

Classification of Organic Brain Syndromes by Cluster Analysis

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Summary. Cluster analysis was carried out on a sample of 92 patients with behavior disorders caused by degenerative, vascular, (alcohol) toxic, and other diseases of the brain. Rating variables of the AMDP system concerning mental state, social behavior, need for special care, sleep disorders, autonomic, physical, and neurologic symptoms were used in the absence of severe degrees of disordered consciousness such as stupor, coma, delirium tremens, and gross cerebral lesions. Results suggested the existence of four major groups of global cognitive impairment combined with neurasthenia and irritability in the first, hypochondriasis and depression in the second, withdrawal symptoms in the third, and severe disorientation in the fourth. At the seven-group level the groups were further distinguished according to severe withdrawal, amnestic syndrome, and dementia by various social and illness behaviors, sleep-wakefulness pattern, hypo- or hyperactivity, additional physical, and neurologic symptoms. Other minor types of organic brain syndromes were identified as individual cases by hallucinations or other circumscribed cognitive, psychomotor, affect, motivation, personality, and/or behavior disorder, symptomatic manic, or schizophreniform psychosis. The findings lent support to old classifications and new ones of organic mental syndromes (DSM-III).

Key words: Organic brain syndromes – Psychiatric evaluation – AMDP – Cluster analysis – Classification.

Introduction

Organic brain syndromes (OBSs) grow in frequency as the age of population increases, and are related to frequent chronic diseases and head trauma; alcohol

This paper is dedicated to Professor Schrappe for his birthday and moving-in to the new Clinical Department of Psychiatry, Fücksleinstraße 15

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and drugs also take their toll. There are many other causes of OBSs, some of which are readily identified clinically such as tumor, syphilis, B₁₂-deficiency, and Huntington's chorea. The great majority of cases, however, are caused either by vascular disease or by primary degenerative disease of the neurons and/or white matter. Clinically (Lipowski 1975) and biochemically (Bowen et al. 1977a; Bowen et al. 1977b; Hoyer et al. 1975), it is evident that OBSs are heterogenous, spanning a wide range of clinical features, mode of onset, duration, and degree of reversibility.

A number of German-speaking authors (Bleuler E 1969; Bleuler M 1975; Bonhoeffer 1912; Conrad 1972; Helmchen and Hippus 1972; Huber 1977; Lauter 1972; Wieck 1978) have classified the OBSs by descriptive categories. Nevertheless, the current international classification of OBSs combining traditional and novel features is riddled with conceptual and semantic confusion (Lipowski 1975) and it has been revised recently within the DSM-III: ICD-9-CM (Spitzer et al. 1977).

Relative few studies have sought to use the newer multivariate techniques of cluster analysis for classifying OBSs. They may be particularly useful in situations where there is clinical and biochemical diversity, but when clear-cut separations between distinct groups do not obviously emerge.

We report the application of such techniques to descriptive data on a sample of OBSs presenting at one mental hospital. The shape of distribution of these psychiatric syndromes described as symptom-sign clusters (SSCs) lends support to old classifications or suggests new ones which may have heuristic or clinical value.

Methods

Subjects

Subjects were 92 patients derived from a study of OBSs ($n=140$) presenting at the acute psychiatric wards of the State Mental Hospital, Weinsberg, Federal Republic of Germany. Some data mainly concerning brain blood flow and metabolism are already published elsewhere (Hoyer et al. 1975; Hoyer 1977; Hoyer et al. 1979; Krüger and Hoyer 1979).

All patients with gross lesions due to trauma, stroke, inflammatory disease, and obviously treatable causes such as vitamin deficiency, or other metabolic problems were excluded from this study. Diagnostic procedures tended to eliminate severe degrees of widespread cerebral damage or metabolic derangement in advanced cases of senile dementia, Alzheimer's, Pick's, and Jakob-Creutzfeldt disease. Huntington's chorea and Parkinson's syndrome were excluded also. We did not wish to overlook the practically most important syndromes: the early, the mild, the potentially reversible, and the most eminently treatable OBSs.

Diagnosis was made using pragmatic guidelines to identify and differentiate vascular and primary degenerative disease of the brain (Hachinski et al. 1975). The empirical ischemic score (the Mayer-Gross score) was based on a scheme for the psychiatric examination of patients with suspected organic cerebral disease (Mayer-Gross and Guttmann 1937). It cannot be bettered (Willis 1976) and may be regarded as identical with the German-language descriptive psychopathology on which the AMDP system had been based (Helmchen 1979; Scharfetter 1971). The object of this type of clinical examination was to back up the basic psychiatric and neurologic examination. It consisted of enquiries and simple clinical tests which could detect organic cerebral impairment (Mayer-Gross et al. 1977). Psychologic data were supplemented by the use of neurologic, electroencephalographic, neuroradiologic, biochemical, and other nonpsychologic techniques for the identification of the type and causation of cerebral disorder.¹

For a period of 31 months, 140 patients were studied. Among these, 48 had no rating scales or had ratings by other scales in pilot studies and were omitted by analysis. Patients were rated at the time before the brain blood flow and metabolism studies between 2 or 3 weeks after admission. Within a period of ten days, no medication was given which might alter cerebral blood flow or metabolism. The cross-sectional study of the psychologic and additional data presented in this paper coincided with the results obtained in cerebral blood flow and metabolism studies. Almost all patients with OBSs were seen on the psychiatric wards of the hospital.

The subjects omitted included patients with delirium tremens, stupor, sopor, coma, and other serious illness as described in the Manual of AMDP system (Helmchen 1979; Scharfetter 1971). As a result these types of organic brain syndrome (Bleuler et al. 1966; Plum and Posner 1972) may be under-represented. They might be observed on the emergency services and intensive care units of the medical, neurologic, and surgical wards (Lipowski 1967, 1972).

