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Epidemiology of bipolar disorders

1.1 CONTRIBUTION OF EPIDEMIOLOGICAL STUDIES TO THE DIAGNOSIS

The variability in the diagnoses of mental illnesses was remarkably well demonstrated around 30 years ago by a diagnostic study called the ‘United States/United Kingdom Diagnostic Project’ (Cooper et al., 1972). This study showed that, on average, psychiatric patients hospitalized in New York were diagnosed with schizophrenia twice as often as patients hospitalized in London – and with alcoholism six times as often. On the other hand, patients in London were diagnosed with mania twelve times more often – and with psychotic depression five times more often – than patients in New York. These results certainly contributed to the realization among researchers and clinicians of the need for common diagnostic criteria to be available. Among the numerous reasons that may explain the inconsistencies in the epidemiological data, two of the most important are an imprecise diagnostic definition and diagnostic thresholds that vary between different studies (Wing et al., 1978; Boyd and Weissman, 1981).

Whatever the precision of the employed criteria, formulating a cross-sectional diagnosis in the absence of longitudinal data remains difficult. A comparison of the results of the New Haven study (Weissman and Myers, 1978) with those of the Iowa 500 study (Winokur, 1975) yields a clear demonstration of this difficulty, with the first study indicating a lifetime prevalence rate for depression and mania of 28% and the second study a rate of only 8%. A large proportion of these differences stems from the fact that the New Haven study employed the RDC research criteria (Research Diagnostic Criteria (Spitzer et al., 1978)), which require the presence of symptoms for at least two weeks, whereas the Iowa study used the Feighner criteria (1972), which require their presence for at least one month. Moreover, the New Haven study included secondary depression, in contrast with the Iowa study.

In order to reduce this variability as much as possible, several diagnostic classification systems were developed over the course of the 1970s, such as the Feighner criteria (1972), the Schedule for Affective Disorders and Schizophrenia (SADS) (Spitzer and Endicott, 1978) that relies on the RDC, and the Present State Examination (Wing et al., 1974). In the following years, diagnostic instruments were developed corresponding to the criteria of the DSM-III (American Psychiatric Association, 1980), such as the Diagnostic Interview Schedule (DIS) (Robins et al., 1981) and, more recently, the Structured Clinical Assessment for Neuropsychiatric Disorders (SCAN) (Wing et al., 1990), the Structured Clinical Interview (SCID) (Spitzer et al., 1990) corresponding to the criteria of the DSM-III-R (American Psychiatric...
One of the main problems of epidemiology lies in the precise definition of what is considered to be a ‘case’, and any comparison of historical data is confronted with the constant evolution of the definition of a disorder over the course of time. As an example, the ‘circular insanity’ suggested by Falret (1854) only partially covers the definition given by Kraepelin (1921) which includes all types of serious, periodically recurring, affective illnesses. We know that Kraepelin’s definition led to an overestimation of the prevalence of bipolar (BP) disorders, because he grouped other periodic affective disorders under this category. Nevertheless, when compared with current definitions that include BP type II disorders (hypomania and depression), Kraepelin’s criteria tend to underestimate the prevalence of these disorders.

1.2 THE DEFINITION OF BIPOLAR DISORDER

The criteria of the diagnostic and statistical manual of mental disorders (American Psychiatric Association, 1994) indicates that the essential characteristic of mood disorders is a disturbance of mood defined as a ‘prolonged emotion that colors the whole psychic life’. Although an elevated mood can be considered as a characteristic of a manic episode, the frequent presence of irritability must be included as well. Manic patients generally suffer from an inflated self-esteem, ranging from an unusual self-confidence to delusional grandiosity. A diminished need for sleep is often associated with hyperactivity, as the subjects feel full of energy and can stay awake all night concocting projects and disturbing neighbours or family with telephone calls and other intrusive interactions. Speech is accelerated and difficult to interrupt and flight of ideas is generally present as well as other symptoms such as sexual hyperactivity or impulsiveness. The disorder can be sufficiently serious to bring about a marked disability in social life, professional activities or interpersonal relationships, sometimes requiring hospitalization.

1.3 DEMOGRAPHIC AND SOCIAL VARIABLES

1.3.1 Gender

Most studies do not show any differences linked to gender, and the Amish study and the ECA study (see Sections 1.4.1 and 1.4.2 below) among others show a one-to-one male–female ratio (Kessler et al., 1994; ten Have et al., 2002). BP type II disorder appears to be more common in women and about 80% of rapid cycling patients are women (Arnold, 2003; Burt and Rasgon, 2004).

