temperature responses to flesinoxan (Ansseau et al., 1993a) whereas ritanserin, a 5-HT2 antagonist, antagonized the prolactin and ACTH responses (Ansseau et al., 1993b).

In the present study, we measured hormonal (prolactin, ACTH, cortisol, GH, total neurophysins and AVP neurophysins) and temperature responses to flesinoxan 1 mg in 12 male inpatients meeting DSM-IIIR criteria for major depression. They had been drug-free for at least 3 weeks before the neuroendocrine procedure and were compared to 12 male healthy controls. Hormones were assayed at −30, 0, +15, 30, 60, 90, and 120 min after the injection of flesinoxan. The two groups differed significantly in their prolactin peak responses (mean ± SD): 165.5±166.5 ng/ml in major depressives vs. 407.1±278.1 ng/ml in controls (F = 5.82, df = 2,21, P=0.025). However, there was no difference between the two groups in their responses in ACTH, cortisol, GH, total neurophysins. AVP-neurophysins and body temperature. These results confirm the implication of 5-HT1A receptors in the pathophysiology of depression.

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P-1-46

The flesinoxan/5-HT1A receptor challenge and suicidal behavior

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Key words: Flesinoxan; 5-HT1A agonist; Neuroendocrine probe; Serotonin; Major depression

A dysfunction in central serotonergic neurotransmission, and particularly in the sensitivity of 5-HT1A receptors, has been widely documented in depression. Agonists of 5-HT1A receptors such as buspirone or ipsapirone stimulate various neuroendocrine responses but lack actual serotonergic selectivity or are not available for intravenous use. Recently, we showed that the intravenous injection of flesinoxan, a highly potent and selective 5-HT1A agonist, induced significant and dose-dependent increases in prolactin, ACTH, cortisol, GH, and total neurophysins and a decrease in body temperature (Ansseau et al., 1992). The tolerance of flesinoxan was excellent and associated with a pleasant feeling of relaxation and slight drowsiness without any GI side effects. Moreover, pindolol, a 5-HT1A antagonist, antagonized the prolactin, ACTH, GH, and temperature responses to flesinoxan (Ansseau et al., 1993a) whereas ritanserin, a 5-HT2 antagonist, antagonized the prolactin and ACTH responses (Ansseau et al., 1993b).

In the present study, we measured hormonal and body temperature responses to flesinoxan 1 mg in 12 DSM-IIIR major depressive patients (10 M, 2 F) in relationship to suicidal behavior. The patients were subgrouped into suicide attempters (n=6) and nonattempters (n=6). The two groups differed significantly in their delta peak cortisol responses (mean ± SD): 12.5±15.6 μg/l in suicide attempters vs. 86.0±65.0 μg/l in nonattempters (F = 7.0, df = 2,10, P=0.02), and in their delta temperature responses: 0.11±0.18°C vs. 0.55±0.33°C (F = 7.9, df = 2,10, P=0.02). However, no differences existed between the two groups for ACTH, PRL, GH, AVP neurophysins and total neurophysins. These results support the 5-HT1A receptor downregulation hypothesis of suicidal behavior.

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P-1-47

Contingent negative variation (CNV) in mood disorders

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Key words: Contingent negative variation; Depression; Antidepressant drugs

The assessment of depressive patients is essentially based on clinical symptomatology, which exhibits considerable limitations. It is therefore of major interest to develop methods able to objectivate clinical outcome during depressive episodes and to predict the response to treatment.

In depression, CNV studies have shown abnormalities in both amplitude (too low or too high) and duration.

In our studies, we found that depressed patients with low CNV amplitude had higher scores on the retardation factor of the Hamilton Depression Scale.

After recovery, patients with low CNV amplitude during the active phase of the illness presented a significant increase of CNV whereas patients with high CNV amplitude during illness exhibited the opposite change. Low CNV amplitude patients had a preferential response to noradrenergic antidepressants whereas high CNV amplitude patients were better improved with serotonergic antidepressants.

Taken together, these results suggest that normalization of CNV amplitude represents a reliable index of positive outcome and that the abnormalities of CNV amplitude (low or high) can predict the response to selective antidepressants. Moreover, low CNV amplitude also appears to characterize depression with psychomotor retardation.

P-1-48

Neurochemical and behavioral evidence for a central indirect dopaminergic agonist activity of the antidepressant medifoxamine in mice

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Key words: Antidepressive agents; Behaviour; Animal; Dopamine; Motor activity

Medifoxamine (*N,N'*-dimethyl-2,2-diphenoxyethylamine fumarate) is an antidepressive agent (Clédial®) marketed in France. In vitro, medifoxamine displays a moderate affinity for various receptors and for serotonin, noradrenaline and dopamine (DA) neuronal transporters. The antidepressant efficacy of medifoxamine may result from an impact on these different molecular targets. We confirm here that medifoxamine binds to the DA neuronal transporter both in vitro and in vivo. This mechanism of action operates in mice at doses which elicit a positive response in the behavioral despair test but are devoid of any stimulant motor effect.

First, the ability of medifoxamine to inhibit the uptake of tritiated dopamine by crude synaptosomal striatal preparations obtained from Swiss albino mice was investigated in vitro. Medifoxamine demonstrated a dose-dependent inhibitory effect on