The evolution of Kraepelin's nosological principles

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Emil Kraepelin developed a new psychiatric nosology in the eight editions of his textbook. Previous papers have explored his construction of particular diagnoses, including dementia praecox and manic-depressive insanity. Here we are providing a close reading of his introductory textbook chapter, that presents his general principles of nosology. We identify three phases: 1) editions 1-4, in which he describes nosological principles in search of data; 2) editions 5-7, in which he declares the mature version of his nosological principles and develops new disease categories; 3) edition 8, in which he qualifies his nosological claims and allows for greater differentiation of psychiatric disorders. We propose that Kraepelin's nosology is grounded in three principles. First, psychiatry, like other sciences, deals with natural phenomena. Second, mental states cannot be reduced to neural states, but science will progress and will, ultimately, reveal how nature creates abnormal mental states and behavior. Third, there is a hierarchy of validators of psychiatric diagnoses, with the careful study of clinical features (signs, symptoms and course) being more important than neuropathologic and etiological studies. These three principles emerged over the course of the eight editions of Kraepelin's textbook and were informed by his own research and by available scientific methods. His scientific views are still relevant today: they have generated and, at the same time, constrained our current psychiatric nosology.

Key words: Kraepelin, psychiatric nosology, psychiatry textbook, psychoses, clinical pictures, disease forms, scientific naturalism, natural kinds, validators

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Emil Kraepelin (1856-1926) proposed the diagnoses of dementia praecox and manic-depressive insanity in an effort to advance the clinical management and scientific study of the psychoses. Previous papers have explored the history of these diagnostic concepts[1-4]. Here we focus on Kraepelin's general principles of psychiatric nosology, which guided his classification of psychiatric disorders. The primary source texts are the eight editions of his textbook, published between 1883 and 1913[5-16].

Textbooks served an important function when psychiatry emerged as an academic discipline in the second half of the 19th century[17-19]. In those early days of academic psychiatry, it was not clear how best to teach the subject and how to develop research programs[17,20]. On a pragmatic level, textbooks provided a source of income and facilitated the teaching of psychiatry to medical students and assistant physicians. More importantly, textbooks allowed authors to articulate and disseminate their perspective of psychiatry in general, and psychiatric nosology in particular.

TEXTBOOKS BEFORE KRAEPELIN

Kraepelin referenced five textbooks that helped him write his own. Three are less relevant here: the fourth edition of Griesinger's textbook[21], published posthumously in 1876; the textbook by Emminghaus[22], published in 1878 when he was Kraepelin's medical school teacher, and a compendium by Weiss from 1881[23]. The other two are crucial for Kraepelin: the textbooks of Schüle (2nd edition in 1880)[24] and Krafft-Ebing (2nd edition in 1883)[25].

H. Schüle (1840-1916) rose to prominence as asylum director (he turned down several offers to chair psychiatry departments) and as journal editor. He published three editions of his widely-read textbook, known for rich, and sometimes convoluted, language[26].

R.F. von Krafft-Ebing (1840-1902), trained with Schüle, subsequently chaired three psychiatry departments (Straßburg, Graz and Vienna), and was a prolific author of several books, including seven editions of his psychiatry textbook. The last edition was translated into English[27].

Kraepelin acknowledged their influence when he introduced his own nosology of psychiatric disorders: "The sequence and delineation I have chosen … follows in its fundamental conception the systems constructed by Schüle and v. Krafft-Ebing"[7, p.239; 8, p.244].

All three authors – Schüle, Krafft-Ebing and Kraepelin – included a chapter in their textbooks that summarized their general principles of psychiatric nosology.

Schüle proposed a complex and confusing psychiatric nosology[28]. He separated psychiatric disorders into psychic, organic and psychic-organic types. He also distinguished cerebropsychoses (diffuse brain diseases that always affect the motor system) from psychoneuroses (diseases of the mind, not accompanied with brain changes). The resulting nosology was a hybrid of clinical description and etiological speculation, supported by neuropathological findings, if available.