There was a wide range of age from 19 to 89 years. The rated cases were alcohol-toxic ($n=44$), then due to cerebrovascular disease ($n=31$), primary degenerative ($n=10$), infectious, metabolic, toxic, and other diseases of the brain ($n=7$) (see Table 1 for distribution). In contrast to other studies (Gustafson 1975) alcoholic patients were included, taking into account the increasing problem of alcoholism and the high hospital incidence of alcoholics with organic brain dysfunction and/or damage. Patients of this category were included unless there was good evidence that the given withdrawal syndrome was not full-blown delirium tremens.

Data Collection

Data collection was by the psychiatrist author (G.K.) responsible for clinical assessment. A pre-coded data recording form was used (AMDP see English translation by Ban 1978; Helmchen 1975). It contained items covering mental state, social as well as illness behavior, needs for special care, sleep disorders, autonomic, physical and neurologic symptoms. Closely defined anchor points for items were given in detail by the Manual. Items were adapted from a wide range of descriptive psychiatric literature allowing a balanced delineation of all psychiatric syndromes (for references see Helmchen 1979; Scharfetter 1971).

The form was completed by the psychiatrist at the first interview, but if necessary, further interviews were held with the patient. Psychiatrists taking a residency at this hospital rotated into the acute psychiatric units in groups of two or three, for half a year or one year. They were trained in the rating procedures while participating in clinical trials of psychopharmacological drugs and were supervised by experienced raters. Almost all OBSs were seen by the psychiatrist after admission. For patients who were too physically ill or drowsy with severe degrees of disordered (clouded) consciousness at the time of presentation, the interview was undertaken later, omitting variants of mental state such as sopor, precoma, coma, and delirium tremens. Further information was obtained one month later in the course of the follow-up study (not reported in this paper).

Assessment Measures

In 1969, documentation records 1 to 4 were published of the AMDP system to assess psychiatric syndromes and the effects and side-effects of psychopharmacologic drugs in clinical trials (Helmchen 1975). Psychiatric disorders were traditionally classified into those caused by demonstrable brain damage and/or dysfunction and those in which evidence of cerebral pathology was either lacking or not considered to be a direct cause of behavioral disorder. The former class of disorders constituted OBSs. Psychiatric syndromes belonging to the second category were referred as 'functional' or 'endogen' in German-language psychiatry. This

1 We have to emphasize that in this prospective clinico-biochemical study we have had to deal with global (widespread, diffuse) organic brain syndromes. We concentrated on a diffuse pathology affecting the cerebral hemispheres symmetrically rather than a focal one. Thus, we used a global method in brain blood flow and metabolism studies (Kety and Schmidt 1948, modified by Bernsmeier and Siemons 1953)

Table 1. Characteristics of seven groups by age (years), sex, and etiology

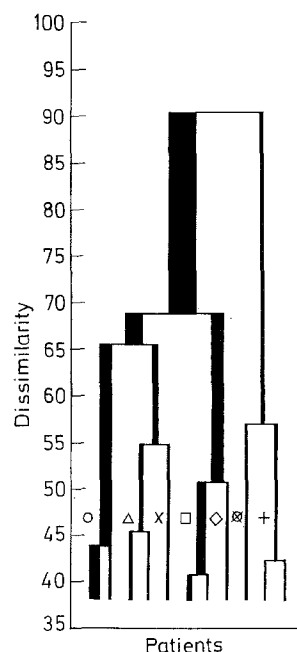
Cluster number	SSC I	SSC II	SSC III	SSC IV	SSC V	SSC VI	SSC VII
Hierarchy	7A	7C	7D	7G	7B	7E	7F
Total:	N = 92 N = 7 ^a	N = 23	N = 10	N = 6	N = 6	N = 6	N = 5
Mean age (years)	56	45	55	42	60	64	72
Range	27–84	23–70	32–73	36–51	46–68	47–79	64–79
Sex: Male	N = 54	21	4	6	4	2	—
Female	N = 31	2	6	—	2	4	5
Etiology ^b							
AD	N = 9		1		2		
MID	N = 29	2	4			4	4
Alcoholism	N = 41	19	2	6	4	2	1
Others ^c	N = 6	2	3				

^a There are seven individual cases that do not fit into any cluster: Heavy metal intoxication, Cushing's syndrome, MID (N = 2), AD (N = 1), and Alcoholics (N = 2) related to the given clinical pictures. AD: Alzheimer's disease; MID: Multiinfarct dementia ('cerebrovascular disease', see Hachinski et al. for references)

^b Etiologic and pathogenic views are neglected on purpose to get descriptive 'cross-sectional' data more transparent

^c The following etiologic diagnoses were made: Heavy metal intoxication (7A), head injury, brain tumor (7C), post-traumatic, glue sniffing, barbiturate intoxication (7D)

Fig. 1. Ward's method: Dendrogram from 11 to 1 symptom-sign clusters (SSCs). ○ Neurasthenia; △ Depression; × Depressed dementia; □ Mild withdrawal; ◇ Severe withdrawal; ⊗ Amnesic syndrome; + Dementia



traditional dichotomy has a practical value, but it should not be viewed as sharp and immutable (Conrad 1972; Huber and Gross 1974; Post 1975; Roth 1978; Schrappe 1972). Many gray areas exist that cannot be fitted readily into one or the other class of disorders (Lipowski 1975).

The items of the AMDP documentation records three and four cover mental state and concern: psychologic impairment and abnormality, or symptom; plus sleep, appetite, autonomic, additional physical and neurologic symptoms in organic cerebral as well as functional syndromes. These syndromes, regardless of their etiology, were described in psychologic terms. There were variables especially relevant to classification of organic brain syndromes, but all items were used in the cluster analysis. These variables are listed in Tables 2 and 3. Components relevant for classification of organic brain syndromes were listed, rather than the original variables of AMDP entered in cluster procedures. The disorder was scored absent, mild, moderate, or severe by zero-, one-, two-, or three-point ratings by the psychiatrist. Additional information was obtained by the resident staff and nurses taking care of the patient on the ward.

