Eur Arch Psychiatry Clin Neurosci (1993) 243:164–170

European Archives of Psychiatry and Clinical Neuroscience

Original articles

Today's perspective on Kraepelin's nosology of endogenous psychoses*

Jules Angst

Psychiatric University Hospital Zurich, Research Department P.O. Box 68, CH-8029 Zurich, Switzerland

Received July 9, 1993

Foreword. Professor Jules Angst, Head of the Research Department at the Psychiatric Clinic of the University of Zurich, member of the Managing Editorial Board since 1971 and Coordinating Editor of the European Archives of Psychiatry and Clinical Neuroscience until 1992, was awarded the Kraepelin Gold Medal. This award is rich in tradition and currently the most distinguishing honour for excellent work in psychiatric research in the Federal Republic of Germany. The Editors of the European Archives take pride in this honour that was bestowed on their colleague for his outstanding services to psychiatric research. Jointly with Springer International they wish to express their hearty congratulations.

The lecture on "Today's perspective on Kraepelin's nosoloy of endogenous psychoses", which J. Angst gave at the Max-Planck-Institute of Psychiatry in Munich on 13 February 1992, is published in the following in its original version.

H. Häfner G. Sedvall

1 Introduction. Kraepelin's nosology

In the 20th century, influenced by psychoanalysis, the classification of psychiatric illness has been neglected over decades, especially in the United States. In the era of antipsychiatry, classification is seen as labelling, stamping, hence as discrimination. The diagnosing psychiatrist thus becomes a diabolus of modern society who declares a healthy person as sick and entangles him in a iatrogenic vicious circle. Yet, as the French structural antropologist Claude Lévy-Strauss (1973) genially proved in his treatise "La pensée sauvage" there is no culture that does not logically classify – that is, among other things, natural objects like rocks, plants, animals and people. In doing so, highly complex totemistic systems emerge. Classification is part of human thinking. To criticize the classification of psychiatric disorders and illnesses because it potentially may be abused is therefore equal to fighting against an ordering principle of the human mind. It would be a fundamental ideologic mistake.

The current classification of endogenous psychoses, that is including affective disorders and schizophrenia, goes back to Emil Kraepelin. Kraepelin was an ardent collector, naturalist and botanist who loved to identify plants (Mayer-Gross 1929). Equally carefully he observed his patients as a clinician both cross-sectionally and longitudinally. He studied their symptomatology, their symptom changes during the course of their illness and finally, after years, the endpoint of their illness. In doing so, he achieved, some 100 years ago, his great synthesis of a psychiatric nosology which, despite all modern developments, has survived to this day.

Max Hamilton (1975) divided the psychiatric nosologists in unifiers or synthesists and subdividers. Kraepelin (1913), without a doubt, was a great unifier. He integrated, as Fig. 1 shows, Kahlbaum's (1863) and Hecker's (1871) hebephrenia, Kahlbaum's catatonia (1874), Diem's dementia simplex (1903) and Ferrarini's dementia paranoides (1905) into the group of dementia praecox, which Eugen Bleuler (1911) later called the "schizophrenias". Kraepelin subsumed the bipolar illnesses [at the time known as Jean-Pierre Falret's folie circulaire (1851) and Baillarger's folie à double forme (1853)], the melancholias, the manias and the milder one or multiphasic affective disorders to the group of manic-depressive illness. Hence, in 1897, after years of hesitation, he accepted the principle concepts of Kahlbaum. Kahlbaum

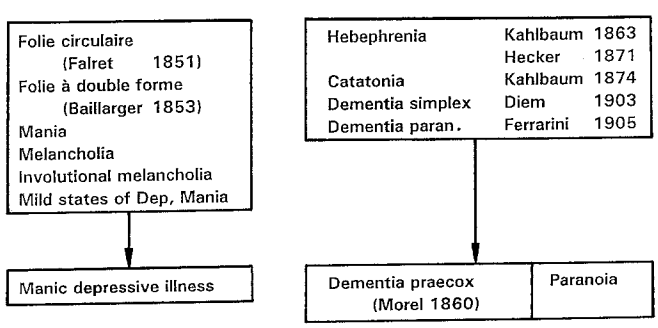

Fig. 1. Kraepelin's subsummations (Kraepelin 1889)

*Lecture held on the occasion of the 75-year jubilee of the Max-Planck-Institute in Munich on 13–14 February, 1992, after receiving the Kraepelin medal in gold

Correspondence to: J. Angst

himself did not succeed with his much too complicated nosology of psychotic illness (1863). He differentiated sharply between symptoms, symptom complexes and illness entities. Additionally, he emphasized the importance of the individual long-term course rather than the usual status of the patient for the classification of psychiatric illnesses.

Kraepelin was a self-critical empirist. As his disciple Gaupp describes, dogmatic rigidity or intolerance for other opinions or results were foreign to him. He tolerated critical doubt and sceptical reserve. He always considered his findings as preliminary. "We are still at the beginning" he wrote in the fall of 1926, shortly before his death.