Krafft-Ebing was more practical. He acknowledged three types of nosologies (anatomical, etiological and clinical) and distinguished three major diagnostic groups: illnesses without pathological findings, illnesses with pathological findings, and neurodevelopmental disorders.

In the first three editions of his textbook, Kraepelin's introductory chapter *The Classification of Psychoses* followed the tradition of Schüle and Krafft-Ebing. In the fourth edition, he broadened the title to *The Nosology of Mental Disorders*. We translated the eight editions of this chapter (which we will refer to as the "nosological chapter"), in order to study the evolution of his nosological principles (see Table 1 for details). In our view,

Kraepelin developed his nosology in three phases: editions 1-4, editions 5-7, and edition 8.

PHASE 1: EDITIONS 1-4

First edition

Kraepelin published the first edition of his textbook in 1883, at age 26. He had completed medical school in 1878 and psychiatric training with the anatomist-psychiatrist B. von Gudden (1824-1886) in 1882. In February 1883, he accepted his first psychiatric position, as first assistant to the department chairman P. Flechsig (1847-1929) in Leipzig. After less than four months, Flechsig dismissed Kraepelin[29].

In his *Memoirs*, Kraepelin wrote: "My situation in Leipzig was very uncertain. I tried to help myself out of my difficulties by accepting the offer to write a compendium of psychiatry"[30, p.25].

The first edition of Kraepelin's textbook was indeed a Compendium, a concise compilation, primarily for students. The next three editions were a Short Textbook and the final four editions became the Textbook. Kraepelin dryly stated: "Nothing new is to be expected in a compendium, however, as far as my own experiences sufficed, I have strived for a degree of independence in the presentation"[5, p.VIII].

The nosological chapter of the Compendium was brief. In three pages, Kraepelin reviewed anatomical, etiological and clinical-symptomatic approaches to psychiatric classification. He considered pathological anatomy and etiology to be of limited value, and concluded that clinical presentations had to provide the basis of a preliminary classification. His assessment was in line with Krafft-Ebing's one: "What it offers us are not illnesses, but merely symptom complexes"[5, p.189].

The Compendium included the chapter *The supporting sciences and methods of psychiatric research*, which was not continued in the subsequent editions of the textbook. Here Kraepelin described, in general terms, how neuroanatomy and experimental psychology can support the pathological study and clinical characterization of mental disorders. The influence of his two mentors – the anatomist B. von Gudden and the experimental psychologist W. Wundt (1832-1920) – is unmistakable. Three years later, Kraepelin used much of this chapter for his inaugural lecture as the new psychiatry chair at Dorpat University[30, 31].

Second and third edition

The next two editions of Kraepelin's textbook appeared during his chairmanship in Dorpat (now Tartu), Estonia (1886-1890). He wrote in his *Memoirs*: "I was forced to publish a second edition of my little text-book, which was completed in 1887; a third edition followed in 1889. The unfavorable circumstances of my clinical activity meant that I had to stay on the tracks already taken, without making any particular progress"[30, p.43].

But this is not the full story. In fact, the nosological chapter in the second edition advanced a new vision for psychiatry: "Were we to be in possession of a thorough and exhaustive knowledge of all details in one of the three fields, namely pathological anatomy, etiology or symptomatology of insanity, not only would each of them allow a uniform and thorough division of the psychoses, but *each of these three groups would also – this requirement is the cornerstone of all scientific research – coincide substantially with the other two*"[6, p.211] (italics added).

This single final sentence captured the essence of Kraepelin's philosophy of science and remained largely unchanged in all subsequent editions. In the third edition, he elaborated on the "three fields of knowledge" and added a fourth set: "The cases of illness which occurred due to the same causes would in each case have to display the same phenomena and the same post-mortem findings. It follows from this fundamental view that the clinical classification of mental disturbances has to be based on all three of the classification aids, to which one must add the experience gained from course, outcome and treatment"[7, p.238].

