

Case Study 3 Treatment-Resistant Chronic Depression and Light Therapy

A 24-year-old single woman in New York with a lifetime history of dysthymia and a history of anorexia and social phobia had suffered from chronic major depression for 6 years. She was unresponsive to multiple drug trials. Treatment with the monoamine oxidase inhibitor tranylcypromine 100 mg induced a full complement of early, middle, and late insomnia. Light therapy at 7 a.m. for 30 min promptly coalesced sleep (11:30 p.m. to 7 a.m.), and within 3 weeks the patient showed complete remission and was discharged. She continued with light + tranylcypromine at home, but was not compliant with light treatment. Whenever she stopped using the light, she would experience relapse within 2 days. On resumption of the light, she would feel improvement within 2 days and complete remission in 4 days. Although light alone might have maintained her improvement, with such a serious chronic depression it is difficult for psychiatrists to withdraw the drug and rely on light monotherapy [32].

3.3

Wake Therapy Added to Medication

The earliest observations in the 1970s of rapid clinical remission under wake therapy prompted the question whether wake therapy might potentiate the response to medication [20]. Rather than increasing antidepressant dosage for non-responders, adding wake therapy can trigger improvement.

Case Study 4 demonstrates that wake therapy can alleviate depression in lithium-treated bipolar patients.

Case Study 4 Bipolar Depression and Wake Therapy

A 51-year-old woman with difficult-to-treat bipolar 1 disorder was hospitalised in the Ospedale San Raffaele in Milano during a depressive episode that had lasted 8 months. After five mood episodes and three forced hospitalisations in 2 years, with so many disappointing therapeutic failures, the patient and her family became very pessimistic about psychiatry in general, so it was no surprise that they were skeptical

Table 5. Medications that have been used with wake therapy

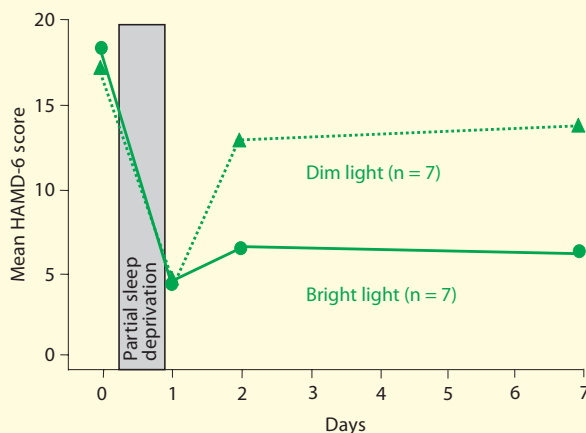
Lithium	Amitriptyline	Desipramine
Clomipramine	Nortriptyline	Amineptine
Fluoxetine	Sertraline	Paroxetine
Fluvoxamine	Duloxetine	Maprotiline
Pindolol		

about trying the chronotherapeutic approach. Upon admission, all medication was stopped, except for lithium, which was increased. She underwent three consecutive cycles of total sleep deprivation, each followed by a recovery night sleep. However, after the first wake therapy she experienced rapid and complete amelioration of the depressive syndrome leading to perceived euthymia in the early morning. The first recovery sleep was followed by a partial but definite depressive relapse. The second wake therapy led again to perceived euthymia, without relapse after recovery sleep, a benefit sustained after the third wake therapy. Euthymia persisted over the following days and the patient was discharged. High plasma lithium levels were maintained for 6 months, and then reduced to a target level of 0.75 mEq/l. Nine years later, the patient is still euthymic. She still takes lithium, which also prevents the moderate seasonal mood fluctuations which had recurred over her lifetime. Her brother, who suffered from severe bipolar disorder, also showed a good response to wake therapy for depression and dark therapy for mania [Benedetti].

Wake therapy appears to be synergistic with antidepressant drugs that potentiate monoaminergic neurotransmission, and lithium salts. Many trials have used both TCAs and newer antidepressants: sleep deprivation hastens and potentiates the response to antidepressants acting on all neurotransmitter target systems (serotonin, noradrenaline, dopamine), and mixed drugs (table 5). The only negative finding comes from a single study combining wake therapy with the antidopaminergic, sedative substance, trimipramine [73]. Indeed, patients do not respond well to sleep deprivation when on neuroleptics (dopamine antagonists).

Research Precedent 7

Responders to partial sleep deprivation in the second half of the night were given dim light (placebo) or bright light for a week. Patients on bright light did not relapse (redrawn from [74], with permission).



Ideally, wake therapy is administered when beginning medication, so rapid mood improvement occurs during the latency of action of antidepressants. From a practical point of view, both the patient and physician can expect substantial improvement during the most painful days when adequate medication has been prescribed, but has not taken effect. Moreover, the short-term response to wake therapy predicts long-term response to drug [20]. Even during the latency of action, medication can sustain the antidepressant effect of wake therapy, and prevent the usual relapse after recovery sleep.

3.4**Wake and Light Therapy Added to Antidepressant Drugs or Mood Stabilisers**

In an expanded protocol, medicated patients with non-seasonal unipolar depression received light therapy and a single session of late-night wake therapy at the start of treatment [74]. There was marked improvement in one day and benefit over a dim light control within one week (Research Precedent 7). In Milano, this model has been extended to general inpatient use, guided by successful treatment studies of non-seasonal major

depression (in conjunction with citalopram) and bipolar disorder (in conjunction with lithium), both of which showed large benefits attributable to morning light therapy.

Case Study 5 demonstrates how a colleague who had never administered sleep deprivation became convinced of its efficacy.

**Case Study 5
Very First Experience of Combined Wake and Light Therapy in a Copenhagen Hospital**

Mrs. K was 65 years old and had a 30-year-long history of bipolar illness. Her depressive episodes often lasted more than 3/4 of a year and did not much improve on antidepressant treatment, whereas her manic periods responded well to low doses of neuroleptics. In her previous depressive episode, which had lasted for 2 months without any sign of improvement, she had heard from her doctor of the possibility of carrying out wake therapy. She was admitted to an open unit, diagnosed with Major Depression with a score of 18 on the Hamilton Depression rating scale. Her medication was left unchanged. She did not have any problem staying up all night. In the morning, her Hamilton score was reduced to 2. After a normal night of sleep she performed two more total sleep deprivations interspersed with a normal night's sleep. During the early morning of the sleep deprivations she received 30 min of light therapy (10,000 lx), which was repeated later that morning. Her Hamilton score remained below 3 and she was discharged after 5 days. At home, she continued daily light treatment and was able to avoid sleep-