

The Influence of Sleep on Cognitive Deficits in Anorexia Nervosa

Onno van den Hoed

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Supervisors: A.J.W Scheurink

Abstract

The present paper aimed to investigate if the cognitive problems often observed in AN patients are caused by AN itself or if they could be a consequence of the sleeping problems also often found in AN patients. The paper also aimed to investigate if sleeping problems in AN patients are caused by AN itself or if they could be a consequence of a low body weight. To this end a total of 7 studies were reviewed. It was found that the cognitive problems in AN are similar to those observed in sleep deprivation, which, paired with the observation that AN patients suffer from sleeping problems suggests that the cognitive problems in AN could stem from the sleeping problem rather than AN itself. It was also found that sleeping problems in AN lessened after weight restoration treatment and that the same sleeping problems are also present in underweight people in absence of AN, suggesting that the sleeping problems in AN are likely a consequence of low body weight rather than AN itself. The treatment of sleeping problems in AN through cognitive behavioural therapy has been suggested as a potential future treatment option for the cognitive problems in AN.

Keywords: Anorexia Nervosa, Eating disorders, Sleep, Insomnia, BMI, Underweight, Memory

Introduction

Anorexia Nervosa (AN) is an eating disorder with several complications. Among these complications are anemia, heart problems as well as a loss of muscles. On top of that, AN patients are often found to suffer cognitive deficits as well, especially in the domain of memory (Keeler et al., 2021; Dahlén et al., 2022). There is also literature suggesting that sleeping problems like insomnia are often present in AN patients (Asaad Abdou et al., 2018).

The notion that AN patients suffer from sleeping problems is rather interesting. Especially so considering that sleeping problems come with their own set of complications. Now, some of the complications observed in sleeping problems are very similar to those often observed in AN patients, especially cognitive problems (Krause et al., 2017; Van Dongen et al., 2003).

With that being the case, it makes one wonder if the cognitive problems found in AN patients are perhaps caused by the sleeping problems they experience rather than by AN itself. The question this paper aims to answer is: *Are the cognitive problems found in AN patients a consequence of the sleeping problems AN patients are found to experience?*

Furthermore, because problems that AN patients experience can often be explained by their significantly low body weight rather than AN itself it is also important to investigate this. Therefore, the second question this paper will aim to answer is: *Are the sleeping problems observed in AN patients caused by AN itself or could they be a consequence of a low body weight?*

To answer these questions it is important to know more about the topics involved. We need to know more about AN, its complications and, most importantly, more about sleep in AN. It is also important to know more about sleep as well as sleeping problems and the complications that come with them. Finally, it is important to know more about the influence weight, specifically underweight, has on sleep.

Anorexia Nervosa

Anorexia Nervosa is an eating disorder that affects both males and females worldwide. While both males and females can suffer from the disorder, it is roughly 13x more common in females compared

to males. The lifetime prevalence rate of AN is up to 4% among females and 0.3% among males. Nowadays, the overall incidence rate of AN is fairly stable but it is increasing in younger people (aged <15 years) (van Eeden et al., 2021). AN is characterised by a few main factors. A restriction of energy intake relative to requirements, leading to a significantly low body weight in the context of age, sex, developmental trajectory and physical health. An intense fear of gaining weight and becoming fat or behaviour that interferes with the gaining of weight even when the patient is at low weight already. And a disturbance in which a patient's body weight or shape is experienced by them, an excessive influence of body weight or shape on self-evaluation or the failure to recognize the seriousness of the low body weight. (American Psychiatric association, 2013).

There is two main subtypes of AN, the restricting type and the binge eating/purging type. In patients suffering from the restricting type, weight loss is accomplished mainly through a restriction of food intake, fasting or an excessive amount of exercise. In the binge eating/purging type patients often eat large amounts of food before forcefully inducing vomiting through misuse of laxatives, diuretics or enemas in order to avoid food absorption. There is also patients with this subtype of AN who do not binge eat but do regularly purge after consuming small amounts of food. Patients are likely to not just fit into one of these subtypes over the course of the entire disorder and crossover of the two subtypes is not uncommon (American Psychiatric association, 2013).

