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## Learning from outcome studies Toward a comprehensive biological-psychosocial understanding of schizophrenia\*

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(Received 22 June 1988, revised received 12 September 1988, accepted 12 September 1988)

According to results from three major European long-term outcome studies on schizophrenia, from other comparable studies, and from additional investigations on rehabilitation and on the influence of psychosocial factors, long-term evolution of schizophrenia is much more variable and considerably better than hitherto admitted. On this basis, the author presents a comprehensive biological-psychosocial evolutionary model of schizophrenia in three phases, centered around the vulnerability- and information-processing hypotheses. Long-term evolution of schizophrenia cannot be sufficiently represented by a linear organic process mainly determined by genetic factors. Environmental and, in particular, psychosocial factors, also seem to play an important role. Vicious biological-psychosocial circles with multiple feedback effects can lead to non-linear escalating processes. Chronic states appear to be the result of complex interactions between preexisting vulnerability and autoprotective counterregulations on a biological, psychological and social level. Some therapeutic consequences and possible future developments of these concepts are presented.

*Key words:* Biological-psychosocial evolutionary model of schizophrenia; Long-term outcome study

### INTRODUCTION

The aim of this presentation is to review the evolution of our understanding of schizophrenia, based on several European long-term outcome studies and additional investigations over the last 2-3 decades, including our own. Our starting point was a series of systematic follow-up studies of the life-long evolution of mental illnesses, especially schizophrenia, initiated in the early 60s by Christian Müller (1981) in Lausanne, Switzerland, and eventually continued by ourselves from 1963 through 1973. As the results changed our under-

standing of schizophrenia and of the nature of its chronic states quite considerably, in a second step we concentrated on the organization and evaluation of clinical services for rehabilitation. These experiences further modified our views of the illness, leading in a third phase to the development of a biological-psychosocial model of its evolution which proved useful for both theoretical and practical purposes. The fourth and so far last step consisted of piloting therapeutic experiences and theoretical explorations based on the concepts mentioned above.

Our survey follows the lines of this alternating interaction between clinical research data and conceptualization. It starts with the situation which confronted us in the early sixties, when we began these long-term investigations.

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\*Stanley R. Dean Award Lecture, presented at the Annual Meeting of the American College of Psychiatrists, Maui/Hawaii, U.S.A., 11-15 February 1987.

THE NOTION OF SCHIZOPHRENIA IN  
THE EARLY 60s AND ITS MODIFICATION  
BY SEVERAL EUROPEAN LONG-TERM  
FOLLOW-UP STUDIES

While challenging new understandings had started to germinate long before in several places, the dominant views on schizophrenia among the European scientific community of the early sixties may be characterized as follows: Schizophrenia was predominantly understood to be a purely 'endogenous' disease, evolving almost inevitably and uniformly toward severe chronicity according to its own, mainly genetically fixed laws. Psychosocial and cultural factors, emphasized at that time by American psychiatry, were attributed, at most, a precipitating and pathoplastical role. The overwhelming importance of genetics seemed to be established by Kallmann's as yet uncorrected concordance rates of up to 86% for monozygotic twins (Kallmann, 1946, 1950); according to the latest reviews (Kringlen, 1986; Gottesman et al., 1987), these rates are 30–50%. The general prognostic pessimism was mainly based on the daily observation of large cohorts of severely impaired chronic in-patients, who at that time populated psychiatric hospitals all over the world. Longitudinal studies usually spanned only a few years; almost completely lacking were follow-up investigations over two or more decades, based on large representative samples of patients, also including those who had long since escaped the attention of clinicians by living in the community.

In this situation, early in the 60s, three major European long-term studies, all based on Kraepelinian or Bleulerian diagnostic criteria (both of which were considerably narrower than the then current American standards—see, e.g., Stephens et al., 1969), were started independently and almost simultaneously in Zurich, Lausanne and Bonn. Their results were eventually published in three monographs written in German, the first one by Manfred Bleuler (1972), the second by Ciompi and Müller (1976), and the third by Huber et al. (1979). So far, only Bleuler's book has been translated into English (Bleuler, 1978). English extracts and summaries of the others do exist (Ciompi, 1980a,c, 1985; Huber et al., 1980). Together, these three studies provided information on 2–4 decades of

evolution of about 1000 cases, our own being the longest one, observing an average of 36.9 years in 289 cases (Table 1).