This text in the second and third edition of the textbook anticipated a core concept of current nosology: any classification is preliminary but, in the end, validators will converge and psychiatric disorders will be defined at the level of the brain. It is remarkable that the text appears so early in Kraepelin's career, considering his own assessment of the limited opportunity for clinical research available to him in Dorpat[32]. Only after his move to Heidelberg in 1891 was he able to collect enough clinical material to develop and then support his new nosology.

Despite a lack of available data, Kraepelin made two important claims. First, psychiatric disorders in general, and psychoses in particular, are what philosophers call *natural kinds*: they reflect the structure of the natural world, being discovered rather than invented[33,34]. He asserted that progress in psychiatric research is possible only if validators converge on natural kinds. This is in contrast to the view that psychiatry should be limited to studying the mind[35,36].

Table 1 The nosological chapter in Kraepelin's textbook

Kraepelin's place of work	Leipzig	Dorpat		Heidelberg				Munich
Year of publication	1883	1887	1889	1893	1896	1899	1904	1910
Edition (volume)	**1**	**2**	**3**	**4**	**5**	**6 (2)**	**7 (2)**	**8 (2)**
Die Klassifikation der Psychosen (pages)	187-189	209-212	235-240					
Die Einteilung der Seelenstörungen (pages)				239-245	311-320	1-9	1-12	1-19

Second and third edition used the spelling "Classification" instead of "Klassifikation". Fourth, fifth and sixth edition used the spelling "Eintheilung" instead of "Einteilung".

Second, the various methods of psychiatric research complement each other. Researchers might start from very different vantage points, but their results will converge.

These conjectures became a focus of criticism for a number of his detractors[37]. Kraepelin already anticipated such criticism of his strong naturalism in the third edition of the textbook: "The more the forms which have been gained from the different views correspond, the greater the certainty that the latter really represent particular disorders"[7, p.238].

Kraepelin recognized that psychiatric disorders are not all the same. Some will likely have higher convergent validity than others. This allowed for a hierarchy within psychiatric nosology, with high convergent validity being the closest to the ideal of a natural kind. It also meant that his classification of psychoses may include diagnoses with only modest convergent validity.

Despite his strong philosophical claims, Kraepelin was a pragmatist when designing his classification scheme: "I have not constructed an actual classification and have contented myself with simply placing a number of empirically gained clinical pictures alongside each other"[6, p.211].

There is considerable tension between Kraepelin's bold vision for a new psychiatric nosology and his traditional classification. The first sign that this tension will lead to a rupture is seen in his fourth edition.

Fourth edition

In 1891, Kraepelin left Dorpat to become chair of psychiatry in Heidelberg. The fourth edition of his textbook, published in 1893, represented a transition towards the more mature form of his psychiatric nosology, which he achieved during this chairmanship in Heidelberg (1891-1903).

Much of the nosological chapter in the fourth edition is unchanged from the two previous ones. But Kraepelin added: "There simply exist no pathognomonic symptoms in the field of insanity; instead only the comprehensive picture of a case of illness, in its development from the beginning to the end, justifies inclusion with other similar observations"[8, p.242].

And he advocated for a new method of painstaking, longitudinal studies: "Every psychiatrist knows that we sometimes encounter cases which in every respect, in the manner of emergence, all details of the symptoms, and further course, present a downright baffling similarity to each other. Such observations will form the natural starting point for our classification endeavors"[8, p.243].

Here he anticipated the significant changes of the fifth edition: for the discovery of natural kinds in psychiatry, clinical observation needs to take the lead.

PHASE 2: EDITIONS 5-7

Fifth edition

The *Foreword* of the fifth edition of the textbook, published in 1896, announced a significant change in Kraepelin's nosology: "In the development of this book, the current edition means the last decisive step from a symptomatic to a clinical perspective of insanity. All pure 'clinical pictures' (*Zustandsbilder*) have thus disappeared from the nosology"[9, p.V].

The change to a clinical perspective is a paradigm shift[38] in Kraepelin's nosology: the *symptom complexes* of the Compendium have been replaced by the concept of unitary diseases[39-41].

Kraepelin elaborated on the clinical perspective in the *Introduction*. First, course and outcome have become primary validators: "As soon as we are able to predict, based on the current condition of a patient, the most likely further development of his affliction with a degree of certainty, then the first important step towards a scientific and practical command of the clinical picture has occurred"[9, p.3].

