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Is depression one thing or many?

Until 1980, manic depressive illness (MDI) was defined as follows: the presence of recurrent severe depressive or manic episodes alternating with periods of normal mood or markedly decreased mood symptoms.[1] In that year, the DSM-III rejected this definition of MDI and replaced it with two different conditions: bipolar disorder and major depressive disorder (MDD). Bipolar disorder meant the presence of manic and depressive episodes, not manic or depressive episodes – a huge difference between bipolar disorder and MDI. Recurrent episodic severe depression, previously called MDI, was redefined as MDD, which also included other varieties of depressive symptoms (such as neurotic depression). In the last few decades, the broad heterogeneous definition of MDD has been accepted by many clinicians as if it was a single entity, completely different from bipolar disorder, without awareness that both conditions were seen as one illness in the past: MDI.

We present the case of a patient with severe recurrent depression who achieved clinical remission after treatment with lithium monotherapy despite non-efficacy of standard antidepressants.

The patient was a 36 year-old White, married woman with a positive family history for bipolar disorder. She had no history of manic episodes.

At 32 years of age, 2 weeks after delivering her first child, she presented feelings of inadequacy and guilt, anhedonia and decreased appetite. She had difficulty falling asleep because of ruminative pessimistic thoughts about the future. These symptoms met DSM criteria for a major depressive episode and improved in the next few weeks without medications.

Six months later, anhedonia increased prominently and she presented depressed mood, feelings of worthlessness and occasional suicidal thoughts. She was admitted to the in-patient service and was treated with sertraline 250 mg/day.

In the following 2 years she had three depressive episodes per year lasting about 2 months each without full interepisode recovery. Her treatment was modified to clomipramine 225 mg/day. Depressive episodes recurred more frequently and lasted about 1 month each.

At age 35, she was admitted to the in-patient service after impulsive ingestion of high doses of benzodiazepine and antidepressants as a suicide attempt. Clomipramine was gradually discontinued and treatment was modified to lithium 600 mg/day (serum level 0.5–0.7 mEq/l). Lithium was maintained in monotherapy; depressive symptoms were well controlled and there were no mood recurrences for the following 12 months.

In this case, four features support the hypothesis of underlying MDI: presence of recurring depressive episodes, positive family history for bipolar disorder, postpartum onset of first depressive episode, and improvement of affective symptoms with a mood stabiliser. Randomised studies indicate that standard therapeutic levels of lithium are effective in recurrent depressive episodes, whether bipolar or unipolar, in both acute and maintenance treatment phases.[2,3]

DSM-III made a radical change in dividing the broad MDI concept into the narrow bipolar and broad MDD concepts. Given decades of research suggesting that MDD is a heterogeneous concept, and the perspective that course (recurrence of mood episodes) may be highly important in diagnosis, rather than symptoms (depression *v.* mania),[4] case examples such as this one raise the question whether therapeutic response also supports a return to the MDI concept that emphasised diagnosis based on recurrence of episodes, irrespective of depressive or manic polarity.

This nosological approach would have important clinical implications if MDI is the disease that produces both depressive and manic symptoms. William Osler's view that the medical profession should primarily treat diseases, not symptoms,[5] would imply that mood stabilisers such as lithium should be the main long-term treatment of choice in patients with recurrent depression. Addition of low doses of antidepressants could be considered for short-term symptom improvement, rather than long-term prevention of mood episodes, while monitoring emerging manic or mixed episodes.

Declaration of interest

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CBT for psychosis: not a 'quasi-neuroleptic'

As members of the recent National Institute for Health and Care Excellence (NICE) clinical guideline update for schizophrenia[1] (M.B. and D.S.), we read with interest the excellent meta-analysis of CBT for symptoms of schizophrenia by Jauhar *et al*.[2] The results are broadly in line with the NICE review and particularly that of Wykes *et al*,[3] which showed that studies with high methodological rigour, including masking, have a small effect size for positive and total symptoms. Clearly cognitive–behavioural therapy (CBT) is no panacea; but neither is it ineffective. Meta-analyses bring together all trials, with patients drawn from heterogeneous populations, including different phases of illness. The tests for

