MENTAL SIDE EFFECTS AND ATTITUDES TOWARDS ANTI-PSYCHOTIC MEDICATION

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In spite of significantly beneficial effects of antipsychotics in positive and negative schizophrenic symptoms, in anxiety, in social functions, and in relapse prevention, it is evident that many patients experience antipsychotic drugs as unpleaseant, something they want to avoid. This attitude is not only due to lack of insight in the disease, to lack of a subjective recognition of the beneficial effects, and to side effects observed. The negative attitude is to a high degree due to mental side effects and a general sceptical opinion towards antipsychotic medication among relatives and in the society.

In a study in 53 chronic schizophrenic out-patients in maintenance depot neuroleptic treatment, we found that 60% were positive to the treatment, 32% ambivalent and 8% negative. Only 60% complained of side effects even though 94% scored as having them. Mental side effects were the most noticed by the patients, while hypokinesia and hyperkinesia were least noticed by the patients, but most by the physician. No correlation was found between patients' subjective assessment of their quality of life and the degree of psychosis and side effects. This raises important questions as to whether we assess the right parameters in clinical trials.

PATIENT REQUESTS AND ATTITUDE TOWARDS NEUROLEPTICS

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Little is known about care delivery systems, patients' requests and appreciation of care of patients attending an outpatient (depot) neuroleptic clinic. Although the concepts of expectancy and satisfaction remain methodologically debatable and are multi-dimensional concepts, they are important variables in the process of care and its ultimate outcome i.e. compliance. In this study, outpatients receiving oral or depot neuroleptics as maintenance therapy are compared using a Patient Request Scale and a Neuroleptic Evaluation and Attitude Scale. No differences were found between either group on sociodemographic and psychiatric history related variables. Both groups of patients have a comparable attitude toward their disease and medication use, as reflected in knowledge of the medication they use and the reasons why. The appreciation of care is comparable, but their treatment requests differ: the patients receiving oral medication are more comparable with the general population and could be described as more psychologically minded. Patient attitude, requests and appreciation of care are of relevance in the quality control systems that need to be developed in the maintenance therapy of psychotic patients.

RATING OF SUBJECTIVE EFFECTS OF ANTIPSYCHOTIC DRUGS. RELATIONSHIPS TO OBJECTIVE PSYCHOPATHOLOGY AND QUALITY OF LIFE

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The benefit of neuroleptic drugs in the treatment of schizophrenic patients is objectively beyond any doubt. However, most patients discontinue their neuroleptic drugs within some months. This low compliance might be caused by adverse effects, not restricted to motor symptoms, but also affecting cognition and emotion. They are often too subtle to be detected by objective examination, but reported by patients who complain of a reduced quality of life with restrictions of emotionality, straight thinking and spontaneity. This syndrome, similar to negative symptoms of schizophrenia, has been named "pharmacogenic depression", "akinetic depression" or "neuroleptic-induced deficit syndrome".

To investigate this issue of major clinical relevance, a self-rating scale was developed to measure subjective well-being under neuroleptic treatment (SWN). First analyses indicate good practicability, reliability, validity and sensitivity. Data obtained from 280 remitted schizophrenic patients showed that the SWN was significantly correlated to objective psychopathology (PANSS; $r = -0.35$), quality of life ($r = 0.60$) and other self-ratings of mood states (SDS, BFS; $r = 0.25$–0.75). The SWN in 40 patients treated with clozapine because of therapy resistance or major side effects was, despite negative selection, significantly better ($t = 1.79$, $p = 0.03$) than in 40 patients under classical neuroleptics. Moreover, even at dismissal, patients who were non-compliant 4–6 months later ($n = 14$), differed significantly ($t = 3.21$ $p = 0.02$) in SWN, but not in PANSS, from those who remained compliant ($n = 34$).

These data indicate that the SWN is a valuable tool for investigating hitherto neglected psychopathological dimension. The scale is used in ongoing trials of potential neuroleptic drugs. Subjective effects of neuroleptics are measurable, affect patients' quality of life and should be considered more thoroughly.

S11. Seasonal affective disorder

Chairmen: S Kasper, C Thompson

EPIDEMIOLOGY OF SAD AND ITS SUBSYNDROMAL FORM

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Depressions that recur on an annual basis in winter and summer have been described in several studies and termed *seasonal affective disorder* (SAD) of the winter and summer type. Clinical studies have documented the presence of the winter syndrome in North America, South America, Europe, Africa, and Australia. There are a few epidemiological studies carried out in the USA but also in Europe which indicate that a substantial part of the population notices seasonal changes of mood and behaviour to varying degrees. The prevalence of winter-SAD and its subsyndromal form (S-SAD) in the general population has been reported to depend on the latitude, with higher rates in more northern countries. Calculations of prevalence rates for SAD and its subsydromal form are therefore dependent on the location where the data are obtained and are for instance for Washington D.C. 4.3% and 13.5%, respectively. Based on data obtained in epidemiological studies and experience in SAD clinics it can be emphasized that patients with subsyndromal SAD are frequently observed in the general population and also in research settings. Since the behavioural and mood changes in subjects with S-SAD fall between those of healthy controls and patients with SAD it would be worthwhile to investigate whether their biological profile also occupies such an intermediate position, and whether they are genetically related to individuals with more severe affective symptoms. Furthermore, data of prospective studies are needed to elucidate the course of S-SAD individuals. These longitudinal studies could contribute to the assumption that seasonality can be viewed as a

dimension, if they document for instance, that vulnerable individuals might develop SAD-like symptoms when they are placed in a light deficient environment, regardless of the time of the year.

