Combining cognitive therapy with medication in bipolar disorder

Edward Watkins

Abstract Although mood stabilisers have substantially improved the treatment of bipolar disorder, recent studies suggest that treatment with lithium is not as effective as originally claimed. Furthermore, patients still have high rates of relapse even when prescribed medication. Recent research has shown that poor coping strategies in response to bipolar prodromes and disruptions of sleep and social routines increase the risk of relapse. Combining a psychosocial approach with medication may improve the rate of relapse prevention. Cognitive therapy teaches patients better self-monitoring and coping skills and is therefore an appropriate means of minimising psychosocial risk factors for relapse. Recent randomised controlled trials suggest that combined medication and cognitive therapy significantly reduce bipolar relapse compared with medication alone.

Bipolar illness is a severe and often very disabling disorder. Although the prognosis can be good, bipolar disorder may be associated with poor social functioning (Bauwens *et al*, 1991), reduced rates of employment (Prien & Potter, 1990), high levels of substance misuse and elevated risk of suicide. Chen & Dilsaver (1996) reported a lifetime rate of suicide attempts in those with bipolar disorder of 30%, compared with 16% in those with unipolar depression and 4% in those with other Axis I disorders, as defined by the DSM–IV criteria (American Psychiatric Association, 1994*a*).

Bipolar affective disorder has a prevalence of about 1.0–1.5% in the adult population, with first onset typically occurring in early adulthood. There seem to be similar rates of prevalence for men and women and there is little evidence that marital status or geographical location influence prevalence, although some studies suggest that bipolar disorder occurs more often in middle and upper social groups.

Relapse and recurrence of bipolar disorder

For many patients, the prognosis of bipolar disorder is not good, as the disorder is associated with frequent relapses and recurrences (Keller *et al*, 1993; Winokur *et al*, 1993). Tohen *et al* (1990) reported that after follow-up over 4 years, nearly 90% of a sample of 75 patients with bipolar disorder had experienced at least one relapse after remission of the index episode. When clinical criteria are used, it is estimated that, on average over a lifetime, a patient with bipolar I disorder will experience 8–12 episodes of depression and 4–8 episodes of mania. These high rates of relapse and recurrence indicate that treatment in bipolar disorder should focus on effective reduction of acute symptoms during a bipolar episode (depression or mania) and effective relapse prevention. Likewise, for each patient, factors that might influence relapse need to be examined systematically. Psychosocial factors related to relapse and recurrence are highlighted below.

Pharmacological treatment of bipolar illness

Medication has been the predominant treatment for bipolar disorder, with lithium carbonate the treatment of choice for three decades. This reflects the prevailing view that bipolar depression is biological in origin, consistent with the evidence of a strong genetic component to the disorder. Lithium, carbamazepine and sodium valproate are used as mood stabilisers, with the intention of treating the acute episodes of mania and depression and preventing relapse and recurrence. In addition, neuroleptics such as chlorpromazine and haloperidol are often prescribed for treatment of acute manic episodes. Similarly, antidepressants are often prescribed for treatment of episodes of acute depression.

Treatment of acute episodes

There is good evidence that lithium is efficacious in the treatment of the acute phase of mania, although

Edward Watkins is a chartered clinical psychologist and research fellow in the cognitive clinical psychology of depression at the Department of Psychology, Institute of Psychiatry (De Crespigny Park, Denmark Hill, London SE5 8AF, UK). His research interests are cognitive processing in affective disorders and psychological treatments of unipolar and bipolar depression.

the addition of major tranquillisers may be clinically indicated for more severely ill patients (American Psychiatric Association, 1994*b*). Although less stringently evaluated than lithium, the current evidence suggests that carbamazepine and valproate have equivalent efficacy to lithium in the treatment of manic episodes. Research on pharmacotherapy for acute bipolar depression is less common and harder to interpret because of methodological difficulties (Prien & Potter, 1990).

Relapse prevention

What about the prevention of relapse and recurrence? How well do mood stabilisers prevent further bipolar episodes? Studies in the 1960s and 1970s suggested that lithium was an effective form of prophylaxis. However, reviews of more recent randomised controlled double-blind trials of mood stabilisers have suggested that these medications are not as effective at preventing relapse as initially reported (Moncrieff, 1995; Solomon *et al*, 1995; Silverstone *et al*, 1998). Whereas the original studies in the 1960s reported that patients on lithium experienced relapse rates of 35% over 2 years, more recent studies find average relapse rates of 50% over a 2-year follow-up. Furthermore, a significant proportion of patients with bipolar disorder do not seem to benefit from mood stabiliser medication. Prien & Potter (1990) estimated that lithium was ineffective in up to 20–40% of cases, either because of inadequate response or poor compliance due to the side-effects of medication. Although further research trials are required to enable a reliable determination of the degree of efficacy for other medications such as carbamazepine and valproate, their efficacy appears to be similar to that of lithium.