In spite of quite different methodological approaches, the major results of these three independent studies are surprisingly similar (Fig. 1). They challenge traditional views in at least three important ways: first, by reporting converging rates between 20% and 29% for complete recoveries or remissions, and between 24% and 33% for only minor residuals; thus, the long-term outcomes in more than half the cases were rather favorable. Severe chronicity, defined by Bleuler as heavily invalidating disorders of thinking, speaking and behaving, was observed in only 14–24% of the cases.

The second, and perhaps just as striking common result, was the enormous heterogeneity of the observed long-term evolutions, contrasting with the classical belief of an almost uniform course toward chronicity. In spite of extreme schematization, like Bleuler (1972, 1978) we distinguished eight different evolutionary forms combining various types of onset, course, and outcome (Fig. 2).

Using their own criteria, Huber et al. (1979, 1980) even found 12 different evolutionary pathways. It seems difficult to explain this polymorphism by the classical concept of a continuously deteriorating process of a purely organic nature. Nor has the identification of stable and clearly distinct nosological subgroups yet been successful. The most plausible—and therefore widely accepted—hypothesis is the one of a *quite open life process in vulnerable individuals* influenced by a variety of interacting psychosocial as well as biological variables (Ciompi, 1983b).

This last notion is also supported by the third common finding, namely the fact that there is hardly any possibility of accurately predicting the long-term outcome in any individual case. The few generally accepted statistical predictors for a better outcome—more stable premorbid personality and social adaptation, acute onset, positive initial symptomatology, and remitting type of course—could certainly be confirmed. But some individual cases with poor statistical prognosis improved surprisingly, or even recovered late in life. In contrast to widely accepted beliefs based, however, on uncertain and contradictory objective findings (see Bleuler, 1978), there was no positive correla-

TABLE 1

Synoptic view of three European longitudinal studies

	Bleuler (1972)	Ciampi/Müller (1976)	Huber/Schuettler/Gross (1979)
Number of cases	208	289	502
Average duration of catamnesis	22 years	36.9 years	21.4 years
Schizophrenia concept	E. and M. Bleuler	E. and M. Bleuler	E. and M. Bleuler, K. Schneider
Catchment area	Zurich	Lausanne	Bonn
Method of investigation	Personal knowledge over decades, all other available information	Personal follow-up examination, all other available information, study of mortality and causes of death	Personal follow-up examination, all other available information

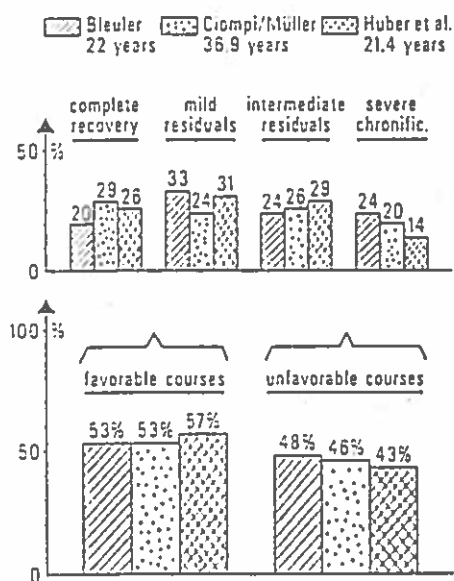


Fig. 1. Long-term outcome ('end states').

