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CHAPTER 1

From Mania to Bipolar Disorder

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From Pinel to Kraepelin

When the first asylums opened, around 1800, mania was a generic term for insanity. Philippe Pinel's *Treatise on Insanity* that appeared in 1800 was accordingly named *Traité sur la Manie*.

For 2000 years before Pinel, the chief determinant of diagnosis in medicine lay in the visible presentation of the patient. These visible presentations could lead to reliable diagnoses of tumours, diabetes, catatonia, epilepsy and insanity. The visible presentations of insanity involved flushing, overactivity and maniacal behaviour. Mania was diagnosed in patients who were overactive and who might now be seen as having schizophrenia, depression, delirium, senility, imbecility and other conditions.

Pinel took a stand on the importance of science in medicine, and was the first to call for an Evidence Based Medicine. Faced with patients hospitalized for years, he was the first to incorporate the course of a patients' disorders into his diagnostic considerations. He recorded outcomes where patients were treated or left untreated, and noting responses followed by relapses, argued that some disorders were periodic or recurrent and that the vast majority of available treatments made the underlying condition worse.

When a final and more complete version of his treatise was published in 1809, it distinguished in its title, *Traité Médico-Philosophique sur l'Aliénation Mentale ou la Manie*, between insanity in general and a new, more specific diagnosis of mania [1]. Once this distinction was made, and mania was separated out from idiocy dementia and melancholia, the rates of admission for mania settled at approximately 50% of all admissions in asylums in Europe and America until around 1900.

While asylum nomenclature remained relatively constant for a century, there was an evolution in the thinking about insanity. The idea that there might be a distinct mood faculty that could be disordered in its own right was put forward in the 1830s by one of Pinel's pupils, Jean-Dominique Etienne Esquirol, who described profound sadness – lypemanie – as a distinct disorder.

The notion of a disease entity took shape in the 1850s when two of Esquirol's pupils, Jean-Pierre Falret and Jules Baillarger, both described disorders that laid the basis for what became circular insanity. Falret outlined *folie circulaire*; Baillarger termed his disorder *folie à double forme* [2].

The idea that mania or insanity might give rise to protean manifestations had posed little difficulty, but as clinicians moved towards the concept of a disease entity, they had difficulties with the idea that two clinical states that looked so different might be presentations of the same underlying disease state. In their efforts to overcome these conceptual problems, both Falret and Baillarger posited a disorder with alternating cycles of mania and melancholia of fixed length and with fixed intervals between episodes. But crucially if neither the superficial features of mania nor the superficial features of melancholia accounted for the disorder, then some common ground between them must be responsible for the disorder. Some substrate must be diseased.

The new disorder was not one that commanded clinical attention. Both men conceded that what they were describing was a rare condition. The condition described was moreover at this point not clearly a mood disorder. Others described alternating or circular insanity. None of these states were bipolar affective disorder, as that term would be understood today.

The first to approach modern bipolar disorder was Karl Kahlbaum who in 1883 described cyclothymia. Where circular insanity was a psychotic disorder, with regular and stable features that led to degeneration, cyclothymia was for Kahlbaum a specific mood disorder from which patients could recover.

Kahlbaum also introduced disease course as a classificatory principle, but this was resisted. Most academics at the time expected a localization of clinical features in different brain areas to provide the key to unlocking the mysteries of mental illness rather than disease course. However disease course was used by Charcot to distinguish between hysteria and Tourette's syndrome, and later to distinguish between Alzheimer's and Creutfeld-Jacob disease.

Bipolar Disorder: Clinical and Neurobiological Foundations
Edited by Lakshmi N. Yatham and Mario Maj

Manic-depressive illness

In 1899, building on a series of syndromes first outlined by Kahlbaum, and on his principle of disease course, but eschewing brain localization, Emil Kraepelin distinguished between two disease entities – dementia praecox and manic-depressive insanity [3]. Dementia praecox was a disorder of cognitive function where the sufferer never returns to normal. Within this group, Kraepelin included three disorders outlined by Kahlbaum – hebephrenia, catatonia and paranoia.