Second, he asserted a causal structure for psychiatric disorders and the special role of clinical observation: "In the course of mental illness, the same causes also have to have the same effects everywhere. If we encounter, as we so often do, seeming deviations from this law, then, without a doubt, either the causes or the effects have not really been the same. Once we have managed to process clinical knowledge to such an extent that we can construct clinical groups with particular causes, symptoms and courses, it will become our task to penetrate the essence of individual pathological processes"[9, pp.4-5].

Finally, a new paragraph in the nosological chapter summarized his mature nosology: "The first task of the doctor at the sickbed is to form a judgment about the further course of the case of illness. The value of each diagnosis for the practical task of the psychiatrist is therefore essentially determined by how far in the future certain forecasts can be made. The same cause of illness will generally also determine the same course of the affliction, and from the clinical symptoms we have to be able to read the further fate of our patients in broad strokes"[9, p.315].

Kraepelin used his new nosological framework to make significant changes to the classification of Schüle and Krafft-Ebing. In fact, with this edition of the textbook and going forward, he no longer referred to them. Kraepelin even added a new subtitle to pages 317 and 319: *Eigene Eintheilung (Own Division)*. He made three major changes.

First, he introduced an etiological dichotomy: acquired mental disorders versus mental disorders due to a pathological predisposition. The former are disorders of a previously normal brain, often with acute onset, and caused by exogenous poisons, brain injury or metabolic disorders; the latter are conditions that arise insidiously in an already abnormal brain.

Second, metabolic disorders are caused by an endogenous poison, a process he called autointoxication, and include endocrine disorders, general paresis and dementing processes. Kraepelin acknowledged that an endogenous poison is only "certain" for the first group, but considered such etiology "most likely" for the other two. The dementing processes are a prequel version of dementia praecox and already include three subtypes: dementia praecox (later termed hebephrenia), catatonia and dementia paranoides.

Third, while dementia paranoides was part of the dementing

processes within the metabolic disorders (i.e., an acquired disorder), paranoia (*Verrücktheit*) was classified as a constitutional mental disturbance (i.e., due to a pathological predisposition).

These were remarkable changes in the classification of psychiatric disorders. Kraepelin made bold claims about distinct disease mechanisms and etiology, especially his speculation about autointoxication and the separation of dementia praecox from paranoia. He now needed to find more evidence from clinical studies to support his new nosologic vision.

Sixth edition

Kraepelin published the sixth edition in 1899, just three years after the previous one. The textbook had grown in size and was now published in two volumes. The nosological chapter was largely unchanged. But Kraepelin revised his classification scheme.

First, he abandoned the etiological dichotomy of acquired and predisposed disorders from the fifth edition. Second, metabolic disorders were split into thyroid conditions and his mature concept of dementia praecox, which now included hebephrenic, catatonic and paranoid subtypes. With this split, he acknowledged more clearly the different forms of autointoxication.

Third, Kraepelin introduced manic-depressive insanity. Together with paranoia (*Verrücktheit*), he defined the new disorder as "an insanity where, in its formation, more and more, a pathological predisposition comes to the fore"[11, p.7].

The sixth edition is of crucial importance for our understanding of the diagnoses of dementia praecox and manic-depressive insanity, but it did not introduce any new general principles to his nosology.

Seventh edition

Kraepelin wrote the *Foreword* to the seventh edition while still in Heidelberg. However, when the two volumes were published, in 1903 and 1904, he was already the new chair of psychiatry in Munich.

The nosological chapter grew from 9 to 12 pages, but did not change substantially. The added new text included an important clarification: "In the course of the same disease process, it was obvious that completely divergent phenomena followed each other, even seeming to indicate the complete opposite. From this arose the clearly recognized necessity, especially by Kahlbaum, to distinguish between temporary clinical pictures and disease forms. A scientific diagnosis can never be content with the determination of a clinical picture, but instead has to shed light on the disease process belonging to a picture"[13, p.4].

