specific QoL-based interventions. The research literature reflects this growth in interest, from the earliest paper in 1931 to the present. Medline entries now stand at 34,624, and for all the major data bases, at 82,849 (including overlap). By comparison, routine QoL measurement is a recent and much less researched phenomenon. The issues in the routine measurement of QoL are not dissimilar to those for any assessment tool, such as reliability, validity, ease of use etc, but there are specific issues such as the nature of the concept being used, the capacity to demonstrate change over time, and responseshoft, that also need to be addressed before routine measurement can be implemented. Data will be presented that relate to these specific issues. Consideration will also be given to the UK government's current attempts to introduce a standard set of outcome indicators, including QoL, for routine use in the National Mental Health Service.

S03.4
Impact of regular outcome assessment on treatment – the MECCA Study

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There are wide spread calls for implementing regular outcome assessment in routine care. Clinicians and patients are more likely to comply with the requirements of regular outcome assessment, if there is a direct positive impact on individual treatment which needs to be demonstrated in research. The MECCA-Study is a randomised, controlled trial conducted in community mental health care services in six European countries. The Study investigates how the regular assessment and feedback of outcome indicators impact on treatment process and treatment outcome in community care of patients with psychotic disorders. Regularly assessed outcome criteria are simple indicators of subjective quality of life, treatment satisfaction and patients' wishes for different and/or additional interventions. We expect a more favourable outcome after one year in the experimental group as compared to standard care and hypothesize that the difference will be mediated through more accurate treatment decisions or a more positive therapeutic relationship or both. The focus on subjective outcome criteria is supposed to shift the communication between key worker and patient towards patients' views and to strengthen a partnership model of care. Concept, methods and organisational approach of the MECCA Study will be presented. This includes how the feedback process is implemented and practiced using simple technology and a special software programme.

S03.5
Estimating treatment effects from trials and observational studies

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The theme is the estimation of the causal effects of treatment. It is based on Rubin's counterfactual model of causality. Basically, in estimating a causal effect, we are trying to compare outcome of the treatment actually received with that which would have been observed if, contrary to fact, the patient had received either no treatmetn or, alternatively, another form of treatment. The arguments will be illustrated using data from a randomized clinical trial in which there are no protocol violations (everyone provides outcome data and fully complies with the allocated treatment). Next, we look at the impact of non-compliance and dropouts in a randomized clinical trial. Finally, we look at the problemsof inferring causality from unstructured, routinely collected, outcome data. One possibility is to use so-called propensity models.

S04. In vivo imaging of neurotransmitter mechanisms. Methods and clinical application

Chairs: A.-L. Nordström (S), P. Grasby (GB)

S04.1
PET and SPECT in psychiatry

A. Catafau. *Spain*

No abstract was available at the time of printing.

S04.2
PET studies of depression

P. Grasby. *UK*

No abstract was available at the time of printing.

S04.3
Dopamine synthesis rate in prefrontal cortex in schizophrenia by use of PET

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Objectives: To investigate the dopamine-synthesis in the brain of drug-free schizophrenic patients in the prefrontal cortex by use of ^{11}C-I-DOPA as the tracer and PET.

Methods: PET was performed in 12 drug-free (10 drug-naive) schizophrenic patients and in 10 healthy volunteers matched for age and gender. The time-radioactive curve from occipital cortex was used as reference area and K_i images in different brain areas were addapted to a brain atlas.A significant overall increase of the K_i value was found in the schizophrenic group.

Results: Significantly higher K_i values were found in the schizophrenic patients compared to the controls in the caudate nucleus, putamen and medial prefrontal cortex (Brod. 24), with the greatest difference in the prefrontal cortex. The K_i values reflect and increased utilization of l-DOPA, presumably due to increased activity of the amino acid decarboxylate enzyme.

Conclusions: Our results give support for an abnormal dopamine synthesis/activity in the prefrontal cortex in patients with schizophrenia.

S04.4
PET and antipsychotic drugs – background

A.-L. Nordström*, M. Talvik, C. Halldin, L. Farde. *Department of Clinical Neuroscience, Psychiatry Section, Karolinska Institutet, Stockholm, Sweden*

Important clinical applications of positron emission tomography (PET) include studies of mechanisms underlying clinical drugs

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effects, treatment optimization and development of new drugs. Several studies have demonstrated that clinical treatment with classical antipsychotics induces a high degree of D2dopamine receptor occupancy. For classical antipsychotics, distinct thresholds in D2occupancy have been shown for antipsychotic effect, prolactin increase and extrapyramidal side effects (EPS) respectively. The atypical antipsychotic clozapine induces a significantly lower striatal D2occcupancy as compared to classical antipsychotics. The hypothesis of a 'limbic selectivity' for clozapine was recently tested with high resolution PET and the high affinity radioligand [11C]FLB457. The finding of a low D2occupancy that was maintained also in extrastriatal regions did not support the hypothesis of a preferential limbic D2occupancy. PET studies of the novel antipychotics risperidone and olanzapine have shown D2occupancy levels similar to those induced by classical antipsychotics. Further studies are needed to test whether D2occupancy thresholds for clinical effects differ between classical and novel antipsychotics.

