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Catatonia as a putative nosological entity: A historical sketch

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Abstract

Kahlbaum was the first to propose catatonia as a separate disease following the example of general paresis of the insane, which served as a model for establishing a nosological entity. However, Kahlbaum was uncertain about the nosological position of catatonia and considered it a syndrome, or "a temporary stage or a part of a complex picture of various disease forms". Until recently, the issue of catatonia as a separate diagnostic category was not entertained, mainly due to a misinterpretation of Kraepelin's influential views on catatonia as a subtype of schizophrenia. Kraepelin concluded that patients presenting with persistent catatonic symptoms, which he called "genuine catatonic morbid symptoms", particularly including negativism, bizarre mannerisms, and stereotypes, had a poor prognosis similar to those of paranoid and hebephrenic presentations. Accordingly, catatonia was classified as a subtype of dementia praecox/schizophrenia. Despite Kraepelin's influence on psychiatric nosology throughout the 20th century, there have only been isolated attempts to describe and classify catatonia outside of the Kraepelinian system. For example, the Wernicke-Kleist-Leonhard school attempted to comprehensively elucidate the complexities of psychomotor disturbances associated with major psychoses. However, the Leonhardian categories have never been subjected to the scrutiny of modern investigations. The first three editions of the DSM included the narrow and simplified version of Kraepelin's catatonia concept. Recent developments in catatonia research are reflected in DSM-5, which includes three diagnostic categories: Catatonic Disorder due to Another Medical Condition, Catatonia Associated with another Mental Disorder (Catatonia Specifier), and Unspecified Catatonia. Additionally, the traditional category of catatonic schizophrenia has been deleted. The Unspecified Catatonia

category could encourage research exploring catatonia as an independent diagnostic entity.

Key words: Catatonia; Psychomotor disturbances; DSM-5; Nosology; History

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Core tip: Kahlbaum was the first to propose catatonia as a separate disease, whereas Kraepelin concluded that persistent catatonic symptoms (particularly negativism, bizarre mannerisms, and stereotypes) were hallmarks of the catatonic subtype of dementia praecox/schizophrenia. Although the Wernicke-Kleist-Leonhard school attempted to comprehensively elucidate the phenomenology and genetics of psychomotor disturbances associated with major psychoses, the complexity of the Leonhardian catatonia concept has hindered its acceptance in mainstream psychiatry. Kraepelin's influence on psychiatric classifications led to the appearance of catatonia only as a subtype of schizophrenia in the first three editions of the DSM. Progress in this field is illustrated by the inclusion of three forms of catatonia in DSM-5, thus paving the way toward an exploration of Kahlbaum's original concept of catatonia as a distinct disease entity.

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INTRODUCTION

Catatonia, which is generally conceptualized as a syndrome and characterized by a variety of autonomic, behavioral, and psychomotor abnormalities, occurs at high frequencies of 2.7%-17% among psychiatric inpatients^[1]. The existence of different diagnostic criteria for catatonia may explain the diverse range of reported prevalence rates. For example, the simultaneous application of the Bush-Francis Catatonia Rating Scale (BFCRS)^[2] and the DSM-IV and DSM-5 criteria to the same 130 acutely ill inpatients yielded catatonia diagnosis rates of 63%, 25% and 17%, respectively^[3]. This paper outlines the historical development of the concept of catatonia as a distinct disease entity.

FIRST DESCRIPTION OF CATATONIA

Most classical authors, including Guislain, Pinel, Kiesel, Griesinger, and Arndt, described clinical pictures such as "Katalepsie und Psychose", "Melancholia attonita" and "Melancholie avec stupeur"^[4]. These descriptions partly overlap with Kahlbaum's view of catatonia as a condition characterized by unusual motor behavior, affective changes, impaired volition and vegetative