Given that clinical course was to be the main determinant of disease status, if in the one case recovery was to be the exception, there had to be a contrasting state in which recovery was the norm. Manic-depressive illness therefore emerged as the foil to dementia praecox. Kraepelin's manic-depressive illness was a disorder where sufferers recovered from acute episodes but were at risk of a relapse.

For Kraepelin, a bipolar alternation between excitement and stupor could not be a classificatory principle in that a similar alternation happens in many states of dementia praecox or general paralysis of the insane. But periodic, circular and simple manias, in addition to melancholic disorders, could all be regarded as manifestations of the one illness if they showed a remitting course.

Involutional melancholia brings out the rigidity with which Kraepelin held to a disease course criterion. These classic depressive psychoses had their onset over the age of 50, when patients typically presented with disturbed sleep and appetite, diurnal variation of mood and either paranoid, nihilistic or guilt-laden delusions. In 1899 Kraepelin thought that these patients were much less likely to recover than other patients with mood disorders. Clinicians now would have no doubt that this condition was a mood disorder. However, because involutional melancholia apparently failed to remit, it posed difficulties for Kraepelin. As a result, he kept involutional melancholia separate from manic-depressive illness until the eighth edition of his textbook.

Kraepelin's distinctions between two almost identical clinical presentations (involutional and non-involutional melancholias) and amalgamation of what appeared to be quite different clinical presentations (unipolar and bipolar affective disorders) produced an illness concept that almost certainly baffled many of his contemporaries.

The puerperal psychoses further clouded the diagnostic picture. Kraepelin's compelling descriptions of a characteristic confusion and fleeting hallucinatory features in these psychoses, as well as their unstable cycling states, made a good case for a separate diagnosis to either dementia praecox or manic-depressive illness. But his disease course criterion left him no option but to argue that they were in all cases either manic-depressive insanity or dementia praecox.

Between these puerperal psychoses and good prognosis psychoses with cycloid features, there was a group of patients accounting for close to 10% of admissions for serious mental illness, double the number of admissions for bipolar affective disorder, but these all disappeared from view, because polarity did not count for Kraepelin as a classificatory principle.

The reception of manic-depressive illness – the academic response

When Kraepelin's work was discussed both within and outside of Germany, it was largely in terms of dementia praecox. For a quarter of a century, there was little mention of manic-depressive illness.

In America, Kraepelin's clinical approach was welcomed by Adolf Meyer as the breakthrough psychiatry was waiting for, although he later criticized it as being too neurological, and failing to place the patient's disorder within the context of their life story.

In Britain, there were regular references to Kraepelin's work at psychiatric meetings and in the academic literature, in a way that did not happen with other German formulations [4]. These references were to dementia praecox; some disliked the term dementia and some disliked praecox, but the concept was widely discussed, whereas manic-depressive illness was rarely raised.

The French did not accept that all psychotic disorders had the same degenerative clinical course, distinguishing instead between acute and chronic psychoses and amongst a variety of chronic non-deteriorating psychoses. The discovery of chlorpromazine in France validated traditional distinctions between the chronic psychoses and schizophrenia, on the basis that schizophrenia was poorly responsive to antipsychotics [5].

Nevertheless, from 1900, dementia praecox swept rapidly into use for a number of reasons. First, many psychiatrists had been struggling with the same issues and had come up with variants of the same idea from primary dementia to adolescent insanity. Kraepelin's formulation balanced simplicity and complexity. It was more complex than simply adolescent insanity but much simpler than making distinctions amongst the chronic psychoses, as the French and Kahlbaum had done.