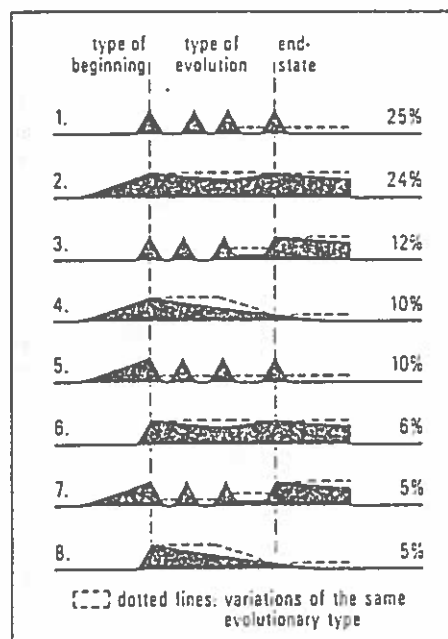


Fig. 2. Long-term evolution of schizophrenia (Ciampi and Müller, 1976).

tion between heavy genetic loading (as measured by several cases of schizophrenia among close relatives) and unfavorable long-term outcome. Bleuler reports only a few psychopathological and evolutionary similarities between the schizophrenias of members of the same family; we found no correlation at all between the outcome and the presence or absence of secondary cases, not even in the subgroups with the heaviest family loading, and in Huber's cohorts there was a paradoxical statistical relationship between better long-term evolution and higher genetic loading! Therefore, the long-term course probably depends on factors

other than strictly genetic ones – including, as we shall see, psychosocial factors.

Before turning to this issue, three major possible objections to these European studies must be discussed: firstly, the favorable outcomes could largely be related to the effects of neuroleptics. Secondly, favorable selective effects generated by sample mortality could be at work; and thirdly, the cohorts studied, dating from the pre-DSM-III era, may have contained a high proportion of prognostically

favorable schizophreniform or schizo-affective psychoses.

The first objection is easy to refute: as 96% of our 289 subjects were hospitalized and treated long before the neuroleptic era, the great majority of observed remissions and recoveries took place without neuroleptics. The same is true for Bleuler's cohorts, but less so for those of Huber. He in fact, reports some, albeit very uncertain, findings in favor of the hypothesis of beneficial effects of neuroleptics on the long-term course of his patients.

The influence of mortality and causes of death were also investigated in detail in our study. Both slightly favorable and unfavorable selective effects were revealed. The former were, however, far too weak to explain the observed outcomes.

The important question of DSM-III or not DSM-III schizophrenias cannot be validly answered on the basis of our data, although we carefully eliminated all marginal cases and utilized such narrow criteria that presumably the great majority of our cases were in fact DSM-III core-schizophrenias\*.

However, the recent highly sophisticated prospective-retrospective study carried out in Vermont, by Courtenay Harding, George Brooks, John Strauss and others, covering an average of 32 years of evolution among more than 150 cases, not only replicated our finding of a high proportion of favorable long-term outcomes (see Harding and Brooks, 1984; Harding et al., 1987a,b), but also succeeded in breaking the cohorts up into DSM-III and not-DSM-III schizophrenias. Surprisingly, they found that long-term outcome in the two subgroups was nearly identical (Table 2).

Concerning DSM-III core schizophrenias, according to Harding (1987b) the analysis of long-term outcome revealed '...that for one-half to two-thirds of these subjects, outcome was neither downward nor marginal. Most people resided in the community, were able to care for themselves, were actively involved with families and friends,

made productive contributions to their families and communities with little or no display of residual symptomatology'.

As our main findings have largely been confirmed by other recent long-term studies from different parts of the world (Tsuang et al. (1979) in U.S.A., Sternberg in Moscow (1981), Marinow (1981) in Bulgaria, Watts et al. (1983) in England, Ogawa et al. (1988) in Japan), the old dogma of a nearly obligatory bad long-term outcome of schizophrenia must be seriously questioned. Knowledge has improved since 25 years ago, not only on the striking heterogeneity and unpredictability of long-term evolutions, but also on the fact that even patients who were severely ill for many years can still recover later in life. This is illustrated by the following example chosen from our cohorts (example no. 7 (Ciompi and Müller, 1976)):

In his late thirties, a former tailor, member of a family heavily charged with schizophrenia, starts to withdraw progressively from all social contacts under the influence of a complicated system of persecution delusions. From the age of 45 to 57, he is constantly hospitalized for a severely chronic paranoid psychosis with multiple sensory hallucinations and delusions. Eventually, however, these disorders decrease. After discharge, he lives with his brother and again works as a tailor until the age of 85. At 88, when the follow-up examination takes place, all psychotic signs have been completely absent for many years; if signs of intellectual impairment were present, these were very minor. The former schizophrenic now lives a very normal and still active and independent life with close and friendly contacts with his many nephews, nieces and friends.

