

tion of neuroleptic relapse prevention appears to be well worth-while.

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## Experimental Psychopathology in Biological Psychiatry and Psychopharmacology

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Main research goals in biologically oriented psychiatry and psychopharmacology are to unravel the etiopathogenesis of psychiatric disorders and to develop causal treatment methods. The workshop was concerned with the application of experimental methods to the psychopathological conceptualization and assessment of psychiatric disorders. An “experimental” approach to psychopathology subsumes the objective and quantitative analysis of spontaneous as well as psychologically or pharmacologically induced abnormal behavior under various controlled conditions.

Highly sophisticated basic biological research methods are not yet sufficiently supplemented by adequate psychopathological concepts and assessment methods (Gaebel). Case identification by means of operationalized diagnostic systems is mainly based on clinically derived signs and symptoms, the neurobiological basis of which is still poorly understood. This is particularly true since complex experiential data, which are rather distant from their biological basis, still prevail in most diagnostic systems. To bridge the gap between “biotype” and “phenotype” of psychiatric disorders, the development of a neurobiologically based taxonomy of elementary psychological (dys-)functions is required (conceptual nervous system). Empirical methods should be adopted from experimental psychology, psychophysiology, and be-

havioral neurology, and should be applied within a general framework of biological research strategies.

Experimental anxiety induction-methods have been crucial tools in elucidating the mechanisms of panic attacks (Ehlers). It was demonstrated that the effect of “biological” panic induction methods (lactate infusion, CO<sub>2</sub>-inhalation, hyperventilation) are mediated by cognitive factors such as expectancy or control beliefs. Panic attacks can be induced by psychological manipulations such as false heart-rate feedback. Experimental methods are not superior to self-reports in the assessment of treatment outcome, but may provide useful additional information.

Various components of emotional reaction patterns after experimental mood induction can be distinguished (de Jong-Meyer). In affective disorders, subjective (feeling state, body awareness), physiological (heart rate, electrodermal activity, EMG of mm. corrugator supercilii, zygomaticus major, and orbicularis oculi), and endocrinological reactions (cortisol in saliva) in mood induction experiments (imagination, film, contingency manipulation), allow an extension of the traditional psychiatric diagnostic approach. Emotional specificity of single components, their covariation, and the influence of intervening factors may all be addressed. Results so far are in favor of a differential concept of emotions. Facial activity is more consistently related to subjective feeling, whereas autonomic nervous system parameters are not. Changes of the latter, however, seem to be contingent on subjective (body awareness) as well as biological (cortisol) variations. Dimensions of a situational taxonomy such as externality/internality and passivity/activity are of potential significance for the optimization of psychological treatment strategies in affective disorders.

Situational influences on behavioral indicators of subjective feeling during psychosis are an important aspect of experimental psychopathology (Ellgring). Relationships between various components (perceptual, subjective, expressive) of emotions appear to be altered. As a consequence, standard stimuli do have specific input which in itself is characteristic of the emotional disturbance and its expression.

Possible reasons for the still poorly developed knowledge of the psychobiological basis of psychiatric disorders are of theoretical, methodological, and technical origin (Wittchen). In particular, psychopathological assessment as a prerequisite to modern diagnostics, e. g. ICD-10 or DSM-III-R, is based on out-of-date concepts, whereas modern experimental approaches have not been considered. Problems of traditional psychopathology are due to insufficient consideration of

- a) temporal instability of (too broadly defined) psychopathological variables,
- b) temporal configurations,
- c) age dependency, comorbidity, and temporal patterning, and
- d) underlying psychobiological regulatory mechanism.

Although the assessment of symptoms is mainly based on the patient's subjective verbal report on “inner” states and processes, little is known about how this report is generated and modified by interoception, information processing ca-

capacity, cognitive sets, learning etc. Accordingly, differences in the incidence rates of depression in younger vs. older patients could be an artifact of differences in speech perception and information processing.

