Psychopsychiatry: Can Psychosocial Factors Cause Psychiatric Disorders?

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THAT MATERIAL FACTORS can disrupt behavior has been differently emphasized in the course of the years, but never seriously refuted. It was seen to happen before one's very eyes. When the brain sustains anatomic damage—due to an accident, a circulatory disorder, a tumor, or inflammation—behavior changes. The same is observed in systemic diseases in which the CNS can be suspected to be involved. An example can be found in endocrine disorders. Alcohol supplies an example of the deterioration of behavior in association with an increasing degree of intoxication.

Viewed in the historic perspective, the theory that psychosocial factors have a similar potential is much more controversial. Since the turn of the century, however, psychopsychiatry has been a vision rooted firmly in psychiatric thinking. I use the term psychopsychiatry as an analogue of the term psychosomatics. Psychosomatics is the discipline that studies the extent to which psychosocial factors contribute to the etiology of somatic diseases. By analogy, psychopsychiatry concerns itself with the significance of these factors in the etiology of psychiatric symptoms.

The scientific bases of psychopsychiatry were, and still are the theory of psychoanalysis and the various sociological/interactional theories on the causation of disturbed behavior. The arguments marshalled in support of these theories are rather one-sided, and mainly consist of casuistics—often very detailed, it is true, but biased because they are presented from a very narrowly defined theoretical vision. A vision that is accepted in advance as axiomatic. The first attempts at more rigorous empirical verification date back to the 1970s, and are still very scanty.

In principle, the question whether (and to what extent) psychosocial factors play a role in the causation of behavior disorders can be approached from several sides. Five of these strategies will be briefly discussed.

LIFE EVENT RESEARCH

Life Events and Psychiatric Disorders

First of all it is necessary to demonstrate that psychosocial stress factors do indeed often precede the development of certain psychiatric syndromes. In the past decade, scales have been evolved for this purpose: the so-called life-event scales. An example of such a scale is that introduced by Paykel et al.[1] This scale can be used to establish the "event profile" over a given period, and also

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to gain an impression of the extent to which these events are unbalancing. By this method, it was demonstrated that numerous psychiatric syndromes (e.g., psychoses, depressions, and various neurotic disorders) are regularly preceded by more or less upsetting life events.[23] Specific correlations were not established. For example, "exits" (disappearance of a person from another person's life environment) often preceded not only depressions but also other psychiatric syndromes.[4]

The validity of life-event research, of the type so far performed, did not remain uncriticized. Most of these studies are retrospective, and the retrospective approach has its imperfections. It is not always easy, for example, to establish with certainty whether an event really preceded a psychiatric syndrome or occurred *during* the period of mental decompensation (and was in fact even determined by it). Moreover, the validity of a life-event history can be reduced by such mental mechanisms as: denial, repression, forgetting, and the search for an explanation of the complaints (effort after meaning). I will not here discuss the correctness of this criticism, but refer for this to another study.[5] In this context, I will confine myself to pointing out that prospective studies overcome many of these objections, and that their results point in the same direction as those of retrospective studies: an accumulation of stress-producing events preceding decompensation.[6] Prospective life-events studies, however, have so far been scarce, and have almost exclusively concerned patients with rapidly recurrent depressions and psychoses. Here, I believe, lies an important avenue of future research.

Estimation of the Pathogenic Importance of Life Events

In view of the above, I believe it is justifiable to conclude that life events play a role in the etiology of various psychiatric syndromes. But how important is this role? In principle, there are two conceivable extremes. On the one hand, without the event in question the syndrome would have developed during the same period, if perhaps slightly later. On the other hand, without the event there would have been no mental decompensation. Two measures have been calculated that make it possible to estimate the risk to mental stability entailed in a given event. The first is the "brought-forward time," introduced by Brown et al.[7] This is a measure of the time by which the event has advanced the manifestation of the psychiatric disorder. This is a clever construction, but one with unmistakable limitations.[8] For example, the value found for the brought-forward time strongly depends on the duration of the period over which the occurrence of life events was investigated. This is definitely a limitation, because we have no adequate knowledge of the duration of the after-effect of a given psychosocial "agent."