AN is the psychiatric illness with the highest mortality rate (Sullivan, 1995). Patients suffering from AN suffer from several complications. Not only do they suffer from medical complications that stem from malnutrition like anemia, heart problems, osteoporosis and a loss of muscles. AN patients are also likely to suffer from mental disorders, approximately half of all adolescent patients suffering from AN meet the criteria for at least one comorbid psychiatric illness (Bühren et al., 2013). Mood disorders like depression as well as anxiety disorders are strongly associated with AN (Westmoreland et al., 2016). Cognitive problems are also often found to be present in AN patients. AN patients show impaired hippocampal memory, achieving lower pattern recognition memory scores (Keeler et al., 2017) as well as impaired working memory (Dahlén et al., 2022) compared to healthy controls. As briefly mentioned before, it has also been suggested that sleeping problems are often found in AN patients, the most discussed one being insomnia. Insomnia is characterised by dissatisfaction in overall sleep quality which includes the inability to initiate sleep, maintain sleep or waking up earlier than desired for at least 3 months at least 3 days a week (American Psychiatric association, 2013).

Sleep

Humans spend about one third of their lives asleep but the reason for this and the exact function of sleep are still unknown. A lot of research on this matter has been done by a great number of different researchers over the years and there is still no definitive answer on the function of sleep. That said, reasonable hypotheses have been formulated and advanced (Frank & Heller, 2018).

Many have suggested the sleep plays a role in physical restoration of the body, serving as a time of growth and repair for the body. One of the arguments in favour of this explanation is the fact that the hormones released during sleep have a predominant anabolic function, such as growth hormone, while hormones associated with wakefulness, such as cortisol, have a predominantly catabolic function and are suppressed during sleep (Assefa et al., 2015). Sleep is also believed necessary to conserve energy, with lower energy expenditure being observed during sleep and sleep deprivation being associated with higher total energy expenditure. Because of the lower metabolic rate observed during sleep, biological processes occurring during sleep may be able to be completed with a lower overall energy costs compared to those during waking. While the full function of sleep in physical restoration is not

yet clear there is clear evidence of the adverse effect of short term and chronic sleep deprivation on function which suggests that sleep at the very least has a positive effect on our bodies (Assefa et al., 2015).

Sleep is also found to play a role in learning and memory. For example, sleep was found to be essential for motor skill learning, a night sleep resulted in a 20% increase in motor speed without loss of accuracy. Similar results have been found in memory formation, an increased result in paired-word association tests was observed after a night sleep (Assefa et al., 2015). On the flip side, sleep deprivation has been found to lead to impaired hippocampal memory (Krause et al., 2017) as well as impaired working memory. Sleep deprived subjects scored significantly worse in a digit symbol substitution task compared to healthy controls (Van Dongen et al., 2003). Interestingly, these cognitive problems associated with sleep deprivation are the same cognitive problems that are observed in AN patients.

Overview of normal sleep

Normally, human sleep consists of two distinct phases. Rapid eye movement (REM) and non-REM (NREM) sleep, which consists of four different stages. Both these phases have distinct characteristics. NREM sleep is defined by a variably synchronous cortical encephalogram (EEG) which includes sleep spindles, K-complexes and slow waves. It is also associated with a low muscle tone and minimal psychological activity. REM sleep is defined by high frequency and low amplitude patterns in the EEG, there is no muscle tone and dreaming is common during this phase (Carskadon & Dement, 2011). These two phases of sleep alternate each other cyclically during sleep.