Several particular subtypes of bipolar depression have been identified as being less responsive to lithium. The rapid-cycling subtype, that is, having four or more mood episodes per year, seems to be less responsive to lithium treatment. Similarly, mixed affective state, that is, the simultaneous occurrence of both manic and depressed symptoms, is a predictor of poor response to lithium. Patients with bipolar disorder with comorbid personality disorders or high levels of neuroticism have also been found to respond poorly to the medication. Patients with higher numbers of previous episodes are also less responsive to lithium treatment. It is still an open question whether the factors that predict poor response to lithium treatment are specific predictors of poor prognosis to this particular medication or general predictors of a poor response to any treatment. If bipolar disorder has any similarities to unipolar depression, some of these factors might be expected to predict poor response to any treatment,

in the same way that chronicity of depression and number of previous episodes in unipolar depression predict poor outcome for both pharmacotherapy and psychotherapy.

It is worth noting that combined medication (e.g. Calabrese *et al*, 1992; Denicoff *et al*, 1997; Frye *et al*, 2000), i.e. lithium plus other mood stabilisers such as carbamazepine or valproate, appears to be superior to monotherapy in achieving prophylaxis. Reduced relapse for adjunctive medication on top of lithium points to a biological basis for the improvement in outcome, consistent with the view that the origins of bipolar depression are biological. Nonetheless, there are still relatively high rates of relapse in those on combined medication. For example, Denicoff *et al* (1997) reported that combined lithium and carbamazepine had some success in only 50% of patients with rapid-cycling bipolar disorder.

Thus, although pharmacotherapy for bipolar disorder has produced significant benefits both in the treatment of acute episodes and in relapse prevention, there are still high rates of relapse and a clear need for the development of improved treatment approaches for bipolar disorder.

Psychosocial approaches to bipolar illness

Given that structured psychological treatments such as cognitive therapy have been found to be effective in both the acute treatment and relapse/recurrence prevention of unipolar depression, it is possible that a cognitive therapy approach would reduce rates of relapse in bipolar disorder. Therapies based on teaching patients new coping skills, as is done in cognitive therapy (see, e.g. Williams & Garland, 2002), may be particularly appropriate for bipolar disorder, given recent evidence that particular coping skills and behavioural responses are important in the course of bipolar illness.

Bipolar prodromes

Prodromes are the early signs and symptoms that can precede a full-blown episode. Recent research has suggested that there are common prodromes for both mania and depression and that patients with bipolar disorder can reliably identify their prodromes (Molnar *et al*, 1988; Smith & Tarrier, 1992; Lam & Wong, 1997; Boxes 1 and 2). It is worth noting that patients find it easier to recognise prodromes for mania than for depression, possibly because the onset of mania is often more acute and more dramatic, whereas bipolar depression seems to develop more insidiously. There appears to be a relationship between residual symptoms and

Box 1 Common prodromes of mania	Box 2 Common prodromes of depression
Reduced sleep/need for sleep Increased goal-directed activity Irritability More optimism Increased sociability/talking more Racing thoughts Distractibility	Reduced interest in people or activities Feeling sad or depressed Disturbed sleep Tiredness Low motivation Increased worry Poor concentration

prodromal symptoms (Fava, 1999) which, given that residual symptoms predict future outcome in depression, further indicates the value of identifying and intervening at the level of these symptoms (e.g. Fava *et al*, 1998).

Importantly, patients with bipolar disorder display different coping strategies to deal with their prodromes, with the type of coping approaches chosen in response to manic prodromes predicting the level of social functioning and number of relapses 18 months later (Lam *et al*, 2001). In general, helpful coping strategies involve behavioural activities that act against the prevailing prodrome, whereas unhelpful coping strategies further reinforce the initial stages of the bipolar episode, fuelling more-extreme mood swings. Thus, for mania prodromes, engaging in calming activities, increasing rest, reducing stimulation and decreasing activity would be useful strategies, whereas increasing activity levels, enjoying the 'high', and 'making up for lost time' would be unhelpful strategies likely to increase the risk of a full-blown manic episode. Similarly, for depression prodromes, keeping busy and maintaining routines are associated with better outcomes, whereas cutting down on activities, withdrawing from other people and going to bed are associated with worse outcomes. For both manic and depressed prodromes, seeing a doctor and increasing the appropriate medication are also useful coping strategies.