However, deeply rooted convictions are difficult to change. It is not astonishing that these new

TABLE 2

Comparison of DSM-I vs. DSM-III outcomes, after 32 years on average (Harding et al., 1987b)

	DSM-III (n = 82)	DSM-I but not DSM-III (n = 71)
Not in hospital past year	82%	86%
Met with friends every week or two	61%	72%
Had one or more moderately to very close friends	68%	86%
Employed in last year	40%	52%
Displayed slight or no symptoms	68%	73%
Required little or no help meeting basic needs	81%	80%
Led moderate to very full life	73%	80%

\* Additional efforts in order to reexamine our data are certainly desirable in spite of considerable methodological difficulties, but could not yet be accomplished, except for the variable 'duration of illness' (in the sense of DSM-III) which was more than 6 months for 81.2%, less than 6 months for 8.9%, and uncertain for 9.9% of the cases.

findings sometimes meet a certain scepticism. Further confirmation, particularly by prospective studies, is certainly needed. But is it not paradoxical that some people literally seem to feel hurt by the idea that long-term prognosis of schizophrenia may be better than they have thought, so that there is still hope even for apparently desperate cases?

In the next section, we shall show that maintaining hope can in itself have positive effects.

### CLINICAL WORK AND RESEARCH INTO THE REHABILITATION OF LONG-TERM SCHIZOPHRENIC PATIENTS

As already mentioned, the reported findings strongly stimulated our interest in rehabilitation. If severely chronic schizophrenics could improve spontaneously and return to the community, it should be possible to discover and reinforce the factors which favor such positive developments. Clinicians from several countries, in particular John Wing's group in England, had already shown the way by developing comprehensive rehabilitation techniques with interesting results (Wing et al., 1964; Freudenberg, 1967; Ekdawi, 1972). In the early 70s, in Lausanne, too, we started to organize a network of half-way institutions including a clinical rehabilitation unit, a day-hospital, a vocational rehabilitation center, a group home, and several sheltered apartments and workshops. In 1976, we undertook a prospective 1 year study of 81 long-term patients treated in these institutions, in order to examine correlations between success or failure and more than 30 possibly important variables (Ciompi et al., 1979). Success was operationally defined as moving up to or remaining in the upper parts (5-7 resp. 6-7) of two scales or axes, the housing and the working axis; failure as moving down to or remaining in the lower parts (1-4 resp. 1-5) of the same scales (Table 3).

Within a year, we observed a 72% success rate on the housing axis and 36% on the working axis (26% on both simultaneously), and the most significant predictors for success turned out to be neither diagnostic subgroups nor psychopathological symptoms or syndromes, but psychosocial variables such as good initial work behavior, positive expectations (i.e., hope) by patients, nurses

and relatives, less than 5 years of unemployment, a certain social competence, and dissatisfaction with the initial situation (see Tables 4 and 5).

The observed rates of success correspond with those reported in the literature, varying between 38% and 73% according to different authors and populations (Wing et al., 1964; Freudenberg, 1967; Ekdawi, 1972; Watts and Bennett, 1977; Katz-Garris, 1983). As positive expectations seemed so important, the next step was to try and influence these expectations in a cohort of severely chronic schizophrenic in-patients, and then to study possible effects on rehabilitation. This work was carried out in Bern at the newly created Social Psychiatric University Clinic. Although the chosen methods of cognitive modification of expectations failed to produce more than short-term effects, positive expectations – at that time especially those of relatives, doctors and nurses – again proved to be better predictors of success than all general or psychopathological variables. It was furthermore striking that with this most unfavorable population, a success of 17% on the housing axis and one of 30% on the working axis could still be achieved within 1 year (Dauwalder et al., 1984). In a follow-up study of 107 mostly schizophrenic patients who underwent vocational training in our industrial rehabilitation center, Hubschmid and Aebi (1986) found that after an average of 7.6 years, more than 2/3 of our former patients were still living and working within the community, in spite of persisting social and financial problems (Fig. 3).