Today, more than 60 years later, the question arises where we stand. Today, more than 60 years later, it is noteworthy that his classification is still valid worldwide. Psychiatry obviously did not grow much beyond her master. Does this mean that psychiatry, despite carefully preserving Kraepelins heritage, did not develop any further?

2 The nosology of affective disorders

In the following, I would like to evaluate Kraepelin's dichotomy in affective disorders and schizophrenias from the perspective of research on affective disorders. The notion of a simple dichotomy will be opposed by the hypothesis of a continuum or a spectrum of endogenous syndromally defined illnesses. The extent of the schizophrenic and the affective components can vary interindividually and intraindividually throughout the longitudinal course of the illness. It initially appears paradoxical to postulate a continuous model of endogenous psychoses on one hand, while defining new subgroups on this continuum on the other hand. Yet, it proves to be useful to subdivide the continuum into clearly defined syndromal subunits, while maintaining the concept of a spectrum. This spectrum or continuum includes not only affective or schizophrenic syndromes, but also the transition of affective syndromes to depressive or euphoric mood changes found in healthy people.

In persuing this goal, the following five points will be discussed:

1. Unification or separation of manic-depressive illness.
2. Psychoses lying between schizophrenia and affective psychoses: mixed psychoses or schizoaffective psychoses.
3. Clinical data on a continuum of affective disorders and schizophrenia.
4. Epidemiologic data on a continuum ranging from health to affective illness: hypomania, recurrent brief psychiatric syndromes.
5. Conclusions for further etiological and pathogenetic research.

2.1 Bipolar and unipolar affective disorders

In his memoir (1983), Kraepelin describes how his observations at Heidelberg on manic stupor, agitated depression, and mania with retarded thinking led to the realisation of the internal unity of "the whole, large, diversely manifesting group" (that is manic-depressive illness). Kraepelin's unification of pure depression and melancholia with bipolar disorder was not accepted by all psychiatrists. Especially Scandinavian authors like C. Lange (1896), Christiansen (1919); Schou (1927) (the father of the lithium researcher) disagreed; likewise the Germans Kleist (1911), Leonhard (1972) and their disciples did not espouse this concept. Yet, in the following time period, there was a lack of genetic studies supporting a differentiation of the two syndromes and withstanding methodological criticism, as Edith Zerbin-Rüdin noted (1965).

In Zurich, a similar noble psychiatric tradition to that in Munich was cultivated, which went back to Griesinger (1867) and Forel (1903) and was further developed by Eugen Bleuler (1911) and Manfred Bleuler (1972). Growing up in this tradition in Zurich, I became acquainted primarily with longitudinal and family studies as important validation methods for psychopathological classification. Starting with a mixed patient population of depressives, manic-depressives, patients with involutional melancholia and depressive mixed psychosis, I concluded in 1966 (Angst 1966) that bipolar disorders – based on the frequent presentation of mania in the relatives of bipolar patients, on clinical criteria on the course of the illness and on the sex distribution – should be separated from purely depressive psychosis. These findings were confirmed by Perris (1966) and Winokur et al. (1969) and promoted the re-emergence of the dichotomy of unipolar and bipolar affective disorders. The development of the last decade confirmed that bipolar and unipolar depressive disorders not only differ in their sex distribution but also in their longitudinal course. The former demonstrate an early age of onset and more frequent phases. Their prognosis is worse than the prognosis of unipolar depression.

A therapeutically induced switch from unipolar depression to bipolar disorder as a iatrogenic worsening hence would have great significance. Let me therefore deviate a little to findings of treatment research. Detlev Ploog was able to show in 1950 in a study on 88 patients treated with ECT that approximately one half of patients developed euphoria or maniform states after treatment with ECT (Table 1). Similar findings were later reported by Max Fink and Kahn in the United States in 1961. Numerous authors, among others Bunney et al. (1977), finally concluded that antidepressant medication was

Table 1. Transformation of depression into hypomania after ECT treatment

		ECT		
		Treated patients	Transformation into hypomania	
		Cases	Cases	%
Ploog	1950	88	44	(50)
Fink and Kahn	1961	73	36	(49)

capable of transforming unipolar depression into bipolar depression – an opinion that became a generally held doctrine.

In analyzing approximately 1300 hospital charts of patients hospitalized at the Psychiatric University Clinic in Zurich since 1920, no increased rate of switching from unipolar depression to mania after the introduction of antidepressants in 1958 as compared to earlier decades could be found (Angst 1992; Angst et al. 1992).

A transitory increase of switches was noted in the years 1944–1957, when depression was primarily treated with ECT or neuroleptics. In 1991, we were able to confirm the finding of Ploog that ECT provokes hypomania particularly frequently: hypomania occurs three times more often than would be expected from the natural course of the illness. Likewise, neuroleptics paradoxically appear capable of provoking such a switch.

