Sleep and Hypnosis
A Journal of Clinical Neuroscience and Psychopathology

Sleep Hypn. 2020; 22(01):1-7
10.37133/Sleep.Hypn.2020.22.0001

CASE REPORT

Efficacy of Modafinil for Dissociative Identity Disorder with Hypersomnia

Adriana Fiszman[1*], Ivan Figueira[2], Camilla Pinna[1], Claudia Cecilia da Silva Rego[1], Soniza Vieira Alves-Leon[1], Carlos H. Schenck[3]

1 R. Prof. Rodolpho Paulo Rocco, 255 - Cidade Universitaria, Universidade Federal do Rio de Janeiro, Brazil
2 Av. Venceslau Bras, 71 - Botafogo, Rio de Janeiro, Universidade Federal do Rio de Janeiro, Brazil
3 420 Delaware Street SE, University of Minnesota Medical School, Minneapolis, USA

ABSTRACT
We report the case of a 22-year-old female victim of childhood sexual abuse with dissociative identity disorder and hypersomnia who remitted from both clinical conditions with the use of modafinil 400 mg/day. We review the literature supporting the sleep-dissociation theory, where trauma-related memories induce a labile sleep-wake cycle allowing dreamlike mentation to intrude into waking consciousness and precipitate dissociative symptoms. The studies examined here found high correlations between dissociation and unusual sleep experiences. This may explain why in our case report modafinil, a medication with wake-promoting properties, improved both excessive daytime sleepiness and dissociation. Future studies are needed to determine which alterations in the sleep-wake cycle are most associated with dissociative disorders. We suggest a new perspective on the use of medications for comorbid hypersomnia, such as modafinil, in the treatment of dissociation.
Keywords: Dissociative disorders, Excessive daytime sleepiness, Sleep disorders, Psychopharmacology, Childhood sexual abuse

Introduction

Dissociative disorders are characterized by disruption (dissociation) in the usually integrated mental processes: perception, memory, identity, emotion, behavior, body representation, and movements. Dissociated mental functions are separated from the primary consciousness and experienced as being outside the individual's control. Dissociative disorders include dissociative amnesia, depersonalization/derealization disorder, dissociative identity disorder, other specified dissociative disorder, and unspecified dissociative disorder (American Psychiatric Association, 2013).

Lifetime prevalence rates of dissociative disorders are approximately 10% (range = 4.3–45.2%) in various psychiatric settings and in the general population (Sar, 2017). These disorders are severe and disabling – therefore exacting a major toll on individuals, as well as being costly to the mental health system. Specialized psychotherapy is the cornerstone of the treatment of dissociative disorders. On the other hand, adjunctive pharmacologi-

***Correspondence:** adriana.fisz@gmail.com, +55 21 999720259, R. Prof. Rodolpho Paulo Rocco, 255- Cidade Universitria da Universidade Federal do Rio de Janeiro, Rio de Janeiro- RJ, 21941-590 Brazil.
Received: 08 September 2020 **Accepted:** 05 May 2021

Sleep and Hypnosis
Journal homepage:
http://www.sleepandhypnosis.org
ISSN:1302-1192 (Print) 2458-9101 (Online)

cal treatment of these disorders is in its infancy. Of all the dissociative disorders, depersonalization disorder has the most accumulated evidence in terms of pharmacological efficacy. A few clinical trials showed that the opioid antagonists (naloxone and naltrexone) have a positive effect on depersonalization (Bohus et al., 1999; Nuller et al., 2001; Simeon & Knutelska, 2005). Two open-label trials reported that lamotrigine benefits depersonalization as add-on therapy with selective serotonin reuptake inhibitors (Sierra et al., 2001; Sierra et al., 2006). Almost no pharmacologic studies have been conducted for dissociative disorders other than depersonalization. To our knowledge, there is no study published showing that modafinil is useful in the treatment of dissociation.

The following case describes a 22-year-old female diagnosed with dissociative identity disorder associated with hypersomnia. Posttraumatic stress disorder (PTSD) was her secondary diagnosis. After a partial remission of PTSD symptoms with paroxetine and psychotherapy, modafinil was added to improve hypersomnia. This symptom improved as expected – but surprisingly, a full remission of the dissociative identity disorder also occurred.

An informed consent was obtained from the patient for writing the case report.

