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Special Feature Article

Management of Hypersomnia in Mood Disorders

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Abstract

Complaints of hypersomnia in mood disorders are more common in women than men, younger people than older people, and those with bipolar rather than unipolar depression. Hypersomnia symptoms such as prolonged nighttime sleep and daytime sleepiness have been shown to be risk factors for recurrence and relapse of depressive episodes and are considered to be clinically important symptoms. Even if patients complain of hypersomnia, objective findings on prolonged nighttime sleep and excessive daytime sleepiness are identified by polysomnography and multiple sleep latency tests only in some patients, suggesting that hypersomnia in mood disorders can be pathologically different from central hypersomnia, such as narcolepsy. In a depressed state, prolonged time in bed due to fatigue, decreased motivation, and lying in bed as an avoidance behavior may also be regarded as hypersomnia symptoms.

When physicians hear complaints of hypersomnia, they should first exclude the sedative effect of the drugs that patients are taking. It is also necessary to exclude excessive daytime sleepiness due to insomnia and other sleep disorders, such as obstructive sleep apnea, restless legs syndrome, and periodic limb movement disorder. A recent study demonstrated that the hypersomnia symptoms of long sleep and excessive sleepiness are independent and not correlated. Therefore, it is also important to distinguish them in order to appropriately manage them.

As for treatment of hypersomnia symptoms in mood disorders, there are a few methods that have been shown to be effective for some subtypes and related diseases. In

seasonal affective disorder, bright light therapy has been reported to be effective not only for depressive symptoms but also for hypersomnia. Low-dose aripiprazole, which has come to be used for delayed sleep phase disorder, may be effective for hypersomnia symptoms in mood disorders, but this has not yet been verified. Bupropion, which has an inhibitory effect on noradrenaline and dopamine reuptake, was reported to be more effective than selective serotonin reuptake inhibitors for hypersomnia in depression. In the present paper, the author reviewed the literature regarding hypersomnia in mood disorders, and described the current approach to its management as well as the author's proposed approach.

Keywords : mood disorders, hypersomnia, long sleep, excessive sleepiness

Introduction

Sleep disturbances are highly prevalent in mood disorders. Insomnia is often observed in depressed patients, but hypersomnia is also frequently reported. Compared with insomnia, hypersomnia has fewer effective treatment methods, and is often difficult to deal with in daily clinical practice. In this article, the author review current knowledge of hypersomnia in mood disorders, and discuss how to deal with it.

I. Prevalence of hypersomnia in mood disorders

Hypersomnia in mood disorders is more frequently reported in women than in men and in younger than in older patients 21)26). By subtype, hypersomnia occurs in 10-20% of patients with unipolar depression 29),

whereas it is present in about half of patients in depressed phase of bipolar disorder 19). Depressive episode in bipolar II disorder is often difficult to differentiate from unipolar depression, but hypersomnia is considered a feature that suggests the possibility of bipolar II disorder, along with racing/crowded thoughts, irritability, and psychomotor agitation 7).

The prevalence of hypersomnia is even higher in seasonal affective disorder (SAD), which causes depression every winter and shows spontaneous remission in spring, and is observed in about 70% of patients 13). This, along with overeating accompanied by carbohydrate starvation, is a characteristic feature of this disorder 30).

II. Relationship between hypersomnia and the course of mood disorders

Insomnia is known to be a risk factor for onset and poor prognosis in mood disorders 33), and hypersomnia is also considered to have a similar effect.

Breslau, N. et al. investigated the association between insomnia and hypersomnia and psychiatric morbidity 3 years later in a general population aged 21 to 30 years, and reported that insomnia and hypersomnia were risk factors for the development of depression with odds ratios of 4.0 (95% confidence interval: 2.2 to 7.0) and 2.9 (95% confidence interval: 1.5 to 5.6), respectively 9).

In major depression, insomnia persists in nearly half of patients even after remission 20), and such persistent insomnia increases the risk of recurrence of depression 12). Hypersomnia also persists after remission in about 70% of patients 37), and persistent hypersomnia has been pointed out to be a risk for recurrence of depression 2). In bipolar disorder, residual hypersomnia in remitted phase has been reported to be a risk for relapse not only in the depressive phase 17) but also in the (hypo)manic phase 18).

Therefore, hypersomnia is as important as insomnia in preventing

the onset, recurrence, and relapse of mood disorders.

III. Confusion regarding the definition of hypersomnia: Two hypersomnolence symptoms

Table 1 shows the main symptoms regarding the diagnostic criteria for hypersomnia in DSM-5 (Diagnostic and Statistical Manual of Mental Disorders, 5th edition) 3), ICD-10 (International Classification of Diseases, 10th edition) 36), and ICSD-3 (International Classification of Sleep Disorders, 3rd edition) 2). In DSM-5 the definition hypersomnia includes recurrent periods of sleep, prolonged main sleep episode, or difficulty being fully awake after abrupt awakening.