Presumably, unipolar and bipolar depressed patients respond differently to prophylactic treatment with antidepressants: antidepressants might worsen the periodicity of bipolar illness in some cases, while in unipolar depression they can prevent recurrences.

2.2 Psychosis between schizophrenia and affective disorders (schizoaffective psychosis, mixed psychosis)

The recent modern classificatory systems, the DSM-III-R of the American Psychiatric Association (1987) and the ICD-10 of the World Health Organization (1991) group the syndromes of schizoaffective psychoses differently. The American diagnostic system subsumes affective psychosis with so-called "mood-incongruent psychotic features" under the affective disorders, while the ICD-10 includes them, in accord with tradition, in the group of schizophrenias. It should be emphasized that both diagnostic systems only take the cross-sectional status within one illness phase into account, although multiple studies demonstrate that this approach does not reflect clinical reality. A simply cross-sectional diagnostic system represents a relapse to the era prior to Kahlbaum and Kraepelin. Hence, the ICD-10, which has just been developed, will have to be revised. Kraepelin himself was well aware of the problematic nosological position of the mixed psychoses between schizophrenia and affective disorders. In 1920, he addressed the difficulties in differentiating reliably between manic-depressive illness and dementia praecox. He literally said: "No experienced diagnostician would deny that cases where it seems impossible to arrive to a clear decision, despite extremely careful observation, are unpleasantly frequent." "..., therefore, the increasingly obvious impossibility to separate the two respective illnesses satisfactorily should raise the suspicion that our question is wrong."

Gaupp (1926), a disciple of Kraeplin, initially was convinced of a pure dichotomy, yet later acknowledged the existence of the so-called mixed psychoses. In a large study together with Mauz, he concluded in 1926: "Today Kraepelin's two groups of illnesses of dementia praecox and manic-depressive illness are no longer rigid entities, yet represent, in their original form, biologically well-founded and, in their symptomatology and course, well-characterized main types. Between them are many connections, mixtures, and transitions" (Gaupp and Mauz, 1926).

Hoffmann (1925) described how mixed psychosis might develop into manic-depressive illness during the course of the illness, and manic-depressive illness might change into a mixed psychosis respectively. Mayer-Gross (1932) discussed the transition of schizophrenia in manic-depressive illness and vice versa. Kasanin (1933) replaced the name mixed psychosis with schizoaffective psychosis, a term that was accepted worldwide. A change from phasic schizophrenia to manic-depressive illnesses (which had already been discovered by Hoffmann in 1925 and Mayer-Gross in 1932) was recently confirmed by the transcultural catamnestic studies of WHO. There are numerous schizoaffective psychoses which can only be diagnosed when considering the longitudinal course.

2.3 Clinical data on a continuum between affective psychosis and schizophrenias

In Zurich in 1985, we examined the results of a syndromal grouping of endogenous psychoses cross-sectionally and longitudinally in a sample of 269 endogenous psychotic probands and their 1577 first-degree relatives. The analysis demonstrates clearly, that the consideration of the cross-sectional psychopathology does not lead to sensible diagnostic entities. Looking at the cross-sectional data, and after a multidimensional scaling the syndromes cluster analysis demonstrates the following spatial distribution (Fig. 2) (Angst et al. 1985): furthest apart, we find the depressive and manic syndromes, in the center there is a group of polymorphous psychotic symptoms, and in between are various transitions or forms. Only when considering the longitudinal data, do we find reasonable agreement with clinical diagnosis. There are two affective clusters, one with primarily depressive and one with primarily manic-depressive symptoms. Additionally, there is a schizoaffective cluster consisting of manic, depressive, and hallucinatory-paranoid syndromes followed by a fourth cluster consisting of primarily schizophrenic, paranoid-hallucinatory syndromes and a fifth cluster consisting primarily of catatonic-hallucinatory symptoms. It is interesting that all five clusters of syndromes contain depressive symptoms. This finding is in agreement with the genetic findings of Wolfgang Maier (Maier et al. 1992): Maier found an in-

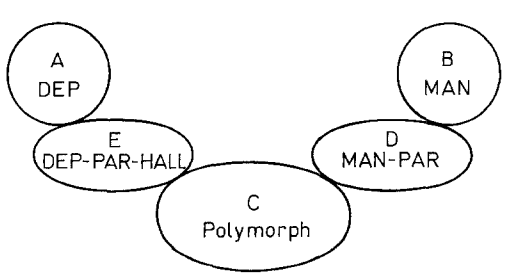

Fig. 2. Cluster analysis (From: Perspektiven der Schizophrenie-Forschung. Herausgegeben von B. Pflug, K. Foerster, E. Straube, Angst et al. 1985: S. 25–38)

creased risk for depression in the relatives of patients with affective disorder and with schizophrenia. He also confirmed our findings that the relatives of patients with unipolar and bipolar affective illness do not differ significantly in their risk of depression, but only with regard to the presence or absence of mania. Depression is a common trait of all subgroups of endogenous psychosis. The presented cluster analytic findings are in good agreement with the hypothesis of a continuum of affective disorders and schizophrenia, according to which schizoaffective disorders represent a middle group.