S04.5

PET and antipsychotic drugs – future

J. Tedroff*. *A Carlsson Research AB, Department of Medicine, Göteborg, Sweden*

For many years PET using displacement studies of PET ligands bound to neuroreceptors has studied the pharmacological action of antipsychotic drugs. Using this approach it has been demonstrated that antipsychotic effects can be achieved by a number of neuroreceptor blocking properties.

During recent years, studies using electrical deep brain stimulation in neurological conditions, have demonstrated that electrical inhibition of very small localized intracerebral targets indeed can affect the function of vast areas of the brain. In a similar manner antipsychotic drugs may, despite different or selective receptor binding properties, affect certain functional domains of the brain, which are common for antipsychotic effects. To visualize such effects PET data have to be analysed differently, employing analysis of connectivity across brain networks such as the corticostriatal pathways. Using this approach it can be demonstrated marked differences between the healthy and schizophrenic states of brain connectivity. Typical and atypical antipsychotic drugs affect these deviations towards a more normalised state, albeit with some differences. Analysis of brain network connectivity in disease and of drugs are likely to expand understanding of the functional effects underlying the antipsychotic properties of various drugs.

S05. Personality disorders – an update

Chairs: L. Ekselius (S), J. Livesley (CDN)

S05.1

Developmental pathogenesis of personality disorder

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Multiple biological and psychosocial variables are associated with the development of personality disorder. Each variable appears to have a small effect and none appear to be either necessary or sufficient to cause personality disorder. Under these circumstances it seems more appropriate to refer to the factors that predispose to the development of personality disorder than to refer to causes.

Behaviour genetic studies indicate that genes and environment contribute to the aetiology of personality disorder and that all personality traits are heritable. It is not possible to distinguish between traits that are largely influenced by genetic factors and traits that are largely environmental in origin. Multiple genetic factors appear to be involved that differ in effect. Some influence the development of specific traits whereas others have wider effects influencing the development of clusters of traits. The broader genetic dimensions appear to be responsible for the clusters of traits that define the different patterns of personality disorder. Each genetic factor appears to involve multiple genes each contributing a small amount of phenotypic variance.

A similar picture emerges from studies of the psychosocial origins of personality disorder. Multiple factors are related to personality disorder including family dysfunction, deprivation, and trauma but none are invariably associated with personality disorder and specific links between different kinds of adversity and specific forms of disorder have not been identified.

These results reveal a complex picture of the aetiological of personality disorder. They suggest that studies of single variables or groups of related variables are unlikely to contribute to understanding pathogenesis. They also suggest the need to re-think our concept of the environment. The environment is not something independent of the individual. Instead individuals shape the environment to which they respond. A theory of the pathogenesis of personality disorder needs to explain the interaction between genetic predisposition and environmental adversity. In particular, it needs to explain the way genetic predisposition and the emerging personality shape the environment to which the individual responds and how this environment in turn influences gene expression and the emerging personality.

S05.2

Personality – different genes or differences in gene activation?

J. Hallman*, H. Garpenstrand, M. Damberg, L. Oreland. *Uppsala University, Uppsala, Sweden*

Monoamine oxidase (MAO) activity in platelets correlates with personality (e.g. sensation seeking, impulsiveness). Low platelet MAO, as well as the personality traits associated with these, have been associated with e.g. type 2 alcoholism, criminality and violent behaviour. The transcription factor family AP-2 is a regulatory factor for prenatal development of monoaminergic nuclei as well as of monoamine turnover in the adult rat forebrain. The gene encoding AP-2b includes a polymorphic region, which is associated with e.g. personality as well as with impulsive binge-eating disorder. In both male and female AP-2β genotypes homozygous with regard to a [CAAA]5 repeat display significantly lower platelet MAO activity than the other genotypes. Thus, it seems likely that the personality disturbances, linked to low platelet MAO, should be associated with the presence of this AP-2β gene allele. In this way, common transcriptions factors regulate the expression of midbrain monoamine structures as well as that of platelet MAO, thereby explaining the association between platelet MAO and personality (see Damberg et al., Mol. Psych.. 6, 503, 2001).

S05.3

Genetics and suicidal behaviour

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Although a familial aggregation of suicide has been observed by many psychiatrists, the reason for this has until recently been

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