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Description of the Disorder: History, Phenomenology, Nomenclature

Delirium: How Its Concept Has Developed

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ABSTRACT. The development of the concept of delirium spans nearly 2,500 years. Its core clinical features were recognized at least as early as the 16th century, while its management reflected a humane approach from the beginning of the modern era. In the 19th century delirium became linked with the concepts of disordered consciousness and confusion, but these two terms were also used in regard to certain functional mental disorders. The most important contribution in this century was the work of Engel, Romano, and associates, who postulated that the syndrome was due to reduction in brain metabolic rate, as reflected in slowing of the EEG background activity. These and other developments are discussed in this article. A list of proposed research priorities is included.

Delirium was one of the first mental disorders to be described by the medical writers (Lipowski, 1990). Greek and Roman writers recognized three main forms of such disorders: mania, melancholia, and phrenitis or delirium. There are many references to delirium in the extant works of Hippocrates (Lipowski, 1990) and thus its history goes back almost 2,500 years.

The term "delirium" was first used by Celsus in the 1st century A.D., but on the whole the word "phrenitis" was used more often in the ancient medical literature (Lipowski, 1990). Aretaeus (Lipowski, 1990), a 2nd century Roman writer, classified diseases as acute or chronic. In the case of mental disorders, phrenitis and lethargy (lethargus) were the chief acute diseases. They were believed to be caused by fever or poisons. While phrenitis typically involved restlessness, insomnia, and hallucinations, lethargy was its opposite, involving undue quietness and sleepiness. Both these disorders were thought to reflect a primary or a secondary brain disease. Despite a strictly organic view of their etiology and pathogenesis, however, the Roman writers recommended treatment for them which included both a physiological and a psychological approach (Lipowski, 1990).

The first description of delirium that I find in the English medical literature appeared in Barrough's textbook *The Method of Physick*, first published in 1583 (Barrough, 1583). He referred to it as "frenesie" and observed that it involved the derangement of three main functions: imagination, cogitation, and memory. It also featured disturbed sleep. Thus, the core clinical features of delirium were already spelled out in the 16th century. In the course of the 16th and 17th centuries a number of dissertations on delirium were published in Germany and Switzerland which elaborated further its characteristics (Lipowski, 1990). In his treatise on mental disorders published in Latin in 1672, Thomas Willis (1683) gave a good description of delirium and pointed out that it was not a disease but rather a symptom, one associated with fever as well as resulting from poisoning, hemorrhage, lack of sleep, and drunkenness. Its core features included "incongruous conceptions and confused thoughts," distorted visual perceptions, and disturbed behavior. One notes that the early writers clearly recognized that delirium involved global cognitive impairment, abnormal psychomotor behavior, and disturbed sleep, that is, diagnostic characteristics that are still considered essential today.

While the description of delirium offered by the early medical writers was strikingly consistent, the relevant terminology was not. The word "delirium" was used in two different senses: first, as a synonym for insanity generally and second, as a designation for an acute syndrome associated mostly with febrile diseases. The first English medical dictionary (Quincy, 1719), for example, stated that mania was "delirium without fever." Quincy asserted that delirium was "the Dreams of waking Persons," a notion that one finds in the medical literature until the end of the 19th century.

In 1746, the first and, to my knowledge, the only early treatise on delirium in English was published by Frings (1746). This author used the term "delirium" to refer to insanity generally and called that which was due to fever "phrensy." Sims (1799) gave a clear definition of delirium as a mental disorder very different from mania and melancholia. It occurred in two main forms: low and raving, respectively.

By far the most sophisticated description of the psychopathology of delirium to appear in the 19th century was that by Greiner (1817). He referred to the syndrome as "febrile insanity," a disorder involving clouding of consciousness (Verdunkelung des Bewusstseins). This was probably the first time that delirium was linked explicitly with disordered consciousness. Greiner offered a remarkably insightful and advanced account of the psychopathology of the syndrome, as well as impressively humane guidelines for its management.

The association between delirium and disordered consciousness was further developed by Hughlings Jackson in the 1860s (Jackson, 1932). He used the syndrome as a modal mental disorder illustrating the application of his concept of the dissolution of the highest nervous centers. Delirium represented a state of reduced consciousness that ranged from the "slightest confusion of thought to coma," and was due to some degree of the dissolution of the topmost layer of the nervous centers and consequent release from inhibition of the evolutionally lower

centers. Thus, delirium came to be viewed as a clinical manifestation of disordered consciousness.

The phrase "clouding of consciousness" became used in this context with growing frequency in the second half of the 19th century, but some writers applied it both to delirium and to certain functional mental disorders such as hysteria (Lipowski, 1990). Bonhoeffer (1912) at the beginning of this century proposed that clouding of consciousness was a core feature of what he called "the exogenous reaction types," that is, acute mental disorders due to systemic diseases affecting the brain secondarily. He viewed delirium as the main such disorder, one that was etiologically nonspecific.