Second, before 1900, diagnoses across medicine were made on the basis of the visible presentations of patients at admission, giving rise to diagnoses of consumption, ague, debility or mania. These diagnoses were essentially descriptions of the presenting problem. Following the triumph of bacteriology, after 1900 there was a move to defer diagnoses to later in the course of the admission, after the appropriate laboratory tests had been done and there had been more time to consider which, amongst a number of differential diagnoses, best accounted for the features of the illness. This

applied also to psychiatry, so that from 1900 diagnoses were less likely to be made on admission, bringing the likely chronicity of a patient's illness to the fore as a diagnostic feature. The time was convenient for Kraepelin's new ideas.

In contrast, while there were many formulations of early onset dementia, Kraepelin's manic-depressive illness concept was quite idiosyncratic. The new illness also introduced a new nomenclature. Why manic-depressive illness? Why not manic-melancholic disease, given that almost all the 'depressions' Kraepelin was faced with were melancholic in terms of their severity and clinical features? The answer may lie in a quirk in the man – he had a partiality for novelty. Melancholia was an old-fashioned word. Depression was creeping into use. The first major paper on depressive illness had come a few years earlier, in 1886, from the Danish neurologist Carl Lange [6].

When it came to manic-depressive insanity, Kraepelin's concept may have ultimately survived, because he had picked a name that worked. Names as well as concepts have survival value. But it took a quarter of a century for the new illness to achieve recognition, as data from North Wales indicates.

The reception of manic-depressive illness: a typical asylum

The North Wales Asylum, which opened in 1848, offers an opportunity to look at the uptake of concepts like Kraepelin's. In North West Wales, the overall population and ethnic mix was almost precisely the same in 2000 as it had been in 1900.

Elsewhere, because of geography and rising wealth, a growing number of people had a choice of hospitals. Because of this choice, it is difficult to know how representative patients, ending up in the public or private asylums across the Western world between 1800 and 1950, were of the mental illness happening in their communities of origin. In North West Wales, because of enduring poverty and geography, those with mental illnesses had nowhere to go except to one asylum.

The resulting asylum records and case registers for modern admissions shed light on a number of issues. The first is the impact of Kraepelin's diagnoses of dementia praecox and manic-depressive illness on clinical practice within Britain. The second set of issues has to do with quantitative aspects of the syndromes underpinning Kraepelin's diagnoses.

The first thing that strikes any reader of the asylum records is that up until 1900 over 50% of patients admitted apparently had mania (Figure 1). As late as 1900, patients who were suicidal, patients with senility, and patients with what now would be called schizophrenia, were all labelled as manic. However, manic-depressive illness was not dramatically more common 100 years ago than it is now. The

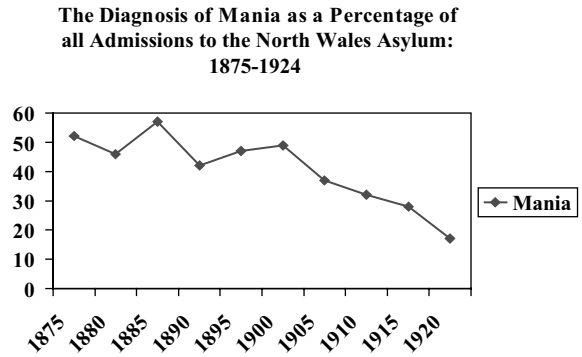

Fig. 1 The diagnosis of mania as a percentage of all admissions to the North Wales Asylum: 1875–1924.

explanation for this finding is, as outlined above, that a diagnosis of mania referred to any state of overactive insanity. Around 1900, primarily in response to Kraepelin's impact, the use of mania as a diagnosis in North Wales began to fall, and it fell progressively to the current rate of less than 5% of patients.

Two questions arise. First, when do modern diagnoses emerge in the records and, second, how many manics had what would now be diagnosed as having in fact bipolar affective disorder? The contrasting reception of dementia praecox and manic-depressive illness helps bring these points out and can be seen in the cases of Bessie Hughes and William Thomas.