Each patient will have his or her own idiosyncratic prodromes so, clinically, it is advantageous to review the weeks preceding each distinct bipolar episode to determine the signs and symptoms that occur as the episode develops. Separating the prodromes into early, middle and late signs is a useful way of structuring the chronology of an episode's development, with late signs reflecting the symptoms of the full-blown episode and early signs reflecting the earliest possible indication of a change in mood state. For example, for one patient, an increase in witticisms and puns may be an early sign of an impending manic episode, while for another it may be that colours appear sharper and more vivid. Because a number of prodromes occur in a social context, involving friends and families in their identification and monitoring can be very productive. The research

evidence suggests that helping patients with bipolar disorder to identify their prodromes and teaching them straightforward responses to counteract them can be beneficial in reducing the risk of relapse. Since the prodromes for mania can precede a full bipolar syndrome by several weeks (Molnar *et al*, 1988; Smith & Tarrier, 1992) early detection followed by effective coping strategies can be very helpful in 'nipping an episode in the bud'.

Life events and routine

There is evidence that life events and routine play an important role in the period prior to the onset of a bipolar episode. Malkoff-Schwartz *et al* (1998) reported that in the 8 weeks prior to manic episodes, a significantly greater proportion of patients had experienced events that disrupted social rhythm than in an 8-week episode-free control period. Such events involve changes to daily or social routine, in particular disruptions of sleep or changes in working schedule. Disruptions to circadian rhythms have been implicated in the onset of bipolar episodes (Wehr *et al*, 1983; Healy & Williams, 1989), and there are reports of patients who relapsed after long-distance travel or jet lag (Jauhar & Weller, 1982). The American Psychiatric Association (1994*b*) recommends regular social and sleep routines within their treatment guidelines for bipolar illness.

Modifying cognitive therapy for bipolar disorder

The psychosocial literature reviewed above suggests that helping patients with bipolar disorder to monitor their prodromes, develop new coping strategies and improve their daily routine, as well as using appropriate psychotropic medication, would help to reduce their risk of relapse. Structured, short-term, problem-focused therapies such as cognitive therapy are particularly suited to developing these skills. Cognitive therapy is built on the view that thinking, mood and behaviour all have a reciprocal influence on each other. Therapists aim to teach patients to become more aware of their thoughts and behaviours

and to then alter dysfunctional thoughts and behaviours. For example, in cognitive therapy for depression, patients are taught to challenge their self-critical thoughts such as 'I am a failure' by looking for evidence and alternative explanations that do not fit the negative interpretations (Box 3). Similarly, patients with depression are encouraged to increase their levels of pleasurable and achievement-related activities, have more structured routines and reduce unhelpful patterns of behaviour such as social withdrawal and avoidance. This combination of monitoring and behavioural change is complementary to the psychosocial research on prodromes and routine in patients with bipolar disorder, indicating that cognitive therapy may be a useful approach in such cases.

Attempts to develop cognitive–behavioural approaches for bipolar disorder have been based within a diathesis–stress model. This approach proposes that there is an inherent biological vulnerability in bipolar illness, as a function of instability of circadian rhythms and of impaired regulation of the motivational system controlling approach and reward (Depue & Iacono, 1989). It is proposed that disruption of sleep and routine can lead to dysregulation of circadian rhythms and the motivational system, leading to prodromal symptoms. The exact nature of life events and social disruptions may determine the specific prodromal symptoms that occur. For example, events involving goal attainment are associated with the development of manic symptoms (Johnson *et al*, 2000*a*), whereas negative life events, low social support and low self-esteem predict the development of depressive symptoms (Johnson *et al*, 2000*b*). The cognitive–behavioural approach to bipolar disorder then predicts that the particular coping strategies adopted in response to prodromal symptoms will determine whether a full bipolar episode will occur, which is more likely if coping strategies are poor. Finally, the consequences of a bipolar episode may further contribute to the maintenance of the episode. For example, impulsive spending may lead to financial problems; irritability coupled with poor concentration may lead to problems at work or the loss of employment; and promiscuous behaviour may lead to problems in intimate relationships. All of these episode-related difficulties could then act as further stressors to interact with the underlying biological vulnerability, to further generate bipolar symptoms.