The last of these evaluative studies was a 1 year cost-benefit analysis of our services in 1983. It not only confirmed that at least partial rehabilitative success was possible in about 3/4 of the nearly 1300 cases we treated annually, but also that overall daily costs of half-way institutions were on average 40-55% lower than those of full-time hospitalizations (Hess et al., 1986).

### THE PROBLEM OF CHRONICITY AND OF A COMPREHENSIVE BIOLOGICAL-PSYCHOSOCIAL UNDERSTANDING OF THE EVOLUTION OF SCHIZOPHRENIA

Along with new insights from other fields of research, these encouraging experiences led to a new

TABLE 3

*The two axes of rehabilitation (Ciompi et al., 1979)*

Housing axis	Working axis
(7) Normal housing	(7) Normal work
↑	↑
(6) Semi-sheltered housing	(6) Semi-sheltered work
↑	↑
(5) Group apartment	(5) Sheltered workshop
↑	↑
(4) Half-way home	(4) Industrial rehabilitation center
↑	↑
(3) Part-time hospitalization (day or night hospital)	(3) Work therapy
↑	↑
(2) Full-time hospitalization (open ward)	(2) Occupation therapy
↑	↑
(1) Full-time hospitalization (closed ward)	(1) No work

TABLE 4

*One year success of rehabilitation (n = 81, Ciompi et al., 1979)*

	% successes
Housing axis	72%
Working axis	36%
Both axes simultaneously	26%

TABLE 5

*Best predictors of success in rehabilitation (1 year, n = 81, Ciompi et al., 1979)*

	Cole coefficient	Level of significance
(1) Good initial work behavior	0.78	$P \leq 0.001$
(2) Positive expectations by patient, team, family	0.49-0.68	$P \leq 0.001$
(3) Unemployment < 5 years	0.68	$P \leq 0.001$
(4) Ego strength: competence	0.36	$P \leq 0.001$
(5) Initial dissatisfaction	0.50-0.59	$P \leq 0.05$

period of reflection on the evolution of schizophrenia. The main question was how to understand the interplay between biological and psychosocial factors in a clinically relevant way. Thanks to the contributions of geneticists and biochemists such as Kallman, Kety, Rosenthal, Carlsson, Axelrod and Wyatt (see Cancro, 1985), to mention only a few, the influence of genetic factors was now clearly established, and the role of neurotransmitters, in particular dopamine, became more and more

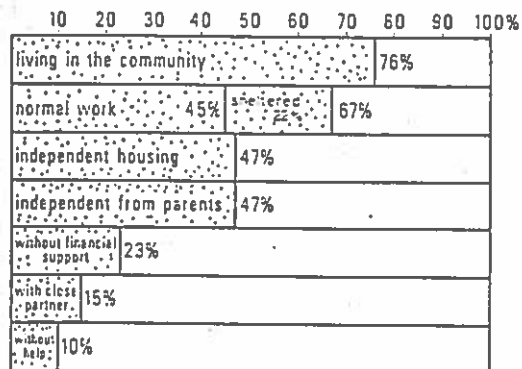


Fig. 3. Long-term results of rehabilitation (n = 107, Hubschmid and Aebi, 1986).

plausible. On the other hand, however, the impact of environmental factors also became more clearly apparent. As Cancro put it in 1981: 'Having the appropriate genes for a schizophrenic illness is not sufficient to produce it', 'Most genes are never activated. In a very real sense, the environment determines which genes are activated' (Cancro and Dean, 1985). Previous investigations around the nature/nurture question had, however, failed to demonstrate convincingly environmental, in particular familial, influences (Wender et al., 1974, 1977). In contrast, the detailed direct examination of different rearing environments by Tienari et al. (1985) in Oulu, Finland, seems to indicate with significance that adopted-away high-risk offspring tend to fall ill in severely disturbed families, whereas healthy adoptive families seem to have a

protective effect. The series of studies carried out since the early 70s by Brown et al. (1972), Vaughn and Leff (1976), Leff et al. (1982) and Berkowitz et al. (1984) on the unfavorable effects of the so-called high-expressed emotions point in the same direction, as well as those by Singer et al. (1978) and Doane et al. (1985) investigating familial patterns of communication and 'affective style' around schizophrenic patients. Other relevant findings concern the well-established opposite effects of social understimulation and overstimulation, the former favoring apathy and institutionalism, and the latter acute relapses (Wing and Brown, 1970), or the repeatedly reported statistical relationships between stressful life events and the outbreak or exacerbation of psychotic symptoms (Brown et al., 1972; Dohrenwendt and Egri, 1981).

