differences. Amisulpride is a selective antagonist at D_2/D_3 receptors with preferential activity at presynaptic autoreceptors. In marked contrast, clozapine and risperidone show higher affinity for $5HT_2$ and α than for D_2/D_3 receptors. Many traditional models used for drug screening involve the antagonism of effects induced by dopamine agonists and may be more relevant to positive symptoms (or even motor side effects) than to negative symptoms. However, a number of recent studies have attempted to develop alternative behavioural procedures modelling different psychotic symptoms. In such studies, amisulpride has been found to exert pro-hedonic activity and clozapine has been reported to reduce spontaneous or drug-induced social withdrawal. Further pharmacological analysis of these models may eventually provide more sensitive procedures and allow the discovery of more effective antipsychotic drugs.

NEURAL NETWORKS, NEUROPLASTICITY, AND NEUROMODULATION: A FRAMEWORK FOR UNDERSTANDING FORMAL THOUGHT DISORDER AND DELUSIONS

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From a neurocomputational perspective, the cortex can be viewed as a computational surface that creates and maintains dynamic maps of representations of important sensorimotor and higher level aspects of the environment and the organism. Most importantly, representations of information in the cortex and in these maps have been demonstrated to dynamically change according to salience and frequency of the input. This feature is referred to as neuroplasticity. The fact that general operational characteristics of computational maps in the cortex can be fine-tuned according to specific processing needs is referred to as neuromodulation. Within this framework of cortical maps and their computational models, the following hypotheses regarding formal thought disorder as well as acute and chronic delusions are discussed:

(1) Formal thought disorder is caused by dysfunctional lexical access which can be modeled in terms of low signal-to-noise ratio within network information processing. Evidence for the crucial role of dopamine modulating signal-to-noise is presented and a model of schizophrenic thought disorder is developed, which allows a parsimonious explanation of a number of otherwise inexplicable or unrelated clinical phenomena and experimental results. (2) Acute delusions may represent a state of too high signal-to-noise, as suggested by some experimental studies and clinical features. (3) In chronic delusions, cortical representations become deformed as the result of long-term dysfunctional activation of the network.

In conclusion, the neurocomputational approach to schizophrenic symptoms provides new insights into psychopathological phenomena. The approach is detailed enough to allow empirical testing and has therapeutic implications.

S8. Craving reduction in alcoholism

Chairmen: H Sass, K Mann

ADDICTIONS AND DEPRESSIVE DISORDERS

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The frequent co-occurrence between addictions and depressive disorders is well established, even if many questions are unsolved concerning the nature of this interrelation. Three situations can be emphasized: Some addictive disorders, especially alcoholism, opiate and cocaine addictions are secondary to depressive disorders, and can be explained through the "self treatment" hypothesis of depression mood by psychoactive substances. The principal data are here discussed, for alcoholism and heroine addictions: the frequency of primary depressive disorders is well established in opiate addiction, better than for alcoholism.

- In most cases, depressive disorders are secondary to addictive disorders: this is especially the case for alcoholism, as well as about 80% of depressive disorders appear after the onset of alcohol abuse and wean with proctacted withdrawal. In those cases, depression could be due to the pharmacological and psychological effects of alcoholic intoxication, as many pharmacological data demonstrate the negative effects on mood of alcoholic during use.

The third hypothesis will be discussed involving an accidental co-occurrence of depressive disorders and addictions, considering the high prevalence of those troubles in the general population.

RESULTS OF A CONTROLLED MULTICENTER STUDY WITH RITANSERIN AND THE EFFECTIVENESS OF OTHER SEROTONERGIC AGENTS IN ALCOHOLISM

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There is considerable evidence from both human and animal studies that serotonergic mechanisms play an important role in the modulation of alcohol intake and dependence (LeMarquand et al 1994). Yet, only a few serotonergic substances have been tested in clinical trials with a satisfying methodological design (Boening 1996). *Fluvoxamine,* a specific serotonin reuptake inhibitor, showed no efficacy in a controlled European multicenter study with 530 alcohol dependents who were treated for six months (Chick, unpbl.). *Fluoxetine* also failed to be superior to placebo in a 12-week trial with 101 alcohol dependent patients (Kranzler et al 1995). In animal studies the $5\text{-}HT_2$ receptor antagonist *ritanserin* was able to significantly reduce both the preference for and the intake of alcohol and cocaine. In an early phase II trial positive effects of *ritanserin* were shown in humans as well (Monti and Alterwain 1991). Therefore, it was hypothesized that *ritanserin* is more effective than placebo in preventing relapse in detoxified alcohol dependents. In a controlled double-blind European multicenter study 493 chronic alcoholics were treated with three doses (2.5/5/10 mg) *ritanserin* versus placebo over a period of six months.

Ritanserin was well tolerated. The most frequent adverse experiences were headache and insomnia. A small increase in weight in the ritanserin-treated patients and a small QTc prolongation in the ritanserin 10 mg group were observed. There was no significant difference between *ritanserin* (2.5/5/10 mg daily) and placebo in the number of relapses, the time to relapse, the craving for alcohol, and the drinking habits after relapse. So far, no serotonergic substance has shown its effectiveness in relapse prevention in clinical trials with demanding methodological designs. Maybe that only subgroups of alcoholics (Cloninger Type II, high impulsivity, etc.) can be considered for the relapse prevention with serotonergic substances.

OPIATE RECEPTORS: ROLE IN ADDICTION AND RELAPSE IN ALCOHOL DEPENDENCE

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The endogenous opiate transmitters, endorphins, are released as one of many acute actions of ethanol on the limbic system. Research in

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