The recognition of a biological vulnerability within the cognitive–behavioural approach to bipolar disorder, coupled with the identified need to improve relapse prevention, means that cognitive therapy for bipolar disorder has been conceptualised only as an adjunct to medication rather than as a replacement for it. Furthermore, cognitive therapy

Box 3 Outline of cognitive therapy for depression

Assessment of current symptoms and problems
Psychoeducation that thoughts, feelings and behaviours influence each other
Scheduling of increased pleasurable and achievement activities
Teaching patients to identify and challenge negative thoughts
Identifying and challenging dysfunctional assumptions that maintain depression

has been designed as a relapse prevention treatment, not as an acute treatment. Thus, attempts to modify cognitive therapy for bipolar disorder have concentrated on working with patients with the illness in a relatively euthymic state, outside of a major depression or manic episode. Clinical experience suggests that attempting cognitive therapy with patients with bipolar disorder who are in a manic episode is difficult and unlikely to be effective. Therefore, for maximum benefit, the cognitive therapy approach needs to be applied when patients are in remission between episodes.

To date, there have been several attempts to examine the efficacy of adding cognitive therapy to medication for bipolar disorder. Lam *et al* (2000) and Scott *et al* (2001) have reported that the addition of cognitive therapy to routine mood stabilisers produced significantly reduced relapse compared with routine mood stabilisers alone. However, both of these were pilot studies with small samples, such that any conclusions from them need to be tentative. Fava *et al* (2001) reported that cognitive–behavioural therapy reduced residual symptoms in patients with bipolar disorder who relapsed on lithium and may improve lithium prophylaxis. However, this study had a small sample size ($n=15$) and there was no comparison treatment group such as treatment as usual. In a randomised controlled trial, Perry *et al* (1999) taught patients with bipolar disorder to detect early warning signs and seek medical help earlier than those on treatment as usual. Although not a trial of a full cognitive therapy package, this study did demonstrate that teaching improved monitoring and better coping skills could significantly reduce bipolar relapse. Zaretsky *et al* (1999) found that cognitive therapy could be helpful in treating episodes of bipolar depression, although this study was also limited by having only a small sample.

More recently, a full-scale randomised controlled trial of cognitive therapy for bipolar disorder has been completed (Lam *et al*, 2003). This study investigated the efficacy of cognitive therapy in conjunction with routine mood stabilisers in the prevention of

bipolar episodes over a 12-month period. It recruited 103 patients with bipolar I disorder, who were being prescribed prophylactic medication at a recommended dose and who were not currently in an acute bipolar episode. To ensure that the patients treated were a group that was highly vulnerable to relapse/recurrence despite the provision of adequate levels of mood stabilisers, all those included in the trial had to have experienced at least two bipolar episodes in the previous 2 years or three episodes in the previous 5 years.

Patients were randomly allocated either to a treatment-as-usual group or to a combined medication and cognitive therapy group. The treatment-as-usual group received mood stabilisers at a recommended level with regular psychiatric follow-up as out-patients. The combined medication and cognitive therapy group received treatment as usual plus cognitive therapy.

The cognitive therapy was based on a previously developed treatment manual (Lam *et al*, 1999) and consisted of 12–18 weekly sessions, followed by 2 booster sessions each after 3-month intervals. The cognitive therapy package was developed from the classic cognitive therapy approach for depression (Beck *et al*, 1979), adapted to take into account psychosocial research into bipolar disorder (Box 4). Teaching better coping responses to prodromes is one core element of cognitive therapy for bipolar disorder. Identifying and challenging dysfunctional thoughts and beliefs is another. Depression-related thoughts and beliefs are challenged as per the standard cognitive therapy for unipolar depression.

In addition to challenging negative thoughts, patients can challenge dysfunctional positive thoughts associated with mania. For example, individuals can be taught to examine grandiose thoughts such as 'I know better than everyone else' and check whether these accurately reflect their past experience and whether such thoughts are dependent on their

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Box 4 Additions to cognitive therapy for bipolar disorder

Psychoeducation explaining the diathesis–stress model, outlining the joint role of medication and psychological treatment
Teaching self-monitoring and self-regulation skills, with an emphasis on identification of prodromes and development of good coping strategies
Promoting the importance of sleep and routine
Therapists gently challenge excessively positive thoughts
Therapists try to reduce the patient's over-striving behaviour and attitudes

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mood. Similarly, patients can be encouraged to examine the longer-term costs and benefits of their more-impulsive thoughts (e.g. 'I need to buy that now'), to prevent overimpulsive behaviour. Patients can also be encouraged to examine grandiose and impulsive plans across a longer time frame ('How many of your ideas still seem good a week later? If this is genuinely a good idea, it should still be a good idea next week. Can you try to leave it for a week?'). Highly driven and extreme goal-attainment beliefs, e.g. 'I should be happy all the time', 'If I put in enough effort, I should be able to achieve everything I want' are hypothesised to be vulnerability factors for mania. Patients with bipolar disorder who have these attitudes are more likely to engage in extreme goal-pursuing behaviour likely to disrupt their sleep and daily routines, precipitating further episodes. Cognitive therapy can involve identifying such beliefs in collaboration with patients and then exploring how realistic and useful these beliefs are.

