thought to reside in the shared socio-cultural and psychological environment, rather than in a shared genetic endowment. Even Franz Kallman, one of the major proponents of the idea of a genetic background of psychiatric disorder, considered a genetic background to suicide unlikely. Accummulating evidence for an association between low serotonin function and an increased risk of suicidal behaviour has, however, made a genetic background for suicide more plausible. Family and twin studies using modern techniqes and controlling for psychiatric illness support the idea that vulnerability to suicidal behaviour is to some extent under genetic control. Several genetic polymorphisms involved in serotonin transmission have been studied for a possible association with suicide. Among them, an modest excess of the tryptophan hydroxylase 17779C allele has repeatedly demonstrated in association with suicide, most recently in a study of surviving cotwins whose monozygotic twin had committed suicide. These, and some studies involving other genetic markers will be briefly reviewed in the presentation.

S05.4

Treatment outcome of personality disorders

P. Tyrer. *UK*

No abstract was available at the time of printing.

S06. Substance P (NK1) receptors – possible role in stress, anxiety and affective disorders

Chairs: T. Hökfelt (S), E. Brodin (S)

S06.1

Anatomy of substance P and NK1 receptors in the brain

T. Hökfelt*. *Department of Neuroscience, Karolinska Institutet, Stockholm, Sweden*

Substance P has a wide distribution in the CNS, including cortical and limbic brain regions, suggesting involvment in multiple functions. Regions with a particular dense substance P innervation include the medial amygdaloid nucleus, the zona reticulata, substantia nigra and the spinal trigeminal nucleus/spinal dorsal horn. There are at least 30 different cell groups expressing substance P in the rat brain. Substance P coexists with classic transmitters, for example with serotonin in the descending system to the spinal cord, but not in the dorsal raphe 5-HT neurons, which project to the forebrain. However, in the human brain a high proportion of the serotonin neurons in the dorsal raphe nuclei has detectable substance P expression. So far three substance P receptors have been identified. The NK-1 receptor has a wide distribution in the rat CNS and is internalized upon stimulation with the ligand. Such internalization can in fact be used as an index of endogenous substance P release. This approach has opened up new possibilities to study substance P functions in the CNS.

S06.2

Pharmacology – a historical overview

E. Brodin*. *Department of Physiology and Pharmacology, Karolinska Institute, Stockholm, Sweden*

Recent studies indicate that neurokinin 1 (NK1) receptor antagonists may be an alternative to selective serotonin uptake inhibitors (SSRI) and other drugs in the treatment of affective disorders. It has been suggested that the antidepressant effect of NK1-receptor antagonists does not involve monoaminergic mechanisms. However, there are preclinical evidence for interactions between substance P (SP), the most important endogenous ligand at NK1-receptors, and serotonin (5-hydroxytryptamine, 5-HT) in limbic structures, the periaqueductal grey (PAG) and other brain regions. Acute and subchronic treatment with SSRI:s and tricyclic antidepressant drugs induce changes of tissue levels of SP, and the other tachykinin neurokinin A, in

these brain regions in the rat. These interactions may involve separate SP- and serotonin-containing pathways or pathways from the dorsal raphe region coexpressing SP and 5-HT. Interestingly, subchronic SSRI treatment and electroconvulsive stimulation have similar effects on SP-levels in the rat cerebral cortex in rats. In addition to these neurochemical data, there are electrophysiological results demonstrating SP/monoamine/-interactions which may be of importance for the antidepressant effect of NK1-receptor antagonists as well as other antidepressant drugs.Preclinical evidence also indicate that SP and NK1-receptors play a key role in the adaptation to stress, a wellknown aetiological factor behind the development of affective disorders. Acute stress induce marked changes in tissue levels of SP in limbic structures and the PAG in the rat that correlate in time with plasma corticosterone levels. Mice lacking the NK1 receptor have been shown to be less aggressive and less anxious than wild type controls and NK1-receptor antagonists have anxiolytic properties in animal models. In our own experiments we have found that the 5-HT1A-receptor agonist 8-OH-DPAT, at low dosage, which also has anxiolytic effect, counteracts stress-induced tachykinin release in the limbic system.

S06.3

Diminished anxiety- and depression-related behaviors in substance P-deficient mice

A. Bilkei-Gorzo, I. Radz, A. Zimmer*. *Laboratory of Molecular Neurobiology, Department of Psychiatry, University of Bonn, Sigmund-Freud Str. 25, 53105 Bonn, Germany*

While the role of substance P (SP) in nociceptive signaling is now well established, its role in the regulation of higher brain functions remains poorly understood. Limbic structures, including the amygdala, contain a high density of SP terminals and NK1 receptor sites, suggesting that SP may be involved in the modulation of emotional behaviors. Indeed, recent clinical and pharmacological studies, and the analysis of NK1 receptor mutant mice suggested that the NK1 receptor modulates emotional responses. In this study, we have analyzed SP-deficient mice (Tac1-/-) in animal models of anxiety and depression. Tac1-/- animals were more active in the forced-swim and tail-suspension test, and displayed a reduced activity change after bulbectomy. Thus, SP deficient mice behaved like wild type animals treated with antidepressants. Tac1-/- also showed a marked reduction of anxiety and stress related responses in the O-maze test, the Thatcher-Britton conflict paradigm, and the social interaction test. Our results suggest a significant role of SP/NKA in the regulation of emotional states and provides further evidence that the NK1 receptor might be a useful pharmacological target in the treatment of affective disorders.

https://doi.org/10.1016/S0924-9338(02)80041-4 Published online by Cambridge University Press