This hypothesis is further supported by genetic findings regarding the risk of psychiatric morbidity in first-degree relatives. We recently developed a model of a continuum between depression and schizophrenia, with the relative morbidity risk taken as the quotient of the schizophrenic and affective burden of the first-degree relatives and under the assumption of a polygenic inheritance of endogenous psychosis (Angst and Scharfetter 1990). The empirical findings correspond quite well to the model, according to which the heredity of pure affective and pure schizophrenic forms differ sharply. In between lie groups of mixed psychoses dominated by affective symptoms on one hand and schizophrenic symptoms on the other hand. It is interesting that neighboring classes do not show statistically significant differences, while the groups as a whole clearly demonstrate statistically significant differences. Kraepelin's dichotomy of endogenous psychosis in dementia praecox and manic-depressive illness primarily used the course and the endpoint of the illness as a validating criterion. The endpoint of the schizophrenias observed by Kraepelin generally consisted in dementia. Newer longitudinal follow-up studies at multiple centers on schizoaffective psychosis uniformly demonstrate that the prognosis of schizoaffective psychosis lies between affective psychosis and schizophrenia, therefore representing a transitional group even from this perspective (Angst 1980; Brockington et al. 1980a, b, 1982; Angst 1986a, b; Marneros et al. 1991).

Research in recent decades demonstrates that schizophrenia tends to have a better and affective disorder tends to have a worse prognosis than previously assumed. Kraepelin's opinion that dementia praecox invariably leads to dementia was not confirmed. In 1909, 468 cases of dementia praecox from Kraepelin's clinic were re-examined by Zendig (1909). He demonstrated that 30% of cases of dementia praecox remitted, a finding which at the time was presumed to be due to a false diagnosis. Further research, however, confirmed that, even with absolutely correct diagnosis, a more favourable course of schizophrenia can be observed. In a 5-year follow-up the group of Möller et al. (1981) found about 50% of patients with schizophrenia to have a bad outcome while to 10–20% remained symptom-free. Repetitively it was demonstrated that schizoaffective illness has to be separated from schizophrenia, because, if they are mixed together, they lead to too favourable a prognosis of schizophrenias.

Our own analysis of hospital charts of the Psychiatric University Hospital of Zurich of the years 1920–1930, when Eugen Bleuler was director, demonstrates that many of the then diagnosed schizophrenias are in fact schizoaffective disorders. The latter appear to be much more frequent than previously assumed. Besides all these findings that support the hypothesis of the continuum in the sense of transitional groups between affective disorders and schizophrenia, I should like to stress once more that all diagnostic classes of endogenous psychosis contain a depressive syndrome. This observation was probably ignored for too long and its significance appears to have been underestimated. A consequence of this underestimation is the myth of a neuroleptic-induced pharmacogenic depression and of a so-called post-psychotic depression in schizophrenics. Von Zerssen and Möller (1988) observed in careful psychopathologic studies of schizophrenic phases that depressive symptoms are already present at the beginning of the episode and tend to abate with remission. Only a small proportion of patients developed a new depressive syndrome for the first time at the end of a schizophrenic episode. These findings are in agreement with results of psychopharmacologic studies from Zurich (Woggon and Angst 1975) and London (Knights and Hirsch 1981). They demonstrate that during the treatment with neuroleptics depressive symptomatology is not a new development but tends to remit in general. Long before the existence of neuroleptic treatment, Mayer-Gross (1920) extensively described a depressive syndrome at the end of schizophrenic episodes, which was assumed to be secondary to psychoreactive moments. Nevertheless, the hypothesis of a pharmacogenic depression is not fully disproved. Should it exist, it would, in analogy to the pharmacogenic mania of depressives, only occur in relatively few cases.

Since it was demonstrated that schizoaffective illnesses are closer in their prognoses to affective disorders, it is not recommended to subsume schizoaffective illnesses under schizophrenia, as Jaspers' (1913) hierarchical rules suggest.

Another important finding is the one by Möller et al. 1981, according to which an affective syndrome, i.e. depressive symptoms at the beginning of hospitalization are of little prognostic value, yet at discharge they appear to influence prognosis. Again it appears that the course predicts the course. Important are the results of Möller and co-workers (1981) that state that psychopathologic variables are the best predictors for the psychopathologic outcome of an illness, while the premorbid social adjustment is the best predictor of the social remission. From a methodologic perspective it is therefore recommended to use a multidimensional approach when assessing course and outcome of psychiatric disorders.

