bral blood flow variations occurring during neurocognitive tasks can also be performed with AD patients.

S31-5

CHOLINERGIC TREATMENT STRATEGIES IN ALZHEIMER'S DISEASE

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Two major pharmacological principles are utilized in cholinomimetic therapy of Alzheimer Disease (AD): the first is direct stimulation of nicotinic or muscarinic receptors with selective agonists, the second is a reduction of acetylcholine hydrolysis by means of cholinesterase inhibition. The cognitive and behavioral effects achieved with the two approaches are different and therefore one can envision either combination or alternative use of these drugs. Cholinesterase inhibitors (ChEI) have been mostly used. The results of therapy with ChEI pose several questions:

1. Do all ChEI act in the same way? What makes the difference in clinical efficacy? 2. Is selectivity for AChE important? 3. Is there a "brain selective" ChEI? 4. Do ChEI produce tolerance? 5. Is there an interaction of cholinergic and non-cholinergic effects?. 6. Is there an effect of cholinergic stimulation on APP release which could be of therapeutic relevance?

If basic principles of pharmacology are applied to the results obtained in the patient one can expect to improve magnitude and duration of effects.

(1) Giacobini. E. Jap. J. Pharmacol. 1997.74. 225–241

S31-6

ANTI-INFLAMMATORY AND ANTIOXIDANT THERAPEUTIC STRATEGIES IN AD

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Accumulating evidence has implicated free radical production and resultant oxidative damage as a major contributing factor in brain aging and cognitive decline. Aβ-induced NO production by microglial cells is one mechanism of the neuronal death in Alzheimer's disease (AD). There is also evidence for cytochrome oxidase dysfunction with oxidative stress and damage in the brains of patients with AD. One additional mechanism of oxidative damage is the nitration of tyrosine residues in proteins e.g. in neurofibrillary tangles of AD but not in controls. Inflammatory processes contribute to the aetiopathology of AD. Interleukin-6 (IL-6), a proinflammatory cytokine, is found in the brains of AD patients, but not in brains of normal control persons. These results support the hypothesis that antioxidant or antiinflammatory compounds could prevent or slow down the course of AD. Several epidemiological studies are in support of a protective effect of antioxidants and anti-inflammatory compounds. In the Prospective Basel Study in people aged 65 and older, higher ascorbic acid and beta-carotene plasma level are associated with better memory performance. Similarly in the EURONUT-Seneca study higher plasma levels of certain vitamins and carotenoids appear to be associated with lower risk of developing dementia. Studies in experimental animals are scarce but in one study chronic PBN (an antioxidant) treatment improved the cognitive performance of aged rats in several tasks. In humans In patients with moderately severe impairment from Alzheimer's disease, treatment with selegiline or alpha-tocopherol slows the progression of disease. Similarly for anti-inflammatory compounds the onset of AD was inversely associated with prior use of corticosteroids or ACTH. Similar but weaker trends were present for history of arthritis or for prior daily use of nonsteroidal anti-inflammatory drugs (NSAIDs) or aspirin. A history of arthritis resulted in a low risk of AD (OR = 0.54; 95% CI, 0.36 to 0.81), as did a history of use of NSAID. In one study the relative risk (RR) for AD was of 0.38 (0.15 to 0.95) when comparing NSAID users (n = 365) to NSAID non-users (n = 5,893). These results not only provide a direct linkage between free radicals/oxidative damage and cognitive performance in old age, but also suggest that synthetic brain antioxidants could be developed to treat or prevent age-associated cognitive impairment and Alzheimer's disease. The results of experimental and epidemiological studies consistently show the close interplay between oxidative stress and inflammatory mechanism in AD. The results indicate the important role played by antioxidants and anti-inflammatory agents in brain aging and may have implications for prevention of progressive cognitive impairments.

S32. Social phobia: developmental risks and impairments

Chairs: JP Lepine (F), H-U Wittchen (D)

S32-1

PREVALENCE, INCIDENCE AND SYNDROME STABILITY OF GENERALIZED AND NON-GENERALIZED SOCIAL PHOBIA IN ADOLESCENTS AND ADULTS

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It is frequently assumed that social phobia is a persistent chronic disorder starting early in life with more or less slowly accumulating disabilities and impairments. In a more recent prospective longitudinal epidemiological sample of 3,021 subjects, we recently investigated prevalence and incidence of generalized and non-generalized social phobia. The baseline findings suggest a lifetime cumulative incidence of about 7%, with women having slightly higher prevalence estimates than men. The 1-year follow-up investigation showed a relatively high incidence. At the same time partial or full remission of previous social phobia was quite high as well, suggesting overall a low stability of social phobia among adolescents. The paper will discuss risk factors for first onset as well as predictors for remission and non-remission and suggests by presenting differential profiles of associated features and complications that generalized social phobia is of primary clinical importance, whereas non-generalized phobia might be a transient disorder with no substantial longterm risks.