Cluster Analytic Procedures

Data were analyzed by Ward's method (Ward 1963) which employs the sum of squared distance of individuals from centroids of their clusters as the clustering criterion, and fuses clusters to minimize this. It has been performed by a Computer program (HGRUP) by A. Rausche, Computer Center, University of Würzburg, Federal Republic of Germany.

Results

Classification Hierarchy

Illustrated in Fig. 1 is the classification dendrogram obtained by Ward's method, fusing from 11 clusters to 1. The length of the vertical line indicates the range of

Table 2. Seven SSCs were significantly different ($P < 0.01$ by χ^2) on the following AMDP variables

Disordered consciousness, orientation, and cognitive functioning: perceiving, remembering, thinking	Psychomotor activity, and social and illness behavior
Twilight state	Exaggerated initiative
Disorientation in time	Motor restlessness
Disorientation in situation	Reduced contact
Disorientation in personal history	Hypochondriasis
Disordered apperception (grasp)	Lack of feeling of being ill
Disordered concentration	Lack of insight into the illness
Disordered attention and immediate memory	
Disordered memory	
Confabulations	Need for special care
Retarded	Patient has to be fed
Restricted	Patient has to be taken care of
Circumstantial	Incontinent of urine and faeces
Perserverating	Difficult to engage in an occupation
Paralogia (tangential talk)	Confined to bed
Mood disorders: Emotional disturbances	Sleep-wakefulness pattern, appetite disorders, and special features of course
Perplexed	
Blunted affect	Difficulty falling asleep
Feeling of affective coldness	Interrupted sleep
Depressed/sad	Only able to sleep for short periods
Hopeless/desperate	Drowsiness during the day
Anxious/fearful	Decreased appetite
Elated/euphoric	Exacerbation at night
Moody/irritable/dysphoric	
Full of complaints	
Emotional lability	
Emotional incontinence	
Emotional rigidity	

fusions over which the cluster was stable. Seven clusters appeared to be the maximum that could be useful. The two-cluster level was stable and worthwhile analyzing, as was the four-cluster level, which was used to examine cluster separation by discriminant function analysis (see below).

Symptom-Sign Clusters (SSCs)

Organic brain syndromes (OBSs) may be defined as psychiatric syndromes presenting as specified psychopathologic symptom-sign clusters (SSCs) that show a regular tendency to occur together (Lipowski 1975). Symptoms and signs were described by the AMDP variables (see Tables 2 and 3).

There was a striking and complete split according to presence or absence of some degree of disordered (clouded) consciousness with severe disorientation (see Fig. 2 for hierarchy). All SSCs, however, manifest clinically a relatively global impairment of cognitive functioning but were differentiated by the degree of severity. The diagnosis of OBSs depends heavily on the evidence of some degree of

Table 3. Seven SSCs were significantly different ($P < 0.01$ by χ^2) on the following AMDP variables

Autonomic symptoms and signs	Neurologic symptoms and signs
Nasal congestion	Increased muscle tone
Dry mouth	Medium or gross tremor
Seborrhea	Nystagmus
Vomiting	Ataxia
Difficulty in urinating	Other neurologic symptoms
Hot flushes	
Chills	
Sweating	
Respiratory disturbances	
Headache: 'Pressure'	
Palpitations	
Dizziness	
<hr/>	
Physical symptoms and signs	
Oedema	
Circulation related symptoms	
Thrombosis-thrombophlebitis	
Menstrual disturbances	
Pruritus	
Parasthesias	
Pale skin	

impairment of these functions, i.e., more specifically, deficits of abstraction, reasoning, and concept formation, generally regarded as impaired information processing. There existed also some differences of other variables such as mood disorders, and affective and emotional disturbances. The SSCs split further on psychomotor activity, social and illness behavior, and need for special care.

1. The largest SSC with 29 subjects was that of Fig. 1. There is some degree of cognitive impairment characterized by disorders of attention, immediate memory, and slowed thought processes. Hypochondriasis and emotional lability are combined with reduced psychomotor activity during the day, nocturnal insomnia, autonomic symptoms, and apathy.

2. The second SSC contained 23 patients, most of whom did not feel ill. They were difficult to engage in an occupation. There was a greater degree of global cognitive impairment and slowed thought processes. They tended to show evidence of blunted (moody, irritable) dysphoric affect. They also showed emotional rigidity and lack of initiative and spontaneity.

3. The third and smaller SSC ($n = 10$) may be regarded as hypochondrical depression described in terms of its component symptoms. Global impairment of cognitive functioning was associated with mood disorder of depression and anxiety. Inner restlessness contrasted with reduced psychomotor activity and social contact. The patients were full of complaint about sweating, hot flushes, headache, dizziness, palpitations, etc. Severe sleep disorders were also present. When feeling ill they rather tended towards regressive dependence on than denial of illness.

4. The fourth SSC contained only six individuals. The SSC was characterized by a high degree of global impairment of information processing and automatic arousal. The most striking features were tremulousness, nystagmus, ataxia, and additional physical symptoms. Patients showed no evidence of insight into the illness. The uncooperative behavior was stressed by tangential talks, reduced contact, and lack of activity. They showed a continuum of disordered mood and affect ranging from the moody, irritable, dysphoric to the elated and euphoric. There were other affective and emotional disturbances such as blunted affect, emotional lability, and rigidity.

5. The fifth SSC also contained only six patients. The combination of memory disorders with gross amnesia for recent events, severe disorientation in time, place, the situation, and personal history, and confabulations made a classical constellation. It was not significant that memory was more disordered than any other cognitive function. They displayed other symptoms, such as defects in perception, impaired concept formation, lack of initiative, and emotional blandness. There was a striking lack of insight into the presence of memory deficit and a tendency to deny its existence.