The second risk measure was introduced by Paykel[9]: the "relative risk" (a concept derived from epidemiology). This magnitude indicates the extent to which a given, presumably pathogenic factor (a life event in this case) increases the risk that a given disease becomes manifest. Paykel calculated that an exit increases the risk of a depressive syndrome by factor 6.5 during the subsequent 6 months, and that it increases the risk of a psychosis of the schizophrenic type by factor 3.9.

It seems to me that the relative risk is a more useful measure than the brought-forward time. Particularly if life events are measured and differentiated in a more sophisticated way than has so far been the case, it should be possible to gain a well-differentiated insight into risk factors of a social nature.

PATHOGENESIS RESEARCH

A second strategy is that of what I would call pathogenesis research. Psychosocial factors do not exert their influence on behavior via a vacuum. If it is true that they play a role in the pathogenesis of psychiatric disorders, then the following sequence of events should be envisaged. The event shocks the personality, causing an excess of intrapsychic tension. As a result of this intrapsychic stress, behavior-regulating systems in the brain are disrupted, and behavioral decompensation ensues. The first part of this sequence has been frequently studied, especially by psychoanalysts: why does a given event cause an excess of intrapsychic tension in a given individual? The second part of the sequence—transduction, i.e., the conversion of psychological to somatic (in this case cerebral) processes—has hardly been studied systematically in human individuals, although the human individual is not in principle inaccessible to such studies. An example in this context is the study made by Powell et al.[10] of the causes of so-called deprivation dwarfism.

In children with this syndrome, stagnation of somatic growth (in spite of normal or even excessive food intake) as well as of mental development is observed. The features are reminiscent of those of idiopathic hypopituitarism, but the fact that the symptoms quickly disappear after hospitalization, without hormonal substitution, contradicts this diagnosis. All these children proved to come from families in which they had long been exposed to serious forms of emotional neglect. Powell et al.[11] related these two findings and postulated a pituitary deficiency caused by psychological stress, with inhibition of growth as a consequence. They demonstrated that the release of growth hormone was in fact diminished at the time of admission and returned to normal during the period in hospital. Growth hormone is an important growth-promoting factor, and in subsequent years it was demonstrated that its release is highly variable and can in fact be influenced by psychological factors.

These findings and their interpretation have not remained uncriticized,[12] but these criticisms need not concern us. I mention this study, not because of the results but in view of the strategy behind it. It is a typical example of what I define as pathogenesis research: investigation of cerebral links between psychosocial stress and the development of physical and mental dysfunctions. Only this type of research can supply incontrovertible evidence that psychosocial factors can be a real cause of disease.

VULNERABILITY RESEARCH

Seed and Soil

A third strategy focuses on the detection of factors that can explain why one individual is so much more vulnerable to psychiatric disorders than another. Let us confine ourselves here to life events. These are usually not really

disastrous. Many people experience them, but relatively few become ill afterwards. Apparently the event per se is not sufficient to induce a syndrome. Let me elucidate this by an example derived from Paykel.[4] He investigated the life events of 185 depressive patients and as many controls during the 6 months preceding the interview in question. Exits had been experienced by 46 depressive patients (25%) and 9 controls (5%), which is an impressive difference, significant at the 1% level. Yet it can only partly explain the development of depressions. This becomes evident when the incidence of depressions is taken into account. Incidence is defined as the number of fresh disease cases per unit of time of a given disease. For depressions, the exact incidence is not known, but let us assume that it was 2% in a given population during the 6 months covered by the study. For a random sample of 10,000 individuals, this means 200 fresh cases of depression and 9,800 persons spared.

Extrapolating from the life-event study under discussion, we find that 5% of the nondepressive persons (490) and 25% of the depressive patients (50) should have experienced an exit, i.e., a total of 490 + 50 = 540 persons. Only 50 of these (less than 10%) actually become depressed. Evidently, therefore, one individual is much more vulnerable to the pathogenic effect of this life event than another.