2.4 The premorbid personality of patients with affective disorder

Kraepelin himself considered the study of personality as quite important for research on psychoses. Nevertheless, there are only very few studies to this day that evaluate premorbid personality prospectively. Investigations of this kind are unfortunately quite expensive. It is possible to study high-risk probands such as the relatives of pa-

tients. Such an approach was used by Parnas (1993 in press) in following children of schizophrenic mothers or by Holsboer in Krieg et al. (1990) in analyzing the relatives of patients with affective disorders in the vulnerability study of Freiburg and Munich. Ultimately, only epidemiologic investigations of a normal population are representative. We are presently persuing such an investigation in Zurich, analyzing approximately 3000 men longitudinally from the age of 19 to 40 years with the Freiburg Personality Inventory (Fahrenberg et al. 1978). We were able to find significant differences in the personality of probands that later developed bipolar affective, unipolar affective and schizophrenic illnesses. Later schizophrenics can be premorbidly differentiated from controls by high neuroticism scores, especially in vegetative lability. Later bipolar manic-depressive patients do not differ in their premorbid personality from normals. Unipolar depressives present early, many years before the onset of illness, vegetative lability, depressive symptoms and a low frustration tolerance (Clayton and Angst, in preparation). Postmorbid assessments of unipolar depressive patients yield much higher pathological values than premorbid assessments for the neuroticism scale, the depression scale and frustration tolerance (equinimity): this indicates that the postmorbid assessment is not necessarily representative of the premorbid state. The design used by Holsboer and collaborators, using a prospective approach in studying high-risk groups, is therefore preferable.

2.5 Epidemiologic data on a continuum between health and affective illness

Kraepelin subsumes under manic-depressive illness: "Certtain mild and very mild, in part periodically in part chronically altered mood states which on one hand can be considered as early phases of more severe disorders and on the other hand may belong to the domaine of personal predisposition, without sharp delineation." Kraepelin did not exclude that there might be subgroups. In the development of DSM-III (1980) and DSM-III-R (1987), American psychiatry attempted to operationally define milder states of depressed or elated mood, i.e. dysthymia and hypomania. In doing so, generally a clinical psychiatric perspective was used rather than an empirical view based on samples from a normal population. Yet this would be necessary to describe a continuum between affective illness and health. Depression research is dominated by studies on severe depressions, so-called major depression; minor depression was totally neglected and its concept has not been validated any further in the last few years.

It is evident that, besides hypomanic or depressive phases of longer duration, there exist shorter episodes that might last only a few days. These were already described in the last century. A classic study is that of Paskind (1929). The question is whether there are individuals that primarily suffer from short episodes and never have a longer phase. In the last 15 years, we collected data in Zurich to evaluate this problem in following a cohort of the normal population from age 20–30 years. Short depressive mood changes occurring once, several times or periodically cristallized, which generally last 1–3 days. These short depressions assume importance as an illness when they occur frequently ("Recurrent Brief Depression") (Angst et al. 1990). The impairment secondary to these short episodes was demonstrated with treatment rates, suicide rates, and a positive family history for affective illness. The relationship of these short mood changes to personality disorders has not yet been clarified and requires further analysis. Analogously, we tried to identify hypomanic phases of short duration in the normal population. We believe that this was successful. Of the population, 5 to 6% suffer from or enjoy hypomanic episodes. This group indicates higher depression scores and a suicide rate equal to the suicide rate of probands with classic depressive syndromes (major depression). Their first-degree relatives have a higher risk for hypomania and depression (Wicki and Angst 1991). From this perspective, we assume that the predisposition to bipolar disorders is much more prevalent in the normal population than classical psychiatry has so far assumed. The significance of these milder syndromes is not only illustrated by the rate of suicide attempts, but also by the social complication secondary to them due to conflicts, divorce, alcohol abuse, and delinquency.

2.6 Conclusions and recommendations for further etiologic and pathogenetic research

The species 'clinical researcher' is becoming ever rarer. Nevertheless, clinical psychiatric research remains indispensible today. It is the only way to advance in conceptual nosologic questions. The methodologic approach of Kahlbaum and Kraepelin, i.e. the careful psychopathologic description cross-sectionally and longitudinally, the study of the course of the illness and the outcome as well as the study of secondary cases among the relatives remain important. Instead of diagnostic classes which are assumed to represent illnesses, we nowadays find syndromal groupings cross-sectionally and longitudinally as well as in genetic research. Research of this kind is tedious. It requires many years, much money and patience. Prospective longitudinal studies like the follow-up study of Wittchen and von Zerssen in Munich (1987) proved to be the best method to reach final conclusions, especially regarding causal hypotheses. It has been demonstrated that the majority of biological findings in endogenously psychotic patients are state-dependent and do not lead to further etiological conclusions. Prospective epidemiologic investigations point out that a valuable approach from a clinical perspective lies in the premorbid assessment.