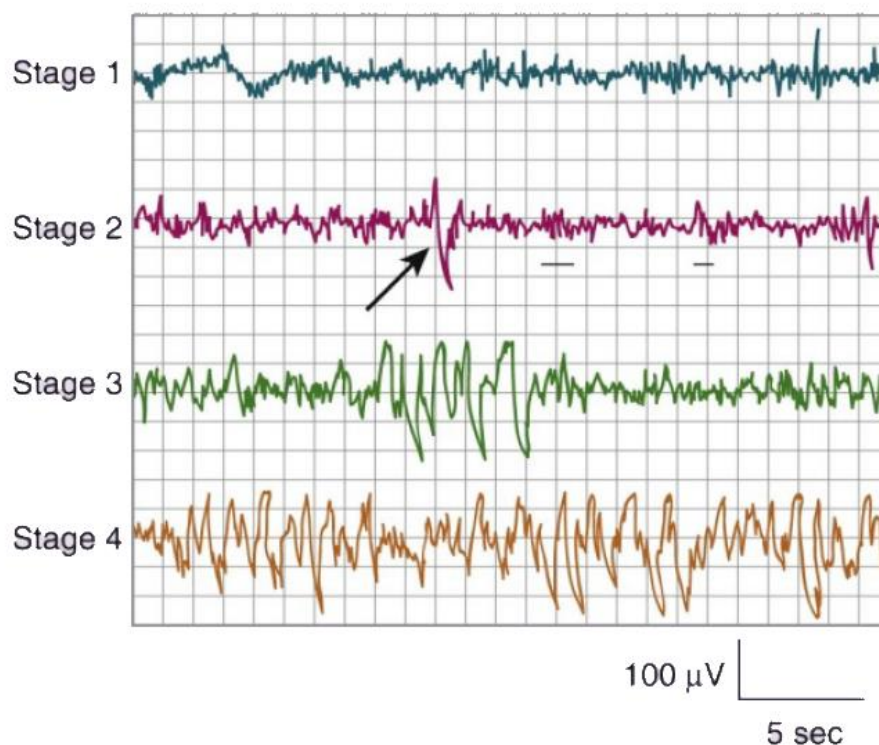


Figure 1. The stages of non-rapid eye movement speed. The arrow in stage 2 indicates a K-complex and the underlining indicates two sleep spindles. Modified from Carskadon & Dement, 2011.

The first cycle of sleep in a normal young adult starts with stage 1 NREM sleep, this stage usually only lasts for a couple minutes and during this stage it is exceptionally easy to wake a person, for example by lightly closing a door in the sleeping person's vicinity.

After stage 1, a person enters stage 2 NREM sleep. This stage is defined by sleep spindles and K-complexes in the EEG. It lasts around 10 to 25 minutes and during this stage it is harder to wake a person compared to stage 1.

Near the end of stage 2 sleep, high-voltage slow-wave activity starts appearing in the EEG until eventually this activity meets the criteria for stage 3 NREM sleep, high-voltage slow-wave activity constituting at least 20% but not more than 50% of the EEG activity). It usually only lasts a few minutes before transitioning into stage 4 NREM sleep where high-voltage slow-wave activity constitutes more than 50% of the EEG activity, this stage usually lasts 20 to 40 minutes. It is exceptionally hard to wake a person from stage 3 and 4 sleep and these stages are often combined and referred to as slow-wave sleep (SWS) or deep sleep (Carskadon & Dement, 2011).

Before transitioning to REM sleep a very brief episode of stage 3 NREM sleep might occur followed by a slightly longer, 5 to 10 minute, episode of stage 2 sleep. In the first cycle of sleep, REM sleep is usually only 5 to 10 minutes long and the amount of stimulus required to wake a person is variably during this phase.

NREM and REM sleep continue to alternate each other cyclically throughout a person's sleep after this. REM sleep episodes generally become longer throughout the night while stage 3 and 4 sleep generally become shorter throughout the night. The NREM-REM cycle usually lasts approximately 90 to 110 minutes (Carskadon & Dement, 2011).

Underweight

Given the importance of underweight to the topic at hand it is important to clearly define what is specifically referred to as underweight. The Centers for Disease Control and prevention (CDC) suggests that people use a body mass index (BMI) to calculate whether they are overweight, underweight or at a healthy weight. BMI is a measure of body fat based on height and weight, it is calculated using the following formula: kg/m^2 , where kg is the amount a person weighs in kilograms and m^2 is a person's height in metres squared. Using a formula like this it is possible to easily determine if a person is overweight or underweight across all sorts of body types. A BMI of 18.5-24.9 is considered healthy and a BMI of less than 18.5 is defined as underweight.

Anorexia Nervosa and Sleep

To obtain an answer to both of the questions in the present paper it is important to assess if there is sufficient evidence suggesting that AN patients suffer from sleeping problems. Furthermore, to assess whether these problems are caused by AN itself or low body weight it is of interest to observe what happens to sleep in AN when weight is restored to a healthy BMI. Several studies have investigated this, recording sleep changes in AN patients before and after weight restoration (El Ghoch et al., 2016; Lacey et al., 1976; Lauer & Krieg 1992). The studies all obtained rather different results in terms of what aspect of sleep was improved but all of the studies reported some degree of improvement in sleep after weight restoration.

