on cardiovascular, noradrenergic and psychological function in 7 healthy male volunteers (mean age 23.4 years) in a placebo-controlled double-blind randomized cross-over design. Blood pressure (noninvasive: FINAPRES-device), heart rate, plasma NOR and MHPG and subjective mood were monitored for a period of 1 h after infusion of CLO or placebo, while in addition NOR and MHPG were analyzed in urine, collected at 1 and 4 hrs after infusion. With 15 min after infusion, dose-dependent decreases were observed for SBP, DBP, plasma and urinary NOR, and dose-dependent increases for subjective sedation (as assessed with the Stanford Sleepiness Scale). CLO did not influence plasma MHPG, but urinary MHPG excretion was significantly decreased after the infusion of 2.0 μg/kg CLO. Since dose-response-patterns of plasma NOR (believed to be a presynaptic and peripheral effect), blood pressure (believed to be a pre- and post-synaptic effect) and subjective sedation (believed to be a central and probably post-synaptic effect) are all similar, our results do not simply provide parameters or doses to discern these mechanisms of action of CLO. However, at a dose of 0.5 μg/kg (a dose much lower than mostly used) clear effects on plasma NOR, blood pressure and sedation were observed, but not on MHPG. When using CLO as challenge test to characterize abnormalities in the noradrenergic system in psychiatric disorders, a design with 0.5 μg/kg, in addition to the traditional 2.0 μg/kg CLO, may prove helpful for interpretation of the results.

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