Thus useful psychological and sociological hypotheses on the influence of partial causes for the development of illnesses can be clarified. Premorbid biological analyses in high-risk groups unfortunately are still rare. Yet they have proven to be of high yield, as the studies of Parnas (1993 in press) and the prospective vulnerability study of Holsboer in Krieg and collaborators (1990) have demonstrated. A premorbidly reduced stability of vegetative regulations and of sleep regulations in schizophrenics has been found in this and our own study. After

the beginning of the illness, it is indicated to further investigate the course of the illness longitudinally. It must be borne in mind that new factors that can modify the course may have to be added to the original cases, as has been demonstrated by Wittchen and von Zerssen (1987). This may also be valid for biological entities, i.e. it might be possible that stress tolerance and immune response can be altered secondarily. Future biological research should orientate itself to syndromal diagnostic concepts that include the course of the illness rather than to the cross-sectional findings. This promises to yield more homogenous patient groups. From a methodological perspective, it is recommended to not onyl concentrate on homogenous illness groups in comparison to a representative control from the normal population but to also include syndromal borderline groups that lie left and right of the target groups and complete the spectrum of endogenous illnesses. Multiple comparisons among these groups yield much more information than the simple comparison of sick patients with healthy people. Historically, psychiatric nosology oscillates between unification and differentiation. Presently, there is an attempt to further differentiate endogenous psychotic illnesses. Yet it appears fruitful to presume a concept of a continuum from healthy to ill, from affective illnesses to schizophrenias, as a syndromal spectrum, a view which is also proposed by Hippius and Selbach (1969). The viewpoint of the unifier and the subdivider therefore do not necessarily collide. Especially biological research starting from such a continuum might be quite interesting, especially if systematic changes can be observed.

Clinical psychiatric nosologic syndromal research therefore remains an elementary basis of biological research and represents the best field to yield its crop. To conclude, let me ask where the main obstacles for research lay today. The answer was given 200 years ago by Lichtenberg (1990): "Nothing is more inimical to the progress of science than the belief that we know what we do not yet known. This in an error to which the inventors of fanciful hypotheses are commonly subject" – "To doubt things which are now believed without any further investigation whatsoever: this is essential always and everywhere".

Acknowledgements. The author wishes to thank Dr. med. Barbara Hochstrasser for translating the original German version into English

References

American Psychiatric Association (1980) Diagnostic and statistical manual of mental disorders (3rd edn) (DSM-III) APA, Washington, DC

American Psychiatric Association (1987) Diagnostic and statistical manual of mental disorders (3rd edn) (DSM-III-R) APA, Washington, DC

Angst J (1966) Zur Ätiologie und Nosologie endogener depressiver Psychosen. Springer, Berlin Heidelberg New York

Angst J (1980) Verlauf unipolar depressiver, biopolar manisch-depressiver und schizo-affektiver Erkrankungen und Psychosen. Ergebnisse einer prospektiven Studie. Fortschr Neurol Psychiatr 48:3–30

Angst J (1985) Switch from depression to mania – A record study over decades between 1920 and 1982. Psychopathology 18: 140–154

Angst J (1986a) Verlauf und Ausgang affektiver und schizo-affektiver Erkrankungen. S 75–87. Diskussionsbemerkungen: S 53–57, 70–73, 102–106. In: Huber G (ed) Zyklothymie – offene Fragen. 2. Hans-Joerg-Weitbrecht-Symposion, Bonn 1985. Tropon Arzneimittel, Köln (Das Ärztliche Gespräch)

Angst J (1986b) The course of major depression, atypical bipolar disorder and bipolar disorder. In: Hipppius H et al. (eds) New results in depression research. Springer, Berlin Heidelberg New York, pp 26–35

Angst J (1992) Drug-induced affective syndromes. In: Keshavan MS, Kennedy JS (eds) Drug-induced dysfunction in psychiatry. Hemisphere, New York, pp 181–190

Angst J, Scharfetter C (1990) Schizoaffektive Psychosen – ein nosologisches Ärgernis. In: Lungershausen E, Kaschak WP, Witkowski RJ (eds) Affektive Psychosen. Schattauer, Stuttgart, 23–31

Angst J, Bänninger R, Nüsperli M, Scharfetter C, Stassen HH (1985) Syndromale Gruppierungen endogener Psychosen in genetischer Sicht. In: Pflug B, Foerster K, Straube E (eds) Perspektiven der Schizophrenie-Forschung. Fischer, Stuttgart, 25–38

Angst J, Merikangas K, Scheidegger P, Wicki W (1990) Recurrent brief depression: a new subtype of affective disorder. J Affect Dis 19:87–98

Angst J, Angst K, Baruffol I, Meinherz-Surbeck R (1992) ECT-induced and drug-induced hypomania. Convuls Ther 8:179–185

Baillarger JGF (1853) De la folie à double forme. Ann Méd Psychol 6:369–389

Bleuler E (1911) Dementia praecox oder Gruppe der Schizophrenien. In: Aschaffenburg G (ed) Handbuch der Psychiatrie. Spezieller Teil 4. Deuticke, Leipzig und Bleuler E (1972) Lehrbuch der Psychiatrie

Bleuler M (1972) Die schizophrenen Geistesstörungen im Lichte langjähriger Kranken- und Familiengeschichten. Thieme, Stuttgart

Brockington I, Kendell RE, Wainwright S (1980a) Depressed patients with schizophrenic or paranoid symptoms. Psychol Med 10:665–675