Overall, Lam *et al* (2003) found that, at 12 months, the combined medication and cognitive therapy group had significantly fewer bipolar episodes compared with the treatment-as-usual group (cumulative relapse 44% *v.* 75%), fewer days in bipolar episodes (27 *v.* 88) and significantly fewer hospitalisations. Those in the combined medication and cognitive therapy group were also significantly better than the treatment-as-usual group at coping with mania prodromes at 12 months, although there was no significant difference between the groups in coping with depression prodromes.

One area that requires future research concerns the impact of cognitive therapy on medication compliance. After 6 months, a significantly greater proportion of patients in the combined medication and cognitive therapy group (88%) than in the treatment-as-usual group (67%) reported missing their medication fewer than three times in the previous month. However, serum levels were available for only 50% of the sample, limiting the power of any calculation to test whether differences in compliance were reflected in serum levels. Nevertheless, more patients in the combined medication and cognitive therapy group (93%) met the criterion of an adequate serum level of mood stabilisers than in the treatment-as-usual group (78%). At this stage, it is not possible to tell to what degree cognitive therapy reduced bipolar relapse simply by improving compliance with mood stabiliser medication or by other mechanisms such as improving coping skills.

The principal limitation of the Lam *et al* (2003) study was that there was no control treatment for the increased level of face-to-face contact that the cognitive therapy patients received compared with

the treatment-as-usual group. Therefore, it is not possible to determine whether the improved outcome was due to specific aspects of cognitive therapy or due to non-specific therapy effects such as increased attention and support. Nonetheless, the study demonstrated that the addition of cognitive therapy to medication for bipolar disorder has benefits in reducing the frequency and durations of relapse/recurrence and in reducing the extent of hospitalisation.

Conclusions

Bipolar disorder is a relatively common and severe condition. Although the use of medication has produced substantial treatment benefits, particularly in the treatment of acute episodes, a substantial proportion of patients with bipolar disorder still relapse despite the use of mood stabilisers. Poor coping strategies in response to prodromes and disruptions of sleep and social routine have been implicated in bipolar relapse. Cognitive therapy is well suited to teach patients better coping strategies to deal with prodromes and stressors and thereby to minimise their risk of relapse. Pilot studies and one large-scale randomised controlled trial have found that the addition of cognitive therapy to routine mood stabilisers significantly reduces the number of bipolar episodes over a 1-year period. Although further large-scale trials with longer follow-ups are required to confirm these findings, the current evidence indicates that the addition of cognitive therapy to medication substantially improves the treatment of bipolar disorder. In clinical practice, helping patients to identify and respond effectively to their prodromes may help to reduce the risk of relapse.

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Multiple choice questions

1 **Over a lifetime, on average, a patient with bipolar disorder will experience:**
a 0–4 episodes of depression and 0–2 episodes of mania
b 4–8 episodes of depression and 0–4 episodes of mania
c 4–8 episodes of depression and 8–10 episodes of mania
d 8–12 episodes of depression and 4–8 episodes of mania
e 12–16 episodes of depression and 10–12 episodes of mania.

2 **More-recent studies suggest that, with lithium, the rates of relapse in bipolar disorder over 2 years are:**
a 20%
b 30%
c 40%
d 50%
e 60%.

3 **Known factors that predict lower response to lithium in bipolar disorder include:**
a a recent severe life event
b comorbid personality disorder
c mixed affective states
d gender of the patient
e rapid-cycling bipolar disorder.

4 **Common prodromes for mania include:**
a reduced need for sleep
b increased worry
c racing thoughts
d withdrawal from people
e increased goal-directed activity.

5 **Lam *et al* found that, compared with medication alone, the addition of cognitive therapy to medication for bipolar disorder:**
a reduced bipolar relapses over 1 year
b improved compliance with medication
c improved coping with depression prodromes
d reduced hospitalisation
e improved coping with mania prodromes.

MCQ answers

1		2		3		4		5	
a	F	a	F	a	F	a	T	a	T
b	F	b	F	b	T	b	F	b	T
c	F	c	F	c	T	c	T	c	F
d	T	d	T	d	F	d	F	d	T
e	F	e	F	e	T	e	T	e	T