Asaad-Abdou et al. (2018) conducted both subjective and objective assessments of sleep in AN patients. 23 patients suffering from AN (23 females) participated in the study. 20 healthy individuals

matched for age and sex were used as a control group. Subjective assessment was done through a questionnaire. It revealed a decrease in sleep quality in AN patients compared to healthy controls. Initial insomnia, characterised by a difficulty in falling asleep, was the most commonly reported problem but there was also a significant difference between groups for all other types of insomnia. Objective assessment was conducted through an all-night polysomnography. The results of the polysomnography are shown in figure 2. The polysomnography revealed a significant increase in sleep latency (the time it takes to go from full wakefulness to sleep) and arousal index (the total number of arousals per hour of sleep) as well as a decrease in sleep efficiency (the percentage of time spent asleep while in bed) in AN patients. On top of that, a significant decrease in both rapid eye movement (REM) and slow-wave sleep (SWS) were observed in AN patients.

	Cases (N = 23)		Controls (N = 20)		p
	SD	Mean	SD	Mean	
Sleep latency	2.57	22.69	2.68	18.05	0.0001 ^b
Sleep efficiency	4.56	79.06	2.24	91.58	0.0001 ^b
Arousal index	0.79	3.06	0.67	1.55	0.0001 ^b
Stage I%	0.72	3.53	0.99	3.26	0.338
Stage II%	1.99	54.82	0.93	50.44	0.0001 ^b
Stage III%	0.87	9.78	0.82	10.54	0.0001 ^b
Stage IV%	1.03	10.38	1.2	11.13	0.041 ^a
SWS% (slow wave sleep)	1.73	20.16	1.66	21.62	0.01 ^a
SWS latency	1.97	30.75	1.57	29.45	0.027 ^a
REM%	1.08	21.79	1.21	24.64	0.0001 ^b
REM latency	6.13	67.55	6.08	70.20	0.178
REM density	0.81	19.34	1.07	20.02	0.031 ^a
Duration of first REM	1.03	7.63	0.96	7.20	0.175
Density first REM	0.85	10.52	1.04	9.28	0.0001 ^b
PLM1	0.62	1.48	0.39	1.14	0.073

PLMI, Periodic Leg Movement Index; REM, rapid eye movement; SD, standard deviation; SWS, slow wave sleep.

^a $p > 0.01$.

^b $p > 0.001$.

Figure 2. Polysomnography results for AN patients compared to healthy controls. Asaad-Abdou et al. 2018.

In an older study Lacey et al. (1976) studied the EEG sleep characteristics of 10 patients suffering from AN (9 females and 1 male) before and after weight restoration. The patients were prescribed a diet of 3000 calories a day and the diet was aimed to result in a 2 to 3.5 lb (0.9-1.6 kg) weight gain a week. Patients were given time to become accustomed to their new environment before the first recording period but the recording period never started later than 12 days after admission. The second recording period was started when patients reached their target weight and each of the periods lasted for three days. The first two days allowed the patients to get used to the experimental situation and the third day was recorded and

examined. Recordings started at 11 pm and lasted at least 7 hours unless the patient woke up earlier.

Patient case no.	Total sleep time (min)	
	Admission	Target
212	380·3	352·7
211	370·0	392·7
256	445·3	478·3
210	381·3	437·7
208	364·3	397·7
204	399·7	469·3
213	351·7	416·0
190	383·7	395·0
215	410·3	496·7
299	383·3	436·3

Figure 3. Total sleep time in minutes. Single night recording before and after treatment. Lacey et al. 1976.

Patients were found to display a significant increase in total sleep time after weight restoration treatment which can be seen in figure 3. One of the patients is shown to have lost sleep time which the authors suggests could be because the patient was on chlorpromazine. Furthermore, the results revealed a significant decrease in overall time spent awake during the night before and after weight restoration in the patients. Figure 4 shows the average time patients spent awake each hour of the recording. It is interesting to note that in hours two, three and four patients spent more time awake after weight restoration compared to before weight restoration but not significantly so. In hours five, six and seven patients spent significantly more time asleep after weight restoration. This also seems to suggest that wakefulness at low body weight is concentrated towards the end of the sleep cycle. The study also obtained results for each individual sleep stage, the results can be seen in figure 5. A slight decrease in stage 1 and 2 sleep was observed though this difference was not significant. Likewise, a slight increase in slow-wave sleep was observed but this difference was, again, not significant. However, the difference observed in REM sleep was significant, showing an increase in REM sleep in patients after weight restoration.

