Both sleep and motor activity have a bidirectional relationship with depression. The existing literature on motor activity during therapeutic sleep deprivation in depressed patients is inconsistent and fragmentary. In the present study we measured motor activity continuously during 40 hours of sleep deprivation in depressed patients. Thirty-four inpatients suffering from a major depression (DSM-IV) underwent sleep deprivation with a continuous waking period of 40 hours. Motor activity of the patients was continuously recorded using an actigraph on the non-dominant wrist. The effect of sleep deprivation was assessed by the Hamilton Depression Scale (six-item version), thus separating the group into responders and non-responders to sleep deprivation. We found no significant differences in motor activity between responders and non-responders on the day before sleep deprivation. During the night, responders to sleep deprivation exhibited a higher motor activity and less periods of rest. On the day after sleep deprivation, responders exhibited a higher activity, too. Motor activity levels differ between the two groups, thus giving more insight into possible mechanisms of action of the therapeutic sleep deprivation. We suggest that higher motor activity during the night prevents naps and leads to better response to sleep deprivation.