Mood disorders: pearls of wisdom from a lifetime of observation

Professor Jules Angst provided a fascinating account of some of the work that has led him to challenge fundamental thinking about bipolar disorder in his Keynote Lecture on the classification, course and treatment of mood disorders, at the ninth Latest Advances in Psychiatry Symposium in London in March 2010. Steve Titmarsh had the privilege of listening and here provides a brief overview.

At 83 years of age, Professor Angst still takes more than a keen interest in research into mood disorders and in particular is actively engaged in analysing the data collected from an epidemiological cohort he began to observe more than 30 years ago. Furthermore, he still does not shy away from questioning perceived wisdom when data he and his colleagues have collected point to a different conclusion.

Prospective trials show that there is a high lifetime prevalence of psychiatric disorders – of the order of 40-50 per cent1-5 – and prevalence rates for mood disorders, anxiety disorders and substance abuse/dependence of 20-30 per cent. Professor Angst personally feels that in reality the prevalence rates for psychiatric disorders may be higher because the figures are based on retrospective data and not lifelong prospective studies.

However, the lifetime prevalence rates of major depressive disorder (MDD) compared with bipolar disorder (BD) have been generally overestimated in Professor Angst’s view. The discrepancy may be due to trial selection criteria largely based on the classification systems, DSM-IV and ICD-10. So, instead of the 1:1 ratio of MDD to BP Professor Angst and colleagues have observed in the Zurich study,1 others have recorded much higher ratios of MDD to BP of around 4:1.2-5

If broader diagnostic criteria that reflect more closely the real-life experience of those with mood disorders are applied to patient populations, then a higher proportion of bipolar disorders would emerge. For example, when Professor Angst’s diagnostic specifier for bipolarity6 criteria were applied to studies where the ratio of MDD to BP is much higher than 1:1, then over-diagnosis of major depressive disorder was reduced, revealing a higher proportion of patients with bipolar disorders; this was the case in a patient study across 18 countries7 and in two well-known prospective epidemiological studies (EDSP Munich,8 NCS-R USA9). Identifying such ‘hidden’ or subthreshold bipolar patients might make it possible to make an earlier diagnosis of bipolar disorder, for which there is an average delay of 10 years from onset of depressive symptoms, and perhaps specific treatment could be employed earlier.

In any case, Professor Angst explained, the risk of someone with depression becoming bipolar is about 1.25 per cent per year – and the risk of becoming bipolar remains the same no matter how many episodes of depression have been experienced before a hypomanic or manic episode manifests. So that, he argued, if people with depression lived to be more than a 100 years old, they would all become bipolar. The risk of switching from mania to depression is 3 per cent per year.

Continuum of mood disorders
Professor Angst explained that his observations, in particular of the male conscripts and female subjects on the electoral role in the canton of Zurich in his native Switzerland, whom he has followed from age 19 and 20 years to age 49 and 50 years, have led him to the conclusion that mood disorders exist on a continuum from depression via bipolar disorders to mania.

He felt that there are no distinct classes between the different disorders. The divisions between the disorders defined by classification systems are arbitrary, but they make sense clinically because they help with treatment decisions.

In reality, almost everyone exhibits at least mild ‘symptoms’ of mood disorders; it is part of normal human experience. For example, people in love have traits similar to hypomania. The difference between those who are in love and those who are pathologically hypomanic is that people in love do not exhibit the kind of dangerous risky behaviours – gambling, driving too fast, etc. – that people who are ill are prone to.

Other clues to the hidden bipolar pathology are family history and comorbid disorders such as anxiety and substance abuse. Mania is significantly associated with family history of mania, Professor Angst explained. Bipolar disorder is significantly associated with anxiety disorders and substance abuse, such as alcoholism, in contrast to major depressive disorder, which is significantly associated with suicide. Around 30 per cent of bipolar patients, as defined by DSM-IV cri-
Jules Angst, MD, is Emeritus Professor of Psychiatry at the University of Zurich and Honorary Doctor of Heidelberg University, Germany. He trained under Manfred Bleuler and was Professor of Clinical Psychiatry and Head of the Research Department of Zurich University Psychiatric Hospital (the Burghölzli) from 1969 to 1994. He continues to work full-time in epidemiological and clinical research.

His 1966 monograph established and validated the distinction between bipolar disorders, depression and schizoaffective disorders on the basis of genetics, course and personality. He was the first to show the unfavourable long-term course of mood disorders.

His recent main research has been in epidemiology covering the classification, comorbidity and course of mood and anxiety disorders including subdiagnostic syndromes (recurrent brief depression, bipolar-II disorders, hypomania, minor bipolar disorder and anxiety), obsessive-compulsive disorder, neurasthenia, perimenstrual syndromes and migraine.


Professor Angst with Dr. David Baldwin, Chairman of PSIG, at the ninth Latest Advances in Psychiatry Symposium in March 2010

Pharmacological myths
Professor Angst was keen to dispel a couple of myths about drug treatment. First, he contended that there is no statistical evidence that antidepressants induce hypomanic episodes more frequently than placebo. The idea is a result of wrong statistical thinking and computations, he said. The natural history of bipolar disorder is an up and down course, by definition, and do not take a number of weeks to have an effect as has been assumed. That has implications for treatment.

Treatment recommendations
Professor Angst’s observations over many years lead him to the conclusion that people with depression should be treated with an antidepressant first – whether they are bipolar or not. If there is a response, such as an increase in activity signalled by something such as the patient sleeping less in the first week or two, then a mood stabiliser should be added. If there is no response, then the dose of antidepressant should be doubled after one week. If there is no response after two weeks, it is fairly certain the patient will not respond to the treatment.

Combination therapy has been shown to be more effective than monotherapy in terms of reducing the number of relapses and in reducing suicide rates. Finally, something perhaps a little more surprising: lithium and clozapine therapy may protect against dementia: several studies show that the drugs attenuate the development of dementia.

References