abnormalities^[5,6]. Kahlbaum was the first to propose that catatonia is a separate disease following the example of general paresis among the insane, which served as a model for establishing a nosological entity^[5]. The oft-cited definition of catatonia clearly refers to a distinct disease: "Catatonia is a brain disease with cyclic, alternating course, in which the mental symptoms are, consecutively, melancholy, mania, stupor, confusion and eventually dementia. One or more of these symptoms may be absent from the complete series of psychic symptom complexes. In addition to the mental symptoms, locomotor neural processes with the general character of convulsions occur as typical symptoms"^[5]. Later in the book, however, Kahlbaum was uncertain about catatonia's nosological position and also considered it "a temporary stage or a part of a complex picture of various disease forms"^[5], that is, a syndrome. Kahlbaum's attempt to describe catatonia as a distinct disease entity received mostly critical comments in the international literature, which failed to question his pioneering efforts to coalesce seemingly disparate psychopathological phenomena into a single clinical concept^[7-16].

A factor analysis of 26 cases reported by Kahlbaum in his 1874 book yielded both "neurological" and "psychotic depression" factors: 11 cases exhibited neurological signs, 9 exhibited epileptic seizures, 2 cases each involved tuberculosis and general paresis, and 1 case was affected by delirium due to peritonitis^[17]. This re-analysis led to the conclusion that "There is a difference between what Kahlbaum actually described and what he thought he was describing at the time"^[17].

In the decades following the publication of Kahlbaum's groundbreaking book, catatonic symptoms were described for a host of psychiatric disorders and medical disorders, including mania^[11,13,15,18], depression^[13,14], infectious diseases, toxic states, delirium, mental retardation and syphilis^[8,11]. By the time that seminal papers on catatonia by Seglas and Chaslin^[8], Urstein^[11], Kirby^[15] and Schneider^[19] appeared, the concept of catatonia as a separate disease had largely been discarded and, with the exception of a few authors^[7], the ubiquitous nature of catatonic signs/symptoms and of the catatonic syndrome itself had been generally accepted in classical continental psychopathology, *i.e.*, mainly German and French psychiatry during the second part of the 19th century and the first few decades of the 20th century.

The concept of catatonia as a syndrome in Anglo-Saxon (English and American) psychiatry was revived and confirmed by Gelenberg^[20] some 60 years later. Until recently^[1,2,6], the issue of catatonia as a separate diagnostic category was not entertained, mainly owing to the misinterpretation of Kraepelin's influential views.

Catatonia as part of dementia praecox (schizophrenia)

In addition to the symptoms, illness course, and autopsy findings, the final outcome was a principle used

by Kahlbaum^[5] to construct his nosology. The outcomes of Kahlbaum's 26 catatonia cases were inconclusive: 8 experienced remission and 8 died or became chronic ("demented"), whereas no follow-up information was available for 10 cases^[5].

Kraepelin^[21] followed Kahlbaum's nosological principles. However, only one of his 63 catatonic patients, who were followed up for an average of 4 years, completely recovered. An additional 39 never remitted, and even those who remitted showed residual symptoms. In his 1908 textbook, Kraepelin estimated that 13% of catatonia patients would remit^[22]. A study of 200 catatonic patients observed between 1901 and 1905 reported a remission rate of 19%^[23]. Based on these data and his own clinical experience, Kraepelin concluded that patients presenting with persistent catatonic symptoms he called "genuine catatonic morbid symptoms", particularly negativism, bizarre mannerisms and stereotypes, had a similarly poor prognosis as did those with paranoid and hebephrenic presentations. Thus, catatonia became a subtype of dementia praecox/schizophrenia^[22]. While acknowledging the catatonic symptoms associated with mood-related and other psychiatric illnesses, Kraepelin emphasized that the above symptoms were "more characteristic (and) scarcely accompanying any other morbid process in a pronounced form throughout a long period"^[22]. Kraepelin also emphasized that catatonic symptoms were not diagnostic criteria for dementia praecox and that the inclusion of the catatonia subtype in his classification was temporary: "So far as judgment on the subject is possible today, we may regard the catatonia of Kahlbaum as in the main a form, though peculiar, of dementia praecox. On the other hand, catatonic morbid phenomena are undoubtedly also observed in many quite different morbid processes to a greater or lesser extent, so that its appearance alone does not justify the conclusion that catatonia in the sense just indicated (*i.e.*, as a dementia praecox subtype) is present"^[22].

