abnormality may underlie the observation of increased impulsive and aggressive behaviors in individuals at risk for suicidal behavior. That biobehavioral characteristic crosses diagnostic boundaries. Most recently, we have reported that serotonergic abnormalites in postmortem brain tissue related to major depression differ significantly in their localization compared to the serotonergic abnormalities associated with suicide. Thus, major depression involves a diffuse change in serotonin transporter binding throughout the prefrontal cortex and temporal cortex, whereas suicidal behavior involves an alteration in serotonin transporter binding in the ventral prefrontal cortex only. Future studies addressing more detailed aspects of the serotonergic and other neurotransmitter systems are required to further differentiate syndromal correlations from temperament and personality correlations in high risk patients.

S33.04
SUICIDE AND YOUNG PEOPLE

B.S. Runeson

No abstract was available at the time of printing.

S34. Imidazolines: novel markers for depression and potential targets of new antidepressants

Chairs: A. Halaris (USA), J.E. Piletz (USA)

S34.01
MIDAZOLINE RECEPTORS: POTENTIAL MARKERS FOR DEPRESSION AND TARGETS OF ANTIDEPRESSANT DRUG DEVELOPMENT

A. Halaris*, J.E. Piletz. *Department of Psychiatry and Pharmacology, University of Mississippi Medical Center, Jackson, MS, USA*

Imidazoline binding sites (I-sites) have been characterized using radioligands like ^{3}H-clonidine. At least two I-sites, I_1 and I_2, have been defined based on differential binding affinities, subcellular localizations and regional brain distributions. Human platelets possess both subtypes and immunologically-related 33 kDa and 45 kDa proteins. Platelet I_1 sites are elevated in depressed patients but downregulated after desipramine, fluoxetine, citalopram, clomipramine and imipramine. We used I receptor binding protein (IRBP) antiserum to quantify I receptors on platelets of depressed patients before and after bupropion. Western blots revealed increased IRBP-immunodensity in a 33 kDa protein band in untreated patients. This band has been positively correlated with I_1 binding sites on platelets. After 6 weeks of treatment, IRBP-immunodensity was downregulated predominantly in treatment responders. Non-responders showed no elevation in IRBP at pretreatment and no downregulation at posttreatment. IRBP-immunodensity was negatively correlated with plasma bupropion concentrations. Thus, a 33 kDa IRBP on platelet plasma membranes is elevated in depression and normalized in treatment responders. We also determined associations between clusters of depressive symptomatology and platelet parameters. Two of the Hamilton Depression clusters, the endogenomorphic and retardation dimensions, showed significant correlations with binding parameters. Thus, platelet I_1 might become a potential marker for affective symptomatology and/or a specific marker for unipolar depression and this could lead to the development of compounds targeting these receptors and exerting antidepressant efficacy.

S34.02
CLONING OF A CANDIDATE IMIDAZOLINE RECEPTOR CDNA FROM HUMAN HIPPOCAMPUS

J.E. Piletz, M. Chen, M.E. Lutrick, H. Zhu, J. Baldwin. *University of Mississippi Medical Center, Dept. of Psychiatry, Division of Neurobiology & Behavior Research, Room G128, 2500 North State Street, Jackson, MS 39216, USA*

Pharmacologically distinguishable imidazoline receptors (IR) and alpha2-adrenoceptors (alpha-2AR) share several common properties in the brainstem. We recently cloned a candidate IR1 cDNA from the human hippocampus using two IR-selective antisera (DNA & Cell Biology, 2000). The clone, designated imidazoline receptor antisera-selected (IRAS-1) cDNA, encodes a 167 kD protein. Transfection of IRAS-1 cDNA into CHO (Chinese hamster ovary) cells resulted in high affinity IR1 sites labeled with [125I]-p-iodoclonidine (PIC). Using phaeochromocytoma PC-12 cells, we also selected a stably-transfected subclone that exhibits a 2-fold increase in IR1-like Bmax. The transfected CHO and PC-12 subclones both showed a 167 kD anti-IRAS band as well as smaller bands (~85 kD). But, transient trasfections into COS-7 and Sf9 cells failed to result in an increase in IR1 binding sites, suggestive that host cell processing of IRAS-1 is critically important for IR1 binding site. Furthermore, CHO cells permanently transfected with human alpha-2AR cDNA were transiently co-transfected with IRAS-1 cDNA. These co-transfectants produced both alpha-2AR and IRAS-1 (immunologically) at expected levels, but there was a surprising 3-fold increase in alpha-2AR binding. Thus, IRAS-1 not only encodes IR1 binding sites in a host-cell specific manner, but also may interact with alpha-2AR to increase their binding capacity for PIC. It is possible that IRAS and alpha-2AR interact with each other in certain brain cells to mediate sympathetic outflow in a coincident detection manner.

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S34.03
BRAIN AND PLATELET IMIDAZOLINE RECEPTORS IN MOOD DISORDERS

J.A. García-Sevilla*, P.V. Escribá[1], J. Guimón. *Department of Psychiatry, University of Geneva, Geneva, Switzerland*
[1]*Laboratory of Neuropharmacology, University of the Balearic Islands, Palma de Mallorca, Spain*

Major depression has been associated with alterations of imidazoline receptors (I_1- and I_{2B}-IR) and related IR proteins in brain and platelets. The immunodensity of a 45-kDa IR (putative membrane I_1-IR) is increased in brains of suicides and depressed suicides, and also in platelets (45- and 35-kDa IR) of depressed patients. Similarly, I_1-sites (^{125}I-p-iodoclonidine binding) and the levels of a 33-kDa IR are increased in platelets of depressed patients (Halaris, Piletz and colleagues). In brains of depressed suicides, the abundance of a 30-kDa IR (putative glial I_{2B}-IR) is down-regulated in parallel with a reduction of ^{3}H-idazoxan binding (I_{2B}-IR), which is in line with recent histopathological studies showing reduced glial density in brains of depressed patients. IR proteins (35- and 45-kDa peptides) are not altered in platelets of euthymic patients with bipolar affective disorder. Antidepressant drugs induce down-regulation of 45-kDa IR protein and I_1-sites in platelets of depressed patients and up-regulation of I_{2B}-sites in rat brain. To foster the knowledge of IR a new IR antibody was