ACTIVITY MEASUREMENTS IN SAD

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Reduced psychomotor activity has been shown to be a symptom in SAD from which nearly all patients suffer. Activity measurement by means of wrist actometers provides an easy method to record physical activity objectively.

We recorded continously for at least seven days motor activity on the non-dominant wrist of SAD patients in their normal living conditions (Actometers by ZAK, Kirchdorf a. Inn).

Quantitative analysis of the recordings showed large interindividual differences in the total amount of activity, which can be attributed to primarily different individual motoric levels and different amounts of socially enforced activity in winter.

In addition activity measurement helped us to assess compliance in outdoor patients in therapy studies that include bright light treatment or the performance of physical exercise at fixed time, thus improving the reliability of results.

Giving the temporal structure of activity, actometry is on the other hand a valuable tool to study the chronobiological implications of SAD. As the temporal pattern of rest and activity periods in the actogram allows better estimation on sleep onset, sleep duration and awakening time, actometry gives a reliable measure of hypersomnia, another common symptom in SAD.

Combined with devices that record body temperature actometry provides data which give insight into the changes of the circadian system of SAD patients during depression and bright light therapy. Our data on SAD patients show phase delay as well as phase advance relationships during depression which are normalized after bright light therapy.

INVOLVEMENT OF THE SEROTONERGIC SYSTEM IN THE PATHOPHYSIOLOGY OF SAD AND LIGHT THERAPY

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Based on published reports in the literature there is some evidence that the neurotransmitter serotonin (5-hydroxytryptamine, 5-HT) plays a fundamental role in the pathophysiology of seasonal affective disorder (SAD) and probably also in the mechanisms of action of light therapy (LT). Patients suffering from SAD differ from healthy controls in 5-HT mediated hormonal and behavioral responses to 5-HT challenges. The atypical symptoms, which represent the core syndrome of SAD, have an important relationship to the 5-HT system and selective 5-HT reuptake inhibitors have been shown to be effective for the treatment of SAD. There is some evidence that the mechanism of action of LT depends on serotonergic mechanisms. With the use of the acute tryptophan depletion technique in double-blind, balanced, placebo-controlled crossover designs we investigated the role of 5-HT in SAD and also in the mechanism of action of LT. It emerged that tryptophan depletion induced an exacerbation of the depressive symptomatology in drug-free patients with SAD who were in a stable remission from depression by the usage of LT. No significant effects on mood were observed during the control testing. Preliminary results from a study with untreated depressed SAD patients revealed no significant deterioration of the depressive syndrome after ingestion of the tryptophan-free amino acid drink (tryptophan depletion). Conclusively, the current results from the literature and our own findings support the hypothesis that a 5-HT dysfunction contributes to the pathobiology of SAD and that the functional integrity of the brain 5-HT system is important for the maintainance of the antidepressant effect of LT.

UPDATE ON CLINICAL ASPECTS OF SAD AND LIGHT THERAPY

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In the 11 years since seasonal affective disorder (SAD) was first described and light therapy was first shown to be effective for the depressive symptoms of this condition, much progress has been made in the clinical aspects of SAD and its treatment. Although SAD was initially presented as a homogeneous disorder, evidence is emerging to suggest that premenopausal women with this condition may constitute a specific subgroup. Premenopausal female SAD patients have been found to differ from their male counterparts on certain biological parameters, e.g. low plasma prolactin levels in young women vs. high levels in men. Puberty and the menopause appear to alter the prevalence of the condition in women, whereas the prevalence in men tends to remain more constant across the life cycle. Women with SAD differ from male SAD patients in that they tend to sleep and crave carbohydrates more and gain more weight than men during the winter. Originally, SAD patients were treated with 2500 lux of artificial light. More recent innovations have included: (1) more intense (10,000 lux) light sources; (2) dawn simulators; and (3) portable head-mounted Light Visors. The relative and/or additive merits of these different approaches will be discussed. One recent comparison between fluoxetine and light therapy suggests that these treatments may be equally effective as antidepressants. In addition, they may have additive or synergistic effects if used in combination, a strategy that may reduce side-effects. The mechanism of action of light therapy in SAD is not yet fully understood, although multiple lines of evidence are converging on brain serotonergic systems as a likely site of action. All these areas will be more fully reviewed during the presentation.

THE BIOLOGY OF SEASONAL AFFECTIVE DISORDER: ARE THERE WINTER SUMMER DIFFERENCES?

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Evidence is growing that patients with seasonal affective disorder have marked biological changes during the winter depressive syndrome compared with the summer, and compared with normal groups during the winter. Prolactin and some behavioural responses to m-CPP are increased in SAD and are reduced in summer and after treatment with phototherapy. This may suggest a presynaptic 5HT reduction in association with the syndrome.

Light sensitivity is increased during SAD in winter compared with the same individuals in summer and compared to normal controls in winter. Light sensitivity is reduced in SAD but not in normals by 5HT reuptake inhibition using fluoxetine, suggesting a possible link between 5HT and light sensitivity.

However, non seasonal depressed patients also show seasonal variations between winter and summer in relevant neuroendocrine variables such as cortisol levels and DST. There are also seasonal variations in the normal population. The evidence that circadian and other biological parameters of SAD vary seasonally in relation to the syndrome will be discussed.