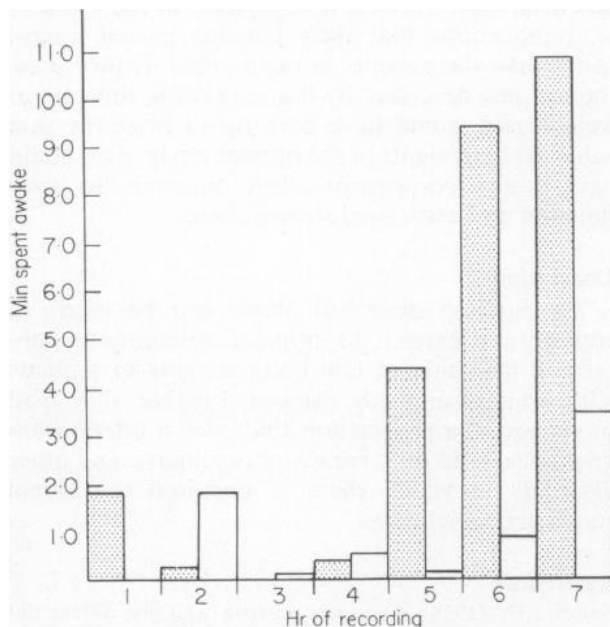


Figure 4. Pattern of wakefulness throughout the night: mean time in minutes spent awake each hour. Before treatment, grey. After treatment, white. Lacey et al. 1976

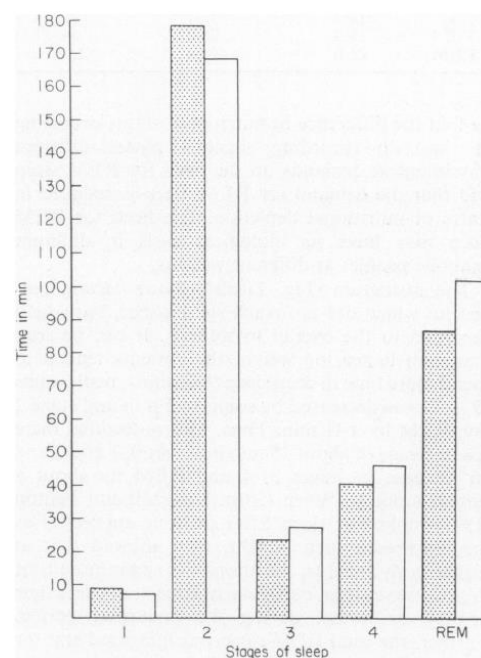


Figure 5. Mean duration of each stage of sleep in minutes. Before treatment, grey. After treatment, white. Lacey et al. 1976

Lauer & Krieg (1992) performed a similar study. They also studied the EEG sleep characteristics of 10 patients suffering from AN (10 females) before and after weight restoration. The main difference between the methods of the two studies is the addition of 10 healthy weight controls in Lauer & Krieg's study. The results of the study are summarized in figure 6. As expected there was a significant difference in body weight between AN patients before and after weight restoration. It is interesting to note that the only significant difference between patients controls observed before weight gain was an increased amount of slow-wave sleep in AN patients, an observation that directly contradicts other studies (Asaad Abdou et al., 2017). Though other differences with controls were not significant they do fit what would be expected in the sleep patterns of AN patients. Particularly more time spent awake during the night, a decrease in the amount of REM sleep and a lower sleep efficiency compared to controls. A significant difference in time spent awake during the night, stage 3 sleep and duration of

the first REM period was found before and after weight restoration. The strong decrease in time spent awake during the night and increase in REM sleep duration after weight restoration match the results obtained by Lacey et al. discussed earlier. However, the significant decrease in stage 3 sleep does not, this is likely due to the earlier discussed finding that the AN patients in the study displayed increased amounts of slow-wave sleep compared to controls. The observed increase in stage 4 sleep after weight gain, while not significant, is expected, though the observation that stage 4 sleep in AN patients is significantly higher compared to healthy controls before weight gain is not.