6. The sixth SSC contained six patients with severe global cognitive impairment corresponding with relatively severe degree of clouded consciousness. Mood disorders and emotional disturbances were mixed, although predominantly elated with reduced impulse control and motor restlessness. There was a total lack of insight into the cognitive deficits and the illness. The constellations of need for special care, exacerbations at night, and exaggerated initiative and spontaneity (disinhibition, impulsiveness) but also drowsiness and tiredness during the day made medical management very difficult. The clinical picture was complicated by neurologic symptoms such as increased muscle tone, tremor, and primitive reflexes.

7. The seventh and smallest SSC contained only five patients. This SSC was also characterized by a relatively severe cognitive impairment, but clouded consciousness was lacking. The patients were not so severely disoriented. The mood disorders were depression and anxiety, although reflecting emotional lability and incontinence. The patients needed special care and their condition was exacerbated at night. They were confined to bed, had to be fed, and were incontinent of urine and feces as the former group. Psychomotor activity was reduced even to the point of apathy. There were many neurologic symptoms such as increased muscle tone, tremor, and primitive reflexes associated with additional circulation related physical symptoms.

New SSCs did appear at further levels. Seven SSCs appeared to be the maximum the data could usefully provide. Seven patients could not be clustered. They represented individual cases. Cluster analysis was well able to discriminate different psychopathological symptoms and circumscribed cognitive, psychomotor, affect, motivation, and/or perceptual disorders and symptomatic functional syndromes relating to paranoid, manic, and schizophreniform psychosis. They may be accompanied by some constellations of cognitive deficits which may be also absent. The following examples show the diagnostic value and security of identifying special syndromes: a female alcoholic patient presented Cushing's syndrome complicated by depression; a second female patient showed a rare

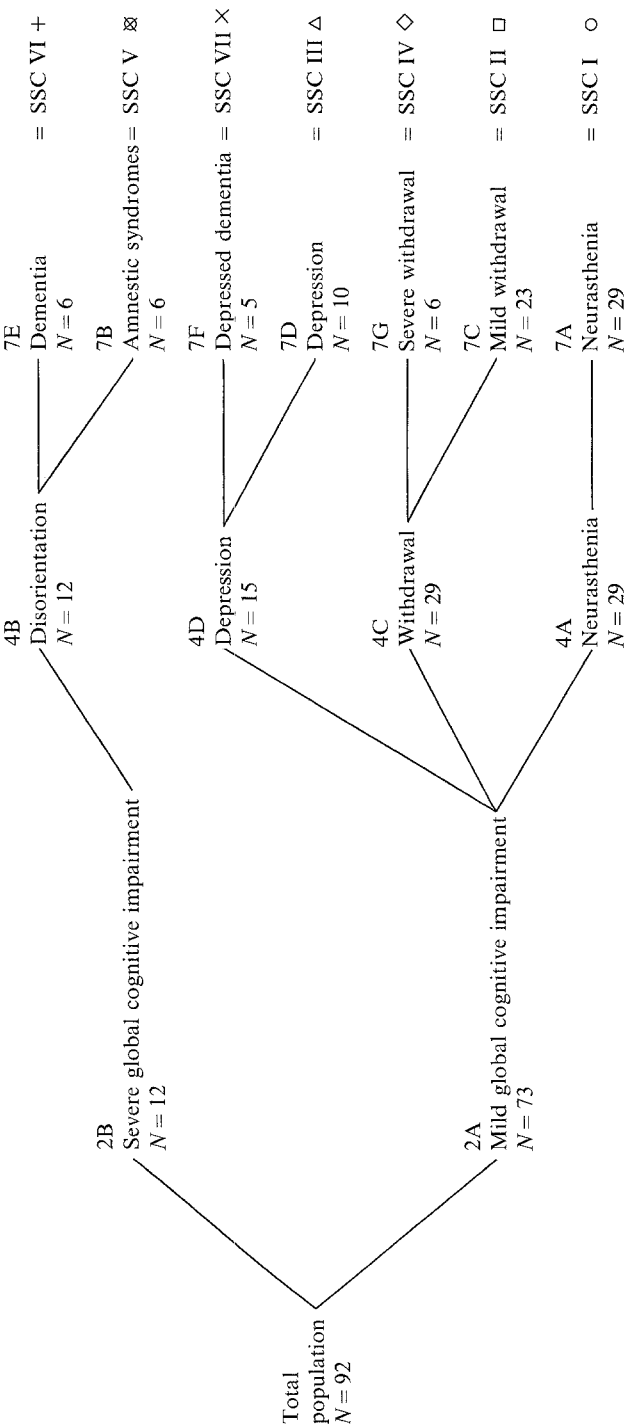


Fig. 2. Hierarchy of symptom-sign clusters (SSCs)

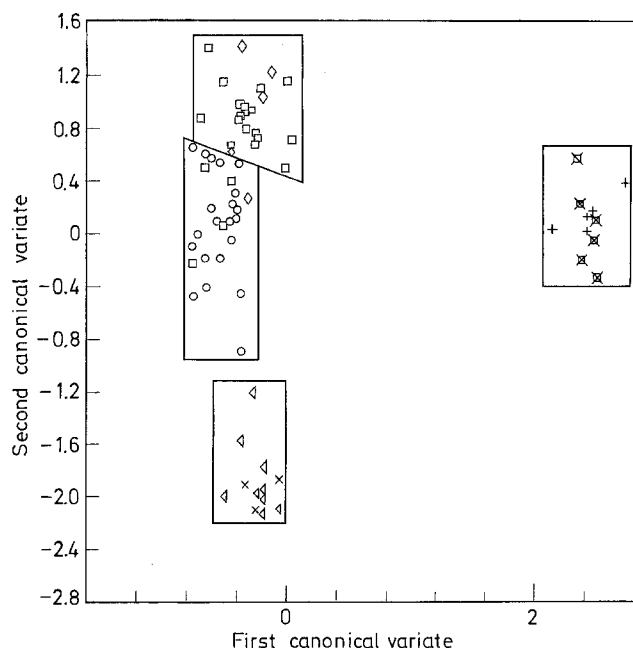


Fig. 3. Four group partition: Plot of patients on first two canonical variates (psychopathology)

clinical picture of bismuth encephalopathy presenting global cognitive impairment, irritability, and specified neurologic features such as tremulousness, myoclonic jerks, ataxia, and clumsiness (Krüger et al. 1976).