Kraepelin inherited the concept of disease form (*Krankheitsform*) from K. Kahlbaum (1828-1899) and E. Hecker (1843-1909), the latter of whom wrote in 1871: "There is an urgent need in psychiatry for a new nomenclature, which allows differentiation between the manifestations and the true clinical disease forms"[42].

What Kraepelin started in the fifth edition had now matured into such a new psychiatric nosology. With his longitudinal observations of large patient samples, he was convinced that he had established true disease forms. The psychiatric researcher could now go beyond a purely descriptive classification and establish a framework for the scientific exploration of psychiatric disorders. Kraepelin built on this in the last edition of his textbook, and used the momentum to build the first research institute devoted to psychiatric disorders.

PHASE 3: EDITION 8

Eighth edition

The eighth and final full edition of the textbook was published in four volumes, between 1909 and 1915. Kraepelin finished writing the last volume in October 1914, three months into World War I[30].

This edition included a wealth of new data (tables, figures, microphotographs of histological specimens) and extensive citations of other researchers. As a result, the nosology was more complex. For example, dementia praecox grew from three to eleven subtypes, as a result of which the dementia praecox chapter grew from 107 to 354 pages. Furthermore, a late-onset subtype was carved out as a novel diagnostic category and given a new name: paraphrenia.

Similarly, the nosological chapter grew from 12 to 19 pages. The ambitious paragraph from the second edition was largely unchanged, but now covered all psychiatric disorders: "If we achieve the goal we have in mind, the recognition of the actual disease processes by means of our clinical descriptions, then the different delineation efforts, whether they occur from a pathological-anatomical, etiological or a purely clinical standpoint, have to finally coincide with each other. I view this requirement as the keystone for the scientific research of mental disturbances"[15, p.14].

It was this unbridled enthusiasm for scientific progress that allowed him to raise considerable funds, in the throes of World War I, for the German Psychiatric Research Institute, which opened in April 1918 and later became the Max Planck Institute of Psychiatry[43-45].

We view the eighth edition as the start of a third, humbler phase of Kraepelin's nosology. As he was approaching retirement in the early 1920s, he published a thoughtful critique of his own classification scheme, questioning the dichotomy of dementia praecox and manic-depressive insanity[46]. But he never changed his mind about the task of psychiatric nosology and the way to make progress in psychiatric research[47].

PRINCIPLES OF KRAEPELIN'S NOSOLOGY

We propose that Kraepelin's nosology evolved over thirty years, from the first (1883) to the eighth (1915) edition of his textbook.

His nosology began with the thesis that psychiatry, like other sciences, deals with natural phenomena. Scientific naturalism is the first principle of his nosology.

At the same time, Kraepelin did not believe that mental states can be reduced to neural states. But he was confident that the proper scientific methods will, in the end, reveal how nature creates abnormal mental states and behaviors. His strong belief in scientific progress is the second principle of his nosology.

Kraepelin was initially undecided about the best approach to make progress in psychiatry. But, after years of longitudinal studies, he concluded that clinical course and outcome were the most important validators in our search for the yet unknown natural disease units. His hierarchy of validators is the third principle of his nosology.

In Table 2 we provide a synopsis of his mature nosology (taken from the eighth edition of his textbook). Table 3 contains a glossary of his main nosological terms. Below we briefly review his three nosological principles.

Scientific naturalism

Psychiatric disorders are natural kinds. They can be validated with the methods of natural science. In the end, all validators will converge on natural disease units. This principle – the first and most important one - attracted many critics[37,48].

A. Hoche (1865-1943), Kraepelin's main academic adversary in the early 20th century, rejected natural disease units and argued that there are only symptom complexes: "We are barking up the wrong tree with this unremitting search for definitive, pure syndromes of a physical kind"[49, p.341].

A. Meyer (1866-1950), who communicated many of Kraepelin's ideas to his American colleagues, remained critical: "Kraepelin bends the facts of psychiatric observation to the concept of disease processes"[50, p.274].

