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