In contrast, ICD-10 considers daytime sleepiness or sleep inertia (prolonged transition from sleep to wakefulness) as hypersomnia symptoms, and does not include prolonged nocturnal sleep. ICSD-3, which is widely used in sleep medicine, considers only daytime sleepiness to be a hypersomnia symptom. Because the definition of hypersomnia differs by diagnostic category, it is possible that different diagnostic criteria may yield different research results even when dealing with the same topic. This inconsistency in diagnostic criteria is

one of the factors hindering the development of research on hypersomnia in psychiatric disorders, and it is hoped that this will be resolved as soon as possible.

Most psychiatrists probably consider daytime sleepiness/drowsiness and prolonged night-time sleep as hypersomnia symptoms. In this respect, DSM-5 criteria seem to be the closest to the clinicians' thoughts. Kaplan, K. A. et al. evaluated hypersomnia symptoms in 159 remitted bipolar patients and conducted factor analysis 18). The results showed that hypersomnia symptoms were divided into two factors: "excessive daytime sleepiness" and "long night-time sleep," and there was no correlation between the two ($r=-0.09$). Based on these results, it is recommended to distinguish between these two types of hypersomnia symptoms and consider how to deal with them individually.

IV. Sleep examination findings in patients with mood disorders complaining of hypersomnia: Differences from central hypersomnia

Several studies have examined nocturnal sleep and daytime sleepiness from a sleep medicine perspective by performing polysomnography (PSG) and the

multiple sleep latency test (MSLT) in patients with mood disorders complaining of hypersomnia.

Billiard, M. et al. performed PSG for 36 untreated patients with mood disorders complaining of hypersomnia (median age: 45 years), and found that the mean total sleep time was 7 hours and 40 minutes, and 13.8% of the patients slept more than 9 hours 8). Given that the average total sleep time of a normal 45-year-old person is about 6.5 hours 22), it is considered that only some patients actually sleep for an extremely long time.

In a study that examined sleep duration using an actigraph in patients with bipolar disorder in remission, the average actual sleeping time was 7.7 hours, even in patients who complained of long night-time sleep. However, the duration of lying in bed was significantly prolonged in such patients, averaging 10.1 hours, suggesting that in mood disorders, lying in bed without falling asleep may also be a complaint of hypersomnia 18). On the other hand, in SAD, total sleep time based on PSG was found to be about 1 hour longer in winter than in summer 4), suggesting that the actual condition of hypersomnia may differ depending on the subtype of mood disorder.

Billiard et al. also examined daytime sleepiness in patients with mood disorders complaining of hypersomnia with MSLT, which is used to diagnosis for central hypersomnia such as narcolepsy, only 22% of the patients showed a mean sleep latency of less than 8 minutes, a criterion for pathological sleepiness 8). This suggests that the sleepiness reported by patients with mood disorders is different from that of those with central hypersomnia.

V. Possible mechanisms and associated conditions

1. Relation with psychiatric symptoms

As mentioned above, daytime sleepiness and prolonged night-time sleep can be confirmed by objective methods in only a small proportion of patients complaining of hypersomnia. This suggests the possibility that prolonged time in bed may also be complained of as hypersomnia in patients with mood disorders. In such patients, decreased motivation and fatigue may be background factors 8). In addition, in a depressed state in which psychological factors are strongly involved, patients may "spend time in bed" to avoid confronting problems 16), and this may be considered as hypersomnia in some cases.

It has been reported that many

depressed patients estimate their sleeping time to be shorter than the time they actually sleep, while one-third of patients estimate their sleeping time to be longer 14). This misperception of sleep duration may also be associated with complaints of hypersomnia.

2. Disturbance of homeostatic mechanisms

Tononi, G. et al. at the University of Wisconsin have been conducting sleep EEG studies of various psychiatric disorders using high-density electroencephalography, and have also studied depressed patients with hypersomnia. They defined hypersomnia as a state of sleeping more than 10 hours per day or sleeping more than usual for two weeks or longer, and recorded all-night EEGs of depressed patients with and without hypersomnia using a 256-channel electroencephalograph 25). Depressed patients with hypersomnia showed less slow-wave sleep in the parieto-occipital region compared with patients without hypersomnia. These results suggest that patients with hypersomnia do not fully recover their cortical function in this region even after night-time sleep, resulting in a prolonged sleep duration and daytime sleepiness.

