

**Narcolepsy beyond sleepiness : endocrine, metabolic and other aspects** Donjacour, C.E.H.M.

## Citation

Donjacour, C. E. H. M. (2014, December 18). *Narcolepsy beyond sleepiness : endocrine, metabolic and other aspects*. Retrieved from https://hdl.handle.net/1887/30243

Version:	Corrected Publisher's Version
License:	<u>Licence agreement concerning inclusion of doctoral thesis in the</u> <u>Institutional Repository of the University of Leiden</u>
Downloaded from:	https://hdl.handle.net/1887/30243

Note: To cite this publication please use the final published version (if applicable).

Cover Page



# Universiteit Leiden



The handle <u>http://hdl.handle.net/1887/30243</u> holds various files of this Leiden University dissertation.

Author: Donjacour, Claire Elisabeth Henrica Maria Title: Narcolepsy beyond sleepiness : endocrine, metabolic and other aspects Issue Date: 2014-12-18



# Delusional confusion of dreaming and reality in narcolepsy

Claire E. H. M. Donjacour\* Erin Wamsley\* Thomas E. Scammell Gert Jan Lammers Robert Stickgold

Sleep 2014, 37:419-422.

# ABSTRACT

**Study objectives:** We investigated a generally unappreciated feature of the sleep disorder narcolepsy, in which patients mistake the memory of a dream for a real experience, forming sustained delusions about significant events.

**Design:** We interviewed narcolepsy patients and controls to establish the prevalence of this complaint and identify its predictors.

Setting: Academic medical centers in Boston and Leiden.

**Participants:** Patients (n = 46) with a diagnosis of narcolepsy with cataplexy, and agematched healthy controls (n = 41).

**Measurements and results:** "Dream delusions" were surprisingly common in narcolepsy and were often striking in their severity. As opposed to fleeting hypnagogic and hypnopompic hallucinations of the sleep/wake transition, dream delusions were false memories induced by the experience of a vivid dream, which led to false beliefs that could persist for days or weeks.

**Conclusions:** The delusional confusion of dreamed events with reality is a prominent feature of narcolepsy, and suggests the possibility of source memory deficits in this disorder that have not yet been fully characterized.

### INTRODUCTION

Each time we recall an event from the past, we are faced with the dual tasks of identifying the source of the memory and evaluating its veracity. In general, we can accurately determine whether a memory originated in our past experience, as opposed to in our imagination, a dream, a film, or a story. However, this process of "source monitoring" sometimes goes wrong.<sup>252-254</sup> Minor confusions about the source of a memory are common in the general population, as when we mistake the source of a quotation, misremember the context in which we met an acquaintance, or even believe that we actually experienced an event that we only heard about. Recently, case reports have described more severe examples of memory source confusion in patients suffering from the sleep disorder narcolepsy, in which false accusations of sexual assault occurred when patients mistook a dreamed assault for the memory of an actual event.<sup>28;29</sup> These reports are remarkable in that dream memories were misinterpreted as representing real, highly significant life events, leading to sustained delusions that became the basis for serious actions. Narcolepsy is a disorder of excessive sleepiness, and is not typically associated with psychotic symptoms.<sup>255</sup> The dramatic nature of these case reports led us to undertake the first systematic study of these "dream delusions" in narcolepsy. In a structured telephone interview, we asked narcolepsy patients and controls a series of questions about sleep, dreaming, and memory. Our goals were (1) to characterize the incidence of this phenomenon in narcolepsy patients, as compared to the general population, and (2) to describe the features of this experience.

#### **METHODS**

#### **Participants**

Narcolepsy patients and age-matched controls were recruited at two collaborating sites, Beth Israel Deaconess Medical Center in Boston, Massachusetts (n = 18), and Leiden University Medical Center in the Netherlands (n = 69). Institutional review boards at both institutions approved this research. Patients (n = 46; age  $34.2 \pm 10.9$  [SD], 59% female) had a definite diagnosis of narcolepsy with cataplexy for a minimum of 6 months prior to the study, according to the standards of the International Classification of Sleep Disorders (ICSD-2) Diagnostic and Coding Manual.<sup>118</sup> Diagnoses were confirmed by interview and review of medical records, including clinic notes, overnight sleep studies, multiple sleep latency tests (MSLTs), and Human Leukocyte Antigen testing. At the time of the interviews, patients

were under treatment with a variety of medications to manage their narcolepsy, including stimulants (72% of patients; includes modafinil, amphetamine, dextroamphetamine, and methylphenidate), antidepressants (15% of patients; includes tricyclics, SSRIs, SNRIs and SARIs), and sodium oxybate (35% of patients). There were no differences in medication usage between those with and without dream delusions (chi-square tests of independence: stimulants: P = 0.82, antidepressants: P = 0.64, sodium oxybate: P = 0.69). Controls were recruited from the general population (n = 41; age 32.7 ± 11.6 SD, 59% female), and were screened (by self-report) to exclude the presence of any diagnosed sleep disorder. There were no differences across study sites in participant age, gender, habitual sleep schedule, dream recall, or incidence of reported confusion.