But the practically and theoretically most intriguing problem is certainly that of the nature of the chronic states usually dominated by negative symptoms such as emotional flatness, social withdrawal, abulia and anhedonia. Our observations have revealed that they can no longer be considered as necessarily irreversible in the long run. Hence, their purely organic etiology becomes questionable. Along with the reported findings which speak more for the impact of environmental than genetic factors on the long-term outcome, the hypothesis arose that these most distressing chronic states were not, as generally assumed, the very core of the schizophrenic illness, but rather a possible consequence of it, perhaps a kind of psychosocial artefact resulting from the interaction of the pre-existing vulnerability with many unfavorable factors, including situational and infrastructural, familial and social, economical and cultural ones (Ciompi, 1980b). The same discussion has currently been reactivated by a forthcoming paper by Harding et al. (1989). Zubin and Spring (1976) have already been defending for more than 10 years the thesis that the very core of the schizophrenic illness is a permanent vulnerability, possibly a defect in information processing (see also Spring and Zubin, 1978; Zubin et al., 1983) which could, but does not necessarily have to lead to acute florid psychotic symptoms under stressful conditions. Chronicity, too, may or may not follow according to favorable or unfavorable overall circumstances (Ciompi, 1983a). Quite similarly, in Germany, Huber et al. (1979), Söllwold (1983) and Söllwold and Huber

(1985) have for many years been exploring the so-called 'basic disorders' (manifesting themselves by a variety of constantly present, discrete disorders of thinking, feeling and behaving), suggesting a permanently underlying vulnerability.

According to our current understanding, the chronic states are in fact most likely to be the result of a complex interplay between a – at least partially biologically rooted – preexisting vulnerability, and overcompensatory autoprotective counterregulations on a biological, psychological and social level against renewed stressful overstimulations. On the biological level, Lecrubier and Domillet (1983) propose a bipolar dopamine hypothesis with compensatory changes of postsynaptic sensibility over time. This could explain the shift from positive to negative symptoms. Thus, it does not seem necessary to think, as Crow (1980) once did, of two different illnesses which he termed schizophrenic syndromes I and II. Rather, the latter appears as the logical consequence of the former, developing under unfavorable conditions, including repeated acute episodes, prolonged institutionalization, social isolation, and underactivity. Neuroleptic long-term effects are also in need of clarification. Neurophysiological as well as psychosocial habituation effects mediated through neural plasticity (see below) doubtlessly play an often underestimated role; they might for instance be responsible for the fact that, contrary to the concepts initially advanced by Zubin et al. (1983), residual disturbances tend to accumulate after repeated psychotic episodes. On similar grounds, perhaps even the atrophic phenomena reported in a minority of cases with ventricular enlargement (Huber et al., 1979, 1980; Andreasen et al., 1982) could be understood as a consequence rather than as a cause of psychosocial restriction and underactivity.

Practically all the above mentioned aspects of evolution can be integrated into a *comprehensive biological-psychosocial model* of three phases, representing their minimal common denominator (Fig. 4). It is based on the vulnerability and information processing hypotheses and it is also compatible with other concepts like the 'stimulus-window model' (Wing et al., 1970), the 'developmental interaction model' (Strauss and Carpenter, 1981; Strauss et al., 1985), or Bleuler's (1972, 1978) notion of a 'disharmonious personality structure'.