1.3.2 Age

Unlike unipolar depression, the age of onset of bipolar disorders is most common in the adolescent to young adult years. The peak age at onset of the first symptoms of BP disorder is between 15 and 19 (Costello et al., 2002; Kupfer et al., 2002). According to the results of a survey by the Depression and Bipolar Support Alliance (DBSA, previously NDMDA) up to 59% of patients with BP disorder had signs of the illness prior to the age of 20 (Lish et al., 1994). Although pre-pubertal onset of BP disorder is rare, an American community
base school survey reported a lifetime prevalence rate of BP types I and II among adolescents aged between 14 and 18 years of 1.4% (Lewinsohn et al., 2003). An ongoing survey (Coby: Cause and Outcome of Bipolar illness in Youth) (Birmaher et al., 2006) indicates that approximately 70% of subjects with BP disorder recovered from their index episode and 50% had at least one syndromal recurrence, particularly a depressive episode with a median of 61 weeks after recovery of the index episode.

Instead of the traditional early and late onset groups of BP disorder, recent findings indicate that there are three age-at-onset groups: early, intermediate and late. The greatest peak is at around age 17, a smaller peak is around 25 and the smallest peak is at around 40 years of age (Bellivier et al., 2003; Leboyer et al., 2005). Age at onset identifies homogenous subgroups of BP disorder patients. Another independent study (Lin et al., 2006) using data from the NIMH genetic initiative for BP disorder is largely consistent with those results.

At the opposite age range, elderly patients can also have symptoms of BP disorder. Onset of mania after age 60 is less likely to be associated with a family history of BP disorder and more likely secondary to medical causes, endocrine, infectious and inflammatory disorders (McDonald and Nemeroff, 1996). A recent report indicates that 6.1% of adults aged 60 and older with BP disorder appear to have illness of relatively recent onset (Sajatovic et al., 2005).

### 1.3.3 Urban and rural

The ECA study (Weissman et al., 1991) indicates that the rate in urban populations is 1.5% as compared with 0.5% for rural zones, and similar differences have also been found in other studies (Blazer et al., 1985; Goodwin and Jamison, 1990). Rihmer and Angst (2005) note that although this distinction provides little information about the real living and social conditions in general, ‘it can be a good marker for the density of population reflecting indirectly the amount and the nature of psychosocial stressors’.

### 1.3.4 Social–economic factors

Most of the studies published before 1980 indicated a higher prevalence in the more privileged social and economic classes (Verdoux and Bourgeois, 1995), but this finding has not been confirmed by more recent studies (Abood et al., 2002). What is certain is that the relationships between social economic factors and mood disorders are extremely complex and multidimensional.

### 1.3.5 Marital status

The ECA study showed that individuals who had divorced or never been married suffered from BP disorders more frequently than those who were married.

### 1.3.6 Cultural factors

Since Kraepelin’s time, we’ve known that the prevalence rates of BP disorders are often higher in certain cultures than in others, particularly in certain population groups living in
Indonesia or among the Hutterites in North America (Dohrenwend and Dohrenwend, 1974). Several studies emphasize the role that emigration may play as a risk factor in the emergence of BP disorders. However, this last point requires a more thorough analysis as it seems difficult to ascertain if BP disorders predispose subjects to emigrate or if the emigration in itself is a precipitating factor (Tohen and Goodwin, 1995).

Parallel with the development of these instruments of evaluation and the refining of the diagnostic criteria, over the last 30 years two periods can be distinguished that have marked epidemiological studies of BP disorders:

- The first period lasts from the 1970s until the mid-1990s. This period is characterized by systematic recourse to structured interviews and precisely defined criteria as well as by a choice to abide by the categories of BP I and II disorders, as they are defined in Appendix I on diagnostic criteria. This trend can explain the relatively low prevalence rates of this period.

- The second period, which began several years ago, is characterized by a loosening of the inclusion criteria and by the recognition of disorders whose severity does not attain the classically defined threshold.

