There exists indirect methods of training. One example is the social skills training methods developed by Robert Liberman.

A different trend is the essays to train cognitive functions by more direct methods. This includes the training of central coherence and social recognition as in the "Integrated Psychological Therapy" and training executive functions in "Cognitive Remidiation". The international research is rewieved and recent Swedish experiences are presented.

S42.3
Work rehabilitation

K.T. Mueser. *USA*

No abstract was available at the time of printing.

S42.4
Interventions for tomorrow

I.-M. Wieselgren. *Uppsala University Hospital, Sweden*

The most important question is the patient's ability to function in the real world. The overall goal is o be able to participate independently in the community. Even at first admission in early schizophrenia, an important part of the patients have an impaired function. It means that interventions had to start at once and run parallel to treatment.

Rehabilitation includes interventions to help a person reduce the functional impairment and adjustment of the environmental together with support. Supported Employment is effective in helping severely mentally ill people to obtain competitive employment.

Social stigma has a significant impact on the quality of life of persons with schizophrenia. Direct interaction with persons who have severe mental illness is the best strategy for changing stigmatizing attitudes. Successful integration in the community is important for many reasons.

Coping strategies to manage their illness and disabilities, social skills training are other possibilities.

Aids for people with psychiatric disabilities for example cognitive impairment, adjustment of place of work, computer/electronic support and other assistive technology are new areas in psychiatric rehabilitation.

PL02. Plenary Nobel Laureate Lecture: The neurobiology of dopamine signaling

PL02
The neurobiology of dopamine signaling

P. Greengard*. *Rockefeller University, Laboratory of Molecular and Cellular Science, New York, USA*

Nerve cells communicate with each other through two mechanisms, referred to as fast and slow synaptic transmission. Fast-acting neurotransmitters, e.g., glutamate (excitatory) and GABA (inhibitory), achieve effects on their target cells within one millisecond, by virtue of opening ligand-operated ion channels. In contrast, all of the effects of the biogenic amine and peptide neurotransmitters, as well as many of the effects of glutamate and GABA, are achieved over hundreds of milliseconds to minutes, by slow synaptic transmission. This latter process is mediated through an enormously more complicated sequence of biochemical steps, involving second messengers, protein kinases, and protein phosphatases. Slow-acting neurotransmitters control the efficacy of fast synaptic transmission, both by regulating the efficiency of neurotransmitter release from presynaptic terminals and by regulating the efficiency with which fast-acting neurotransmitters produce their effects on postsynaptic receptors.

LS03. Schizophrenia: a journey from first episode to long-term stability (Sponsored by Janssen Cilag)

Chair: A. David (GB)

LS03.1
First episode schizophrenia: a targeted treatment approach

L. Kopala*. *University in Halifax, Nova Scotia, Canada*

Optimising treatment of a first episode of psychosis sets the stage to influence long-term management of illness. The primary aim of treatment is to achieve rapid remission of the acute psychotic episode using the most effective and best-tolerated treatment. The morbidity and mortality of schizophrenia can be diminished for patients treated early and consistently with second generation antipsychotics such as risperidone. It is widely recognised that recovery is related to the number and severity of relapses and thus success in the initial treatment phase influences the long-term course. Risperidone is a rapid, effective and well-tolerated medication, which can be safely used in the treatment of a first episode of psychosis. Current data indicate that one-year of consistent treatment with oral risperidone or one of the other newer atypicals results in a reduction in rehospitalisations as low as 8% compared with previously reported annual rates of 50%. There was a reduced suicide rate for the population studied. In addition to this, negligible levels of neurotoxicity, in the form of EPS, were observed along with a reduction in pre-existing baseline motor abnormalities.

In summary, early intervention in an acute or chronic first episode of psychosis with a second generation antipsychotic such as risperidone, can provide effective control of symptoms, limit neurotoxicity and reduce the incidence of non-adherence. Importantly, mortality and morbidity can be diminished.

LS03.2
Chronic symptoms of schizophrenia: improving the outlook

J. van Os. *University of Maastricht, The Netherlands*

In a substantial proportion of individuals with psychotic illness, a cascade of events starting with non-clinical psychotic experiences may develop into chronic psychosis over many years. The majority of individuals with non-clinical psychotic experiences in the general population will not develop a psychotic disorder. However, a smaller but increasing number of individuals will experience progressively more severe psychotic states, culminating in the first psychotic episode. This is known as the *psychosis toxicity hypothesis*. A large longitudinal survey has demonstrated that non-clinical psychotic experiences in the general population have the potential to become more 'toxic' with increasing length of exposure and do have a negative impact on clinical outcome. The possibility that psychotic experience itself has adverse prognostic

https://doi.org/10.1016/S0924-9338(02)80173-0 Published online by Cambridge University Press

consequences provides a powerful rationale for continued treatment with antipsychotics. In the first five years of illness, patients who discontinue their antipsychotic medication have a five times higher risk of relapse than those who do not, and may have a poorer outcome in the long term. However, clinicians and chronic patients often develop treatment discordance, i.e. disagreement on the need for continued antipsychotic medication, or patients may develop disabling side effects. Predictors of decreased use of antipsychotics were tardive dyskinesia and severe illness. In the same study, reduction in time exposed to antipsychotic medication was associated with *more* clinical needs, *more* hospital admissions and *more* suicidal thoughts. This again suggests that patients who reduce their medication intake have a poorer clinical outcome than those who do not. The new generation of antipsychotics may have advantages over the older medications in terms of reduced risk of side-effected related medication discontinuation and subsequent relapse.