Neurological symptoms and syndromes can be experimentally modified by simple activation tasks such as finger tapping and asking the patients to perform calculations (*Fleischhacker*). Although these procedures are frequently used by clinicians, for instance to provoke symptoms of tardive dyskinesia in patients where the diagnosis is doubtful, there are only few scientific data which corroborate empirical observations. It appears that the disorders commonly attributed to disturbances in the dopaminergic nigrostriatal system are aggravated by mental (e. g. serial subtraction) and motor (finger tapping) activation tasks. Most experts in the field agree that this is true for tardive dyskinesia, dystonia, and parkinsonism. Akathisia, which is believed to have a different pathophysiological mechanism has been shown to have a differential response to mental and motor activation. Mental activation clearly decreases the symptoms of akathisia, motor activation had no effect in one study and increased akathisia in the other. This has important clinical consequences when the diagnosis of akathisia is unclear. It also shows that experimentally induced alterations of motor states can be used to differentiate pathophysiologically different disturbances. Experimental neurology does seem to be helpful for the clinician and the basic scientist.

A further aspect of applied behavioral research is concerned with the development of appropriate animal models for symptoms/syndromes of psychopathology (*Lehr*). Retrospective behavioral models rely on behavioral changes which are caused by treating animals with clinically validated reference drugs. The disadvantages of this method are that the model depends on existing therapeutic agents, that there is a risk of searching for side effects rather than main effects, and that they aim at copying without any innovation. Prospective behavioral models make use of ethological know-how of transspecific comparisons. The advantage of this method is that novel therapeutic targets and mechanisms can be addressed. However, there has only been a limited awareness of such strategies up to now.

From a methodological point of view, an experimental approach to psychopathology is based on two general assumptions (*Cohen*).

1. The psychopathological state in principal is variable and alterable; this seems to be true, although the conditions under which panic attacks, hallucinations, stereotypies etc. occur are far from clear.
2. Differential reactions between groups are more important aspects of psychopathology than mere differences in the degree of their general impairment. Accordingly, "interaction" effects instead of "main" effects are the matter of interest. However, four problems have to be taken into account:
  - a) Interactions between groups and conditions, though important, are rarely replicated. This is due to the fact that they are usually embedded in interactions of higher order, the statistical confirmation of which requires enormous experimental efforts, large sample

size, and is nevertheless hardly intelligible because of its abstractness.

- b) Abandoning global psychopathological terminology in favor of narrowly defined and operationalized partial aspects, experimental research is confronted with the problem of their multifactorial determination. Although it is impossible to control for everything, uncontrolled confounding variables invalidate any interpretation.
- c) The choice of certain experimental parameters is always arbitrary. Accordingly, by means of data manipulation and transformation statistical interactions may wax and wane. Unfortunately, "double dissociations" which are more robust against data treatment are very rare in psychopathological research.
- d) Adequate reliability and discriminatory power of experimental measures, as well as balanced task difficulty are prerequisites for the detection of a differential deficit. Otherwise, differences in performance could only be due to group differences in illness severity.

In conclusion, biological, psychological, and situational (social) aspects of psychopathology should be given more attention. This requires the application of experimental methods within a multidisciplinary approach, bringing together psychiatrists, psychopharmacologists, psychologists, neurologists, biologists, and other basic scientists interested in brain/behavior relationships. Future research should be more concerned with nosologically unspecific, but pathogenetically specific dysfunctions of psycho-neuro-biological systems ("functional psychopathology").

## Drug Monitoring in Psychiatric Patients: Which Approach is Useful to Improve Psychopharmacotherapy?

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The measurement of serum or plasma levels of psychotropic drugs in psychiatric patients has become a routine during the last two decades. It was the aim of this workshop to highlight its current status in Austria, Germany and Switzerland.

In the three countries therapeutic monitoring of psychoactive drugs is restricted to psychiatric inpatients of university clinics in collaboration with laboratories within the psychiatric department or in closely associated institutes of clinical pharmacology. Commercial laboratories do not play a significant role.