#### **Interview procedures**

Participants completed a ~30-min structured telephone interview in which they were asked a series of questions pertaining to sleep, dreaming, and memory. Following questions about their habitual sleep schedule and dream experiences, participants were asked, *"Have you ever had the experience of being unsure whether something was real, or if it was from a dream?"* Delusional episodes were defined as incidents in which *a fully awake participant was uncertain if a memory was dreamed or real, or was convinced that a memory was real, only later to discover that it was actually dreamed.* To be included, a delusional episode was required to clearly persist into the waking state – Fleeting feelings of confusion during the transition to wakefulness were excluded because brief confusion is a well-known consequence of the hypnagogic and hypnopompic hallucinations characterizing narcolepsy. For purposes of analysis, participants were categorized as a "Yes" for having dream delusions if they claimed to have experiences that met this definition, and were able to provide at least one detailed example of an instance when this had occurred.

To compare general features of dreaming between narcolepsy patients and controls, participants also rated the frequency, emotionality, and intensity of their typical dream experiences on a 5-point scale.

At the conclusion of the interview, two standardized questionnaires were verbally administered – the *Boundary Questionnaire* and the *Prospective-Retrospective Memory Questionnaire*. Ernest Hartmann's *Boundary Questionnaire*, assesses the personality construct of psychological boundaries.<sup>256,257</sup> A "thin" boundary score (higher values) is associated with frequent and intense dreaming, as well as high interest in dreams, and the

report of unusual sleep experiences such as sleep paralysis and sleep-related hallucinations, both of which are features of narcolepsy. We administered the 18-item short form of the Boundary Questionaire.<sup>256</sup> The *Prospective-Retrospective Memory Questionnaire* (PRMQ) assesses subjective complaints of difficulties in remembering to carry out intentions (prospective memory), and in remembering the events of the recent past (retrospective memory).<sup>258;259</sup> Seventeen participants who reported dream/reality confusions meeting our criteria additionally reported to the laboratory for a face-to-face interview in which they described the qualities of these experiences in greater detail.

### RESULTS

Dream delusions were extremely common in narcolepsy. Overall, 83% of narcolepsy patients reported that they had confused dreams with reality, compared to only 15% of controls ( $\chi^2$  = 40.1, *P* < 10<sup>-10</sup>; Figure 9.1). The severity of these delusions was striking. One man, after dreaming that a young girl had drowned in a nearby lake, asked his wife to turn on the local news in full expectation that the event would be covered. Another patient experienced sexual



**Figure 9.1** Prevalence of dream-reality confusion. Patients with narcolepsy were much more likely to report mistaking dream experiences as true memories, in comparison with age-matched healthy controls.

dreams of being unfaithful to her husband. She believed this had actually happened and felt guilty about it until she chanced to meet the 'lover' from her dreams and realized they had not seen each other in years, and had not been romantically involved. Several patients dreamed that their parents, children or pets had died, believing that this was true (one patient even made a phone call about funeral arrangements) until shocked with evidence to the contrary, when the presumed deceased suddenly reappeared. Although not all examples were this dramatic, such extreme scenarios were not uncommon.

All narcolepsy patients reporting dream delusions provided multiple examples of such occurrences. Two-thirds of patients (65%) who completed the follow-up interview reported experiencing dream delusions at least once a week, and all but two (95%) had the experience at least once a month. In contrast, of the 6 control participants who reported delusions, only 2 (5% of all control subjects) had experienced this more than once in their lives.

The classic hypnagogic and hypnopompic hallucinations of narcolepsy are fleeting images and feelings linked to the current environment, and patients recognize the hallucinatory nature of the experience within seconds of awakening. In contrast, the experiences reported here were much longer lasting, persisting into stable wakefulness. In follow-up interviews (see Methods), patients reported that although some delusions resolved within minutes after awakening, they often persisted for hours, days, or even weeks.