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heterogeneity not accounted for by chance (I^2) in this meta-analysis were all high. The question therefore arises, 'For whom is CBT in psychosis most effective and for what outcome?' Likely groups are individuals at ultra-high risk for psychosis,[1] those in the early phase of psychosis[1] and perhaps those with chronic stable symptoms, appearing to benefit the most; the Prevention of Relapse in Psychosis trial suggests that those beginning treatment early in the course of recovery from acute symptoms do not benefit. These trials focus on individuals in receipt of medication, with enduring symptoms. They therefore ask the question, 'Does CBT offer added value compared with medication alone?' We might also ask the converse, 'Does antipsychotic medication offer added value to CBT alone?' It is known that up to 50% of individuals will not adhere to medication; a recent pilot trial of CBT in those not taking medication showed an effect of CBT equivalent to that of drugs.[4] Given the low acceptability of antipsychotic medications and their serious impact on health, this is an important question for further research.[1] We note that our trial of CBT for commanding hallucinations is included in the analysis for hallucinations; however, this trial did not predict a reduction in hallucinations, but reported a 'high' effect size for harmful compliance (not reported), which has been the subject of a large multicentre trial, soon to report. We argued some time ago that CBT for psychosis should not be conceived and evaluated as a 'quasi-neuroleptic':[5] the dimensions of delusions (power, distress) and general affective dysfunction are, we believe, among the most appropriate targets for CBT, with strong theoretical justification. Given the evidence from systematic reviews of antipsychotics[6] that the improvements claimed for antipsychotics are of questionable clinical utility, with most trials failing to demonstrate minimal clinical improvement using the Positive and Negative Syndrome Scale, with effect sizes smaller than for adverse side-effects, there is clearly much work to be done to improve care, as the Schizophrenia Commission outlined in their 2012 review of current treatment and services (www.schizophreniacommission.org.uk).

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Jauhar and colleagues'[1] review and meta-analysis of cognitive–behavioural therapy (CBT) for the reduction of particular symptoms associated with schizophrenia is interesting but incomplete. For example, the review does not examine the clinical significance of dose or duration of CBT treatment. This limitation is considerable, as an analysis of effective elements of CBT for psychosis found that 'consistent delivery of full therapy, including specific cognitive and behavioural techniques, was associated with clinically and statistically significant increases in months in remission, and decreases in psychotic and affective symptoms', while 'delivery of partial therapy involving engagement and assessment was not effective'.[2]

Jauhar *et al* have also excluded measurement of long-term outcomes from their analysis, measuring only end-of-study data. This is another considerable limitation, as symptom reductions maintained at 9- or 18-month follow-up represent a substantial benefit of effective CBT. Further, although reduction of psychotic symptoms is an important treatment outcome to measure, CBT is particularly focused on reducing distress associated with such symptoms and improving an individual's ability to cope with them. As psychotic symptoms can continue even with administration of powerful antipsychotic medication, improvements in these areas may be clinically significant for many CBT recipients. Indeed, a comprehensive synthesis of qualitative research into patients' experiences of CBT for psychosis[3] found that the most commonly identified 'key ingredients' of CBT included increased understanding of psychosis and of coping strategies, reappraisal of distressing beliefs, and normalisation: 'Participants did not necessarily experience an actual reduction in the frequency or distressing content of psychotic experiences, but instead gained an increased ability to cope and an increased perception of personal power'. It is also important to consider that not all individuals want their 'symptoms' eradicated, and such appraisals are common in the wider literature on recovery from psychosis or schizophrenia: 'Learning to cope to accept that you hear voices or whatever your symptoms are. Recovery is . . . to be able to live with it'.[4] So, although analyses of CBT that focus only on psychotic symptom reduction are important, they are also incomplete; 'secondary' outcomes such as reduced distress or self-defined recovery may be valued more highly than symptom reduction alone by many patients, and such outcomes are increasingly well measured in CBT trials.[5] Future meta-analyses of CBT will contribute more meaningfully to our understanding of its effectiveness by examining these wider outcome domains and acknowledging their value as long-term benefits.

Declaration of interest

R.E.B. was a member of the National Institute for Health and Care Excellence guideline development group 'Psychosis and schizophrenia in children and young people', and is involved in National health Service-funded CBT for psychosis research.

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