Brockington I, Wainwright S, Kendel RE (1980b) Manic patients with schizophrenic or paranoid symptoms. Psychol Med 10: 73–83

Brockington IF, Perris C, Kendell RE, Hillier VE, Wainwright S (1982) The course and outcome of cycloid psychosis. Psychol Med 12:97–105

Bunney WE Jr, Wehr TA, Gillin JC, Post RM, Goodwin FK, Van Kammen DP (1977) The switch process in manic depressive psychosis. Ann Intern Med 87:319–335

Christiansen (1919) cited by Schou HJ (1927)

Clayton PJ, Angst J (in preparation) Premorbid personality traits of men who develop unipolar or bipolar disorders

Diem O (1903) Die einfach demente Form der Dementia praecox. Arch Psychiatry 37:111–187

Fahrenberg J, Selg H, Hampel R (1978) Das Freiburger Persönlichkeitsinventar FPI Handanweisung. 3., ergänzte Auflage, Hogrefe, Göttingen

Falret JP (1851) De la folie circulaire ou forme de maladie mentale caractérisée par l'alternative régulière de la manie et de la mélancolie. Bull Acad Méd (Paris)

Ferrarini C (1905) Demenzia precoce paranoide (diagnosi differenziale dalla paranoia). Riv Sper Freniatr 30:876

Fink M, Kahn RL (1961) Behavioral patterns in convulsive therapy. Arch Gen Psychiatry 5:30–36

Forel A (1903) Hygiene der Nerven und des Geistes im gesunden und kranken Zustand. Moritz, Stuttgart

Gaupp R (1926) Die Frage der kombinierten Psychosen. Z Gesamte Neurol Psychiatr 101:73–80

Gaupp R, Mauz F (1926) Krankheitseinheit und Mischpsychosen. Z Gesamte Neurol Psychiatr 101:1–44

Griesinger W (1867) Die Pathologie und Therapie der psychischen Krankheiten für Ärzte und Studierende. Krabbe, Stuttgart

Hamilton M (1975) Anxiety and depressive states. What is the difference? In: Boissier JR, Hippius H, Pichot P (eds) Neuropsychopharmacology. Proceedings of the IXth Congress of the Collegium Internationale Neuropsychopharmacologium, Paris 1974. Excerpta Medica, Amsterdam, American Elsevier, New York, pp 32–34

Hecker E (1871) Die Hebephrenie. Ein Beitrag zur klinischen Psychiatrie. Virchows Arch Pathol Anat Physiol Klin Med 52:394–429

Hippius H, Selbach H (1969) Das depressive Syndrom. Urban und Schwarzenberg, München

Hirsch SR, Knights A (1982) Gibt es die pharmakogene Depression wirklich? Beweismaterial aus zwei prospektiven Untersuchungen. In: Ergebnisse psychiatrischer Therapieforschung [Do pharmacogenic depressions really exist? Proof from two prospective studies]. In: Kryspin-Exner K, Hinterhuber H, Schubert H (eds) Results of research on psychiatric therapy. Schattauer, Stuttgart

Hoffmann H (1925) Familienpsychosen im schizophrenen Erbkreis. (Psychosen bei den Eltern von Dementia-praecox-Kranken.) Karger, Berlin

Jaspers K (1913) Allgemeine Psychopathologie. 1. Aufl., Springer, Berlin 1913

Kahlbaum KL (1863) Die Gruppierung der psychischen Krankheiten und die Einteilung der Seelenstörungen. Kafemann, Danzig

Kahlbaum KL (1874) Die Katatonie oder das Spannungsirresein. Hirschwald, Berlin

Kasanin J (1933) The acute schizoaffective psychoses. Am J Psychiatry 90:97–126

Kleist K (1911) Die Streitfrage der akuten Paranoia. Ein Beitrag zur Kritik des manisch-depressiven Irreseins. Z Gesamte Neurol Psychiatr 5:366–387

Knights A, Hirsch SR (1981) "Revealed" depression and drug treatment for schizophrenia. Arch Gen Psychiatry 38:806–811

Kraepelin E (1889) Compendium der Psychiatrie, Leipzig

Kraepelin E (1913) Das manisch-depressive Irresein. In: Psychiatrie. Ein Lehrbuch für Studierende und Ärzte. 8. Aufl. Bd III/II. Teil, Barth, Leipzig, pp 1183–1395

Kraepelin E (1983) Lebenserinnerungen. Springer, Berlin Heidelberg New York

Krieg JC, Lauer CJ, Hermle L, Bardeleben von U, Pollmächer T, Holsboer F (1990) Psychometric, polysomnographic, and neuroendocrine measures in subjects at high risk for psychiatric disorders: Preliminary results. Neuropsychobiology 23:57–67

Lange C (1896) Periodiske Depressioner. Copenhagen 1985. Deutsche Übersetzung: Periodische Depressionszustände und ihre Pathogenese auf dem Boden der harnsaueren Diathese. Leopold Voss, Hamburg

