produced. Rabbit liver membranes were solubilized with CHAPS and IR purified using a ReactiGel-amiloride resin. The purified protein (I_2-type) was used to immunize rabbits, and the IgG fraction was used after purification. The antibody immunoprecipitated the binding of ^{3}H-2-BFI (I_2-IR) in rabbit liver. Western blot analysis of human brain membranes (prefrontal cortex) with this antibody (AMI, 1:12,000 dilution) resulted in the labeling of a unique protein of about 77 kDa (putative I_2-IR). In a well-defined population of depressed suicides, the immunodensity of this 77 kDa IR protein in the prefrontal cortex was marginally increased (41±21%, n = 10, $p > 0.05$) compared to that in matched controls. This increase was clearly apparent in antidepressant-free (69±29%, n = 6, $p < 0.05$) but not in antidepressant-treated (1±20%, n = 4) depressed suicides. These preliminary data suggest that this putative I_2-IR, in contrast to the 30-kDa IR protein, is up-regulated in brains of depressed suicides and down-regulated by antidepressant drugs. The functional relevance of altered IR in the pathogenesis of mood disorders (e.g. modulation of monoaminergic neurones by IR) is unknown, but brain $I_{1/2}$-IR appear to be targets for the effects of antidepressant drugs.

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S34.04

IMAGING NORADRENERGIC AND NON-ADRENERGIC BINDING OF [^{3}H]CLONIDINE IN BRAINS FROM PSYCHIATRICALLY CHARACTERIZED HUMANS

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Clonidine is a partial agonist at brain α_2-adrenoceptors (α_2AR), and also has high affinity in homogenate binding assays for non-adrenergic imidazoline-binding sites (I-sites). This study utilized receptor autoradiography to compare the density distributions of binding of [^{3}H]clonidine to α_2AR and I-sites and in sections of human brain. The α_2-adrenoceptor component of [^{3}H]clonidine binding was masked with either norepinephrine (α_2AR agonist) or with methoxy-idazoxan (selective α_2AR antagonist) and the remaining I-sites were displaced with the imidazoline compound, cirazoline. Densities of [^{3}H]clonidine binding to α_2AR and I-sites, determined in adjacent tissue sections, were positively correlated across 27 brain regions ($p = 0.0003$; $r^2 = 0.385$). Despite this significant correlation, closer inspection within the hippocampus, using quantitative transepts drawn across hippocampal images, revealed α_2AR enrichments in the CA-1 and inner molecular layer of the dentate gyrus, areas not enriched in I-sites. Competition curves were generated for I-sites in caudate sections using 10 ligands reported to distinguish between I_1 and I_2 subtypes. The rank-order of affinities was cirazoline > harmane > BDF6143 > idazoxan = tizanidine (affinities of agmatine, efaroxan, moxonidine, norepinephrine, and oxymetazoline were too low to be reliable). [^{3}H]clonidine binding to α_2AR and to I-sites in 6 layers of the left, rostral orbitofrontal cortex (area 47) were measured in 7 psychiatrically normal control subjects and 8 subjects with major depression, of whom diagnoses were confirmed by retrospective psychiatric autopsy. Ratios of α_2AR/I-site binding were significantly higher (approximately 2-fold) across all layers of the cortex of control subjects relative to major depressive subjects. In conclusion, (1) the distribution of non-adrenergic [^{3}H]clonidine binding sites in human brain sections is correlated with, but distinct from, α_2AR, (2) the pharmacology of these sites is distinct from α_1AR, α_2AR, I_1 or I_2 sites as previously defined in membrane binding assays, and (3) major depression is associated with an abnormality in the ratio of α_2AR/I-sites in the orbitofrontal cortex.

S34.05

NEW APPROACHES TO IMIDAZOLINE RECEPTORS

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In view of the potential role of imidazoline receptors in both psychiatric (depression, addiction) and neuropsychiatric (Alzheimer's, Huntington's) disorders, there is a great need to have selective and potent probes for them. Our group has been working in this field for a number of years and have characterised a series of high affinity, high specificity ligands such as 2-BFI and BU224. The pharmacological actions of these compounds are intriguing in that, to varying degrees, they increase the release of noradrenaline and dopamine in 5HT in brain. We have previously shown 2-BFI to have efficacy in the Porsolt forced swim test. In a rat model of opiate withdrawal, we noted that BU224 could alleviate some symptoms of the syndrome such as diarrhea (Hudson et al., 1999). This suggests that these compounds may have some utility as therapeutic agents. More recently, we have synthesized a high affinity irreversible ligand of these receptors which offers the promise of studying the effects of long term ablation of imidazoline receptors on neurochemistry and behaviour (Coates et al., 2000). Moreover, it will allow us to identify the imidazoline proteins and therefore proceed towards purification and cloning. The implications of this for psychiatry will be discussed.

S35. Somatoform disorders and related disorders: the clinical concepts and the neurobiological basis

Chairs: M. Ackenheil (D), N. Sartorius (CH)

S35.01

SOMATOFORM DISORDERS AND CONCURRENT CONCEPTS IN INTERNAL MEDICINE

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Around the world and across different cultures, medically unexplained somatic symptoms are characteristic of psychosocial distress and indicative of somatoform disorders. However, when a medically unexplained somatic symptom (or a syndrome) is explained (which is sometimes due to the advancement of our medical knowledge and more often due to the reclassification of our existing knowledge), it tends to move from the area of psychiatry to the area of internal medicine. The most recent examples include Chronic Fatigue Syndrome, Fibromylagia and Irritable Bowel Syndrome.

In this paper we will discuss the concept of somatoform disorder and compare it to concurrent concepts in internal medicine including the above-mentioned conditions. Our discussion points will be based on a comparative analysis of symptom profiles and diagnostic features of these disorders and for such purpose we will use the data collected in the International Study of Somatoform Disorders-a large epidemiological project carried out by the World Health Organisation in eleven countries spaning four continents.