Summarizing very briefly what has been fully

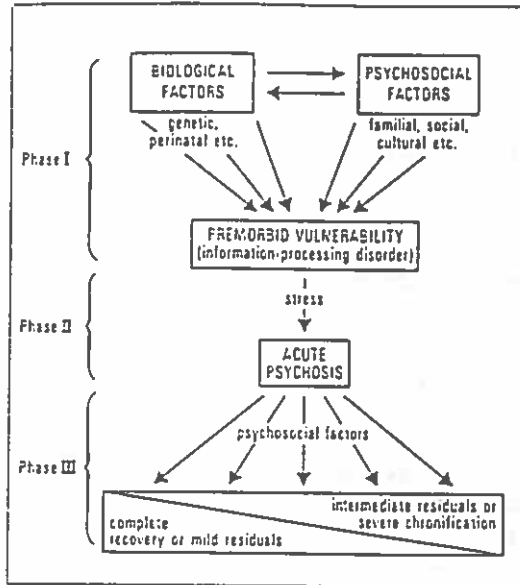


Fig. 4. Three-phase biological-psychosocial model of schizophrenia (Ciompi, 1982).

developed in our book on the <sup>bound</sup> boundary between affectivity and logic (Ciompi, 1982, 1988), the first, premorbid phase from birth, or rather conception, to the outbreak of psychosis is characterized by the building-up of partly defective 'programs of behavior', that is of coping or information processing systems in a wide sense. In this view, based on a synthesis between Piaget's and psychodynamic or systems theoretic concepts, inborn and/or acquired deficiencies in these affective-cognitive 'programs' learned through repetitive action represent the very place or substratum for the mentioned vulnerability. They manifest themselves, on the psychosocial level, as disorders of attention, categorization and time sequentiality, emotional oversensitivity and overreactivity ('overinclusion'), according to studies on cognition (see, e.g., Venables, 1963; Salzinger, 1973; Patterson et al., 1985) and investigations on high-risk children by Mednick et al. (1978), Erlenmeyer-Kimling et al. (1982), and others. Also interesting are the results of a 40-year prospective observation of 1000 children by Hartmann et al. (1984), which argue for specific premorbid lacunae in the field of interpersonal relationships among 24 future schizophrenics.

The proposed model postulates constant circular interactions between biological, psychosocial and

psychodynamic factors. Among the latter, convergent findings by Kernberg and Piaget (see Ciompi, 1982, 1988) on the genesis of the inner self and object representations deserve a special mention. These not only regulate our interpersonal relationships, but also the distinction between the inner and outer world.

The second phase is reached when the vulnerable information-processing system is critically overtaxed by stressful situations and life events. Again biological and psychosocial factors, e.g., genetically rooted information-processing disorders and disturbed familial communication patterns, may interact in vicious circles which finally escalate into acute psychosis. On the psychosocial level, mainly complex interpersonal relationships with contradictory existential demands necessitating 'impossible' changes seem to be involved. An interesting hint as to the biological dynamics of these same situations may be the fact that the dopamine metabolism seems to be sensitive to stress (Blanc et al., 1980; Reinhard et al., 1982; Trulson and Preussler, 1984), and that it can get into chaotic behavior (King and Barchas, 1983).

As to the third phase, long-term evolution, its enormous variability and the many interacting factors which seem to be responsible for it have already been discussed extensively.

#### PRACTICAL CONSEQUENCES AND POSSIBLE FUTURE DEVELOPMENTS

In this final section, we shall point briefly to some practical implications of the proposed model of understanding. If schizophrenia-prone persons suffer from permanent difficulties in processing complex 'informations' in the widest sense, first of all, every kind of confusion and overtaxing should be avoided as much as possible. Clarity and continuity, simplicity and authenticity (that is cognitive-affective congruence) of all kinds of communications and other incoming stimuli may become crucially important. This also concerns therapeutic settings and programs, which usually contain many counterproductive elements. The human environment of schizophrenics, especially the family, but also the work situation and the general way of living deserve special attention. In



order to avoid confusing feedbacks, clear information about the illness and about preventive measures, as well as information about the persistent vulnerability and oversensitivity, should be shared by all relevant persons in an atmosphere of close collaboration. By combining these measures, it should be possible to reduce considerably the need for neuroleptic protection from overstimulation (Ciompi, 1983b).