Leonhard K (1972) Aufteilung der endogenen Psychosen in der Forschungsrichtung von Wernicke und Kleist. In: Psychiatrie der Gegenwart. 2. Aufl. Bd. II. 1. Teil Klin. Psychiatrie. Springer, Berlin Heidelberg New York, pp 183–212

Lévi-Strauss C (1973) Das wilde Denken. Suhrkamp Taschenbuch Wissenschaft 14

Lichtenberg GC (1990) Aphorisms. Translated with an Introduction and Notes by R.J. Hollingdale. Penguin, London, pp 158–159

Maier W, Lichtermann D, Oehrlein A, Fickinger M (1992) Depression in the community: a comparison of treated and non-treated cases in two non-referred samples. Psychopharmacology [Suppl] 106:79–81

Marneros A, Deister A, Rohde A (1991) Affektive, schizoaffektive und schizophrene Psychosen. Springer, Berlin Heidelberg New York

Mayer-Gross W (1920) Über die Stellungnahme zur abgelaufenen akuten Psychose. Eine Studie über verständliche Zusammenhänge in der Schizophrenie. Z Gesamte Neurol Psychiatr 60: 160–212

Mayer-Gross W (1929) Die Entwicklung der klinischen Anschauungen Kraepelins. Arch Psychiatr Nervenkr 87:30–42

Mayer-Gross W (1932) Die Schizophrenie. Die Klinik. Handb. d. Geisteskrankheiten, Vol. IX, pp 293–578. Springer, Berlin

Möller HJ, Zerssen D von, Wüschner-Stockheim M, Werner-Eilert K (1981) Die prognostische Bedeutung psychopathometrischer Aufnahme- und Entlassungsbefunddaten schizophrener Patienten. Arch Psychiatr Nervenkr 231:13–34

Möller HJ, Werner-Eilert K, Wüschner-Stockheim M, von Zerssen D (1982) Relevante Merkmale für die 5-Jahres-Prognose von Patienten mit schizophrenen und verwandten paranoiden Psychosen. Arch Psychiatr Nervenkr 231:305–322

Morel BA (1860) Traité des maladies mentales. Masson, Paris

Parnas J (1993 in press) Basic disorder concept from the view point of family studies in schizophrenia. In: Gross G (ed) Perspectiven psychiatrischer Forschung und Praxis. Schattauer Stuttgart New York

Paskind HA (1929) Brief attacks of manic-depressive depression. Arch Neurol (Chicago) 22:123–134

Perris C (1966) A study of bipolar (manic-depressive) and unipolar recurrent depressive psychoses. Acta Psychiatr Scand Suppl 194:1–89

Ploog D (1950) "Psychische Gegenregulation" dargestellt am Verlauf von Elektroschockbehandlungen. Arch Psychiatr Z Neurol 183:617–663

Schou HJ (1927) La dépression psychique. Quelques remarques historiques et pathogéniques. Acta Psychiatr Scand 2:345–353

WHO (1991) ICD-10. In: Dilling H, Mombour W, Schmidt MH (eds) Internationale Klassifikation psychischer Störungen. Huber, Bern

Wicki W, Angst J (1991) The Zurich Study. X. Hypomania in a 28–30-year old cohort. Eur Arch Psychiatry Clin Neurosci 240:339–348

Winokur G, Clayton PJ, Reich T (1969) Manic depressive illness. CV Mosby, Saint Louis

Wittchen HU, Zerssen D von (1987) Verläufe behandelter und unbehandelter Depressionen und Angststörungen. Eine klinisch-psychiatrische und epidemiologische Verlaufsuntersuchung. Springer, Berlin Heidelberg New York

Woggon B, Angst J (1975) Einzelne Aspekte der Behandlung mit Depotneuroleptika. In: Huber G (ed) Therapie, Rehabilitation und Prävention schizophrener Erkrankungen [Some aspects of treatment with "depot"-neuroleptics. In: Therapy, rehabilitation and prevention of schizophrenic disorders] pp 191–200. 3. Weissenauer Schizophreniesymposion [3rd symposium on schizophrenia at Weissenau]. Lübeck-Travemünde. Schattauer, Stuttgart

Zendig (1909) Beiträge zur Differentialdiagnose des manisch-depressiven Irreseins und der Dementia praecox. Allg Z Psychiatr 66:932–933

Zerbin-Rüdin E (1965) Die endogenen Psychosen. Thieme, Stuttgart

Zerssen D von, Möller HJ (1988) Affektive Störungen. Diagnostische, epidemiologische, biologische und therapeutische Aspekte. Springer, Berlin Heidelberg New York

Zerssen D von, Zaudig M, Cording C, Möller HJ, Wittchen HU (1990) The predictive value of grouping schizoaffective psychoses together with affective psychoses: Jaspers' hierarchical rule revised. In: Marneros A, Tsuang MT (eds) Affective and Schizoaffective Disorders. Springer, Berlin Heidelberg New York, pp 33–52