functioning, serotonin-related behaviors, and psychopathological disorders. A similar polymorphism, believed to be homologous, also exists in nonhuman primates. We have recently analyzed the relationship between the rhesus macaque serotonin transporter (rh5-HTTLPR) genotypes, CSF 5-HIAA concentrations, and aggression. Our results show that rhesus macaques with the short rh5-HTTLPR allele have low CSF 5-HIAA concentrations, and are highly aggressive. However, the phenotypic expression of this short allele is environmentally-dependent, with the short allele associated with low CSF 5-HIAA concentrations only in subjects reared in age-matched peer groups that lack adult influence. Aggression was shown to be higher in subjects with the short allele than in subjects with the long allele regardless of early rearing experiences. In humans, the 5-HTTLPR is associated with early infant temperament. Similar data for neonatal rhesus monkeys were collected during assessments on days of life 7, 14, 21 and 30. Subjects with the short allele exhibited diminished orientation, attention, and increased emotional responses. Consistent with our earlier findings, these differences were generally exaggerated by parental deprivation. These findings illustrate the interacting influence of genotype and early rearing experiences on the developing phenotype.

36. CLINICAL PROFILE OF SUBSTANCE P ANTAGONISTS


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Based on limbic co-localization of tachykinins (i.e. Substance P; [SP]) with monoamines, and behavioral pharmacology data, we postulated that the selective NK1 antagonist, MK-0869, would be antidepressant with potential anxiolytic activity, and support a role for SP acting at the NK1 receptor in the pathophysiology of depression and perhaps anxiety. As available, data from additional studies may be presented and discussed.

37. REDUCED EXPRESSION OF PKC ISOZYMES IN THE BRAINS OF TEENAGE SUICIDE VICTIMS

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We have recently reported that the binding of [3H]phorbol dibutyrate to protein kinase C (PKC), which is an important component of the phosphoinositol (PI) signaling system, is significantly reduced in Broadmann’s Areas (BA) 8/9 of teenage suicide victims. We have now determined PKC activity; and protein and mRNA expression of PKC isozymes by immunolabeling and quantitative RT-PCR, respectively, in BA 8/9 and hippocampus of teenage suicide victims and matched control subjects. Postmortem brain samples were obtained from the brain collection program of the Maryland Psychiatric Research Center and the diagnosis was made by DSM-IV and diagnostic evaluation after death (DEAD) instruments. We found that PKC activity was significantly lower in BA 8/9 and hippocampus in suicide victims as compared with the control subjects. We also observed that the immunolabeling of PKCo, β, and γ isozymes was significantly decreased in both the brain areas of the suicide victims. To examine if the a decrease in protein expression of PKC isozymes is associated with decreased mRNA level, we are currently determining mRNA levels of PKC isozymes using RT-PCR method and so far have observed that the PKCo mRNA expression is significantly decreased in BA 8/9 of suicide victims. Further results are awaited. Our results suggest that the reduction in PKC recognition sites in BA 8/9 of teenage suicide victims is associated with decreased PKC activity as well as the immunolabeling of PKCo, β, and γ isozymes, and further suggests that teenage suicide may be associated with an impaired PI signaling system.

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38. MOTOR PROGRAMMING DEFICITS IN DEPRESSION: SUPPORT FOR A DOPAMINERGIC MECHANISM

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Several investigators have reported parallels between motor and cognitive slowing in patients with major depression (MD). Such a relationship between depression and motor function suggests the possibility of a shared neuropathologic mechanism. This mechanism has remained elusive largely because depression may involve any of several neurotransmitters. While others have shown that MD and parkinsonism share a number of features, especially in the motor domain, previous technologies have not delineated the cognitive from neuromotor aspects of the motor impairment in MD. The aim of the present study was to examine motor programming in MD patients...