What applies to life events also applies to other potentially pathogenic factors. Not every person becomes depressive after cortisol medication; not every woman develops amential symptoms after childbirth; not every patient becomes delirious after an operation. In this context, too, the crucial question is "What is it that makes an organism (or personality) hypersensitive to such influences?"

Levels of Vulnerability Research

In principle, vulnerability research can be carried out on three levels.

Biological level. Do cerebral behavior-regulating systems show weak spots, as a result of which disruption occurs abnormally quickly? Possibilities to be mentioned in this respect are a primordially marginal enzyme system or a limited number of synapses between certain neuronal systems. I mention two examples of this type of research.

First, the study of Buchsbaum et al.,[13] who demonstrated that low activity of the enzyme monoamine oxidase (MAO) in blood platelets increases the risk of psychiatric morbidity. MAO is involved in monoamine degradation, e.g., that of serotonin (5-hydroxytryptamine: 5-HT), dopamine, and noradrenaline. In the central nervous system (CNS) these amines serve as neurotransmitters, and there are indications that disturbances in the metabolism of these compounds can play a role in the pathogenesis of vital depressions and certain types of psychosis.[14] If the reduced MAO activity should be localized in the brain, then it would be possible in the context of these so-called monoamine (MA) hypotheses to demonstrate the plausibility of disturbed MAO activity increasing the vulnerability to these psychiatric disorders.

The second example is based on personal observations. We found indications that cerebral 5-HT deficiency exists in certain types of vital depression.[15—17] In depressions of this type, 5-hydroxy-tryptophan (5-HTP), a precursor of

5-HT that is converted to 5-HT in the brain, exerts a therapeutic effect.[18–20] This finding supports the hypothesis that the metabolic defect plays a role in the pathogenesis of these depressions rather than being a result of them.

Next, we demonstrated that signs of central 5-HT deficiency persist in a majority of these patients even after abatement of the depressive symptoms. On this basis we postulated that the central 5-HT deficiency is not a factor of direct causal significance but a predisposing factor. A factor that might be the biologic expression, so to speak, of the increased tendency of some individuals to respond to threatening endogenous or exogenous stimuli by a pathologic deterioration of mood. If this is correct, then 5-HTP administration can be expected to have a stabilizing, depression-preventing effect. We did find indications to this effect.[14] This is why we maintained that reduced availability in the brain of 5-HT is a factor that increases the vulnerability to vital depressions. We found two indications in further support of this hypothesis. The frequency of depression in the group of patients with signs of persistent disorders of the central 5-HT metabolism exceeded that in the group without these metabolic disorders. Moreover, the familial depression frequency was higher in the former group than in the latter.[21]

Psychological level. Does the personality structure show weak spots that explain an increased vulnerability to (certain) life events? Von Zerssen[22] provided an example of such research when he demonstrated that the compulsive personality is depression-prone, i.e., runs an increased risk of reacting to various more or less marked stressors with a vital depression.

Sociological level. Which circumstances of life enhance the pathogenic valency of a given event that, in principle, is unbalancing? Brown et al.[23] were able to distinguish four: loss of the mother before age 11; the presence at home of three or more children under age 14; poor relation with the marital partner; unemployment.

COMBINED THERAPIES

If it is true that (1) psychosocial factors can play a causal role in psychiatry, and (2) that they can exert their pathogenic influence on behavior exclusively via changes in cerebral behavior-regulating systems, then it is to be expected that the effect of combined pharmacotherapy and psychotherapy is superior to the effect of each of these therapies separately. Psychotropic drugs exert a direct influence on the brain, and are in principle expected to normalize or improve the disturbed cerebral functions. Psychotherapy is applied on the side of the pathogenic input. It aims at harmonization of the psychic structure and, consequently, elimination of a disease focus that constantly threatens the stability of the cerebral functions in question. As a rule, one has a better chance of winning a (therapeutic) fight with both hands than with one hand tied behind one's back. The above-formulated expectation is valid only in so far as there are more or less specific therapeutic methods for a given syndrome.

