for 5-HT3 receptor in mediating the CCK-induced anxiety. On the other hand, a decrease in 5-HT neurotransmission after tryptophan depletion augments CCK-4-induced neuroendocrine activation. To further explore the spectrum of CCK-5-HT interactions we study the biochemical and behavioural markers of CCK activity under conditions of an altered presynaptic availability of 5-HT. Specifically, we investigate in separate studies the effect of tryptophan depletion on the composition of CCK peptides in the cerebrospinal fluid and the influence of a serotonin precursor 5-HTP on the CCK-4-induced panic attacks in healthy volunteers.

S32.4

Cholecystokinin and anxiety disorders

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There is evidence for the role of the cholecystokinin (CCK) neurotransmitter system in the neurobiology of panic disorder. The CCK receptor agonist, CCK-tetrapeptide (CCK-4) fulfils criteria for a panicogenic agent and there is evidence that panic disorder might be associated with an abnormal function of the CCK system. CCK receptors, which have been cloned, have been classified into two subtypes: CCK-1 and CCK-2. Recently, it has been reported that genetic dissection of the CCK system suggests that CCK-2 receptor gene variation and CCK peptide gene variation may be factors in the neurobiology of panic disorder. These findings support the hypothesis that panic disorder might be associated with an anomalies of the CCK peptide and CCK-2 receptor system. This session will review research to date on the role of CCK in anxiety disorders, suggests future research strategies and review potentials for therapeutics.

S32.5

Cholecystokinin in cerebrospinal fluid

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Cerebrospinal fluid (CSF) concentrations of the cholecystokinin (CCK) tetrapeptide (CCK-4) and the sulphated octapeptide (CCK-8S) were analysed in three groups of healthy subjects, in hypothyroid patients before and during treatment, and in panic disorder (PD) patients.

On performing lumbar puncture with the patient in the sitting position, the concentrations of CCK-4 and CCK-8S were influenced by age, bedrest prior to lumbar puncture, neuraxis distance, position during lumbar puncture, height, atmospheric pressure and storage time. No such influences were found when lumbar-puncturing the subjects in the decubitus position. This might imply that lumbar puncture in the decubitus position is to be recommended when performing CSF studies on CCK.

In hypothyroid patients, serum levels of thyroid hormones correlated with both CCK peptides in the CSF. A negative correlation between CCK-4 and the subjects level of anxiety was found.

In PD patients, suicidal ideation correlated positively with CCK-4. There was also a positive correlation between tyrosine and CCK-8S. No other correlations were found between monoamines and CCK peptides in any of our studies.

S32.6

Pentagastrin, anxiety and personality

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Rationale: CCKB receptor agonists such as pentagastrin or CCK-4 have panic-like anxiogenic effects in humans. It has also been shown that CCK-4 can stimulate insulin release and thus C-peptide release from pancreatic islet cells. Combined, these mechanisms may provide a basis for a bio-assay.

Objectives: Our aim was to study if a pentagastrin bolus injection evokes C-peptide release, correlating to the anxiogenic effect of pentagastrin and whether personality characteristics might predict the response.

Methods: Bolus i.v. pentagastrin was administrated at increasing doses. The Karolinska scale of personality (KSP) and anxiety sensitivity index (ASI) were used to characterize the individuals. Pentagastrin-induced discomfort was rated.

Results: A significant increase in the plasma level of C-peptide, heart rate (HR) and galvanic skin response (GSR), accompanied by increases in discomfort rated on SAS, were observed within the same time-frame (2–4 minutes) following pentagastrin. ASI correlated to the increase in discomfort following pentagastrin.

Conclusions: The results support the predictive value of ASI for fearfulness and indicate that C-peptide levels in plasma might predict the biological response to pentagastrin.

SAL08. Current and Future Treatments for Dementia

SAL08

Current and future treatments for dementia

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Cholinesterase inhibitors (ChEI) are currently the most established treatment strategy in Alzheimer's Disease (AD). The treatment effect appears mainly to be symptomatic. Nicotinic agonists may have cytoprotective effects. Glutamatergic (NMDA)-antagonists (memantine) have been successfully tested in severe dementia. Estrogen replacement therapy may give a lower risk for AD in elderly women. However, the reported treatment studies on AD have been negative. Anti-inflammatory drugs have shown to reduce risk for AD. Growth factors are important for neuronal development and maintenance. Nerve growth factor (NGF) stimulates outgrowth of cholinergic neurons but gave severe side effects. Anti-amyloid substances might be used to target directly to the production of Aβ in order to increase the removal of Aβ and/or to decrease the aggregation of Aβ. Immunisation studies of APP transgenic mice with Aβ42 before the onset of pathology prevented development of β amyloid plaques and when given to mice already with pathology, the progression was reduced. This might open the way for immunisation/vaccination against AD. Clinical studies have started.

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