More recently, Weber and Engstrom examined Kraepelin's *Zählkarten* (diagnostic cards) and criticized his "positivist clinical research agenda": "Condensing patient reports was already an interpretative process – a cognitive discrimination and scientific assessment impossible without preconceived categories which Kraepelin had acquired outside, before, or perhaps despite his clinical observations"[51, p.379].

Many contemporary critics of Kraepelin have focused on scientific naturalism as an indefensible philosophical position[35,40,52]. In contrast, the psychiatrist-turned-philosopher K. Jaspers (1883-1969) viewed Kraepelin's principle more favorably[53,54]: "The idea of the disease-entity is in truth an idea in Kant's sense of the word: the concept of an objective which one cannot reach since it is unending; but all the same it indicates the path for fruitful research and supplies a *valid* point of orientation for particular empirical investigations"[54] (italics added).

The view that natural disease units have heuristic value is relevant for Kraepelin's next nosological principle, his unshakeable trust that psychiatry will make progress.

Scientific progress

Kraepelin finished the introduction to the fifth edition of his textbook on an optimistic note: "Psychiatry is a young, still developing science, that must, against sharp opposition, gradually achieve the position it deserves according to its scientific and practical importance. There is no doubt that it will achieve this position – for it has at its disposal the same weapons which have served the other branches of medicine so well: clinical observation, the microscope and experimentation"[9, pp.10-11].

He kept the paragraph in all subsequent editions. Where did Kraepelin see the "sharp opposition" against psychiatry? In his 1918 monograph *One Hundred Years of Psychiatry*[55], he described how empirical research had overcome unscientific views of the human mind.

But Kraepelin was acutely aware that the scientific understanding of psychiatric conditions was uneven. For some clinical presentations there was a clear cause, e.g., an exogenous agent. For many other clinical syndromes, however, disease mechanism and etiology were unknown. Kraepelin viewed advances in scientific methods as the primary drivers of progress. For example, he cited the histological stains by Nissl and Weigert[55, p.86]

Table 2 Synopsis of Kraepelin's nosology (quotes from the 8th edition of his textbook)

"The task of psychiatric nosology is the delineation of individual *disorders* (*Krankheitsformen*) and their grouping according to unified viewpoints. The completion of the first task occurred previously almost exclusively according to the most prominent illness phenomena."[15, p.1]
"Only the purposeful distinction between *clinical pictures* (*Zustandsbilder*) and disorders has made an adequate nosology possible. A diagnosis currently means the recognition of the underlying *disease process (Krankheitsvorgang)* of a particular type in the given clinical picture."[15, p.1]
"We can only view a *disease concept* (*Krankheitsbegriff*) as final and clearly delineated once we are precisely informed about the causes, the phenomena, the course and outcome of the affliction, finally, also about the peculiar anatomical changes."[15, p.2]
"The careful splitting of the forms into their smallest and seemingly insignificant variations… is thus the indispensable precursor for the obtainment of truly uniform *disease pictures which correspond to nature* (*der Natur entsprechende Krankheitsbilder*). Analysis is followed by synthesis… Only observation of the further course will clarify which of the numerous small deviations in the illness phenomena have a close relationship to the nature of the disease process, and based on this permit a recognition of its peculiarity."[15, p.11]
"The method of conducting experiments – in the border region between two illnesses – with diagnostic features, until predictions have achieved the greatest possible degree of reliability, delivers practically useful disease concepts, of which we can assume that they are as close as possible to *natural disease processes* (*natürliche Krankheitsvorgänge*)."[15, p.13]

Table 3 Glossary of Kraepelin's main nosological terms

Nominalist terms
***Disorder (Krankheitsform)*:** The basic unit of psychiatric nosology.
***Clinical picture (Zustandsbild)*:** The cross-sectional description of psychopathology.
***Disease concept (Krankheitsbegriff)*:** Initially a nominalist definition of a psychiatric disorder. When final, it links causes with all clinical phenomena and explains course and outcome.
***Disease process (Krankheitsvorgang)*:** The evolution of clinical pictures over time. Only longitudinal observations can reveal this active process.