Case Report

The patient is a 22-year-old female, white, single, catholic, born in Rio de Janeiro. When she was eighteen, her mother and boyfriend witnessed sudden episodes of "zoning out" and "a vacant and distant gaze," with no response to the environment. These "absences" lasted from one to fifteen minutes. After regaining consciousness, she could not remember what had happened. The crises occurred in the absence of any triggering factor. A few months later, the patient also experienced fainting with flaccid body and eyes closed lasting up to an hour. During nocturnal sleep, she sat on the bed with eyes fixed, no contact with surroundings, and no response to requests from others. She looked around with a fearful facial expression running towards the door as if going away. She did not recognize when the mother or boyfriend held her and pushed or kicked them away. After that, she passed out for some time. These episodes also occurred in the waking state during the day. Periods of age regression were also frequent. Upon awakening from a deep sleep at night the patient spoke with the voice, vocabulary, and gestures of a seven-year-old girl. She asked someone to call her father (who died when she was nine): "where is my father? I want to call him." After another deep sleep period, she regained adult identity, not remembering what had transpired. During some regression events, the patient did not recognize the boyfriend and instead used her sexual assailant's name, which occurred at six-years-old.

The patient was sexually abused in childhood from age six to eight years by her adolescent cousin. She described the following traumatic episodes: "he would take off my pants, stay on top of me and rub his organ against mine...he said that I could not tell anyone; if I did, no one would ever like me...his words left me without a reaction". Since the abuse, the patient has had daily intrusive memories, which she tries to avoid because of intense distress, shortness of breath, and palpitations causing sleep initiation insomnia. A recurring memory at bedtime is "when he put his penis in my mouth, I was extremely disgusted." She never remembered if vaginal penetration occurred. The patient avoided sexual intercourse throughout her life. She started a relationship with her current boyfriend at seventeen but never had sex with him. She once told her doctor that she was "lucky" because her boyfriend "couldn't" have sex due to back pain.

The first time she was seen by a psychiatrist and then by a neurologist, she was misdiagnosed with panic disorder and epilepsy. After two years of unsuccessful treatments of both conditions with sequential trials of venlafaxine, valproic acid, sertraline, fluoxetine, carbamazepine, and clonazepam, the patient was admitted to an Epilepsy Center for the differential diagnosis between epileptic seizures and psychogenic nonepileptic seizures (PNES). PNES are events that mimic epileptic seizures but do not have the electroencephalographic features that typify epilepsy (Devinsky et al., 2011). Most presentations of PNES fulfill the diagnostic criteria of conversion disorders or dissociative disorders,

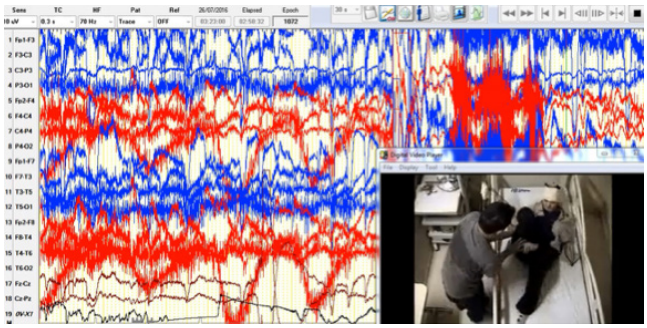

Figure 1: Psychogenic nonepileptic seizure with aggressive behavior

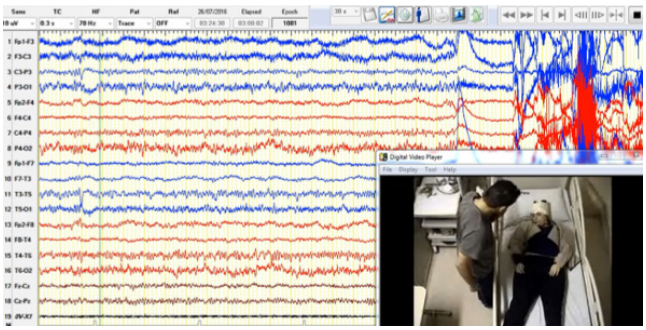

Figure 2: Fainting with EEG wakefulness

according to the DSM 5 (American Psychiatric Association, 2013).

The patient was monitored through video-electroencephalography (EEG) for 24 hours. During the day, the patient experienced periods of drowsiness and spontaneous sleep, correlating with a decrease in the posterior alpha rhythm and the presence of sleep spindles, K-complexes, theta and delta waves, indicating well-established intermediate and deeper stages of sleep. At certain times, the delta rhythm prevailed throughout the tracing. During the night, the patient rarely fell into deep sleep; she switched between waking and drowsiness, which correlated with the presence of posterior alpha rhythm and diffuse theta activity.