Patients with Anorexia Nervosa				MANOVA T1 vs T2 F(1,9) p
	Before	After	Healthy subjects (HC)	
	Weight gain			
	(T1)	(T2)		
Age (yr)		20.9 ± 3.0	23.1 ± 3.1	
Ideal body weight (% IBW)^a	70.2 ± 7.4	83.8 ± 4.6	96.0 ± 5.9	27.5^b
Sleep period time (min)	403.9 ± 35.9	390.7 ± 55.6	413.7 ± 17.0	0.7
Sleep efficiency index (%)	87.9 ± 8.3	89.8 ± 11.1	93.3 ± 4.2	0.2
Sleep onset latency (min)	16.8 ± 16.6	11.8 ± 8.0	19.0 ± 10.6	0.8
Intermittent time scale (min)	21.2 ± 23.8	2.0 ± 2.4	7.8 ± 11.0	6.0^c
Stage 1 sleep (% SPT)	7.0 ± 4.8	4.7 ± 3.4	5.9 ± 1.8	1.3
Stage 2 sleep (% SPT)	44.2 ± 7.4	46.8 ± 9.3	52.1 ± 5.7	1.0
Slow-wave sleep (%SPT)	26.7 ± 5.9	26.2 ± 6.7	19.6 ± 7.6	0.1
Stage 3 sleep (min)	53.9 ± 21.2	36.0 ± 13.8	47.9 ± 19.3	9.4^c
Stage 4 sleep (min)	54.1 ± 25.8	65.9 ± 27.8	33.1 ± 19.6	3.3
REM sleep (% SPT)	16.3 ± 6.8	21.2 ± 4.4	19.4 ± 3.7	2.9
REM latency (min)	62.9 ± 12.3	65.4 ± 10.6	72.0 ± 31.5	0.5
Duration of first REM period (min)	9.3 ± 6.7	17.8 ± 11.3	14.6 ± 8.6	5.4^c
First REM density index	2.1 ± 0.8	2.4 ± 1.0	2.2 ± 0.9	0.0
Mean REM density index	2.7 ± 0.9	2.8 ± 0.9	3.2 ± 1.1	0.1

^aAccording to the tables of the Metropolitan Life Insurance Company (1959): *Stat Bull Met Life Insur Co*

^bp < 0.001.

^cp < 0.05

^dp < 0.025

Figure 6. EEG-sleep parameters in AN patients before and after weight gain as well as in 10 healthy controls. Lauer & Krieg 1992.

While both of the previously mentioned studies yielded results that could suggest sleep problems in AN patients are in fact caused by a low BMI on its own, both of the studies suffer from a rather low sample size. In a more recent study done by El Ghoch et al. (2016) a higher sample size was used, 50 patients suffering from AN (50 females) and 25 healthy controls, matched to the patients age and gender. The general proceedings of the study are almost identical to those performed by Lacey et al. and Lauer & Krieg but the present study did not investigate EEG characteristics. Instead, the Sense Wear Armband, a device that uses average variations in body movements, differential and proportional changes in heat-flux and skin temperature and the galvanic skin response to determine if the wearer is awake or asleep at 60 second intervals, was used. While this device is able to provide objective, accurate and reliable data on patients' sleep it cannot provide data on the different stages of sleep. Figure 7 contains the data obtained from the study. The results revealed various significant differences between AN patients before weight restoration and healthy controls. AN patients before weight

restoration had a significantly lower weight and BMI compared to healthy controls which is to be expected. Also expected was the significantly lower total sleep time observed in AN patients before weight restoration compared to healthy controls. However, the results revealed a significantly lower sleep onset latency in AN patients before treatment compared to healthy controls, something that has not been observed before and contradicts several other studies (Asaad Abdou et al., 2017). Aside from the expected observation that AN patients before treatment had significantly lower weight and BMI compared to AN patients after treatment only a single significant difference was observed before and after treatment. AN patients before weight restoration had a significantly lower total sleep time compared to AN patients after weight restoration, a result that is backed up by the study conducted by Lacey et al. The other results, while not significant, are rather unexpected. The observations that sleep onset latency and the time spent awake after sleep onset both increased after treatment in AN patients as well as the observation that sleep efficiency went down after treatment are unexpected and directly contradict results obtained by various other studies (Asaad Abdou et al., 2017). Even so, these results were not significant and especially the data for sleep onset latency and sleep efficiency could suffer from the way the study was conducted, patients were asked to record the time they turned off the light and started trying to sleep as well as the time they woke up themselves. Relying on patients themselves to perform tasks like these increases the chance of inaccuracies. As mentioned before, due to the limitations of the Sense Wear Armband, no data on the specific sleep stages could be obtained and only general sleep patterns could be discussed.