3. Related sleep disorders causing hypersomnia

Hypersomnia in patients with mood

disorders may be a symptom of the mood disorder itself or may be caused by other sleep disorders. Obstructive sleep apnea (OSA) is a relatively common sleep disorder among psychiatric disorders. The prevalence of OSA in the general population is estimated to be 3-7% in adult males and 2-5% in adult females, but depression and bipolar disorder are reported to be comorbid with OSA at high rates of 36.3 and 24.5%, respectively. OSA causes airway obstruction during sleep, resulting in oxygen desaturation and disruption of nocturnal sleep. This results in daytime sleepiness. The reasons why mood disorders are more likely to be complicated by OSA are considered to be related to obesity 15) caused by inactivity and overeating, the effects of smoking and alcohol 27), and the effects of medications. In addition, it has been pointed out that not only serotonin function in the brain but also serotonin function acting on the cervical musculature is decreased in depression, which may lead to muscle hypotonia and the development of OSA 35). Since OSA and depression are mutually aggravating factors 5), it is clinically important to suspect the presence of OSA in the background of hypersomnia 5).

Restless legs syndrome (RLS) is a sleep disorder in which abnormal sensations in the lower limbs cause marked

difficulty in falling asleep. RLS is characterized by the urge to move the legs, which is relieved when moving the legs. Antidepressants and antipsychotics are known to cause RLS. It is also important to suspect that RLS may be induced by the medications being administered, resulting in a worsening of night-time sleep quality and daytime sleepiness.

One of the most common sleep disorders complicated by RLS is periodic limb movement disorder (PLMD). Sleep is disrupted by periodic jerking of the lower limbs (dorsiflexion of the ankle joint is accompanied by dorsiflexion of the big toe and flexion of the knee joint) during night-time sleep. Patients with PLMD complain of "waking up with a jerking leg" or "not being able to sleep because of the jerking leg. As well as RLS, antidepressants and antipsychotics can cause PLMD.

If the patient complains of hypersomnia, it is important to consider whether the patient's nocturnal insomnia has been well-treated, as daytime sleepiness may also occur if insomnia is not adequately treated.

VI. Assessment of hypersomnia in mood disorders

At present, there are no established clinical guidelines for hypersomnia in mood disorders. Therefore, based on

what has been described so far, the following is the author's draft of an assessment procedure when hypersomnia symptoms are observed (Table 2).

1. Could it be due to the drugs?

When daytime sleepiness or prolonged nocturnal sleep is observed, the first thing to consider is the influence of medications being taken. If the patient is being treated with antidepressants or antipsychotics that have sedative effects, check for hypersomnia symptoms caused by these drugs. The carryover effect of prescriptions for insomnia should also be considered. This is most likely the case when a patient who originally complained of insomnia becomes a hypersomniac as his/her insomnia improves.

2. Is the patient getting enough sleep at night?

The most common sleep disorder in depression is insomnia, which is observed in about 85% of patients (32). Daytime sleepiness can also occur when insomnia has not improved sufficiently, so it is necessary to check for insomnia. It is also important to suspect the possibility that OSA, RLS, or PLMD may be interfering with nocturnal sleep, since it may cause prolonged sleep duration and daytime

sleepiness. The presence or absence of snoring, discomfort in the lower limbs when falling asleep, and twitching of the legs during sleep should be confirmed with the patient and family members.

3. Distinguishing between types of hypersomnia

Hypersomnia symptoms can be divided into daytime sleepiness and prolonged sleep, and recent studies have shown that there is no correlation between the two (18). Therefore, consciously evaluate whether it is one of the two types of hypersomnia symptoms, or both.

4. Distinguish between actual sleep and lying in bed

In mood disorders, time spent lying in bed without sleeping may also be considered hypersomnia. If the question is asked: "How long have you been sleeping?", the patient may answer: "I have been sleeping all day.", even if he/she has been lying down because of fatigue. It is necessary to ask specific questions, such as whether the patient is actually sleeping, or whether the patient is awake but spends time lying down due to difficulty in leaving the bed. If the latter is the case, treatment for depressive symptoms should be strengthened, rather than

for hypersomnia. Some patients may consciously try to sleep to avoid confronting a problem, in which case stressors need to be addressed.

VII. How to deal with hypersomnia in mood disorders?

If a patient experiences excessive daytime sleepiness or prolonged nighttime sleep, interventions should be considered. At present, however, there are a few methods that have been shown to be effective for some subtypes and related diseases. In SAD, bright light therapy (BLT) has been reported to improve daytime sleepiness and depressive symptoms 24). Since the shortening of daylight hours in winter is associated with the onset of depressive symptoms in SAD, BLT is used to create a light environment similar to that of summer. Figure 1 shows standard phototherapy apparatus using white fluorescent lamps, which deliver 2,500-10,000 lux high-intensity light for 30 minutes to 2 hours in the morning. Recently, wearable light-illuminators such as those shown in Figure 2 have also become available, and it has been pointed out that there are many similarities between SAD and bipolar disorder, and some researchers consider SAD as a type of bipolar spectrum disorder 1). Considering these points and the fact that high-intensity light itself has an arousing effect 10), BLT

may be effective for hypersomnolence symptoms of mood disorders other than SAD, especially for hypersomnolence in bipolar disorder. Several studies have shown that BLT is effective for depressive symptoms of bipolar disorder 34), but its effect on hypersomnia symptoms has not been fully investigated.