It has always been one of our main concerns to derive simpler approaches from sophisticated therapeutic techniques that would be accessible for nurses, relatives a.s.o., thus becoming profitable to the great majority, and not only to a few highly privileged patients. By combining useful tools from individual and family therapy with other successful experiments such as Mosher's Soteria house approach (Mosher et al., 1975; Matthews et al., 1979), Anderson's (1983), Leff's et al. (1982) and Berkowitz's et al. (1984) educational programs, and the low and targeted medication strategies by Carpenter et al. (1977), Herz et al. (1982), Carpenter and Heinrichs (1983), Kane et al. (1983) and other authors, we devised an experimental 2 year standard program including acute treatment, rehabilitation, and relapse prevention. It is based on the following six principles:

(1) *Special therapeutic setting*

Small, transparent, open, close to the community and as normal as possible therapeutic setting with a relaxing and supporting atmosphere.

(2) *Special therapeutic team and attitude*

Continuous personal support through the psychotic crisis with stimulus-protection by a few permanently present and specially selected and trained helpers.

(3) *Continuity of care*

The same team from acute psychosis through rehabilitation, post-care and relapse prevention.

(4) *Targeted and/or low dosage neuroleptic medication*

Neuroleptic medication only in case of danger for self or others, prolonged psychotic agitation, lack of improvement over several weeks, or signs of relapse beginning during the post-care phase.

(5) *Systematic collaboration with the family and other relevant persons*

Elaboration of straight-forward common goals (e.g., on the housing and working axes) based on realistic expectations of risks and opportunities.

(6) *Commonly shared information for professionals, relatives and patients*

Information concerning the nature and course of the illness, the therapeutic methods and goals, the importance of systematic post-care, the possible preventive measures.

Preliminary experiences with more than 50 cases treated in a Soteria-like setting in Bern, Switzerland, are encouraging, particularly because they in fact allowed a drastic reduction of neuroleptic medication (Ciompi and Bernasconi, 1986; Ciompi et al., 1988). A final appreciation, however, will only be possible in a few years' time, when other results are available, i.e., results of an ongoing systematic comparison of relapse rates, social and psychopathological outcome, and costs for four matched-pair control groups treated mainly by drugs in various, more traditional, psychiatric hospital settings in Switzerland and Germany.

Two other possible extensions of the concepts described above can only be mentioned briefly. On the one hand, in a joint effort with Manfred Bleuler from Zurich and John Haracz from the U.C.L.A. Brain Research Institute, we are currently trying to integrate the phenomenon of neural plasticity – certainly one of the most promising links between biological and psychosocial factors – into the proposed comprehensive understanding of schizophrenia and derived research programs (see Cotman, 1978; Haracz, 1984; Haracz et al., 1989). On the other hand, we have started to explore the possible theoretical and practical implications of Prigogine's concepts of 'order through fluctuation' and 'dissipative structures' (Prigogine and Stengers, 1984; Nicolis and Prigogine, 1985) for a better understanding of the vicious biological-psychosocial circles mentioned above, leading from vulnerability to overt psychosis (Ciompi, 1989).

It is not possible to go into these fascinating future perspectives here. Coming to a conclusion, the evolution of our understanding of schizophrenia can be summarized in the following way. The evolution of schizophrenia is certainly not, as we once

thought, a simple, linear, organic process. It rather appears to be the result of complex life-long interactions between numerous biological and psychosocial factors evolving in at least three great phases: first by creating a vulnerable 'premorbid terrain' characterized by partly deficient, internalized cognitive-affective 'programs of behavior', or coping systems. Secondly, by giving way to productive psychotic disorders beyond a critical level of acute or chronic overtaxing, and thirdly by a wide spectrum of possible long-term evolutions between complete recovery and different degrees of chronicity, representing the result of complicated compensatory and adaptive interactions over decades between the vulnerable individual and his whole environment.

By looking closer and closer, we discover different intermediate stages and multiple feedback mechanisms of a biological and psychosocial nature. It is this last insight which logically leads to the above mentioned assumption of non-linear escalating circular interactions between an overreacting, vulnerable individual and a disturbing environment. We regard it as one of our main tasks for the future to continue to explore these mechanisms carefully.

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