	Pre-treatment AN(N=50)	Post-treatment AN(N=42)	Control group (N=25)	Comparison between pre-treatment AN and control group values (T0)		Comparison between pre-treatment and post-treatment AN values (Completers N=42)	
				Paired t-test	P	Paired t-test	P
Weight (kg)	37.7 (5.3)	49.2 (5.3)	57.9 (5.8)	15.15	<0.001	18.85	<0.001
BMI (kg/m ²)	14.5 (1.6)	18.9 (0.9)	21.5 (1.8)	16.95	<0.001	20.69	<0.001
Sleep parameters							
Total sleep time (min)	390.4 (78.4)	423.3 (67.6)	432.6 (56.0)	2.40	0.019	2.25	0.030
Sleep onset latency (min)	6.9 (6.4)	7.6 (5.9)	10.4 (5.8)	2.28	0.026	0.51	0.613
Sleep efficiency (%)	87.6 (7.1)	86.3 (5.9)	89.4 (3.4)	1.16	0.249	1.04	0.303
Wake after sleep onset (min)	49.2 (33.8)	60.4 (30.2)	41.8 (18.9)	1.00	0.235	1.83	0.074
Eating disorder and general psychopathology							
Global EDE score	3.8 (1.4)	2.0 (1.3)	—	—	—	9.71	<0.001
BSI Global Severity Index	89.3 (19.9)	63.0 (16.1)	—	—	—	10.16	<0.001

Figure 7. Weight, BMI and sleep parameters in AN patients before and after weight gain. El Ghoch et al. 2016.

Underweight and Sleep

Results obtained from weight restoration studies provide solid evidence to suggest that sleeping problems are caused by a low BMI rather than AN itself. However, it could still be the case that sleeping problems are caused by another aspect of AN that is solved with weight restoration rather than weight itself. If sleeping problems are in fact caused by weight on its own, one would expect the sleep problems observed in AN patients to also be present in people without an eating disorder but just a low BMI. Several population wide studies in all parts of the world have been conducted (Awadalla

& Al-Musa, 2019; Sivertsen et al., 2014; Ade et al., 2021) and results seem to back up this expectation.

Awadalla & Al-Musa (2019) conducted a large scale study in all primary health-care centers in Abha city in the Aseer region of Saudi Arabia. A total of 3166 adult subjects from ages 18 to 90 participated, most of the participants were from the 25 to 40 years age group. Participants filled out a questionnaire and the responses to this questionnaire were used for data collection. Sleep performance was assessed through the Arabic versions of internationally accepted scales such as the Athens Insomnia Scale and Epworth Sleepiness Scale, both questionnaires consisting of eight different questions related to insomnia and sleepiness during the day. Out of all the participants a total of 1903 participants were found to suffer from insomnia. According to figure 8, insomnia was more common in adults in the age group 25-40 and adults over the age 40 compared to those in the age group 18-25. It was also found that females are slightly more likely to suffer from insomnia compared to males.

Characteristics	Total N. (%)	No Insomnia N. (%)	Insomnia N. (%)	cOR. (95%CI)
Overall	3166 (100)	1263 (39.9)	1903 (60.1)	-
Age (years)				
18-25	881 (27.8)	387 (43.9)	494 (56.1)	Ref
25-40	1528 (48.3)	594 (38.9)	934 (61.1)	1.23 (1.04-1.46)
> 40	757 (23.9)	282 (37.3)	475 (62.7)	1.32 (1.08-1.61)
Sex				
Male	1432 (45.2)	581 (40.6)	851 (59.4)	Ref
Female	1734 (54.8)	682 (39.3)	1052 (60.7)	1.05 (0.91-1.21)

Figure 8. Insomnia prevalence associated with age and sex. Modified from Awadalla & Al-Musa 2019.

Figure 9 shows the prevalence of insomnia in the normal and underweight BMI groups. Underweight adults were found to be far more likely to suffer from insomnia compared to those with a normal weight. Out of the 3166 participants of the study only 116 were classified as underweight but nevertheless 80 out of these 116 suffered from insomnia.

	Total N. (%)	No Insomnia N. (%)	Insomnia N. (%)	cOR (95%CI)
BMI grouping				
Normal weight	1117 (35.3)	494 (44.3)	623 (55.7)	Ref
Underweight	116 (3.7)	36 (31.6)	80 (68.4)	1.86 (1.14-3.06)

Figure 9. Insomnia prevalence associated with BMI. Modified from Awadalla & Al-Musa 2019.