Bessie Hughes was a 17-year-old girl admitted on 16 October 1905 with hebephrenic and catatonic features. She was noted to be a good case of dementia praecox. The records indicate that up until then a case like Bessie's would have been diagnosed as melancholia with stupor. The term dementia praecox thereafter rapidly came into use in North Wales, and was not replaced by schizophrenia in these records before 1949.

In contrast, William Thomas had been admitted in 1891 at the age of 45, having been looked after at home by his family for a number of years. A businessman, who had travelled back and forth between Wales and Argentina, his family wondered if his first breakdown 17 years previously, from which he had recovered at home, had stemmed from an engagement to a Catholic woman, or whether it had been triggered by the general alarum that had accompanied an outbreak of Yellow Fever. He had recovered and continued working until his early 40s, when his family committed him to the asylum where he remained until his death.

On admission, in contrast to most patients, he seemed far from manic in the sense of agitated or overactive. After some days, grandiosity and probable delusional beliefs became apparent. Periods of elation alternated with mute and almost catatonic states, and he settled down to a cycle of episodes of depression, followed by overactivity and periods of lucidity. In 1904, 13 years after admission, the notes

indicate that his alternating states were being viewed as circular insanity. The reference to circular insanity is the first of its kind in these records, but the overall diagnosis remained mania and never became manic-depressive illness.

In 1906, a national conference on the classification of insanity in Britain introduced a new set of diagnoses. This system proposed a new disorder, primary dementia, which was the equivalent of Kraepelin's dementia praecox.

The new national classification system subdivided mania and melancholia into recent, chronic and recurrent mania or melancholia, and introduced the term alternating insanity. None of these terms were used in North Wales but dementia praecox was and it was this that led to the fall in the frequency of diagnoses of mania.

Within the affective disorders domain, RO, who was admitted in 1908 and discharged in 1909, was diagnosed with maniacal depressive insanity – a disorder not on the list. In fact, this odd use of words was a better description of his case than a diagnosis of manic-depressive insanity would suggest, in that he only presented on one occasion, showing features of agitated (or maniacal) depression without any alternation of mood.

Despite the example of RO, except for clearcut cases of dementia praecox, other cases continued to be diagnosed as having mania or melancholia rather than alternating insanity or manic-depressive illness. It was not until the 1920s that we begin to find diagnoses of manic-depressive illness appearing.

In September 1920, a 30-year-old sailor, RP, was admitted with grandiose beliefs and violent behaviour. He remained in hospital for over a year, during which time he had attacks of agitation at regular intervals. On discharge he was diagnosed as manic-depressive. This man was readmitted two years later and spent most of the following 15 years as an inmate of the asylum, during which time he was noted to have a clinical state that alternated from manic to depressive poles on a one month cycle.

The diagnosis only came into regular use in 1924. In that year, three cases were diagnosed as manic-depressive. One was AA, whose records from 1924 outline a 60-year-old woman who had two admissions for what would now be diagnosed as psychotic depression – no hint of mania. ER, also admitted and diagnosed in 1924 as manic-depressive, had a postpartum psychosis. In 1924, WH had her tenth admission, and during this admission she was diagnosed as manic-depressive. There had been nine previous admissions starting from May 1900, mostly for mania, none of which led to this diagnosis. Later in the 1920s, the pattern of taking previous episodes into account takes hold, and also a willingness to make the diagnosis if the person during the course of one admission has distinct spells of elevated and depressed moods.

In addition to mirroring the wider resistance to Kraepelin's concept of manic-depressive illness, the asylum records reveal a quantitative factor to this resistance. During the historical period 1875–1924, there were 3872 admissions from North West Wales. These came from 3172 patients. Amongst patients admitted for the first time during the 1875–1924 period, only 127 (4%) had what retrospectively appears to be a bipolar disorder. Against the background population of North West Wales, this rate of admission gives rise to 10 cases per million per year, a rate that remained constant across the 50-year period, and continues to hold true today [2,7].