Separation of Symptom-Sign Clusters (SSCs)

To examine separation of specified SSCs, the four-cluster level was subjected to a discriminant function analysis, using the original scores on the psychologic and physical symptoms. For the clarity of presentation this level was preferred to the seven-cluster level. Figure 3 displays the clusters on the four discriminant function axes of the four-cluster level. There was good separation between clusters. Discriminant function analysis does not mean a direct attack on the classification problem, because it requires an existing two (or more) cluster classification as a starting point. Given two clusters, weights can be calculated so that the total weighted score ($T = \sum ax$) maximizes the distance between the two clusters. When there are more than two clusters, multiple discriminant function analysis, sometimes called canonical variate analysis, can be used to find those canonical variates which maximize the ratio of between clusters to within group covariance of three or more existing clusters (Garside and Roth 1978).

Discussion

The findings suggest that patients of one psychiatric hospital showing behavior disorders caused by degenerative, vascular, toxic, and other diseases of the brain

can be classified in seven symptom-sign clusters (SSCs) (see Fig. 2). The evidence that seven SSCs comprise the maximum number that can be usefully acquired rests on the hierarchical structure and on conceptual meaning, i.e., reasonable interpretation. The SSCs are ranked due to the number of patients constituting a definite SSC rather than to hierarchical structure, i.e., 7A, 7B, 7C, etc. The largest SSC comprises patients who may be diagnostically labelled in terms of 'emotional hyperesthetic fatigue state' (Bleuler 1975), 'organic neurasthenia' (Mayer-Gross et al. 1977) or 'subacute amnestic-confusional state' (Lipowski 1975). A second smaller SSC is distinguished by denial of cognitive impairment and illness from the first one. A third smaller SSC is characterized by 'depression and hypochondriasis'. The fourth and moderately small SSC covers the 'confusional state' in alcoholics (Victor et al. 1971) reflecting some kind of withdrawal in the absence of delirium tremens according to DSM III (Gross et al. 1974; Spitzer et al. 1977). The fifth and small SSC comprises patients with 'amnestic syndrome' in which clear-cut separation between distinct relatively global (widespread) and selective (focal) organic brain syndromes relating to this cluster of psychopathologic symptoms is not easy. Diagnostically, however, Korsakoff's syndrome is obvious in those patients. The sixth and seventh SSC are characterized by severe degrees of 'global cognitive impairment' with some degree of clouded consciousness in the former. They are distinguished by denial of illness and hyperactivity in the sixth, and regressive dependence and hypoactivity featuring anxiety and depression in various patterns in the seventh.

Comparison with Traditional and New Classifications

Organic brain syndromes often include symptoms readily explained in the term 'emotional-hyperesthetic fatigue state' (Bonhoeffer 1912). Bleuler pointed out that the most frequently encountered organic brain syndromes of this type featured simple moodiness with irritability, anxiousness, or whining (Bleuler 1975). Lipowski distinguished an organic brain syndrome characterized by a potentially reversible global cognitive impairment as 'subacute amnestic confusional state' usually called 'reversible dementia'. This psychiatric syndrome was not only described in terms of its component symptoms, but also by its mode of onset and course. It is usually featured by insidious onset and/or protracted course. In our cases the first and second, and probably the sixth and seventh SSC may fit in this category. This syndrome consists of various constellations of cognitive deficits occurring in the absence of or with only a mild degree of clouding of consciousness. It may be viewed as intermediate form between delirium and dementia.

In the English-speaking psychiatry there is disagreement (Wells 1977 and 1978) about further subgroups between delirium ('acute confusional state', 'acute-on-chronic brain syndrome') and dementia ('chronic brain syndrome') described (Lishman 1978). There is a strong argument in favor of classifications related to etiology and pathogenesis rather than descriptive psychopathology, thus resulting in contradictions between viewpoints of American and the European psychiatry (see ICD 1972; German translation with introduction remarks by Degkwitz et al. 1975). This point was considered recently in the latest

revision of the American Psychiatric Association's Diagnostic and Statistical Manual of Mental Disorders (Spitzer et al. 1977).

Pinsker and Spitzer have stated that the division of organic mental disorders into two disparate categories—the psychotic and the nonpsychotic—was a characteristic of the ICD alien to most American psychiatrists. In organic conditions it is easy to see the severe (psychotic) degree of illness and the mild (nonpsychotic) degree as a continuum. In organic disorders, the individual patient may shift from nonpsychotic to psychotic and back again, as the underlying brain disease changes. The patient with mild cerebrovascular disorder may progress to severe cerebrovascular disorder. Therefore, as in other sections of the classification, many of the organic mental disorders will be classified as mild, moderate, or severe. The term 'organic brain syndrome' was replaced by the broader term, 'organic mental disorders', thus recognizing that there is a spectrum of both physical and mental pathologic processes, and that diagnosis should be made before the degree of global impairment required for the old 'brain syndrome' is reached. The organic mental disorders are divided into three groups: those with relatively global impairment of cognitive or information-processing capacity, those with relatively selective impairment, those that are clinically indistinguishable from some of the nonorganic disorders, such as the affective, paranoid, schizophrenic, and anxious. The etiology of cerebral disorders should be specified, if known (Lipowski 1975; Pinsker and Spitzer 1977).

Depression, which dominated in the third group is to be referred either to depressive psychosis as symptomatic functional affective syndrome or depressive neurosis representing maladaptive modes of coping with autonomic symptoms and global cognitive impairment or both (Folstein et al. 1977; Lipowski 1976; Roth 1978). Irregularly progressive cerebral pathology, as in cerebrovascular disease, introduced elements of uncertainty and unpredictability for the patient and especially, in the early stages may give rise to severe depression and/or anxiety, sometimes with suicidal tendencies (Lipowski 1975; Quandt 1972). This holds true also for deviant illness behavior in organic brain syndromes. Self-destructive lack of compliance with or avoidance of medical management, massive denial of illness on the one hand (Weinstein 1955), and regressive dependence and hypochondrical depression on the other may be regarded as two opposite poles of a continuum with common mixed forms in between (Lipowski 1977).