Another term to be linked with delirium in the 19th century was that of "confusion." Introduced by German and French writers (Berrios, 1981; Lipowski, 1990) the word "confusion" referred to an impaired ability to think logically and coherently, impairment of memory, and disordered perception. Like the phrase "clouding of consciousness," "confusion" was often used in relation to the symptomatology of delirium as well as to certain functional mental disorders. Thus, both these usages were really not specific to delirium. From the word "confusion" several terms became derived in the 19th century, notably "acute confusional states" and "acute confusional insanity" (Lipowski, 1990). The meaning of the term "confusion" has never been precise, yet despite its vagueness, it is still commonly used in clinical practice (Simpson, 1984). "Clouding of consciousness, " equally vague, is also often used, even though it has been dropped from DSM-III-R (1987).

The most important contribution to the concept of delirium and its boundaries in this century was the work of Engel and Romano (1959) carried out in the 1940s. They concluded on the basis of their clinical and experimental studies that delirium was a disturbance in the level of consciousness, one manifested by cognitive-attentional disturbances. The syndrome was due to a reduction in the brain metabolic rate, as indicated by slowing of the EEG background activity. The degree of cognitive impairment tended to vary pari passu with the EEG slowing: the greater the impairment, the greater the slowing.

The psychological variables correlating best with the EEG slowing included thinking, memory, and attention. Features such as the level of psychomotor behavior displayed by the patient, that is, hypo- or hyperactivity, as well as his or her emotional state, were not diagnostic. Delirium tremens was viewed by these investigators as a variant of the unified concept of delirium proposed by them, in that the EEG was either normal or showed fast rather than slow activity.

The most innovative aspect of this concept of delirium was the addition of a laboratory indicator of its diagnosis in the form of the diffuse EEG abnormality, as well as the formulation of a hypothesis in regard to its underlying pathophysiology. This hypothesis was further expanded by Blass et al. (Blass, Gibson, Duffy, & Plum, 1981), who proposed that impairment of oxidative metabolism in the brain resulted in reduced synthesis of certain neurotransmitters, notably acetylcholine, whose relative deficiency in the brain was a "common denominator" in metabolic-toxic encephalopathies.

In the 1960s a number of investigators studied delirium induced experimentally in volunteers by administering drugs with anticholinergic activity (Lipowski, 1990). This work highlighted the pathogenic role of cholinergic blockade in delirium and provided a clue to the generally acknowledged proneness of patients with Alzheimer's disease to develop the syndrome. Central cholinergic deficiency in this disease is considered to be one of the putative pathogenic factors in the associated dementia (Cummings & Benson, 1987).

The last phase in the development of the concept of delirium was the formulation of its diagnostic criteria in DSM-III (1980). Until then a terminological chaos had prevailed in the whole area of organic mental syndromes (Lipowski, 1980). "Acute organic brain syndrome" had been used to designate delirium in the official American classification of mental disorders, but medical writers had applied numerous other labels more or less synonymously (Lipowski, 1989, 1990). As a result, communication among clinicians was liable to be poor, and research was hampered.

As a member of the DSM-III Task Force, I was asked to revise the classification of organic brain syndromes (Lipowski, 1980). I proposed that for the sake of historical continuity we should reintroduce the ancient terms "delirium" and "dementia" into the official classification. This proposal was accepted, and a uniform terminology resulted. Moreover, the essential clinical features of the syndrome were spelled out and diagnostic criteria for it were formulated. There is reason to believe that this development has facilitated communication, research, and teaching.

Yet some problems remain: The diagnostic criteria for delirium will need to be sharpened to be more precise for research purposes. The boundary between delirium and dementia, two mental disorders featuring global cognitive impairment, is not clearly demarcated at this time, and this impedes differential diagnosis between them (Lipowski, 1989, 1990). Finally, the distinction between delirium, an organic mental syndrome, and what I refer to as pseudodelirium (Lipowski, 1983) remains unresolved. The elderly patient especially, when experiencing depression, mania, or an anxiety disorder, may exhibit deliriumlike symptoms or "confusion." The same holds for some postpartum psychoses and brief reactive psychosis (Lipowski, 1990). I would propose that a diffusely abnormal EEG record should be introduced as a diagnostic criterion for delirium in contrast to other confusional states.

In conclusion, the concept of delirium has been developed by countless medical writers for over two millennia and has reached a state of relative clarity, consistency, and clinical usefulness. This development should encourage badly needed research on all aspects of the syndrome, notably its epidemiology,pathogenesis, pathophysiology, and prognosis. As the numbers of the elderly throughout the western world increase, one may expect to encounter delirium with increasing frequency. Thus, research is essential in order to develop more effective methods for its prevention and treatment. To stimulate interest in this subject I have listed ten proposed research priorities (see Appendix).

APPENDIX

Delirium: Research Priorities

1. Study aimed at clinical differentiation of delirium from dementia and pseudodelirium.
2. Development and validation of a diagnostic scale for delirium.
3. PET study of the two main variants of delirium: the hypoalert-hypoactive and the hyperalert-hyperactive, respectively.
4. Study of the relationship between disordered sleep-wake cycle and delirium: Is the former a pathogenic mechanism or an independent concomitant of the latter?
5. Study of the relative frequency of etiologic factors in delirium.
6. Study of the incidence of mortality and transition to dementia and other organic mental syndromes.
7. Study of differences in the phenomenology of delirium between older and younger patients.
8. Study of the etiologic role of psychosocial stress in delirium in the elderly —Is hypercortisolemia implicated?
9. Study of the reasons for surgery for a femoral neck fracture being complicated by a high incidence of postoperative delirium.
10. Study of the relationship between delirium and the sundown syndrome.

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