In conclusion, Kraepelin devised a rather nuanced clinical concept of catatonia, as briefly outlined above. This concept was glossed over for decades, which ascribed to him the simplified view that catatonia equals schizophrenia^[6].

DISTINCT CATATONIA SUBTYPES AS PUTATIVE NOSOLOGICAL ENTITIES

Despite Kraepelin's decisive influence on psychiatric nosology throughout the 20th century, only isolated attempts have been made to describe and classify catatonia outside of the Kraepelinian system.

Lethal (malignant) catatonia

In 1934, Stauder based a description of "lethal catatonia" on 27 cases, with the intent to delineate a separate clinical entity^[24]. Stauder noted that sudden

death in a catatonic state with or without autopsy findings had been well recorded in the psychiatric literature under different names such as acute delirium, Bell's mania, delirious mania, or amentia. Currently, the preferred term is malignant catatonia^[25]. Stauder's lethal catatonia was characterized by a sudden, acute onset occurring mostly in young adults presenting with severe excitement ending in stupor, confusion alternating with mutism, rigidity and other catatonic signs and symptoms, vegetative disturbances, fever, dehydration, cardiovascular collapse and negative findings at autopsy^[25]. Although the outcome in most of Stauder's cases was fatal, mortality has become relatively rare, with a rate of 9% among the 77 cases published since 1986^[25,26]. The consensus view is that malignant catatonia is not a separate entity but a severe form of catatonic syndrome^[25,26]. Advances in neurosciences and clinical neurology have led to the determination of the etiologic agents in cases of malignant catatonia, such as paraneoplastic encephalitis^[27] or anti-NMDA encephalitis^[28].

Most but not all^[29] modern authors regard neuroleptic malignant syndrome (NMS) as an antipsychotic drug-induced variant of spontaneously occurring malignant catatonia^[30]. While the two syndromes share several clinical characteristics and possibly an underlying pathophysiology, notable differences include the lack of a prolonged excitement phase in NMS and the dynamics how the symptoms develop; typically, a few days of extreme excitement ushers in malignant catatonia followed by exhaustion and stupor^[25].

Wernicke-Kleist-Leonhard school of psychiatry

The Wernicke-Kleist-Leonhard school of psychiatry has made a comprehensive attempt to elucidate the complexities of psychomotor disturbances associated with major psychoses^[31,32]. Following Wernicke and Kleist's path-breaking work, Leonard devised the final classification of psychomotor disturbances^[31,32]. While a variety of motor signs and symptoms may appear in several neurological and psychiatric conditions, catatonic symptoms aggregate into persistent, stable syndromes associated with specific cognitive, affective, and psychotic patterns that sharply delineated categories within the schizophrenic and cycloid psychoses. Leonard's system differentiates two major groups of psychomotor syndromes: Cycloid motility psychosis and the systematic and non-systematic catatonic schizophrenias. Motility psychosis, described originally by Wernicke, presents with akinetic and hyperkinetic poles both characterized by episodic course, good prognosis and motor symptoms which, although excessive, differ only quantitatively from normal movements, *i.e.*, lack odd/bizarre qualities). Most modern authors would undoubtedly regard motility psychosis as catatonia^[33].

The six subtypes of systematic catatonias and non-systematic periodic catatonia are distinguished from normal psychomotor patterns by their qualitative and quantitative differences. Unlike motility psychosis,

these catatonia subtypes have a poor prognosis. Once they emerge, systematic catatonias never remit, and the initially episodic course of periodic catatonia may also become chronic. The sophisticated descriptions of catatonic and akinetic-hyperkinetic syndromes cover 57 psychomotor signs and symptoms^[31,32]. A number of cross-sectional and large-scale, long-term (15-20 years) follow-up studies conducted by Kleist, Leonhard and their co-workers confirmed the reliability and stability of Leonhard's classification^[31,32,34-37].