Realist terms
***Disease picture which corresponds to nature (der Natur entsprechendes Krankheitsbild)*:** A nosological entity that represents nature.
***Natural disease process (natürlicher Krankheitsvorgang)*:** A process occurring in nature, giving rise to clinical phenomena.

Kraepelin blends nominalist with realist views. The nominalist terms are descriptive and preliminary: they allow us to assign a diagnostic label. The realist terms capture what nature has revealed to us. For Kraepelin, psychiatric nosology progresses, through conjecture and refutation, from constructivism to realism. Kraepelin was not always consistent in the use of his terms[48].

and the serological test by Wasserman[55, p.90] for their impact on revealing new disease mechanisms.

His pragmatic approach to classification included the recognition that mental states cannot be reduced to neural states. In fact, Kraepelin embraced the psychophysical parallelism of his mentor W. Wundt[56] in the Compendium: "Only with the close connection of brain pathology and 'psycho-pathology', it is possible to discern the laws of the interrelationship between physical and mental disturbances and thus advance to a true, deeper understanding of the phenomena of insanity"[5, p.3].

The juxtaposition of scientific naturalism and psychophysical parallelism in Kraepelin's nosology has puzzled many, including W. de Boor in his 1954 review of psychiatric nosologies: "It is astonishing to see how Kraepelin put the need for a dualistic methodology with regard to the somatological and psychopathological side of psychiatry programmatically at the beginning of his work, in order to largely neglect this principle in its nosology"[57, p.20].

As Kraepelin developed his nosology, he recognized that psychiatric disorders are not created equal. As a consequence, he had to determine the method best suited to reveal the etiology and disease mechanism of each psychiatric disorder.

Hierarchy of validators

During Kraepelin's time, some psychiatric disorders had already been validated with biological measures. The neuropsychiatric syndrome in the end stage of syphilis, known as dementia paralytica or general paresis, may serve as the most compelling example[58].

But, for the majority of psychiatric disorders, biological validation was not available to Kraepelin – and is still lacking today[59]. Kraepelin disagreed with T. Meynert (1833-1892), the prominent anatomist and inaugural chair of psychiatry in Vienna, and his student C. Wernicke (1848-1905), that neuroanatomy is the premier method in psychiatry: "The statement by Wernicke that all mental disorders with anatomical findings have approximately the same underlying disease process, can be refuted due to the advances of science"[15, p.3].

Following Kahlbaum[60], Kraepelin established disease course and outcome as the primary validators for psychiatric disorders. But it was not until the fifth edition of his textbook, after he and his assistants had collected longitudinal data in Heidelberg, that Kraepelin declared his hierarchy of validators. Once he had established it, he embraced prediction (of course and outcome) as the most important task of the psychiatrist. This hierarchy of validators might be Kraepelin's most impactful contribution to psychiatric nosology[61,62].

CONCLUSIONS

The principles of Kraepelin's nosology are still relevant today[39]. But we have not been able to hold them together in the way Kraepelin did.

On the one hand, current diagnostic systems (such as the DSM[63] and ICD[64]) have implemented a simpler, nominalist view of mental illness[65]. In such nosologies we diagnose *disorder*, rather than *disease*, which suffices for clinical and forensic practice[66]. *Disorder* avoids premature assumptions about etiology and, by doing so, may reduce stigma and bias[67]. Psychiatric diagnoses also serve many functions in society, only some of which are scientific[68,69].

On the other hand, psychiatric research favors a realist view: causal models of disease allow for stronger hypothesis testing[70]. Accordingly, research communities have established hierarchies of validators that fit their research methods and inference testing[62,71].

The DSM-5 Scientific Review Committee embraced a hierarchy of validators to guide the revision process[72]. But psychiatric clinicians and researchers assess validators differently and often speak a different language[73,74]. As a result, the training of psychiatrists has lost its footing[75]. This is different from the start of the 20th century, when Kraepelin's nosology promised progress in the education of both clinicians and researchers[76,77]. We are still searching for the best avenue to make progress in the nosology of psychiatric disorders[71].

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