behaviour and depression. Both the physiological and the psychological consequences of this reaction are important factors in the further development of atherosclerosis and will be described in the lecture.

S13.5

Prevention of work-related stress and ill health: options and obstacles

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The Swedish EU Presidency Conclusions of 23–24 March, 2001, read that "regaining full employment not only involves focusing on *more* jobs, but also on *better* jobs. Increased efforts should be made to promote a good working environment for all".

According to WHO (2001), mental health problems and stress-related disorders are the biggest overall cause of premature death in Europe. Based on such considerations, the European Council of Ministers (15 November, 2001) concluded that "stress and depression reled problems ... are of major importance ... and significant contributors to the burden of disease and the loss of quality of life within the European Union" and underlined that such problems are "common, cause human suffering and disability, increase the risk of social exclusion, increase mortality and have negative implications for national economies".

In essence, this means an urgent need for preventive measures across societal sectors and levels, aiming at minimising unemployment, underemployment, and over-employment, promoting "the healthy job" concept, and humanising organisational restructuring.

The challenge to science of all this is to find out *what* to do, for *whom*, and *how*, and to bridge the science-policy gap.

According to the EU Framework Directive, employers have a "duty to ensure the safety and health of workers in every aspect related to the work". The Directive's principles of prevention include "avoiding risks", "combating the risks at source", and "adapting the work to the individual". In addition, the Directive indicates the employers' duty to develop "a coherent overall prevention policy". The European Commission has published its Guidance* to provide a basis for such endeavours.

Based on surveillance at individual workplaces and monitoring at national and regional levels, work-related stress (and its outcomes in terms of both cardiovascular and mental morbidity) could be prevented or counteracted by job-redesign (e.g., by empowering the employees, and avoiding both over- and under-load), by improving social support, and by providing reasonable reward for the effort invested by workers, as integral parts of overall management systems. And by adjusting occupational physical, chemical and psychosocial settings to the workers' abilities, needs and reasonable expectations – all in line with the requirements of the EU Framework Directive and Article 152 of the Treaty of Amsterdam, according to which "a high level of human health protection shall be ensured in the definition and implementation of all Community policies and activities".

Supporting actions should include research, but also adjustments of curricula in business schools, schools of technology, medicine and behavioural and social sciences, and in the training and retraining of labour inspectors, occupational health officers, labour union representatives, managers and supervisors. – Again, the challenge to science is to provide evidence-based guidelines for all such endeavours.

(1) Levi, L and I: Guidance on Work-Related Stress. Spice of Life or Kiss of Death? Luxembourg: European Commission, 2000 (ISBN 92–828–9806–7).

S14. Functional Imaging In Schizophrenia

Chairs: W.W. Fleischhacker (A), F.A. Henn (D)

S14.1

Dynamics of working memory in schizophrenia

N.F. Ramsey*, J.M. Jansma. *Functional Neuroimaging Section, Department of Psychiatry, University Medical Center of Utrecht, The Netherlands*

Various studies have associated the working memory deficits observed in schizophrenic patients with hypofunction of prefrontal brainstructures. It is however not clear whether reduced frontal activity is the cause of reduced processing capacity, or the consequence of disengagement from working memory tasks that are simply too difficult for schizophrenic patients. Several recent studies have shown that if the task is modified in such a way that patients can perform adequately, frontal activity is either normal, or enhanced. This suggests that working memory capacity may not be impaired, but that utilization of working memory resources may be inefficient, leading to excessive demands on those resources. To examine this hypothesis, we conducted a study to assess the dynamics of working memory, i.e. the change in demands on working memory when a task becomes familiar after practise. In healthy subjects, activity in the working memory system reduces with practise, which is associated with automatization of cognitive processes. The degree to which this activity reduces may reflect the capacity to free processing resources that can subsequently be utilized for processing other information. In schizophrenic patients, automatization of stimulus processing during a working memory task was normal in behavioural terms (responses became more accurate and faster), but brain activity did not decrease in several frontal and parietal regions of the working memory system. These results are taken to reflect inadequate neurophysiological adjustment of working memory to automatization. We hypothesize that the working memory deficits in schizophrenia may be a consequence of a reduced neurophysiological benefit from automatization of cognitive processes, leading to excessive demands on working memory resources.

S14.2

Sensory information processing in schizophrenia: effect of atypical medications as monitored by fMRI

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Using a simple sensory paradigm which involves a visual input, an alternating checkerboard, and an acoustic input, drum beats, we are able to demonstrate disturbed thalamic and prefrontal function as well as changes in the dorsal visual processing stream and right acoustic cortex of never medicated first episode paranoid schizophrenic patients.

