

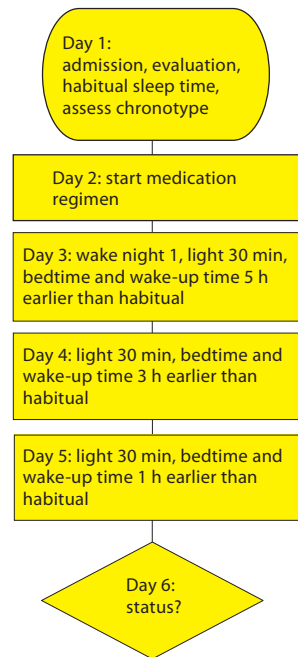
According to MEQ-derived internal time is important in order to optimise phase stabilisation. Furthermore, morning light both stimulates alertness and potentiates the onset of the antidepressant effect.

4.6

Wake Therapy + Light Therapy + Sleep Phase Advance

We converge on the triple chronotherapeutic ensemble by adding a 3-day course of sleep phase advance therapy after one night of wake therapy and initiation of light therapy. Sleep phase advance therapy has been shown to sustain the acute improvement following a single night of sleep deprivation, thus forestalling relapse. As in the previous section, the procedure follows a similar course, illustrated in flowchart 3. After day 6, the procedure follows that of flowchart 1.

- Following wake therapy on day 3 and initiation of light therapy, the patient remains awake until a scheduled bedtime 5 h before habitual sleep onset. Sleep is allowed for the patient's habitual sleep duration (in the example, 8 h). If not already awake, the patient is awakened 4 h before the scheduled light therapy session on day 5.
- The goal is a minimum of 5 hours' sleep on sleep-phase-advance nights. If the patient awakens before the end of the scheduled sleep period and cannot resume sleep, he or she may rise and remain in low-level room light of approximately 30 lx at eye level (e.g. from a shaded reading lamp with an incandescent 25-watt bulb, and without overhead lights). An alternative is the use of blue-blockers under normal room light in the unit (fig. 19).
- From the time of scheduled wake-up to the time of the morning light therapy session, the patient remains in low room light of approximately 30 lx. The low level is required to fore-



Flowchart 3

- stall circadian rhythm phase delays during a procedure designed to foster phase advances.
- On day 5, bedtime is delayed by 2 h, placing it 3 h before habitual bedtime.
- On day 6, bedtime is again shifted 2 h later, placing it 1 h before habitual bedtime. This is the target for sleep onset under continued morning light therapy, since light therapy truncates habitual sleep and shifts the circadian clock earlier.
- As in the earlier procedures without sleep phase advance therapy, if there are only mild residual depressive symptoms on day 6, light exposure duration is increased from 30 to 45 min on day 7. If the patient remains depressed or there has been relapse after transient improvement, the chronotherapeutics protocol is further elaborated (examples below).
The recommended combination therapy protocol is illustrated in figure 24.
The protocol as described times the phase advance precisely, which may not always be possible.

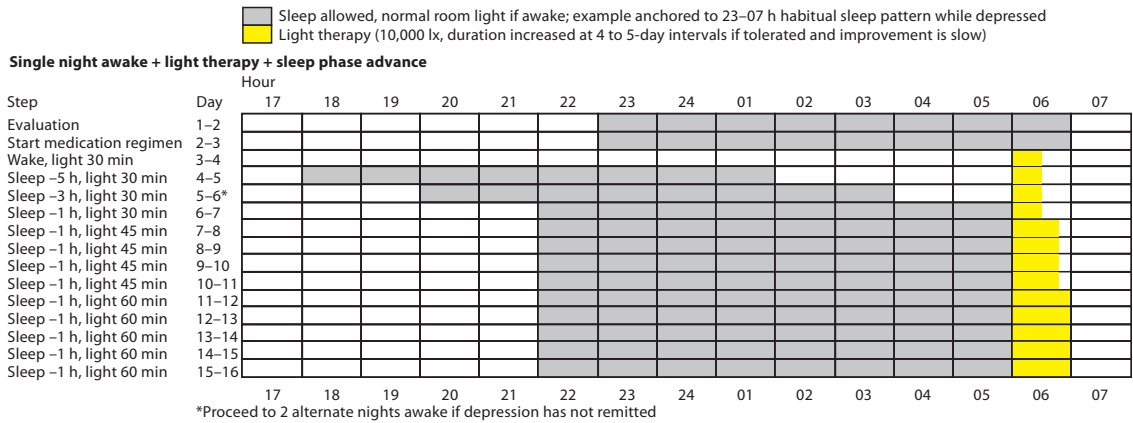


Fig. 24. Timeline for the same patient as in figure 22, encompassing spontaneous sleep while depressed, the starting time of morning light therapy from the MEQ algorithm, sleep deprivation, and a sleep phase advance. After earlier awakening on the nights of sleep phase advance, room light is kept low until the start of the light therapy session in order to forestall counteracting phase delay of the circadian clock.

Patients can also be left the freedom to choose when to go to bed (and be given a protected environment to enable early sleep), and be allowed to sleep as long as they like. This patient-friendly version of the protocol typically leads to a spontaneous phase advance of sleep onset by about 2 h (as measured by actimetry) [80]. However, in this flexible version of the phase advance protocol the patients are not required to wake up early, and in fact experience shows that they sleep longer in the recovery night after sleep deprivation. Clearly, however, in a research protocol, phase-advanced bedtime should be scheduled according to the patient’s chronotype.

4.7
Three Alternate Nights of Wake Therapy + Light Therapy + Freely Chosen Sleep Phase Advance

The fully elaborated chronotherapeutics ensemble has been established in Milano as the procedure of choice for the treatment of by a major depressive episode without psychotic features in

the course of bipolar disorder. It can also be used for patients who have been non-responsive at the earlier steps.

The complete triple wake protocol requires 6 days.

- Three nights of wake therapy alternate with 3 nights of freely chosen sleep phase advance.
- When wake therapy is repeated three times, we defer increasing light therapy duration from 30 min until day 9, giving precedence to the sleep-wake procedures, which are more likely to have an immediate effect.
- If the patient remains symptomatic, but with partial improvement at day 13, light therapy duration is increased to 60 min. Many patients with non-seasonal depression have settled on a 60-min maintenance regimen. In such long sessions, one may stand up and stretch for a few minutes, away from the light box, after half an hour of exposure.