Comparative studies of combined therapy and one-dimensional therapy have been made in recurrent psychoses of the schizophrenic type and in recurrent depressions that symptomatologically are of the vital (endogenous) type. The results of these studies were practically unequivocal.[1,24,25] Combined therapy

was superior to one-dimensional therapy of either type. Moreover, the useful effects of the two one-dimensional approaches became manifest in different areas. Pharmacotherapy with neuroleptics or tricyclic antidepressants reduced the risk of a relapse of the psychosis or depression; psychotherapy exerted no distinct influence in this respect. The latter's useful effect became manifest in an improved quality of life during the intervals between the various psychotic depressive phases.

Of course, these experiments are not definitive, if only because there are so many different types and intensities of psychotherapy. They are mentioned here as exemplifying a research strategy, suitable in principle to gain an impression of the pathogenic potency of psychosocial stress factors.

The experiments mentioned have yielded no indications of a negative interaction between pharmacotherapy and psychotherapy. Psychotherapy was not unfavorably affected by simultaneous medication with psychotropic drugs. Nor was the reverse the case. The claim of some psychotherapists that psychotropic drugs have an unfavorable effect on psychological attempts to influence behavior has so far not been supported by empirical data.[26]

FURTHER SOPHISTICATION OF LIFE EVENT RESEARCH

Stable and Interactional Events

Life-events research has so far focused for the most part on readily definable, readily objectifiable events of everyday life in which the patient played a passive role (death of a dear one), an active role (divorce), or a combined role (loss of a job). As a rule, events of this type are the end products of a certain process, and as such immutable and irreversible. Perhaps somewhat paradoxically, I would call them "stable events." They are relatively easy to trace in an interview with the patient, to be recorded and verified in cross-interviews.

There are more life events that can unbalance the psyche. These events take place in the interaction between two or several individuals, in the family or outside. A sharp exchange of words; a token of affection, irritation, denigration, or hatred; rejection of an attempt at reconcilitation—these are merely samples of possible events that I would call "interactional." They are volatile, not readily defined, nodal points in a continuous relation, but they may be decisive for the quality of life. For a more profound understanding of the relations between life situation and psychiatric morbidity, empirical study of these interactional events is perhaps of even greater importance than that of stable events.

While the importance of this problem statement is evident, the study of these events is exceedingly difficult. However, the problems are not insurmountable, as demonstrated in studies made by Wing and Brown and their coworkers. Some aspects of these studies may be discussed here.

Expressed Emotional Involvement

In an effort to trace interactional variables in the families of psychiatric patients, Brown and Rutter[27] evolved a structured family interview. Two types of data can be collected in this way. To begin with, data on the patient's

behavior at home over a given period: i.e., is the patient still doing his work; what are his activities at home; how are his contacts at home; how are his contacts away from home; has his behavior towards family members changed, etc. Data of the second type concern the feelings of the family members towards the patient. These are assessed on the basis of such factors as a number of critical remarks that the interviewed person makes about the patient; tone and pitch of expression of certain feelings towards the patient; the emotional load of certain remarks, etc.