It is plausible that at least some of the psychopathologic states having their onset in close temporal relationship to organic disease are manifestations of disordered cerebral metabolism or neurophysiologic dysfunction. The practical implication of this is that the clinician must always keep in mind the possibility that any given psychiatric disorder may be a manifestation of a somatic disease whose other symptoms it may overshadow and mask (Krüger 1977; Lipowski 1975; Schrappe 1971).

Victor et al. 1971 carried out a careful study on organic brain syndromes in chronic alcoholism and stressed psychological impairment, deficits, and abnormalities, or symptoms different from delirium tremens and amnesic syndrome. The term they used was 'global-confusional state' in which clouded consciousness might be slight or absent (Victor et al. 1971). In other words, this

syndrome may be described as severe withdrawal without delirium tremens (Gross et al. 1974; Spitzer et al. 1977).

The diagnostic term *amnesic syndrome* designates an organic brain syndrome characterized predominantly by memory pathology. It is reasonable to distinguish this syndrome from memory pathology which represents part of global cognitive impairment resulting from widespread cerebral damage and/or metabolic derangement. This syndrome is regarded as selective in its psychologic manifestations and results from lesions of diencephalic-temporal structures (Talland 1964; Victor 1969; Zangwill 1977). The syndrome can be classified according to the revised DSM III as Wernicke-Korsakoff syndrome or, in other words, amnesic syndrome in a patient with Wernicke-Korsakoff encephalopathy, head injury, encephalitis, carbon monoxide intoxication, and so forth (Spitzer et al. 1977). The disorder of memory does not wholly account for the perceptual disorder and other cognitive abnormalities that characterize Korsakoff's psychosis (Victor et al. 1971). The latter observation confirms the great masters of the clinical and ethological methods (Bürger-Prinz and Kaila 1930; Bleuler 1975). Thus, their descriptions survive because they were based on clear hypotheses.

Dementia is an organic brain syndrome due to cerebral cortical damage and characterized by a relatively global impairment of cognitive function as evidenced in the sixth and seventh group. It has been suggested that the term dementia is antiquated, ambiguous, and misleading (Stengel 1964). Lipowski proposed that the term be retained, if it can be generally agreed to confine its use to essential criteria of descriptive features, the degrees of severity, and the concepts of compensability and modifiability of cognitive deficits. The latter may account for fluctuations in the patient's intellectual performance, which is to some extent independent of the severity of cerebral damage. The cluster of symptoms described herein, represents static and cross-sectional symptom clusters. The value of the descriptive classification is enhanced if temporal features of symptomatology are included. The mode of onset and behavior over time of the psychiatric disorder provide additional etiologic, diagnostic, and prognostic clues. The syndrome should be judged retrospectively on the basis of its course and response to appropriate treatment, if such is currently available (Lipowski 1975; Post 1975).

Comparison with Other Studies

A few studies have used similar methods. Mombour et al. subjected AMDP ratings on 51 patients with organic brain syndromes to factor analytic procedures. The patients were derived from a total of 454 cases with functional syndromes, psychoses, neuroses, behavior, and personality disorders. Workers at the Max Planck Institute have extracted a factor—'organic brain syndrome'—partly covering the items of Lorr' IMPS (Impatient Multidimensional Psychiatric Scale) such as 'disorientation' and 'conceptual disorganization'. The factor 'organic brain syndrome' was more extensive and described all features of the 'diffuse organic psychosyndrome' by Eugen Bleuler (Mombour et al. 1973).

Freudenthal et al. compared the AMDP system and BPRS rating scale as most widely used in English-speaking countries (Overall 1974). They described the factor 'organic brain syndrome' which was not extracted in Zürich by Baumann and Angst (1974) but at the MPI in Munich by Mombour (1973). Their results suggested that the psychopathologic symptoms of AMDP system may allow a more accurate and consistent classification on this type of patient than the BPRS which did not include any disorder of orientation, attention, memory, etc. (Freudenthal et al. 1977). There appears to be much agreement about the usefulness of the AMDP system in classifying organic brain syndromes in those and in our own studies.

Gustafson (1975) has studied psychiatric symptoms in 57 patients with signs of organic dementia beginning in the presenile period (40–65 years of age) by factor analytic procedures. Alcoholics were not included in this study, thus, syndromes of this etiology were not comparable. Some of the factors found in the groups as 'amnesia-apraxia, amnesia-confusion, depression, paranoid, delusion, ixophrenia, hypochondria, explosive temper, affective lability, unsteady gait, anarthria-mutism, psychomotor retardation, and psychomotor overactivity' are described as specified constellations of symptoms in the seven groups of patients classified by cluster analysis in our sample. The latter technique provides a direct attack upon the problem of classification of patients into groups (Garside and Roth 1978). Gustafson et al. (Gustafson and Risberg 1974; Gustafson and Hagberg 1975) had a different aim in using the regional (local) blood flow method.

The present study used Ward's cluster analytic method which produced useful and stable clustering. The symptom-sign clusters obtained lend support to old classifications and the new ones (DSM-III). They suggest the practical value in clinical trials of circulatory agents and metabolic stimulants proving their usefulness as appropriate treatment for some types of organic brain syndromes or lack of response (Hoyer et al. 1977). They require replication against other variables such as cerebral oxidative metabolism and blood flow, follow-up outcome, or response to treatment.