At night, the patient exhibited groaning, grunting, and extreme trunk movements. Her boyfriend's approach triggered defensive behavior through kicks and slaps (Figure 1). These events were followed by fainting and occurred several times throughout the night (Figure 2). Since no epileptic discharges were noted, the diagnosis of PNES was made. PNES emerged from periods of sustained EEG-wakefulness. The patient's PNES manifestations of "zoning out" and defensive and violent behavior followed by amnesia constituted a marked discontinuity in the sense of self and sense of agency typical of dissociative phenomena. The additional and well-characterized episodes of fugue and age regression – followed by amnesia – led to the diagnosis of dissociative identity disorder.

The patient was also diagnosed with PTSD due to intrusive and recurrent memories of sexual abuse, accompanied by anguish, palpitations, breathlessness, difficulty sleeping, nightmares, efforts to avoid traumatic memories and sexual contact, and blaming herself for not having reacted to the sexual assault. The patient also complained of excessive daytime sleepiness, with perceived sleep lasting up to twenty hours. Hypersomnia could not be an adverse drug effect because, during the diagnostic process, all medications were discontinued, and yet this symptom persisted. Upon waking up in the morning, the patient frequently felt extreme drowsiness, which caused her to miss important commitments**.** Despite her complaint of hypersomnia, the patient had no other narcolepsy symptoms, such as sleep attacks, cataplexy, sleep paralysis, or hypnagogic/hypnopompic hallucinations. She had no neurological diseases, nor history of sleep disorders in the family. Her BMI was 32.4 kg/m^2, but she didn't snore.

Initially, paroxetine was introduced up to a dose of 50 mg/day to treat PTSD. A moderate improvement in intrusive memories, symptoms of distress, shortness of breath, and palpitations was noted. However, all manifestations of dissociative identity disorder remained, resulting in disability and great suffering. After one year of treatment of PTSD with paroxetine, modafinil was added (for hypersomnia) at 100 mg/day and titrated up 100 mg, monthly, to a total of 200 mg in the morning and 200 mg in the afternoon. Modafinil is a novel wake-promoting drug approved for treating hypersomnia that is distinct from the traditional central nervous system stimulants such as amphetamine or methylphenidate, and does not share their known adverse effects, involving euphoria and other altered mood states, abnormal behaviors, and dosage tolerance. Although its mechanism of action is incompletely understood, it is a partial alpha 1-adrenergic agonist.

Surprisingly, not only the hypersomnia complaint completely remitted with modafinil, but also the dissociative identity disorder. Minor PTSD symptoms remained after the modafinil add-on to paroxetine, but of no clinical significance. After 3 years of continuous use of modafinil – along with paroxetine –, the patient is still in psychiatric treatment, with no recurrence of dissociative symptoms, or hypersomnia. Through the first year of treatment the patient had undergone psychotherapy. At the beginning of the second year, she started working and resumed her master's degree studies in social sciences. However, she still avoids sexual intercourse, saying that "this is not missed."

Discussion

Despite being common and highly disabling, dissociative phenomena remain one of the major puzzles in neuropsychiatry and are usually refractory to pharmacological treatment. Clinicians have few treatment options to alleviate the suffering of persistent dissociation, apart from specialized psychotherapy that is often difficult to find and can involve a lengthy and expensive treatment course; therefore, the use of agents to treat comorbid sleep disorders, such as modafinil, has therapeutic and also pathophysiological implications related to dissociative phenomena.

Here, we report the first published case showing the complete and sustained efficacy of modafinil on dissociation. A 22-year-old female patient with a well-documented dissociative identity disorder and hypersomnia completely remitted from both clinical conditions with the use of modafinil 400 mg/day. A previous communication reported a similar finding, but this was an Abstract that had limited information. Dang and Kokkin (2013) reported a female patient with dissociative identity disorder and idiopathic hypersomnolence diagnosed by polysomnography. Dissociative episodes and hypersomnia improved with modafinil. However, the dose of modafinil, the extent of benefit, and the length of treatment were not mentioned, nor the age of the patient. The authors hypothesized that hypersomnia and dissociation could constitute the same phenomenon at the spectrum extremities.

The sleep-dissociation model

Dissociative disorders seem to be the result of exposure to traumatic events, especially in childhood. Individuals rely on dissociation to escape from painful memories (Bremner & Marmar, 2005; Vermetten et al., 2007). van der Kloet et al. (2012a) claimed that the connection between trauma and dissociation articulates why, but not how, trauma produces dissociative symptoms. The authors hypothesized that as a result of intrusions of trauma-related memories, some individuals endure a labile sleep-wake cycle that may support intrusion of sleep phenomena (i.e. dreamlike mentation) into waking consciousness, which in turn triggers dissociative symptoms.

