

as in the normal elderly population. Antipsychotics and most antidepressant medications impair sexual function even further, leading to non-compliance and relapse. The prevalence of sexual dysfunction in schizophrenics treated with typical and atypical antipsychotics is 30–60%. Attempts to treat sexual dysfunction using dopaminergic drugs such as L-dopa, apomorphine, amantadine and L-deprenyl were disappointing. Sildenafil citrate (Viagra) seems to be an effective treatment in less deteriorated male patients who are capable of maintaining a reasonable relationship with their partners. A variety of strategies have been used in the management of SSRI-induced sexual dysfunction: waiting for spontaneous resolution, dosage reduction, drug holidays, adjunctive pharmacotherapy or switching antidepressants. Adjunctive agents are SHT<sub>2</sub> antagonists (cyproheptadine, mianserin, mirtazapine), dopamine receptor agonists (psychostimulants, bupropion) and Viagra. Substitute antidepressants are bupropion, nefazodone, mirtazapine and reboxetine. In an open-label study with 10 male SSRI-treated PTSD patients who complained of sexual dysfunction, the use of sildenafil (50 mg) significantly improved their erectile function and intercourse satisfaction. Sildenafil (25–50 mg) was efficacious also for antidepressant-induced erectile dysfunction in elderly male depressed patients (n=11, age 70–81, mean age 73 yrs). In 8 out of 11 patients, erectile function returned to a normal level. Side effects were noted in two patients (headache). It appears that sildenafil co-administration is efficacious, safe, and well-tolerated in special populations.

## S09. Is schizophrenia really just a neurodevelopmental disorder?

*Chairs:* E. Johnstone (GB), S.M. Lawrie (GB)

### S09.1

Recent evidence on the neurodevelopmental model of schizophrenia

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No abstract was available at the time of printing.

### S09.2

Clinical and cognitive markers of the development of schizophrenia

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Neuropsychological impairments have been reported in patients with schizophrenia, in the adult relatives of such patients, and in children at high genetic risk for the disorder. In the Edinburgh High Risk for Schizophrenia Study we examined the relationship between neuro-psychological impairments and risk for schizophrenia, and the development of psychotic symptoms in subjects at enhanced genetic risk for schizophrenia. The results from a battery of neuro-psychological assessments were compared among 157 high-risk subjects, and 34 normal controls. Findings were related

to a quantitative measure of genetic risk, calculated for the high-risk group according to the number of ill and well relatives in the family and their relationship to the subject, and to development of psychotic symptoms. Neuropsychological differences were identified in many areas of function and were not accounted for by the presence of psychotic symptoms in some subjects. The quantitative measure of genetic liability was not associated with either neuropsychological function or with the development of psychotic symptoms. These results suggest that what is inherited is not the disorder itself, but a state of vulnerability manifested by neuropsychological impairment occurring in many more individuals than are predicted to develop the disorder.

### S09.3

Structural and functional MRI in the Edinburgh High Risk Study

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MRI studies of the brain in schizophrenia have demonstrated structural abnormalities, particularly of the temporal lobes, and disruptions of fronto-temporal functional connectivity. We conducted sMRI scans in 150 high risk subjects aged 16–25 at baseline and 66 of them after approximately 2 years, and have now conducted sMRI and fMRI scans in almost 100 after a further 2–3 years. Healthy age-matched controls have also been scanned.

We have found associations between pre-frontal and basal ganglia volumes with genetic liability, and reductions in medial temporal lobe and thalamus volumes in the high risk group compared to controls, at baseline. Those with psychotic symptoms had relatively large brains at baseline as well as reductions in temporal lobe volumes over two years. More detailed analyses of temporal lobe abnormalities and fronto-temporal dysconnectivity are in progress.

Overall, the results suggest that some abnormalities of the brain in high risk subjects are genetically mediated and developmental, that others may only become apparent in late adolescence for unclear reasons, and that psychotic symptoms are associated with further structural changes.

### S09.4

An MRI study of subjects in the prodromal phase of psychosis

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**Introduction:** Recent prospective neuroimaging studies have suggested that there are progressive volumetric changes in grey matter over the course of psychotic disorders. We sought to investigate this issue using magnetic resonance imaging (MRI) to examine brain structure in subjects before and after the first episode of psychosis.

**Methods:** a) *Cross-sectional comparison:* Subjects identified as being at ultra high-risk (UHR) of developing psychosis were scanned using MRI; at 12 month follow-up 31% had developed a psychosis and 69% had not. The MRI data from these 2 subgroups at baseline were compared by ANCOVA, controlling for age. b) *Longitudinal comparison:* Subjects were scanned at baseline and again, either after the onset of psychosis, or at least 12 months

later for patients who had not developed a psychosis. The MRI data from the 2 time points were compared within each group.