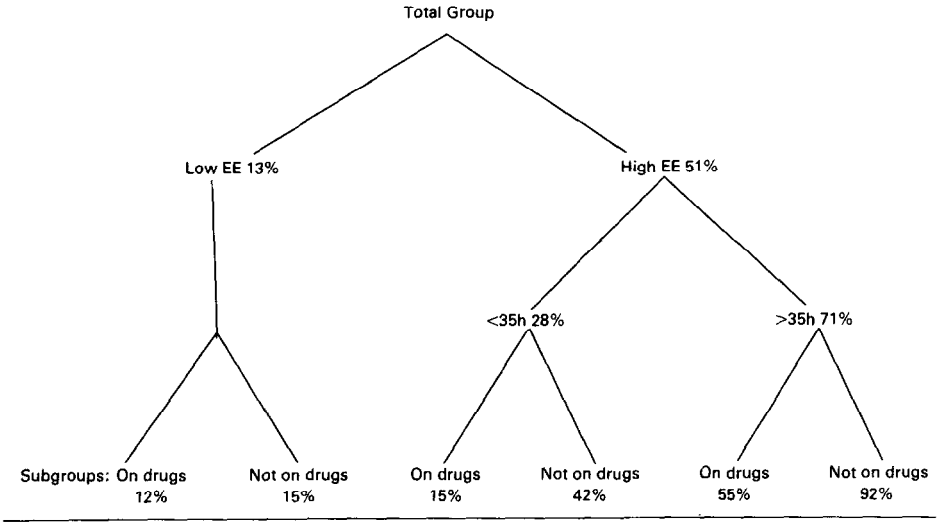
On the basis of data of the second type, the concept of "expressed emotion" was evolved.[28,29] This is an index of the degree of emotional involvement of a given family member with the patient's existence. It should be stressed that this concept has largely negative overtones because it is made up of scores for (1) critical remarks about the patient; (2) expressed hostile feelings towards him, and (3) the extent to which the family member concerns himself with the patient's life. It should therefore be borne in mind that this index is one-sided. It may reveal only a negative, not a positive attitude towards the patient.

Expressed Emotional Involvement and Psychoses of the Schizophrenic Type

This index of expressed emotional involvement (EE index) proved to be of value in predicting the risk of relapse of psychoses of the schizophrenic type. The first study of relevance in this respect concerned 116 patients with schizophrenic psychoses in whom the ability of chronic neuroleptic medication to prevent relapses was tested:[30] 50% received a placebo, and the other 50% received the active principle. In one group—those who showed a relapse after active medication—the number of stable life events in the 5 weeks preceding manifest psychosis exceeded that in the other groups, i.e., patients who showed no relapse after active and placebo medication, and those who showed a relapse after placebo medication. The following conclusion was formulated. Patients receiving neuroleptics relapse when exposed to upsetting (stable) life events, but they are protected from everyday tensions. Those receiving no active medication relapse either spontaneously or in response to normal interactional tensions of everyday life (interactional events). In other words on the interactional level there are concealed factors that can promote a relapse. The hypothesis that the expressed emotional involvement with the patient could be such an interactional factor was tested.

A follow-up was made over a 9-month period on a group of 125 patients discharged from hospital after a schizophrenic psychosis.[31] The group treated with neuroleptics clearly had the advantage over the patients treated with placebo, showing less than half as many relapses. Next, the patients were classified on the basis of the EE index of the family to which they had returned. Patients in families with a high EE index were found to run a much graver risk of relapse than comparable patients in families with a low EE index. Moreover, in the group with a high EE index a further distinction was made between patients in frequent direct (eye-to-eye) contact with their family members, and those whose contacts were less frequent because they had work outside or frequently retired while at home. The prognosis was best in the subgroup with little eye-to-eye contact (Table 1). A correlation matrix showed that the factor

Table 1. Nine-Month Relapse Rates of Total Group of 125 Schizophrenic Patients*



* Low EE (expressed emotion index) = 69 patients; high EE = 56 patients.[32]

relapse rate correlated closely with both the EE index and the nonuse of neuroleptics (Table 2).

Another important question arises. How did the patients limit their eye-to-eye contacts with relatives: by outside activities or by social reticence at home? Leff[32] found a significant correlation between low eye-to-eye contact and social reticence. This could suggest that this autism is not so much a symptom of the disease per se as a method of self-protection used by schizophrenic patients in families with a high EE index. It should be borne in mind that protection is a relative concept in this context. A measure that makes sense in principle can overshoot its goal and then turn into a detrimental, pathogenic factor. This happens in somatic medicine also. Inflammatory reactions protect the organism from invading pathogens. However, an inflammatory reaction can become excessive and thus an additional threat to health.