These studies demonstrate that early in the disease, without any medication exposure, sensory processing is defective. This involves a task with no performance component and one that is minimally sensitive to attention, the patients must simply look and listen, which in the circumstances they cannot avoid. This suggests that there are defects in the connections which mediate the processing of sensory information independent of medication. A group of these patients have been treated with atypical antipsychotic medications and followed for periods of up to 18 months. The atypical medications show a tendency to reverse the prefrontal deficits after just 6

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months. Data on several atypical medications including clozapine, olanzapine and amisulpride will be reviewed.

S14.3

Executive functions in schizophrenia

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Studies of patients with schizophrenia have repeatedly shown a wide range of neurocognitive disturbances, including deficits in executive functions, memory and attention. Executive impairments are among the earliest described and clinically most prominent cognitive deficits that are present in schizophrenia and appear to be related to long term outcomes, disability and quality of life. Many domains of executive functions are impaired in patients with schizophrenia including forward planning, concept formation, set shifting, initiation, self-monitoring, ABSTRACT ion and the ability to direct attention and memory. A variety of neuropsychological tasks have been used in examining these functions, such as the Wisconsin Card Sorting Test, the Stroop Test, object-sorting tests, proverb tests and mazes. Specific executive deficits appear to be related to specific symptom clusters in schizophrenia and are linked to structural and functional brain abnormalities.

Anatomic and functional neuroimaging studies have begun to identify specific cortical deficits. Although no single brain region has been found to identify schizophrenic pathology, specific hypotheses about fronto-temporo-limbic system dysfunctions have been consistently implicated in the pathogenesis of schizophrenia.

S14.4

FMRI and cognitive dysfunctions in schizophrenia

R. Schlösser*, H. Sauer. *Department of Psychiatry, University of Jena, Germany*

Cognitive dysfunctions in the domains of attention, working memory, and executive functions are a core feature of schizophrenia and a major challenge for treatment interventions. We directed our research efforts to the question, whether schizophrenic patients demonstrate changes in fMRI-activation patterns in the entire cortical-subcortical information processing network while performing different cognitive tasks.

In a series of studies, the Wisconsin Card Sorting Test (WCST) has been employed to challenge executive functions. Blunted prefrontal activation could be detected even after patients where matched for task performance. Another paradigm adapted, the Continuous Performance Test (CPT) is the classical procedure to detect attention deficits in schizophrenic patients compared to normal controls. Since this task consists of different subcomponents such as feature detection, selective attention and working memory, tests for each of these subcomponents have been constructed. Already in the feature detection task exploring basal visual analysing performance, schizophrenic patients exhibited activation deficits particularly in temporal lobe areas belonging to the ventral visual stream. These findings suggest a disturbed early visual processing pathways in schizophrenic patients. The "2-back" working memory task was implemented, since it is particularly related to working memory and executive functions. Effective connectivity analysis using structural equation modeling revealed that atypical antipsychotic drugs as compared to the conventional neuroleptic haloperidol enhanced prefrontal-thalamic and prefrontal-cingulate connectivity during task performance. This finding may be interpreted as restored integrity of fronto-striato-thalamo-cortical circuitry.

Taken together, the findings are consistent with the notion of an imbalance of different processing components in terms of a "cognitive dysmetria". The results provide evidence that both early and later steps of sensory and cognitive information processing might be affected in schizophrenic patients. And finally, the findings suggest that a disruption of widespread neural networks in schizophrenia can be favorably influenced by atypical antipsychotic treatment – an observation which could at least partially be attributed to the atypical receptor binding profiles of atypical antipsychotic drugs.

S14.5

The influence of antipsychotic treatment on cortical activations in patients with schizophrenia using functional magnetic resonance imaging

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Cognitive dysfunction is an enduring deficit in schizophrenia. It may underpin some of the psychopathology of schizophrenia as well as contribute to the patient's impaired social and vocational functioning. Treatment with atypical antipsycotics have shown that there is a significantly greater improvement in several domains of cognitive function, especially attention and verbal fluency, compared to classical antipsychotics, a result which may be due to the effects of 5HT and other neurotransmitter systems and normalisation of dopamine function by these compounds. Social cognition perhaps the domains most likely to have relevance to functional outcome. It is thus possible to map the functional anatomy of neurocognitive improvement with atypical antipsychotics in schizophrenia using functional magnetic resonance imaging and investigate the effects of atypical antipsychotics on social cognition.

Our group has previously shown the effects of atypical antipsychotics on brain activation in schizophrenia using a working memory task (Honey et al, 1999). In that study there was a possible ceiling effect in patients with schizophrenia and normal controls thus preventing any conclusions about the neural correlates of cognitive improvement with atypical antipsychotic medication. We have now completed a study of a new cohort of patients where we have parametrically increased cognitive load to examine cortical activation in patients switched to newer atypical antipsychotics. This presentation will outline new methods of brain imaging and how these methods may allow us to understand the effects of antipsychotic drugs in schizophrenia. The new data set will be presented and discussed.

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