

Plenary Lectures

PL2. Plenary Lecture — The Lilly Dista Psychiatry Lecture

HUMAN BRAIN IMAGING — A FORCE FOR PSYCHIATRY AND PSYCHOPHARMACOLOGY

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Developments in molecular biology and genetics have disclosed an enormous molecular complexity of signalling mechanisms within the human brain. Hypotheses on pathophysiological mechanisms in neuropsychiatric disorders imply perturbations in the expression or function of such molecular components. Most, if not all currently used psychopharmacological agents mediate their actions by binding to molecular components as neuroreceptors and amine transporters. Among the brain imaging modalities only positron emission tomography (PET) and single photon emission tomography (SPECT) have the sensitivity required to image molecular components of the human brain. The development of selective radioligands binding with high affinity to neuroreceptors and transporters gives the possibility to image the distribution and quantities of these molecules and also the possibility to examine how clinical treatment with pharmacological agents affect the molecular targets in the brain. Using suitable radioligands for monoamine receptors belonging to the D1, D2 and 5HT2 receptor families it has been possible to compare the characteristics of these receptors in some brain regions in patients and healthy control subjects. Such PET studies have disclosed molecular alterations of both pre- and post-synaptic type in patients with Huntington's chorea and schizophrenia. In schizophrenic patients treated with antipsychotic drugs this PET methodology has also allowed the analysis of relationships between the degree of drug effects on receptors directly in the living brain and the clinical manifestations of the treatment. Such studies have consistently demonstrated that antipsychotic action can appear at occupancy levels of D2 dopamine receptors in the brain which are lower than those required to produce extrapyramidal manifestations. These brain imaging studies point to the possibility to use lower clinical doses of antipsychotic drugs than previously used routinely. The results also point to the possibility to further refine the analysis of relationships between the degree of occupancy of central monoamine receptors in drug-treated patients and the various action components of antipsychotic drugs such as the differentiation of positive and negative symptoms and side-effects as sedation and motor disturbances. It can be expected that as more selective radioligands become available for molecular components not accessible so far, the relevance of brain imaging for diagnostic purposes and to further refine drug treatment for the individual patient will be increasingly appreciated.

- [1] Sedvall G and Farde L: Chemical brain anatomy in schizophrenia. *Lancet* 346: 743–749, 1995.
- [2] Sedvall G et al: Utilization of radioligands in schizophrenia research. *J Clinical Neuroscience* 3: 112–121, 1995.

PL3. Plenary Lecture

INTEGRATING EASTERN EUROPE

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Countries in the Eastern and Central parts of Europe are many and they have little in common. They use a multitude of languages — ten or so of them Slovak, the remainder languages belonging to other groups (e.g., Romanic, Germanic, Albanian, Altaic, Caucasian); they have a different history and different religious traditions; different cultures; and different geophysical and social environments. What makes them similar above all is more than a thousand years of separation from the countries in the West of Europe. Although, on a number of occasions, ideas and people moved freely and in large numbers from East to West, there have been long periods during which contacts were sporadic and even seen as undesirable by the governments in power.

The consequences of the most recent period of intensive separation stretching over most of the second half of the twentieth century are numerous. Most of them are detrimental to the development of countries in Eastern and Western Europe. The political situation is now such that it is possible to create a bridge between the East and the West of Europe and to dream of benefits of a community of nations and countries containing more than 800 million people inhabiting the European territory.

Science and medicine stand to gain from intensive and extensive collaboration across Europe. Proposals about ways to establish productive links and work together are now before the scientific community. Possibilities for cooperation have been identified and opened: yet, few of the opportunities are taken up and the gap remains as wide — if not wider than before.

PL6. Plenary Lecture

LITHIUM PROPHYLAXIS OF BIPOLAR DISORDER: LONG-TERM OUTCOME IN ORDINARY CLINICAL CONDITIONS

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In recent years, there has been an increasing interest in the effectiveness (i.e., outcome in ordinary clinical conditions) as opposed to the efficacy (i.e., potential usefulness as emerging from double-blind randomized clinical trials) of lithium prophylaxis in bipolar patients.