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References

- Ban TA (1978) The AMP-system in English. In: Deniker P, Radonco-Thomas C, Villeneuve A (eds) Proc X. Cong CINP. Pergamon Press, London, pp 15–75
- Baumann U, Angst J (1974) Methodological development of the AMP-system. Neuropsychopharmacology Proc IX. Cong CINP. Paris, cited by Freudenthal et al.
- Bernsmeier M, Siemons K (1953) Die Messung der Hirndurchblutung mit der Stickoxydul-methode. Pflügers Arch Gesamte Physiol 258:149
- Bleuler E (1969) Lehrbuch der Psychiatrie, 11. Auflage. Springer, Berlin Heidelberg New York
- Bleuler M (1975) Acute mental concomitants of physical disease. In: Benson DF, Blumer D (eds) Psychiatric aspects of neurologic disease. Grune & Stratton, New York
- Bleuler M, Willi J, Bühler HR (1966) Akute psychische Begleiterscheinungen körperlicher Krankheiten. Thieme, Stuttgart

- Bonhoeffer K (1912) Die Psychosen im Gefolge von akuten Infektionen, Allgemeinerkrankungen und inneren Erkrankungen. In: Aschaffenburg GL (Hrsg) Handbuch der Psychiatrie, Spezieller Teil 3. Deuticke, Leipzig
- Bowen DM, Smith CB, White P, Goodhardt MJ, Spillane JA, Flack RHA, Davison AH (1977) Chemical pathology of the organic dementias I. *Brain* 100:397
- Bowen DM, Smith CB, White P, Flack RHA, Canasco LH, Gedye JL, Davison AH (1977) Chemical pathology of the organic dementias II. *Brain* 100:427
- Bürger-Prinz H, Kaila M (1930) Über die Struktur des amnestischen Symptomenkomplexes. *Z Gesamte Neurol Psychiatr* 124:553
- Conrad K (1972) Die symptomatischen Psychosen. In: Kisker KP, Meyer JE, Müller M, Strömgen E (Hrsg) Psychiatrie der Gegenwart, 2. Aufl, Bd II/1. Springer, Heidelberg
- Degkwitz R, Helmchen H, Kockott G, Mombour W (1975) ICD: 8. Revision. Diagnoseschlüssel und Glossar psychiatrischer Krankheiten. Springer, Berlin Heidelberg New York
- Freudenthal K, Gebhardt R, Pietzcker A (1977) AMP (PAS) and BPRS: A comparison of two assessment methods. *Psychopharmacopsychiat* 10:57
- Garside RF, Roth M (1978) Multivariate methods and problems of classification in psychiatry. *Br J Psychiatry* 133:53
- Gross MM, Lewis E, Hastey J (1974) Acute alcohol withdrawal syndrome. In: Kissin B, Begleiter H (eds) The biology of alcoholism: Clinical pathology III. Plenum Press, New York
- Gustafson L, Brun A, Ingvar DH (1977) Presenile dementia: Clinical symptoms, patho-anatomical findings and cerebral blood flow. 8th Salzburg Conference on cerebral vascular disease 1976. In: Meyer JS, Lechner H, Reivich M (eds) Cerebral vascular disease. *Excerpta Medica*, Amsterdam, pp 5–9
- Gustafson L, Hagberg B (1975) Dementia with onset in the presenile period. A cross-sectional study. Part I: Psychiatric symptoms in dementia with onset in the presenile period. *Acta Psychiatr Scand (Suppl)* 257:7
- Gustafson L, Risberg J (1974) Regional cerebral blood flow related to psychiatric symptoms in dementia with onset in the presenile period. *Acta Psychiatr Scand* 50:516
- Hachinski VC, Iliff LD, Zilka E, DuBoulay GH, Allister VL, Marshall J, Ross Russell RW, Symon L (1975) Cerebral blood flow in dementia. *Arch Neurol* 32:632
- Helmchen H (1975) The AMP-system as a method in clinical pharmacopsychiatry. In: Hippus H (ed) Assessment of pharmacodynamic effects in human pharmacology. Schattauer, Stuttgart, pp 87–134
- Helmchen H (1979) Das AMDP-System. Manual zur Dokumentation psychiatrischer Befunde. Dritte korrigierte und erweiterte Auflage. Springer, Berlin Heidelberg New York
- Helmchen H, Hippus H (1972) Therapie der organischen Psychosen. In: Kisker KP, Meyer JE, Müller M, Strömgen E (Hrsg) Psychiatrie der Gegenwart. 2. Aufl, Bd II/1. Springer, Berlin Heidelberg New York
- Hoyer S (1977) Blood flow and oxidative metabolism of the brain in different phases of dementia. Workshop—Conference on Alzheimer's disease, senile dementia and related disorders. Bethesda: NIH
- Hoyer S, Krüger G, Weinhardt F (1979) Brain blood flow and metabolism in relation to psychiatric status in patients with organic brain syndromes. 9th Salzburg Conference on cerebral vascular disease 1978. In: Meyer JS, Lechner H, Reivich M (eds) Cerebral vascular disease. *Excerpta Medica*, Amsterdam, pp 151–154
- Hoyer S, Krüger G, Oesterreich K, Weinhardt F (1977) Drug effects on cerebral circulation and oxidative brain metabolism in demented patients. 8th Salzburg Conference on cerebral vascular disease 1976. In: Meyer JS, Lechner H, Reivich M (eds) Cerebral vascular disease. *Excerpta Medica*, Amsterdam, pp 25–28
- Hoyer S, Oesterreich K, Weinhardt F, Krüger G (1975) Veränderung von Durchblutung und oxidativem Stoffwechsel des Gehirns bei Patienten mit einer Demenz. *J Neurol* 210:227
- Huber G (1977) Klinik und Psychopathologie der organischen Psychosen. In: Kisker KP, Meyer JE, Müller M, Strömgen E (eds) Psychiatrie der Gegenwart. 2. Aufl, Bd II/1. Springer, Berlin Heidelberg New York
- Huber G, Gross G (1974) Schizophrenie und Pseudo-Schizophrenie. In: Das ärztliche Gespräch. Köln, Tropon