### 1.4 A FEW IMPORTANT HISTORICAL EPIDEMIOLOGICAL STUDIES

#### 1.4.1 Amish study

This study (Egeland and Hostetter, 1983) examined affective disorders among the Amish community, a Protestant population that has remained culturally isolated and genetically homogenous. The old order Amish were represented by a population of 12,500 people who live for the most part in the county of Lancaster, Pennsylvania, USA. Their genealogical tree and medical files date back for 30 generations. This study followed individuals with affective disorders over a period of six years. It was carried out in a population that is rarely confronted with criminal acts and is free from alcohol or drug dependence. The prevalence of BP type I and II disorders in the population aged 15 years or older was 0.46%.

#### 1.4.2 Epidemiologic Catchment Area (ECA) study

The ECA study gathered data on BP disorders according to the DSM-III criteria by means of the DIS diagnostic interview (Robins et al., 1981), allowing for the calculation of prevalence rates for BP I and II disorders, but not for cyclothymic disorders. The lifetime prevalence rate of the manic episode was 0.8% (Robins et al., 1984), with no differences between gender or ethnic groups. The rate of BP II disorder was 0.5%, likewise with no differences between gender and ethnic groups. It is noteworthy, however, that the prevalence rates vary noticeably among the five study sites. For example, for BP I disorder, the rate varied between 0.6% in Baltimore and 3.4% in Durham. The average age of onset was 21 years (Weissman et al., 1988).
1.4.3 New Haven study

Weissman and Myers (1978) published the first epidemiological study carried out by means of diagnostic research criteria, the Schedule for Affective Disorders and Schizophrenia and the Research Diagnostic Criteria (SADS-RDC) (Spitzer et al., 1978). This study indicates a lifetime prevalence rate of 0.6% for BP I disorder and of 0.6% for BP II disorder, with significantly higher prevalence rates, up to 4.6%, in groups with more elevated social and economic status.

1.4.4 National Comorbidity Survey (NCS)

This study (Kessler et al., 1994), which surveyed a national sample of the non-institutionalized population of the United States, aged between 15 and 54, was carried out with the Composite International Diagnostic Instrument (CIDI) (Robins et al., 1988) developed by the University of Michigan. 8,098 individuals were included in the survey and the methodology was designed with the experience of the ECA study in mind, thus special attention was paid to risk factors and comorbidity issues. The study reported a lifetime prevalence rate of 1.6% for BP disorder and of only 0.6% for non-affective psychoses (schizophrenia, schizophranform disorder, schizoaffective disorder, delusional disorder and psychotic disorder not otherwise specified). This rate, which is particularly low for the non-affective psychoses in comparison with preceding studies, can be partially explained by the methodology employed, which included a reevaluation of each case by means of the clinical interview using the SCID.

1.5 OTHER STUDIES CARRIED OUT WITHIN THE GENERAL POPULATION

The Florence study (Faravelli et al., 1990) reported a one year prevalence rate of 1.4% in women and 0.65% in men for BP I disorder and a prevalence of 0.2% for BP II disorder regardless of gender.

The Dutch NEMESIS study (ten Have et al., 2002), using the CIDI, indicated a prevalence of 1.9%. These results issue from a study aimed at gaining a better understanding of the prevalence of mental disorders as well as their consequences and the use of health systems. For example, the study revealed that more than a quarter of BP patients did not have any access to care of any type.

A study carried out in Taiwan (Hwu et al., 1989) by means of the DIS reported a prevalence varying between 1.6% in the city of Taipeh and 0.7% in rural zones.

A study carried out in Alberta, Canada (Bland et al., 1988), also by means of the DIS, indicated a lifetime prevalence rate of 0.7% in men and 0.4% in women for BP I disorder.

A recent screening for BP disorder in a US community (Hirschfeld et al., 2003) was carried out to estimate the rates of BP I and II disorders in the general population. The study used the Mood Disorder Questionnaire (MDQ) mailed to the heads of 100,000 demographically representative households, with a supplemental mailing to 27,800 individuals selected to make the combined sample more representative for matching adults (18 years of age or older) from the US population, according to the 2000 US census data. The response rate was 66.8%.
When adjusted for non-response bias, the rate of positive screens for BP I and II disorders was 3.7%, an estimated prevalence that the study’s authors consider conservative.