In contrast, there were 1041 patients with non-affective psychoses, who between them had 1304 admissions, and 658 admissions from 568 individuals for severe depression or melancholia. These melancholias account for 17% of all admissions and over 80% of the manic-depressive cohort. Without inclusion in a larger manic-depressive group, bipolar patients would have been close to invisible, and this may have been a factor that led Kraepelin to collapse these disorders into one entity.

From this perspective, it is clear why concepts such as *folie circulaire*, *folie a double forme* or alternating insanity were simply not used in a working asylum like Denbigh before 1900. Too few patients were involved. The viability of the modern concept of a bipolar affective disorder depends critically on the diagnosis of hypomanic or cyclothymic states in the community.

Of the patients with retrospective bipolar diagnoses admitted to the North Wales Asylum, 60% were female, compared to the 66% Kraepelin reported. The average age of first admission was 32 years old, with the youngest admission being for a 17 year old. The average length of stay in hospital for any one episode was 6 months. Almost all patients went home well, with only a very small proportion having continuous fluctuations in clinical state that precluded discharge. This group of 127 patients had 345 admissions and on average each person had 4 admissions every 10 years.

Today the district general hospital unit serving the same area has a slightly higher proportion of female admissions. The average age of first admission is 31 years old. The average length of stay is a month. But bipolar patients have 6.5 admissions every 10 years. There is therefore a substantial increase in admission prevalence [7].

In the 1875–1924 cohort, 80% of the admissions for bipolar disorder were for manic presentations. Today, over 50% of the admissions from bipolar patients are for depression. Thus either the presentation of the illness is changing, or treatment is having an impact on presentations, or we have a greater sensitivity to episodes of depression that would formerly not have led to admission.

The records also shed light on involutional melancholia. When patients with melancholia admitted to North Wales Asylum between 1875 and 1924 were tracked for length of stay and rates of recovery, broken down by age, one

might have expected, if Kraepelin was right, that those who had an episode of melancholia in their 50s and 60s would have much longer lengths of stay and a much lower rate of recovery. Also patients with melancholia in their 50s and 60s had a somewhat lower rate of recovery, but this was in fact governed by the greater likelihood that they would die in hospital from physical illness. The length of stay of those patients who did not die in hospital was the same as those who had an onset of the disorder earlier in life. Overall patients admitted in their 30s or 40s were 1.2 times more likely to recover than patients admitted in their 50s or 60s, hardly the behaviour of a distinct disorder [8].

Between 1875 and 1924, puerperal psychoses accounted for close to 10% of admissions of women of childbearing years and 3% of admissions overall (Table 1). This disorder was as common as bipolar affective disorder. Two different sets of women were admitted with postpartum psychoses. The larger of the two sets were women who had no mental illness prior to the postpartum period. A smaller group (20%) were women with a prior mental illness [9].

In the modern period, psychoses with a first onset in the postpartum period in North West Wales have all but vanished, while the incidence of postpartum psychoses in women with a pre-existing mental illness remains the same. Data from across Europe support these findings. If so, this would support claims that these disorders are distinct from other disorders. Alternately, if regarded as affective disorders, establishing the basis for the apparent decline in frequency of these disorders may have implications for other affective disorders.

Table 1 The incidence of postpartum psychoses in North West Wales: 1875–1924 vs. 1994–2005.

	1875–1924	1994–2005
All Female Admissions	1946	3956
All Women	1577	1827
All Women of Child-Bearing Age	1100	1032
All Postpartum Psychotic Admissions	103	7
All Women with Postpartum Psychoses	101	7
Women with no prior Mental Illness	80	1
Women with Prior Mental Illness	21	6
Postpartum Cases/All Admissions from Women of Child-Bearing Age	9.2%	0.68%
All Postpartum Cases/1000 Births	0.34	0.19
Postpartum Onset Cases/1000 Births	0.26	0.03
All Postpartum Cases/100 000 Childbearing Yrs	3.43	0.94
Postpartum Onset Cases/100 000 Childbearing Yrs	2.70	0.13

The emergence of bipolar disorder

A new chapter in the affective disorder story opened up in the psychotropic era. By this time, Manic-Depressive Illness had become a stable and accepted category, and anomalies such as calling someone who only ever had depressive episodes manic-depressive no longer registered.