In a pioneering study on dissociation and sleep in two large student samples, Watson (2001) noted that unusual sleep experiences were related to dissociative symptoms. To test the sleep-dissociation theory, van der Kloet et al. (2012a) reviewed 23 studies, mostly relying on nonclinical samples. Based on more than 5,600 participants, these studies consistently provided evidence establishing moderate to strong correlations (0.30 to 0.55) between unusual sleep experiences and dissociative symptoms.

The link between sleep and dissociation was replicated in further studies. van Heugten-van der Kloet et al. (2014) used the path analysis approach to study 139 undergraduate students and showed that associations between dissociation and early-childhood traumatic experiences were mediated via unusual sleep experiences as nightmares, sleep paralysis, and hypnagogic hallucinations. In a sample of 372 undergraduate students, Selvi et al. (2017) found meaningful associations between pathological dissociation, insomnia, and sleepiness. Consonant with the literature, insomnia and sleepiness significantly contributed to pathological dissociation.

Lately, Nobakht and Dale (2019) evaluated 200 university students. They found that nightmares and other sleep disorders mediated the relationship between trauma and dissociation. In particular, nightmares' mediation role seemed to be of considerable importance on the trauma–dissociation relationship. These findings suggested that traumatic events might engender both sleep disturbances and

nightmares, which may play a pivotal role in dissociative symptoms. It is also consistent with the Levin and Nielsen (2007) theory, which emphasized that the processes involved in producing nightmares are also engaged during the expression of pathological signs and symptoms during the waking state. When dreaming and waking states become undifferentiated, the dreamlike mentation may intrude into waking consciousness and contribute to dissociative experiences.

van der Kloet et al. (2012b) studied the correlation between unusual sleep experiences and dissociation in a diverse inpatient sample at a private psychiatric clinic (N = 195). The association was measured on arrival and at discharge, six to eight weeks later. It was demonstrated that gains in sleep quality (specifically, decreases in narcoleptic symptoms) were related to the reduction of dissociative experiences. Narcoleptic symptoms included hypnagogic imagery, sleeping in social occasions, sleep attacks, cataplexy, and sleep paralysis. The authors used the Dissociative Experiences Scale (DES). A score of 30 is the cutoff above which patients with dissociative disorders are identified (Carlson & Putnam, 1993). The DES Taxon (DES-T) is a modified version of the DES relying on a subset of eight items. DES-T is sensitive to extreme forms of dissociative pathology (Waller et al., 1996).

Interestingly, at baseline assessment, 24% of the patients who completed therapy exceeded the DES clinical cutoff. However, only 12% of the completers met this cutoff at follow-up. Similarly, when DES-T was considered, 24.6% of participants met the taxon membership criteria at baseline versus only 9.7% after treatment. Sleep gains were associated with a decrease in other psychiatric symptoms, particularly anxiety and depression. However, this decrease did not account for the substantial and definite beneficial effects of decreasing narcolepsy-like symptoms on dissociation, as indexed by DES and DES-T scores.

Relevant to the case presented here was the finding by van der Kloet et al. (2012b) that the reduction in narcoleptic symptoms was the best predictor of improvement of severe dissociative pathology – as measured by the DES-T. This result raises the hypothesis of a pathophysiologic association between dissociation and narcolepsy. Narcolepsy is a sleep disorder whose chief characteristic is excessive daytime sleepiness, for which modafinil is one of its preferred therapeutic agents. Therefore, it is not surprising that, in our case, modafinil improved both excessive daytime sleepiness and dissociation.

Our case contains additional information that reinforces the relationship between dissociation and sleep disorders. The dissociation presented by our patient is classified as a psychiatric sleep disorder by the International Classification of Sleep Disorders (second edition ICSD-2) (American Academy of Sleep Medicine, 2005) because her dissociative events occurred near sleep–wake transitions. This type of dissociation is called "sleep-related dissociative disorder" by the ICSD-2. Sleep-related dissociative disorders arise from well-established EEG wakefulness, either during the period of transition to sleep or following awakening from stages N1, N2, or rarely from rapid eye movement (REM) sleep (Genchi, 2017). As with most patients with sleep-related dissociative disorders (Agargun et al., 2001; Angulo-Franco et al., 2015; Schenck et al., 1989), our patient was amnestic of the nocturnal events and presented with corresponding daytime dissociative disorders and history of traumatic events in childhood. Recently, the revised version of the American Academy of Sleep Medicine Manual of Sleep Disorders (ICSD-3) did not include sleep-related dissociative disorders in any of its major categories (American Academy of Sleep Medicine, 2014).