S32-2

PSYCHOSOCIAL IMPAIRMENTS AND QUALITY OF LIFE IN SOCIAL PHOBIA

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It seems that social phobia is one of the most neglected psychiatric disorders, both in terms of its prevalence and the amount of suffering and disability it creates. Recent estimates from epidemiological surveys suggested that the life time prevalence may be as high as 13.3%, if intensive questioning is carried out. Superficial

interviewing often does not lead to a diagnosis of social phobia, because these persons do not seem to be inclined to regard their objectively restricted life as especially burdening, whereby the impairment criterion required by operational diagnostic criteria is not fulfilled. However, persons suffering from social phobia are restricted in many aspects of their life: they are socially isolated, less well educated, less productive in work and impaired in many other aspects. However, because of the usually long duration of the disorder before it is recognised, for social phobia has become a "way of life" for many sufferers. Since social phobia is an early onset disorder - the generalised subtype has an age of onset of around 15 - an important component of the reduction of patient's quality of life seems to be due to the lack of social skills which are usually acquired in late adolescence and early adulthood. Due to the avoidance of social learning situations at this life stage disabilities develop and contribute to the reduction of functioning in social roles and prevent the creation of an adequate living environment, i.e. an adequate standard of living. Persons suffering from specific social phobia (e.g. performance anxiety) seem to be less disabled than those suffering from the generalised subtype. Early recognition, already at school age and in non-psychiatric services (e.g. in primary care), is the most important strategy for reducing the prevalence of social phobia.

S32-3

FAMILIAL AGGREGATION AND HIGH RISK STUDY OF SOCIAL PHOBIA

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This paper presents the results of a family study of comorbidity of anxiety disorders and alcoholism. The 165 probands were selected from both treatment and community settings and best estimate diagnoses were assigned to 1053 adult first-degree relatives. After controlling for potential confounders such as age, sex and comorbidity in both probands and relatives, there was a strong degree of specificity of familial aggregation of anxiety disorders and of the specific subtypes of anxiety including social phobia and panic as well. Different patterns of co-aggregation of alcoholism with social phobia and panic were found, thereby suggesting different mechanisms for comorbidity of the subtypes of anxiety and alcoholism. The results of a prospective longitudinal study of the children of these probands will also be reported. Both the child and adolescent offspring of parents with anxiety disorders had significantly greater rates of anxiety symptoms, behavioral inhibition and anxiety disorders, as well as psychophysiologic indicators of anxiety, than those of either controls or other affected parental groups. The strong degree of specificity of transmission of anxiety disorders suggests that there may be underlying temperamental vulnerability factors for anxiety disorders which may already manifest in children prior to puberty.

S32-4

DEVELOPMENT AND ANXIETY DISORDERS: CONTRIBUTION OF FAMILIAL AGGREGATION

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Prospective follow-up studies are commonly used, in order to precise continuity or discontinuity between disorders according to the developmental approach. Family studies also may contribute to the knowledge of these links. Previous studies had demonstrated that there was a familial component involved in the pathogenesis of anxiety disorders such as separation anxiety disorders, social phobia, or simple phobia (Last et al., 1987, Reich and Yates, 1988, Fyer et al., 1995). Last observed differences between separation anxiety disorder and phobic disorder for maternal psychiatric history, and suggested that it could exist differences in familial aggregation of anxiety disorders in the two subgroups of anxious school refusing children.

Objective: We designed a study to test the existence of differences in familial aggregation between a group of children suffering from school refusal related to separation anxiety disorder and a group suffering from phobic disorder-based school refusal.

Method: Using a blind standardized diagnostic evaluation we compared parental lifetime psychiatric illness for the two groups of refusers.

Results: Increased prevalences of anxiety and depressive disorders were found in mothers and fathers of anxious school refusing children. Relationships between specific anxiety disorders in children and their parents revealed increased prevalences of simple phobia, and simple and/or social phobia among the fathers and mothers of phobic disordered school refusers, and increased prevalences of panic disorder and panic disorder and/or agoraphobia among the fathers and the mothers of separation anxiety disordered school refusers.

Conclusion: Our data showed the high prevalence of both anxiety and depressive disorders in fathers and mothers of anxious school refusers. Significant differences were observed in familial aggregation considering the subgroups of anxious school refusing children, supporting the distinctions of these two different subgroups.

S32-5

THE ROLE OF THE FAMILY IN EARLY STAGES OF GENERALIZED AND NON-GENERALIZED SOCIAL PHOBIA: A FAMILIY AND PROSPECTIVE LONGITUDINAL EPIDEMIOLOGY STUDY

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Social phobia is characterized by the fear/avoidance of situations where an individual who is subject to the evaluation of other persons fears that he or she will do something painful or will appear anxious. Motivated by previous studies about familial liabilities of social phobias, we wanted to elucidate the role of specific family factors in the development of social phobia.

In detail, we want to find answers to the following questions:

1. Can we confirm the results of previous findings of a higher rate of social phobia in first-degree relatives of social phobics?
2. Can our data support the distinction between generalized and nongeneralized subtypes of social phobia on the basis of family data?
3. Is there a relationsship between parental alcoholism and social phobia in their children?
4. Is specific parental rearing behavior associated with social phobia in children?

The findings which will be presented are based on a face-to-face interview family study. Subjects were predominantly mothers of 1053 14- to 17-year-old adolescents and young adults which have been examined in the first and second wave of the EDSP-Study, a prospective epidemiological study which investigates the prevalence, comorbidity and course of mental disorders in this age group. Social phobia and the addressed family factors were assessed using