In line with prior literature,<sup>260;261</sup> narcolepsy patients rated their dreams as substantially more vivid ( $t_{83} = 3.79$ ; P = 0.0003) and more emotional ( $t_{82} = 5.25$ ;  $P < 10^{-6}$ ) than the age-matched controls. They also reported recalling dreams more frequently than controls ( $t_{84} = 3.16$ ; P = 0.002), and scored higher on the *BQ* than controls (indicating that patients had "thinner" boundaries;  $t_{85} = 1.98$ ; P = 0.05). However, we found no evidence that dream delusions were related to an abnormal quantity or quality of dream experience in narcolepsy. Within the narcolepsy sample, neither *BQ* scores nor any other measure of dreaming differentiated between those who did and did not experience confusions (all Ps > 0.1).

While prior research has largely failed to find objective memory dysfunction in narcolepsy,<sup>26;262;263</sup> subjective complaints of memory difficulty are common.<sup>264</sup> Here, narcolepsy patients scored higher than controls on the PRMQ for both retrospective memory problems ( $t_{85} = 3.71$ , P = 0.0004) and prospective memory problems (difficulties in remembering to carry out intentions;  $t_{85} = 4.20$ , P = 0.00007). However, memory impairment as measured by the PRMQ did not discriminate between narcolepsy patients with and without dream delusions.

## DISCUSSION

Our data reveal an underappreciated memory problem in narcolepsy, in which patients are prone to delusionally believe that dreamed events actually occurred. These "dream delusions" are a special case of memory source confusion, a well-described phenomenon in which the origin of a particular memory is misattributed.<sup>253</sup> The conflation of dream experiences with actual events has previously been described in healthy controls.<sup>265;266</sup> However, in this sample of narcolepsy patients, the incidence and severity of dream delusions was striking, and far greater than that seen in controls. These observations suggest that something about the pathophysiology of narcolepsy leads to a profound confusion of memory source. Although the mechanism of dream delusions cannot be determined at this time, several possibilities present themselves. First, on the phenomenological level, our observations confirm previous reports of frequent and intense dreaming in narcolepsy. Thus, it is possible that patients mistake dream experiences for real events because the vividness of their dreams prevents the use of perceptual realism as a cue in discriminating the dreamed from the real. Our data did not provide support for this hypothesis, as dream vividness ratings did not discriminate between patients with and without delusions. However, the possibility that these delusions are caused by an abnormal intensity of dream experience in narcolepsy certainly cannot be ruled out.

Alternatively, dream delusions may be just one manifestation of a more general memory deficit in this disorder. Consistent with this possibility, we found evidence of subjective memory difficulties in narcolepsy, as assessed by the PRMQ. Again, however, this measure did not discriminate between patients with and without delusions. To our knowledge, no prior study has examined any form of memory source confusion in narcolepsy. Thus, it cannot be said at this time whether the delusions observed here are specific to dreaming, or whether narcolepsy patients might be equally prone to confuse the origin of other memories, for example mistaking imagined events or stories they have heard as personal experiences. Future studies employing standard source monitoring tasks in narcolepsy patients should be able to better determine the specificity of this complaint.

Finally, dream delusions could result from an abnormality of memory encoding specific to the sleep state. The failure to discriminate memories formed during sleep from waking life experiences could be a direct consequence of the well-described neural mechanisms of narcolepsy. Narcolepsy is caused by destruction of orexin/hypocretin neurons in the lateral hypothalamus. Normally, the orexin system helps stabilize wake/sleep states, and loss of the orexin neurons results in "state dissociation" characterized by frequent transitions between states and the intrusion of aspects of rapid eye movement sleep into waking.<sup>267</sup> As monoaminergic and cholinergic neurons involved in the control of sleep states are major targets of the orexin neurons, we speculate that abnormal activity in these neurons during sleep could alter the encoding of dream content in long-term memory stores, leading to its misattribution as waking memory. Disruption of sleep neuromodulation, for example, could cause features of wakefulness to bleed into REM sleep, strengthening the typically poor memory encoding during this state.

Though the underlying mechanism of dream delusions is unknown, it is clear that many people with narcolepsy have a surprising and intense difficulty distinguishing the dreamed from the real. In concert, these patients perceive themselves as having more general difficulties with both retrospective and prospective memory. These observations highlight the possibility of source memory deficits in narcolepsy that have not yet been fully characterized.