The main limitations of our case report are lack of polysomnography (PSG) and multiple sleep latency test (MSLT) to objectively confirm and characterize hypersomnia and lack of actigraphic monitoring over a 2-week period to assess the extent of hypersomnia. Using PSG/MSLT, Becker et al. (1992) were the first to describe patients with dissociative disorder who also presented "psychological" (dissociative) hypersomnia rather than true hypersomnia. Schenck and Mahowald (1993) diagnosed nocturnal dissociative disorders in 25 patients; among them, 16 complained of excessive daytime sleepiness. PSG/MSLT revealed that there were 6 cases of organic hypersomnia and 10 cases of dis-

sociative hypersomnia. In our case, despite the lack of PSG/MSLT, the prolonged electroencephalogram monitoring showed that the patient's episodes of excessive daytime sleepiness were at least in part true sleep instead of subjective (dissociative) sleep.

Other limitations of our case report include lack of generalization; impossibility to establish a cause-effect relationship; possible over-interpretation. Also, many studies reviewed here documenting the sleep-dissociation link were from the same group (van der Kloet et al.) and were based on undergraduate student samples. Furthermore, most studies rested on correlational data. One inherent restriction of this type of study is that it does not allow the deduction of causal relationship between the variables.

On the other hand, due to the scarcity of the literature on the sleep-dissociation link, our case report gains importance for revealing the efficacy of modafinil in the treatment of dissociative identity disorder with hypersomnia. This allows us to suggest that research on dissociation might benefit from the literature on the treatment options for sleep disorders.

Future studies can discern what unique sleep disruptions in the sleep-wake cycle are most reliably associated with dissociative disorders. This could open new avenues of treatment for dissociative disorders using medications for sleep disorders such as modafinil, which carry the major potential benefit of rapid and sustained efficacy. Finally, the "take-home" message from our case report is that clinicians should investigate for the presence of hypersomnia in patients with dissociative disorder because of the potential beneficial treatment implications.

In that context, the validated Epworth Sleepiness Scale (Johns, 1991) can be a quick screen for hypersomnia in dissociative disorder patients, as it is an 8-question self-administered scale (with a score range of 0-3 per question on "chance of dozing" in various everyday situations). A score>10 indicates excessive daytime sleepiness (EDS), and a score >16 indicates a high level of EDS. In conclusion, our case report encourages further research between sleep and dissociative symptoms.

Conflicts of interest

Apart from Carlos H. Schenck (who is a Consultant for Axovant Sciences; not relevant to this manuscript), the other authors declare no conflict of interest.

Informed consent

Informed consent was obtained from the participant included in the study.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

References

Agargun, M.Y., Kara, H., Özer, O.A., Semiz, U., Selvi, Y., Kiran, U., & Tombul, T. (2001). Characteristics of patients with nocturnal dissociative disorders. Sleep and Hypnosis, 3, 131–134.

American Academy of Sleep Medicine. (2005). International Classification of Sleep Disorders (2nd ed.). Westchester.

American Academy of Sleep Medicine. (2014). International Classification of Sleep Disorders (3rd ed.). Darien.

American Psychiatric Association. (2013). Diagnostic and statistical manual of mental disorders. (5th ed.). Washington, DC.

Angulo-Franco, M., Bush-Martinez, A., Nenclares-Portocarrero, A., & Jiménez-Genchi, A. (2015). Trichotillomania and non-epileptic seizures as sleep-related dissociative phenomena. Journal of Clinical Sleep medicine, 11(3), 271-273.

Becker, P.M., Brown, W.D., & Jamieson, A.O. (1992). Dissociative disorder with hypersomnia mimicking symptoms of narcolepsy: description of four cases. Sleep Research, 21, 173.

Bohus, M.J., Landwehrmeyer, G.B., Stiglmayr, C.E., Limberger, M.F., Böhme, R., & Schmahl, C.G. (1999). Naltrexone in the treatment of dissociative symptoms in patients with borderline personality disorder: an open-label trial. Journal of Clinical Psychiatry, 60(9), 598-603.

Bremner, J.D., & Marmar, C.R. (2005). Trauma, memory, and dissociation. Washington, DC: American Psychiatric Press.