Two factors brought about a change. First, in 1954, Mogens Schou demonstrated that manic states responded to lithium. Second, in 1957, Karl Leonhard distinguished amongst affective disorders on the basis of polarity, separating manic-depressive illness from pure melancholia and pure depression. Several prominent European and American researchers picked up his lead. The effect of lithium appeared both to endorse the existence of a bipolar subgroup within manic-depressive illness, and put a premium on the diagnosis of a mood disorder rather than a psychotic disorder. Combined, these developments underpinned the emergence of bipolar disorder in the mid-1960s and its incorporation into DSM III in 1980. DSM III was badged as a neo-Kraepelinian revolution in psychiatry.

As of 1980, bipolar disorder was still embedded within the affective disorders, of which depression was the most important. The research focus was on distinguishing between subtypes of depression so that biological markers might be discovered. The failure to discover such markers was widely attributed to the heterogeneity of the samples being studied and this had led to proposals to distinguish between neurotic and psychotic, primary and secondary, reactive and endogenous depressions and other distinctions including bipolar and unipolar depression. In the early 1970s, the bipolar/unipolar dichotomy looked amongst the less fruitful avenues of research, in that clinically there was less to distinguish bipolar and unipolar depression, for instance from neurotic and psychotic depressions or endogenous and reactive depressions.

As of 1980, the effects of pharmacological and biological dissection of nervous disorders seemed more likely to lead to distinctions between ever smaller groups of disorders rather than the reverse. Lithium, for instance, seemed only helpful for a proportion of either manic-depressive or bipolar patients.

In the decade from 1980 to the mid-1990s, manic-depressive illness and bipolar disorder co-existed, with Goodwin and Jamison's 1990 monograph on the illness still entitled *Manic-Depressive Illness* [10]. It was only in 1992, with ICD 10, that the term bipolar disorder spread beyond America. But with the launch of Depakote as a mood-stabilizer in 1995, the bipolar offspring ate its manic-depressive parent.

The term mood-stabilizer essentially had not existed before 1995. Sedatives had been widely used to manage manic patients prior to that, but demonstrating a sedative effect in mania is quite different to showing a drug is

prophylactic for bipolar disorder. Depakote was licensed for the treatment of mania but its adverts claimed it was a mood-stabilizer. Had Abbott said Depakote was prophylactic, they would have broken the law, as it had not been shown to be prophylactic but the term mood-stabilizer had no precise meaning. It suggested prophylaxis and this suggestion led to the use of Depakote and other anticonvulsants for maintenance purposes, despite a failure in controlled trials to demonstrate these agents are prophylactic.

Bipolar disorder, in my view, has become more a brand than a well-grounded scientific term – as successful a brand as the creation of the terms tranquilizer and SSRI. A brand is something whose value lies in the perception of a consumer rather than in a tangible benefit. Where there had been almost no uses of the term mood-stabilizer before 1995, by 2000 there were over 100 articles per year featuring this term in their titles.

The dramatic and rapid switch from Manic-Depressive Illness to Bipolar Disorder in the mid-1990s took place in the absence of any clinical or research facts to underpin the switch. The term bipolar disorder is rarely found in the titles of articles listed in Medline before 1992, but its use rapidly escalates from 1995 to reach 500 articles per year by 2005, while the term manic-depressive vanished. Estimates of the frequency of bipolar disorder in the population soared to a 100-fold compared with figures for admissions to the North Wales Asylum in the period from 1875 to 1924.

The possibilities offered by 'mood-stabilization' and 'bipolar disorder' led companies producing second generation antipsychotics into the market, greatly expanding the use of these terms. Bipolar affective disorder is unquestionably a distinct clinical type; this does not mean it is necessarily a distinct disease entity. We still do not know enough about the bases for any remitting disorders to carve nature definitively at its joints in these domains.