1.5.1 Studies extending the boundaries of bipolar disorder

The DSM-IV (American Psychiatric Association, 1994) and the ICD-10 (World Health Organization, 1993) define mania and hypomania as the presence of a certain number of symptoms that are present for a defined duration. The diagnosis of mania requires a duration of at least one week whereas at least four days are required for hypomania. This minimum threshold of four days would not account for more than half of the patients who suffer from brief hypomania, that is to say, an episode that lasts between one and three days.

Akiskal (2000) directed numerous studies that led to a reevaluation of the classically accepted prevalence rates and a redefinition of the limits of BP disorders by including mixed states of the BP disorder spectrum, including ‘soft’ bipolar forms (see Chapter 2).

Angst (1995) produced a review citing 13 studies that all report a lifetime prevalence rate of BP disorder below 1% in the general population, whereas two large American studies, the ECA study (Weissman et al., 1991) and the National Comorbidity Survey (NCS) (Kessler et al., 1994), indicate that the prevalence rate is between 1.2 and 1.6%. Angst (1995) contests these figures, considering them to be too low due to methodological errors. The article primarily criticizes these studies for not taking into account the fact that mania and hypomania are widely under-diagnosed because the subjects often tend to feel better than the average person in the general population. As a result they do not report their suffering and play down the possible social consequences of their disorder. With this observation as foundation, the article defends the idea that epidemiological studies cannot neglect the essential source of information provided by collateral informants in order to better detect certain behavioural modifications. In addition, the article questions the practice of resorting to non-specialized interviewers, which takes place in the majority of studies carried out by means of the DIS, and lists several American and European studies that report significantly higher prevalence rates, ranging from 3 to 6.5%. These latter studies include not only mania, but also atypical BP disorders such as hypomania and cyclothymia, thus widening the BP disorder spectrum accordingly, in comparison with the prevalence rates defined by the DSM.

In the Zurich study (Angst, 1995), the lifetime prevalence rate was 5.5% for mania and hypomania and 2.2% for brief hypomania (lasting between one and three days), thus yielding a total prevalence rate reaching 7.7%. This study was based on the examination of a cohort of 591 subjects aged between 10 and 20 years and followed over four evaluations until the age of 35. A certain percentage of patients presenting with brief hypomania (lasting between one and three days), thus yielding a total prevalence rate reaching 7.7%. This study was based on the examination of a cohort of 591 subjects aged between 10 and 20 years and followed over four evaluations until the age of 35. A certain percentage of patients presenting with brief hypomania, and recurring mood changes associated with episodes of depression, must be added to the rate obtained. Angst hypothesizes that the symptoms of this group would largely overlap with those of cyclothymia and that it must be included in the spectrum of BP disorders. The most recent analysis of the Zurich study (Angst et al., 2003) also takes into account the inclusion of groups defined as ‘soft categories’ of BP disorder. The study indicates a total lifetime prevalence rate for the entire BP disorder spectrum as high as 24% (0.55% for BP I, 11% for BP II including hard and soft criteria, 9.4% for minor BP disorders and 3.3% for pure hypomania, see Chapter 2 on classification).

Confronted with such high prevalence rates in comparison with the majority of previous studies, the question necessarily arises of whether certain cases that were classified as belonging to the BP disorder spectrum were not diagnosed in an excessive fashion, which would
reduce accordingly the clinical validity of this diagnosis. This possibility cannot be ignored, but these proposals are founded on ‘modern’ practices of epidemiology, which are not limited to the definition of a diagnosis, but also take into account the social consequences, a large amount of data concerning the evolution of treatment and, a new and essential aspect, the quality of life. The attention paid to quality of life makes it possible to show that subjects suffering from mania or hypomania tend to evaluate their quality of life negatively (for example, see Vojta et al., 2001).

In conclusion, certain recent criteria of the BP disorder spectrum, such as the duration of the presence of the symptoms, the consideration of quality of life and the information provided by collateral informants, have led to a reevaluation of the lifetime prevalence rate of BP disorders, which would be between 3 and 6.5% (Kessler et al., 2003).

1.6 KEY POINTS

- When we consider the BP disorder spectrum, numerous experts now evaluate the lifetime prevalence to be at least 3% of the general population.
- The diagnostic criteria that are currently used to define the duration of hypomania are quite probably too restrictive and do not account for brief hypomanic episodes lasting fewer than four days.
- The information provided by collateral informants can be extremely valuable in the formulation of the diagnosis, notably for BP II disorder.

REFERENCES

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