Due to its complexity and dissimilarity to mainstream classifications, Leonhard's nosological system has never been subjected to the scrutiny of investigations using modern methods to validate these putative disease entities beyond the works of dedicated proponents of the Wernicke-Kleist-Leonhard school.

Although Leonhard's catatonia subtypes have been subsumed under the group of schizophrenias, they form distinct entities and have been sharply delineated from the rest of schizophrenia subtypes, thereby constitute relatively independent, albeit putative catatonic disease entities.

Periodic catatonia

Periodic catatonia is not recognized by the ICD-10 or any version of the DSM. This nosological category is not well established, and there is no consensus regarding the relevant diagnostic criteria except for the Wernicke-Kleist-Leonhard classification, which has hardly been acknowledged by mainstream psychiatry. Discussions regarding periodic catatonia have always raised two continuously unresolved nosological issues: Whether it is a separate disease entity or just a variant of catatonia with an episodic course and whether it is a clinical form of bipolar affective disorder^[22,26].

Catatonia with episodic presentation was recognized as early as 1894, when Nacke coined the term "Katatonie alternans"^[38]. Bleuler^[38] described similar cases and stated that "we recognize catatonias which run a periodic course". Kraepelin^[22] presented several vignettes on periodic catatonia while discussing periodic, agitated, and circular dementias, and the catatonic forms of dementia praecox, but concluded rather dismissively that "some of the smaller groups will in course of time be got rid of [...] namely for the cases [...] with a periodic course"^[22]. However, he did not proceed with an argument regarding why these cases should not be included among the catatonias^[22].

Despite its marginal place in nosology, in clinical practice periodic catatonia attracted the first rigorous investigations in biological psychiatry that spanned more than four decades. The father and son duo Rolv and Leiv Gjessing devoted a lifetime of research to periodic catatonia, a special form of schizophrenia. The subjects of their investigations were patients in whom catatonic stupor and excitement occurred with rhythmic periodicity over long periods and were regarded as two facets of the same pathophysiological process. The

catatonic condition was painstakingly recorded and correlated with biochemical variables. Cyclic alternations in the nitrogen balance were observed to follow changes in the clinical presentation simultaneously with the catecholamine metabolism, autonomous nervous system, and EEG findings^[39,40]. These findings have not been confirmed or refuted by other investigators using modern methods of neurobiology. The treatment of periodic catatonia with large doses of thyroid hormone to correct the nitrogen imbalance was made obsolete by the introduction of antipsychotics and lithium, which proved to be effective^[41].

The Wernicke-Kleist-Leonhard school paid much attention to the clinical and genetic aspects of periodic catatonia, one of the three non-systemic schizophrenic psychoses characterized by polymorphous clinical presentation and a cyclic/bipolar course, which not infrequently becomes chronic^[31]. In addition to psychotic symptoms, the specific catatonic features include the tendency of the two poles (stupor and excitation) to alternate, or appear simultaneously with signs/symptoms of impulse/aggression preparedness, affective tension, parakinesis, stiff/choppy movements, grimaces (particularly in the upper part of the face), iterative motor stereotypes, and negativism. Extensive clinical genetic studies conducted by Leonhard and his pupils confirmed the high familial incidence of homotypical psychoses in periodic catatonia, yielding a cumulative morbidity risk of 26.9% among first-degree relatives^[32,42]. Subsequent and ongoing genome-wide linkage investigations identified two susceptibility loci on chromosomes 15q15 and 22q13^[43]. These findings await replication by independent investigators.

Idiopathic catatonia

Ever since Kahlbaum conceptualized catatonia as a putative disease entity, there have been proponents of this idea although it has never gained currency in mainstream psychiatry. Recent reports suggest that in a significant minority of cases a catatonic syndrome appears without any underlying diagnosable psychiatric disorder or medical condition^[33,44-49]. Case reports of presumably idiopathic catatonia describing clinical presentations that did not meet modern diagnostic criteria for any psychiatric illness^[33,47-49] correspond to the traditional Leonhardian categories of periodic catatonia or motility psychosis^[33]. Two studies from India compared idiopathic catatonia with catatonic schizophrenia ($n = 13$ vs $n = 21$)^[45] and depression with catatonic schizophrenia ($n = 30$ vs $n = 35$)^[46]. Idiopathic cases differed from the controls by shorter duration of illness, a preponderance of female patients^[45], reduced overall psychopathology as measured by the Brief Psychiatric Rating Scale (BPRS), and higher scores regarding specific catatonia features, particularly negativism, waxy flexibility, Mitgehen, and ambitendency^[46]. Further studies are warranted to replicate and extend these preliminary findings. The new DSM-5 diagnosis of Unspecified Catatonia will be the