Carlson, E.B., & Putnam, F.W. (1993). An update on the Dissociative Experiences Scale. Dissociation, 6(1), 16-27.

Dang, D., & Kokkinn, K. (2013). Dissociative identity disorder and central hypersomnolence: comorbid diagnoses, or the same phenomena at different ends of a spectrum?. Sleep & Biological Rhythms, 11, 8-9.

Devinsky, O., Gazzola, D., & LaFrance, W.C., Jr. (2011). Differentiating between nonepileptic and epileptic seizures. Nature Reviews Neurology, 7(4), 210-220.

Genchi, A.J. (2017). Sleep Related Dissociative Disorders. Elsevier Inc.

Johns, M.W. (1991). A new method for measuring daytime sleepiness: the Epworth sleepiness scale. Sleep, 14, 540-545.

Levin, R., Nielsen, T.A. (2007). Disturbed dreaming, posttraumatic stress disorder, and affect distress: a review and neurocognitive model. Psychological Bulletin, 133(3), 482–528.

Nobakht, H.N., & Dale, K.Y. (2019). The mediational roles of sleep disorders and nightmares in the relationship between trauma and dissociation. Dreaming, 29(1), 79–90.

Nuller, Y.L., Morozova, M.G., Kushnir ,O.N., & Hamper, N. (2001). Effect of naloxone therapy on depersonalization: a pilot study. Journal of Psychopharmacology, 15(2), 93-95.

Schenck, C.H., Milner, D.M., Hurwitz, T.D., Bundlie, S.R., & Mahowald, M.W. (1989). Dissociative disorders presenting as somnambulism: polysomnographic, video and clinical documentation (8 cases). Dissociation, 2(4), 194-204.

Schenck, C.H., & Mahowald, M.W. (1993). Somatoform conversion disorder mimicking narcolepsy in 8 patients with nocturnal and diurnal dissociative disorders. Sleep Research, 22, 260.

Selvi, Y., Kandeger, A., Boysan, M., Akbaba, N., Sayin, A.A., Tekinarslan, E., Kocf, B.O., Uygurg, O.F., & Sar, V. (2017). The effects of individual biological rhythm differences on sleep quality, daytime sleepiness, and dissociative experiences. Psychiatry Research, 256, 243–248.

Sierra, M., Phillips, M.L., & Lambert M.V. (2001) Lamotrigine in the treatment of depersonalization disorder. Journal of Clinical Psychiatry, 62(10), 826-827.

Sierra, M., Baker, D., Medford, N., Lawrence, E., Patel, M.X., Phillips, M.L., & David, A.S. (2006). Lamotrigine as an add-on treatment for depersonalization disorder: a retrospective study of 32 cases. Clinical Neuropharmacology, 29(5), 253-258.

Simeon, D., & Knutelska, M. (2005). An open trial of naltrexone in the treatment of depersonalization disorder. Journal of Clinical Psychopharmacology, 25(3), 267-270.

van Heugten – van der Kloet, D., Merckelbach, H., Giesbrecht, T., & Broers, N. (2014). Night-time experiences and daytime dissociation: a path analysis modeling study. Psychiatry Research, 216, 236–241.

van der Kloet, D., Merckelbach, H., Giesbrecht, T., & Lynn, S.J. (2012a). Fragmented sleep, fragmented mind: the role of sleep in dissociative Symptoms. Perspectives on psychological science, 7(2), 159-175.

van der Kloet, D., Giesbrecht, T., Lynn, S.J., Merckelbach, H., & de Zutter, A. (2012b). Sleep normalization and decrease in dissociative experiences: evaluation in an inpatient sample. Journal of abnormal psychology, 121(1), 140-150.

Sar, V. (2017). Dissociative disorders: epidemiology. In A. Wenzel (Ed.), The SAGE encyclopedia of abnormal and clinical psychology. Thousand Oaks: SAGE publications Inc.

Vermetten, E., Dorahy, M.J., & Spiegel, D. (2007). Traumatic dissociation: neurobiology and treatment. Washington, DC: American Psychiatric Publishing Inc.

Waller, N., Putnam, F.W., Carlson, E.B. (1996). Types of dissociation and dissociative types: A taxometric analysis of dissociative experiences. Psychological Methods, 1(3), 300-321.

Watson, D. (2001). Dissociations of the night: individual differences in sleep-related experiences and their relation to dissociation and schizotypy. Journal of Abnormal Psychology, 110, 526–535.