Many clinicians and scientists associate history with post-modernism, an all but psychiatric disorder in its own right, where academics refuse to concede there is any reality to human behaviours, or to the physical underpinnings of disorders of human behaviour. That which scientists regard as hard data or even facts, post-modernists treat as texts to be interpreted and re-interpreted without external constraint.

The analysis of Kraepelin's concept of manic-depressive illness outlined above demonstrates how complex his concept was, and how open to revision, but it also makes clear that clinical realities were once the primary determinant of clinical concepts. Concepts arose from the clinical material. In contrast, the post-modernism at which the marketing departments of pharmaceutical companies excel think nothing of shaping the clinical material to fit a marketing concept.

In the decade from 2000, all of the companies producing antipsychotics have targeted bipolar disorder as a means to enhance sales. The companies have recognised that to do this the attitudes of primary care physicians would have to change. Market research had shown that these doctors were reluctant to use antipsychotics, but they could be re-educated to the possibilities of mood-stabilizers. These were doctors who thought that bipolar disorder was a severe mental illness comparable to schizophrenia whose treatment appropriately was either in secondary care rather than primary care – they would need to be re-educated to recognise that many of the anxious and depressed patients going through their practices could be re-conceptualized as having bipolar disorder.

These points are illustrated using the documents in the public domain from litigation involving Zyprexa, but a similar scenario applies to other drugs in the group. Thus: 'As the current market leader in primary care, Zyprexa will continue to revolutionize the way complicated mood disorders are treated by primary care physicians. Just as Prozac revolutionized the treatment of depression in the late 1980s and throughout the 1990s, so too will Zyprexa forever change the way primary care physicians view and treat bipolar disorder' [11]:

> The facts: up to 30% of patients with a diagnosis of depression or anxiety may actually have bipolar disorder
>
> *[12].*

Scenarios like Donna's have been put forward as typical: 'Donna is a single mom, in her mid-30s appearing in your office in drab clothing and seeming somewhat ill at ease. Her chief complaint is "I feel so anxious and irritable lately". Today she says she has been sleeping more than usual and has trouble concentrating at work and at home. However, several appointments earlier she was talkative, elated, and reported little need for sleep. You have treated her with various medications including antidepressants with little success. . . You will be able to assure Donna that Zyprexa is safe and that it will help relieve the symptoms she is struggling with' [13].

There is clearly a nexus of nervous problems that patients endure in the community without ever coming to the attention of mental health services. Company marketers have been adept at framing the symptoms these give rise to in a manner most likely to lead to a script for the remedy of the day. Donna could have featured in adverts for tranquilizers from the 1960s to the 1980s, or for antidepressants in the 1990s, and would have probably been more likely to respond to either of these treatment groups than to an antipsychotic, and less likely to be harmed by them than by an antipsychotic.

There have traditionally been difficulties in seeing these conditions simply as anxiety or as depression [14]. But

while bipolar affective disorders probably exist in the community without coming to the attention of the secondary services, it flies in the face of a century of psychiatric thinking to see conditions that patients like Donna have as bipolar disorder.

The concept of juvenile bipolar disorder flies even more in the face of a century of psychiatric thinking, but as of 2008, upwards of a million children in the United States, in many cases preschoolers, are on 'mood-stabilizers' for bipolar disorder, even though the condition remains unrecognized in the rest of the world [2].

While this was happening, the cycloid disorders, which provided sound clinical grounds to unpick or go beyond the Kraepelinian synthesis, remained neglected. Instead, in a return to a pre-Kraepelinian psychiatry, company marketing departments have used a template of a supposedly neo-Kraepelinian medical science to promote a form of bipolar disorder based more on the visible presentations of patients rather than on any valid classificatory basis. This new disorder would have been unrecognizable to Kraepelin, whose tombstone bears an inscription – 'your name may vanish but your work remains' – that has become ironic.

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