Dr van Os will discuss the psychosis toxicity hypothesis, a cascade of events starting with non-clinical psychotic experiences leading to chronic psychosis in a small but increasing number of people. These individuals experience progressively more severe psychotic states, culminating in the first psychotic episode. A longer duration of untreated psychosis (DUP), poor premorbid functioning and number of acute relapses are associated with poorer outcome. Evidence is emerging that the experience of psychosis itself may be toxic, the risk of relapse increases with each successive episode, providing a powerful rationale for continuous use of antipsychotic medication. The new generation of antipsychotics may have advantages over the older medications in terms of lower risk of side-effects, which will reduce discontinuation rates and subsequent relapse.

LS03.3

Long-term treatment benefits: a lesson from the past

A. David*. *University of Glasgow, Department of Psychiatry, UK*

Schizophrenia is a relapsing and remitting condition. Despite the large number of effective treatment options for patients – both pharmacological and psychosocial – many have a poor outcome. One reason is that treatment is frequently interrupted. This may be a reflection of how patients perceive their illness as well as their experience of treatment and the alliance they have with their physician. One means of reducing the risks associated with interrupted treatment is mode of delivery. Long-acting intramuscular forms of antipsychotic drugs guarantee the delivery of a measured quantity of drug. However, the use of traditional depot formulations of conventional antipsychotic drugs is often limited by concerns about side effects, and misgivings about the mode of administration. Patient and clinician acceptance can therefore be variable. Nevertheless, attitudes of patients who actually receive depots, indicate preference over oral medication. In efficacy terms, long-acting injectable medication may also confer benefits in terms of global outcome, with no proven adverse effects. A recent postal survey of practising UK psychiatrists was done to establish current attitudes to depot medication. Most agreed that they facilitated better monitoring of adherence for a range of patents. Further, over 90% of the survey respondents agreed that they would prescribe a long-acting intramuscular atypical antipsychotic if one were available. Other recent surveys of clinicians in Europe have revealed similar attitudes. Hence, long acting atypical antipsychotic drugs are set to become an important addition to the clinician's armamentarium in the treatment of patients with schizophrenia who can benefit from continuous therapy.

LS03.4

Treatment delivery: a hope for the future

M. Eerdekens*. *Janssen Research Foundation, Beerse, Belgium*

Risperidone long acting injection is the first atypical antipsychotic drug formulated for controlled release that combines the advantages of both atypical antipsychotics and long-acting formulations for enhanced clinical outcome and improved long-term stability. The new formulation encapsulates risperidone in 'microspheres' made of a medically accepted biodegradable polymer which is injected into the muscle. Single-dose pharmacokinetic characteristics of risperidone long acting injection show a post-injection latent period of three weeks, followed by a rapid rise in plasma levels, maintenance at therapeutic levels from weeks 4–6, followed by a rapid decline of plasma levels by week seven post injection. Thus pharmacokinetic profile explains why additional antipsychotic treatment is needed during the initial latent period. Multiple-dose pharmacokinetic data indicate that undue accumulation does not occur with long-term use. Risperidone long acting injection 25mg and 50mg showed superior efficacy over placebo based on PANSS total score, PANSS positive subscale, PANSS negative subscale and CGI score (RIS-USA-121). A 37.5mg dose will also be made available for enhanced dosing flexibility. Risperidone long acting injection was well tolerated with no unexpected systemic adverse events and very good local tolerability. The discontinuation rate in the active treatment group was found to be significantly lower than in the placebo group. Long-term trials have shown this favourable tolerability profile to be maintained for at least 50 weeks. Risperidone long acting injection delivers effective and well-tolerated control of symptoms and can be recommended for patients with psychotic illness for whom treatment and continuous drug delivery is required.

LS04. Escitalopram – redefining SSRI therapy (Sponsored by H. Lundbeck AB)

LS04.1

Exploring the pharmacology of enantiomeric drugs

J. Arnt. *Denmark*

No abstract was available at the time of printing.

LS04.2

Escitalopram – progression in antidepressant therapy

S. Montgomery. *UK*

No abstract was available at the time of printing.

LS04.3

Increasing the efficacy of antidepressant therapy without compromising the tolerability

A. Wade. *UK*

No abstract was available at the time of printing.

https://doi.org/10.1016/S0924-9338(02)80173-0 Published online by Cambridge University Press