appropriate category for idiopathic catatonia in psychiatric classification.

CATATONIA IN SUCCESSIVE EDITIONS OF DSM

In the first three editions of DSM catatonia appeared only as a subtype of schizophrenia following a narrow and simplified version of Kraepelin's catatonia concept.

A landmark paper by Gelenberg^[20] heralded the rediscovery of catatonia as a syndrome based on knowledge known since Kahlbaum's time that catatonic signs/symptoms are found in several medical and neurological conditions. Reflecting this paradigm shift in modern psychiatry, the new category of Catatonic Disorder Due to a General Medical Condition was introduced in DSM-IV while still retaining the category of Schizophrenia, Catatonic Type^[50]. As catatonic syndromes were observed with increasing frequency in patients with mood disorders^[51], Catatonic Features was added as a specifier to describe mood disorders more accurately. Catatonic features could be diagnosed if 2 of the 5 composite signs/symptoms were present. Over the past 20 years, the number of publications on catatonia has grown significantly^[52]. Rating scales^[53] have been constructed and clinical^[54], treatment^[55], and biological studies^[56] have appeared. Books^[26] and review papers^[57-59] have helped make clinicians cognizant of the clinical significance of catatonia. The development in the field is mirrored in DSM-5^[60], which includes three forms of catatonia: Catatonic Disorder Due to Another Medical Condition, Catatonia Associated with Another Mental Disorder (Catatonia Specifier) and Unspecified Catatonia. The traditional category of catatonic schizophrenia was deleted. The diagnostic criteria for the first two categories are identical and require the presence of 3 out of 12 common catatonic signs/symptoms, including stupor, catalepsy, waxy flexibility, mutism, negativism, posturing, mannerism, stereotypy, agitation, grimacing, echolalia and echopraxia.

Unspecified Catatonia, an independent category in DSM-5, is an entirely new, potentially important development in the recognition of catatonia as a distinct diagnostic entity^[61]. However, this category remains ambiguous toward catatonia as a separate diagnosis because it was intended to be applied to conditions where "either the nature of the underlying mental disorder or other medical condition is unclear, full criteria for catatonia are not met, or there is insufficient information to make a more specific diagnosis". Uncertainty about the nosological position of catatonia is demonstrated by the placement of the three catatonia diagnoses in the Schizophrenia and other Psychotic Disorders section. Nevertheless, the catatonia concept espoused by DSM-5 constitutes a major step forward and will stimulate the exploration of a separate catatonia diagnosis in clinical practice. Additionally, this concept will foster research^[1], particularly if the soon-to-

be published ICD-11 follows a similar path.

CONCLUSION

The validity and clinical utility of catatonic schizophrenia in the traditional Kraepelin-Bleuler classificatory system is limited. In an attempt to replace the Kraepelin-Bleuler model, the dimensional approach reaches beyond the classical concept of catatonic schizophrenia. Complex neurobiological and clinical investigations, including the quantification of individual or clusters of catatonic signs and symptoms, have recently taken shape within broadly defined groups of mood disorders and psychoses^[62-64]. This dimensional approach reduces bias attributed to the narrow and uncertain nosological categories.

The catatonia concept espoused by DSM-5 constitutes a promising step forward by stimulating the exploration of a separate catatonia diagnosis in clinical practice. It could also foster research^[1], such as whole-genome association, epigenetic, and metabolomics studies, particularly if the soon-to-be published ICD-11 is similar to DSM-5.

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