However, currently available studies in this area are not numerous, and often suffer from multiple methodological flaws. Furthermore, it is seldom realized that the assessment of "response" to lithium prophylaxis is a very complex task, for several reasons, including the irregularity of the natural course of bipolar disorder, the multiplicity of the dimensions on which "response" has to be evaluated, and the frequent inadequacy of the exposure of bipolar patients to lithium.

The present lecture, based on the 20 years of experience of the Naples group, aims to answer the following questions: a) how many bipolar patients started on lithium prophylaxis are still on treatment after five years? b) what are the most frequent causes of interruption of prophylaxis before that term? c) what are the patterns of outcome of prophylaxis which can be identified after five years? d) what are the most significant clinical and demographic correlates of those patterns? e) what are the prevalence and predictors of "late non-response" to prophylaxis (i.e., reappearance of multiple affective episodes after five years or more of completely successful treatment)? f) what are the prevalence and predictors of "lithium-discontinuation-induced refractoriness" (i.e., refractoriness to reinstated lithium prophylaxis in bipolar patients who had relapsed after discontinuation of successful lithium treatment)?

PL8. Plenary Lecture — William Sargant lecture

DRUG TREATMENT FOR ANXIETY DISORDERS: A LEGACY OF WILLIAM SARGANT

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In 1962 Sargant and Dally published their seminal paper on "The treatment of anxiety states by antidepressant drugs". Since that time several kinds of progress have made on the basis of these original findings: (a) the classification of anxiety disorders has been extended and improved; (b) new antidepressant drugs have been introduced; (c) the original clinical observations have been followed by randomized controlled trials; and (d) new psychological treatments have been developed. These developments will be reviewed to determine the value of antidepressant treatment for the various anxiety disorders and how psychological and drug treatments can best be combined. The lecture will end with a reference to the implications of these findings about treatment for theories of the aetiology of anxiety disorders.

PL10. Plenary Lecture

NOSOLOGO-MANIA AND COMORBIDITY IN PSYCHIATRY

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The term "Nosologo-mania" [1] signifies the inflation of psychiatric diagnostic categories as illustrated by the development from DSM I to DSM IV. In addition the modern non-hierarchical approach makes for a multitude of cross-sectional and longitudinal psychiatric diagnoses, and so for further complexity. What is the future of this development?

Given the low validity of the majority of diagnostic sub-categories, the spectrum concept suggested early on by Kety et al. [2] for schizophrenia and by Klerman [3] for mania is to be recommended. This synthetic view, which assumes homogeneity, simplifies the diagnostic complexity, and advocates of other concepts have the burden of proving heterogeneity. Further spectra worth considering are anxiety states including panic and social phobia including avoidant personality disorder.

Comorbidity between psychiatric syndromes is a frequent phenomenon, which can be highly specific, for instance mania plus depression, or very unspecific, for instance the association of recurrent brief spells of anxiety with GAD, panic disorder or OCD.

Whether two or more psychiatric diagnoses occur simultaneously or sequentially is of practical relevance for treatment and prognosis. From a theoretical point of view a clinical association needs to be studied through epidemiological samples, including family data, and data on the temporal sequence of syndromes. Retrospective data based on patients' recall of onset raise problems of reliability, which not even prospective studies can solve completely. Controversies around primary and secondary syndromes, for instance agoraphobia related to panic disorder, belong to this context. Our epidemiological data show that the age of onset of psychiatric syndromes is usually identical, whether they occur as pure or comorbid conditions, which questions the principle of the distinction between primary and secondary syndromes.

- [1] van Praag HM (1995) Concerns about depression. *Eur Psychiatry* 10: 269–275.
- [2] Kety SS, Rosenthal D, Wender PH, Schulsinger F (1968) The types and prevalence of mental illness in the biological and adoptive families of adopted schizophrenics. In: Rosenthal D, Kety SS (eds) *The transmission of schizophrenia*. Pergamon, Oxford, 345–362.
- [3] Klerman GL (1981) The spectrum of mania. *Compr Psychiatry* 22: 11–20.