In recent years, low-dose aripiprazole administration for delayed sleep-wake phase disorder (DSWPD) has become a frequently used technique in the field of sleep medicine. In DSWPD, the body's internal clock is delayed, making it difficult to fall asleep until late at night or early in the morning, and difficult to wake up in the morning. It has been reported that the administration of 0.5 to 3 mg of aripiprazole in DSWPD shortens the duration of sleep and makes it easier to wake up, and its agonistic effect on dopamine receptors is considered to be involved as a mechanism 23). It is expected to be effective for hypersomnia symptoms of mood disorders, especially for prolonged sleep, but there have been no systematic studies on its efficacy to date.

The efficacy of psychostimulants such as modafinil and methylphenidate has been investigated 28)38), but no solid evidence has been obtained that they are beneficial in the treatment course of depression 11). Therefore, hypersomnia in mood disorders is considered a

separate condition from central hypersomnia such as narcolepsy.

In addition, there is a report that bupropion (not approved in Japan), an antidepressant with noradrenaline and dopamine reuptake inhibitory effects, was more effective than SSRIs for hypersomnia in depression 6).

Conclusion

This paper reviewed the literature regarding hypersomnia in mood disorders, and described the current approach to its management as well as the author's proposed approach. Compared with insomnia, hypersomnia remains largely unknown, and only a few methods have been shown to be effective in treating some subtypes and related disorders. Hypersomnia in mood disorders may be caused by a mixture of biological and psychological factors, the proportion of which may vary greatly from subtype to subtype. It is important to distinguish hypersomnia by subtype of mood disorders and symptom (prolonged nocturnal sleep or daytime sleepiness) in order to develop an effective treatment.

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表 1 各診断基準における気分障害の過眠の定義（著者作成）

1) 精神疾患に関連する過眠障害 (DSM-5 ³⁾)
過剰な眠気の訴えがあり、以下のうち 1 つ以上
・繰り返す睡眠
・9 時間以上の睡眠エピソードがあっても回復感がない
・急な覚醒後、十分に覚醒を維持できない
2) 非器質性過眠症 (ICD-10 ³⁶⁾)
昼間の過剰な眠気、あるいは睡眠不足によらない睡眠発作、お
よび/または目覚めから覚醒への移行が長引くこと（ねぼけ）
3) 精神疾患に関連する過眠症 (ICSD-3 ²⁾)
耐え難い睡眠要求や日中に眠りこんでしまうこと

Table 1 Definitions of hypersomnia for mood disorders in each diagnostic criterion (prepared by the authors)

- 1) Hypersomnolence disorder associated with psychiatric disorders (DSM-5³⁾)
Complaints of excessive sleepiness, and one or more of the following:
Repetitive sleep
No sense of recovery after a sleep episode of 9 hours or more
Inability to stay awake sufficiently after sudden awakening
- (2) Non-organic hypersomnia (ICD-10³⁶⁾)
Excessive daytime sleepiness, sleep attacks not due to sleep deprivation, and/or prolonged awakening-to-wakefulness transition (sleepwalking)
- (3) Hypersomnia related to psychiatric disorders (ICSD-3²⁾)
Intolerable sleep demands or falling asleep during the day

表 2 気分障害の過眠のアセスメント

1. 薬剤の影響（鎮静）ではないか
2. 夜間睡眠は十分にとれているか
不眠や他の睡眠障害の合併には注意が必要
e.g. 睡眠時無呼吸, レストレスレッグス症候群
3. 過眠のタイプを区別（長時間睡眠 or 日中の眠気）
4. 実際の睡眠なのか臥床なのか区別

Table 2 Assessment of hypersomnia in mood disorders

1. Is the patient under the influence of drugs (sedation)?
2. Is the patient getting enough sleep at night?
Insomnia and other sleep disorder complications should be noted,
e.g., sleep apnea, restless legs syndrome
3. Distinguish between types of hypersomnia (prolonged sleep or daytime sleepiness)
4. Distinguish between sleeping and lying down



図 1 卓上型光療法器

Figure 1 Desktop Phototherapy Device



図 2 ウェアラブル型光療法器

Figure 2 Wearable Phototherapy Device