The above is mentioned only in passing. What matters to me in this respect is to emphasize the importance of this type of sociobiologic research. What we need above all else in psychiatry is rationalization of therapeutic programs—

Table 2. Factors Associated With Relapse[32]

Relapse	Behavior Disturbance	Critical Comments	Drug Treatment	Face-to-face Contact	EE*
1.00	−0.20	0.11	−0.39†	0.14	0.45†
		0.34†	0.32	−0.01	0.24
			0.24	0.13	0.58††
				−0.01	0.01
					0.10

* EE, expressed emotion index.
† $p < 0.05$.
†† $p < 0.001$.

not everything is helpful for everything—and purposeful prevention. In my opinion, such data as the above discussed are suitable par excellence to bring us closer to this goal.

CONCLUSIONS

I have discussed a number of research strategies that, in my opinion, can provide a firmer foundation for the view that psychosocial factors can seriously disrupt behavior. It may be evident from the above that in this context I tend to emphasize sociobiologic and psychobiologic research. This is because the following questions are fundamental.

How Do Psychosocial Factors Act on the Biologic Substrate?

The central question in this respect is "in which way do they disrupt cerebral regulatory systems?" Such a disruption is a conditio sine qua non, (1) for the development of dysfunctions on the level of behavior, and (2) for disorders of somatic functions outside the CNS.

Research of this type can provide convincing proof that psychosocial factors do play a role in the causation of disease (of any kind).

Which Requirements Should be Fulfilled Before Common Events Can Start to Play a Pathogenic Role?

I am alluding here to vulnerability research which, as discussed, can be carried out on three different levels: the biologic, the psychological, and the sociological. Research of this type can reveal how psychosocial factors are operative in the causation of disease.

How Can We Reduce the Vulnerability of Individuals to the Effects of Psychosocial Stress?

Will it be possible to ensure more adequate (re)programming of the cerebral machinery? Can balance within the personality structure be enhanced? Can resistance-reducing environmental factors be eliminated? It is by this approach that we may be able to prevent the pathogenic action of psychosocial factors. This is the true foundation of purposeful prevention.

The notion underlying this argumentation is in fact a cliché: psychosocial and biologic factors do not operate independently but in constant interaction. This should be the central concept in the approach to any disorder of behavior. It should be a cliché, but is not. A recent example is to be found in the turbulence that arose when, in the Netherlands, the Leiden criminologist Buikhuizen announced his intention to carry out biologic research in delinquents. His problem definition as such is not under attack (hardly anything about this has emerged in the press), but the mere fact that his research is to be biologic is.

Comparable turbulence is currently evident in the United States with regard to Yochelson and Samenov's work on the "criminal personality."[33] Criminal behavior is considered to be socially determined. Attempts to elucidate criminal behavior in pathopsychological and pathobiologic terms are viewed with the greatest mistrust and aversion by "politically liberal academic."[34]

A door that is closed, but should have been open, is rarely opened by kicking

against it. It is much more effective to find a key to fit the lock. I am enough of a positivist to be confident that empirical research will in the end provide such a key.

SUMMARY

It is a widely accepted view today that psychosocial factors can cause psychiatric disorders. However, this view has, as yet, no firm foundation of verifiable facts. This paper outlines some research strategies that can provide data in favor of or against this theory: (1) systematic analysis of life events preceding psychiatric disorders, covering both stable events and interactional events; (2) vulnerability research on three levels (biologic, psychological, and sociological), aimed at factors that could explain the increased vulnerability of some individuals to the detrimental effects of life events; (3) pathogenesis research, aimed at analyzing how psychosocial stress disrupts cerebral systems, and discovering which of these disruptions is responsible for disturbed behavior, and (4) research into the efficacy of combined biologic (mainly pharmacotherapeutic) and psycho(socio)therapeutic methods. Some results obtained in these areas of research are discussed.

The central idea of this study is that psychosocial and biologic factors do not operate independently but in close interaction. This seems a cliché, but is not, as clearly indicated by the scantiness of relevant research so far carried out. This gap is to be filled if psychiatry is to maintain and reinforce its status as a medical discipline.

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