**Results:** (a) *Cross-sectional comparison:* relative to the group who did not become psychotic, those going on to develop psychosis had smaller grey matter volumes in right temporal temporal and inferior frontal cortex, and in the cingulate cortex bilaterally. (b) *Longitudinal comparison:* in the group who became psychotic there were reductions in grey matter volume in the medial temporal and anterior cingulate cortex bilaterally, the left fusiform and inferior frontal cortex and in the cerebellar cortex. There were no changes in the group who remained non-psychotic.

**Discussion:** There were marked differences in regional grey matter volume between high-risk subjects who later developed psychosis and those who did not, despite the absence of clinical differences at the time of scanning. The group who went on to develop psychosis showed longitudinal reductions in regional grey matter volume in association with the expression of frank psychotic symptoms. These data suggest that in psychotic disorders some abnormalities of grey matter volume predate the onset of frank symptoms while others appear in association with the first episode of psychosis.

### S09.5

Disordered brain development and abnormal connectivity

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There is some evidence both for schizophrenia as a disorder of brain development and for schizophrenia as a disconnection syndrome. Imaging evidence for dysconnectivity in adult schizophrenia is reviewed and possible mechanisms by which abnormal early development might lead to adult dysconnectivity are rehearsed. One experimental approach to securing a more robust link in general between mechanisms of abnormal neurodevelopment and patterns of abnormal adult brain structure is to study rare neurogenetic syndromes where a specific genetic lesion is associated with well-characterised developmental abnormalities in animal models. An example of this approach is provided by a structural and functional MRI study of a human family with heterozygous mutation in PAX6, a highly-conserved neuro-developmental control gene which is important for inter-regional boundary demarcation and guided axonal growth in mice. The adult human phenotype is characterised by deficits in major white matter tracts and distributed functional deficits in fronto-striatal circuits. The implications for schizophrenia as a syndrome of abnormal development of neurocognitive networks are discussed.

## S10. Eating disorders

*Chairs:* H. Wijbrand Hoek (NL), J. Treasure (GB)

### S10.1

Evidence based treatments for anorexia nervosa

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Evidence based medicine (EBM) is the *integration* of best research evidence, together with clinical expertise and patient values (Sackett et al., 2000). All too often when the evidence based medicine approach has been considered there is a tendency to focus on the quality of the evidence for treatment. The second part of Sackett's definition, which discusses clinical expertise and patient's values,

tends to be overlooked. There is very little in the way of Level I and II evidence about the efficacy treatment in anorexia nervosa. However the fact that there is no evidence from RCT's should not be interpreted as if these treatments are of no value. It is not appropriate to dismiss treatment of the starvation state because of paucity of specific evidence in anorexia nervosa, as the natural history of starvation is known and effective treatment of starvation is also known. Thus there is an argument for not requiring evidence from RCTs to resuscitate and embark on treatment. There is a detailed, coherent body of research, which documents prognostic features and the factors that have to be considered in terms of the acute medical risk. Medical risk is critically important to guide the acute management of anorexia nervosa. The acute risk management involves a combination of the medical risk and psychological capacity set against the possible resources of motivation and psychosocial support.

Once we are out of these "fire fighting" stages there is evidence that specific psychotherapies are more effective than supportive counselling and dietary advice. It is useful to involve families in management but how and by how much is less certain. The early phase of research into pharmacotherapy produced little benefit, but new drugs and new paradigms such as using drugs to prevent relapse rather than to treat starvation are of interest.

### S10.2

Evidence based treatment for bulimia nervosa

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Eating disorders are mental disorders occurring mainly among young females. The prevalence of bulimia nervosa according to DSM-IV criteria among young females is 1%. Bulimia nervosa leads to serious physical, psychological and social consequences. Women suffering from bulimia nervosa are so ashamed of their disturbed eating behaviour that they hardly look for professional help. Only 6% of all women with bulimia nervosa in the population do come into mental health care.

Systematic reviews of large randomized controlled trials found that cognitive behavioural therapy compared with remaining on a waiting list reduced the symptoms of bulimia nervosa and improved non-specific symptoms such as depression. The NNT (Number Needed to Treat) of CBT is 3. The absolute remission rate of bulimia nervosa for CBT is around 40%. One 5-year follow-up study showed that the effect of CBT remained. Selfhelp based on CBT seems also to be effective.

Systematic reviews of RCT's with antidepressants compared to placebo have found a significant short-term reduction of bulimic symptoms.

### S10.3

Osteopenia and bone mass increase in adolescent anorexia nervosa

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The percentage of patients with osteopenia, the variables related and the bone mass increase after recovery were studied. Bone mass was measured by dual-energy-x-ray absorptiometry in 180 female and 20 male adolescents with anorexia nervosa. The results were compared with normative values for bone mass in Spanish adolescents. In 108 females and 15 males a second examination was carried out after a follow-up of six to thirty four months. At lumbar spine 44.1% of girls and 35% of boys had osteopenia. The variables related to osteopenia were duration of illness and