- Krüger G (1977) Das funktionell gefärbte, dadurch maskierte organische Psychosyndrom als psychiatrischer Akut- und Notfall. *Z Gesamte Neurol Psychiatr* 218:277
- Krüger G, Hoyer S (1979) Psychiatric evaluation of organic brain syndromes in cerebrovascular disease. 7e satellite congrès international de pharmacologie: Pathophysiologie, biochimie et méthodologie pharmacologique des maladies cerebrovasculaires. Reims 1978. Excerpta Medica, Amsterdam
- Krüger G, Thomas DJ, Weinhardt F, Hoyer S (1976) Disturbed oxidative metabolism in organic brain syndrome caused by Bismuth in skin cream. *Lancet* 4:485
- Lauter H (1972) Organisch bedingte Alterspsychosen. In: Kisker KP, Meyer JE, Müller M, Strömgen E (eds) *Psychiatrie der Gegenwart*. 2. Aufl, Bd II/1. Springer, Berlin Heidelberg New York
- Lipowski ZJ (1967) Review of consultation psychiatry and psychosomatic medicine. Part II: Clinical aspects. *Psychosom Med* 29:201
- Lipowski ZJ (1967) Delirium, clouding of consciousness and confusion. *J Neurol Ment Dis* 145:227
- Lipowski ZJ (1972) Psychiatric liaison with neurology and neurosurgery. *Am J Psychiatry* 129:136
- Lipowski ZJ (1975) Physical illness, the patient and his environment: Psychosocial foundations of medicine. In: Arieti S (ed) *American Handbook of Psychiatry*, Vol 4. Basic Books, New York
- Lipowski ZJ (1975) Psychiatry of somatic diseases: epidemiology, pathogenesis, classification. *Compr Psychiatry* 16:105
- Lipowski ZJ (1975) Organic brain syndromes: Overview and classification. In: Benson DF, Blumer D (eds) *Psychiatric aspects of neurologic disease*. Grune & Stratton, New York
- Lipowski ZJ (1977) Physical illness and psychopathology. In: Lipowski ZJ, Lipsitt DR, Whybrow PC (eds) *Psychosomatic medicine: Current trends and clinical applications*. University Press, Oxford
- Lipowski ZJ, Kiriakos RZ (1972) Borderlands between neurology and psychiatry: Observations in a neurological hospital. *Psychiatry Med* 3:131
- Mayer-Gross W, Slater E, Roth M (1977) *Clinical psychiatry*. Tindall, London
- Mayer-Gross W, Guttmann E (1937) Schema for the examination of organic cases. *J Ment Sci* 83:440
- Mombour W, Gammel G, Zerssen D von, Heyse H (1973) Die Objektivierung psychiatrischer Syndrome durch multifaktorielle Analyse des psychopathologischen Befundes. *Nervenarzt* 44:352
- Ogilvie JC (1977) Cluster analysis. In: Wolman B (ed) *International Encyclopedia of Psychiatry, Psychology, Psychoanalysis and Neurology*. Aesculapius, New York
- Overall JE (1974) The brief psychitric rating scale in psychopharmacology research. In: Pichot B (ed) *Psychological measurements in psychopharmacology*. Karger, Basel
- Pinsker H, Spitzer R (1977) Classification of mental disorders, DSM-III. In: Wolman B (ed) *International encyclopedia of psychiatry, psychology, psychoanalysis and neurology*. Aesculapius, New York
- Plum F, Posner JB (1972) *The diagnosis of stupor and coma*. Davis, Philadelphia
- Post F (1975) Dementia, depression and pseudo-dementia. In: Benson DF, Blumer D (eds) *Psychiatric aspects of neurologic disease*. Grune & Stratton, New York
- Quandt J (1973) Significance of psychopathological criteria in initial arteriosclerosis. 6th Salzburg Conference on cerebral vascular disease 1972. In: Meyer JS, Lechner H, Reivich M, Eichhorn O (eds) *Cerebral vascular disease*. Thieme, Stuttgart
- Roth M (1978) Psychiatric diagnosis in clinical and scientific settings. In: Akiskal HS, Webb WL (eds) *Psychiatric diagnosis*. Spectrum Publications, New York
- Scharfetter CH (1971) *Das AMP-System. Manual zur Dokumentation psychiatrischer Befunde*. Springer, Berlin Heidelberg New York
- Schrappe O (1971) Symptomatische depressive Bilder bei Rückbildungsprozessen. In: *Das ärztliche Gespräch*. Tropon, Köln
- Schrappe O (1972) Zur Psychopathologie und Klinik von Psychosen im Involutions- und späteren Lebensalter. *Z Allg Med* 48:1589

- Spitzer RL, Skeehy M, Endicott J (1977) DSM-III: Guiding principles. In: Rakoff VM, Stancer HC, Keckward HB (eds) *Psychiatric diagnosis*. Brunner & Mazel, New York
- Stengel E (1964) Psychopathology of dementia. *Proc R Soc Med* 57:911
- Talland GA (1964) The psychopathology of the amnesic syndrome. *Mod Probl Psychiatr Neurol* 1:443
- Victor M (1969) The amnesic syndrome and its anatomical basis. *Can Med Assoc J* 100:1115
- Victor M, Adams RD, Collins HG (1971) *The Wernicke-Korsakoff syndrome*. Davis, Philadelphia
- Ward JH (1963) Hierarchical grouping to optimize an objective function. *Am Stat Assoc J* 58:236
- Wells CE (1977) *Dementia* 2nd. Davis, Philadelphia
- Wells CE (1978) Chronic organic brain syndromes. *Amer J Psychiatry* 135:1
- Weinstein EA, Kahn RL (1955) *Denial of illness*. Thomas, Springfield
- Wieck HH (1978) Relationship between somatic and psychopathometric variables in disorders of consciousness. *Arch Psychiatr Nervenkr* 225:193
- Willis JH (1976) *Clinical psychiatry*. Blackwell Scientific Publications, London
- Zangwill OL (1977) The amnesic syndrome. In: Whitty CWM, Zangwill OL (eds) *Amnesia*. Butterworths, London

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