On top of that, out of all the parameters in the study found to be significantly associated with insomnia in figure 10, underweight was found to have the second strongest association, only being behind fatigue. Even so, the range of underweight is a lot larger compared to that of fatigue, ranging from 1.22 odds of insomnia all the way up to 3.48 odds of insomnia, the highest odds observed in the study.

Factors	β	S. E	aOR. (95%CI)
Age (years)	-	-	-
18–25	0.016	0.115	1.02 (0.81–1.27)
25–40	-0.134	0.148	0.87 (0.65–1.17)
> 40			
Income			
Sufficient	-	-	-
Insufficient	0.667	0.159	1.95 (1.43–2.66)
Smoking status			
Non-smoker	-	-	-
EX- smoker	0.316	0.150	1.37 (1.02–1.84)
Smoker	0.385	0.136	1.47 (1.13–1.92)
Caffeine (cups)			
=<3	-	-	-
>3	0.219	0.108	1.24 (1.01–1.54)
Presence of chronic disease	0.223	0.105	1.25 (1.02–1.54)
BMI grouping			
Normal weight	-	-	-
Underweight	0.724	0.267	2.06 (1.22–3.48)
Overweight	0.185	0.114	1.18 (0.94–1.47)
Obesity	0.165	0.147	1.23 (0.96–1.58)
Fatigue	0.947	0.096	2.10 (1.72–2.56)
Daytime sleepiness	0.453	0.100	1.57 (1.29–1.91)

Figure 10. Multivariable analysis of factors associated with insomnia. Awadalla & Al-Musa 2019.

Ade et al. (2021) conducted a highly similar study in Parakou, a sub-saharan African city. The amount of participants in this study was considerably lower compared to the previous study, 930 randomly selected adult (Age >18) residents of Parakou participated in the study. Sleep performance was assessed through the Pittsburg Sleep Quality Index, the Insomnia Severity Index and the Epworth Sleepiness Scale, much like those used in the previous study these are all questionnaires filled out by the participants. Figure 11 reveals that poor sleep is more common with increasing age. Insomnia was already more common in adults in the age group 35-44 compared to those in the age group 18-34 though not significantly so. However, insomnia in adults in the age groups 45-54 and >55 was significantly more common compared to those in the group 18-34. It was also found that females are significantly more likely to suffer from insomnia compared to males. Underweight adults were also found to be significantly more likely to suffer from insomnia than those adults with a normal weight. Interestingly, the results obtained during this study perfectly match the results obtained in the study of Awadalla & Al-Musa. That said, the odds found during this study tend to be a fair bit higher compared to those found in the study of Awadalla & Al-Musa. For example, while Awadalla & Al-Musa only found an odds ratio of 1.05 for females compared to males the present study found an odds ratio of 1.95 for this same comparison. This difference could simply be caused by the far lower amount of participants in the present study.

	Poor sleeping <i>n/N (%)</i>	cOR	<i>P</i> value	aOR	95%CI	<i>P</i> value
Age groups (years)			< 0.001			
18-34	220/636 (34.6)	1		1		
35-44	55/124 (44.4)	1.51		1.48	0.95-2.30	0.078
45-54	41/84 (48.8)	1.80		1.78	1.05-3.03	0.032
≥ 55	33/54 (61.1)	2.97		3.61	1.82-7.36	< 0.001
Sex			< 0.001			
Males	166/517 (32.1)	1		1		
Females	183/381 (48.0)	1.95		1.84	1.37-2.48	< 0.001
Nutritional status			< 0.001			
Normal range	185/555 (33.3)	1		1		
Overweight/obesity	153/324 (47.2)	1.65		1.53	1.12-2.08	0.007
Underweight	11/19 (57.9)	2.75		2.90	1.12-7.84	0.030

Figure 11. Age, Sex and BMI associated with poor sleep. Modified from Ade et al. 2021.

Sivertsen et al. (2014) conducted a study similar in method in Norway. A total of 9396 subject participated, unlike in previous studies, the participants in this study were all adolescents aged 16 to 19 years old. Participants were asked to fill out a questionnaire with questions on BMI and sleeping behaviour. Sleep specifically was assessed through questions on bedtime, rise time, sleep onset latency and wake after sleep onset. Specific questions on insomnia were also included in the questionnaire. Figure 12 shows that 145 of the participants were considered underweight and it was found that girls were more likely to be underweight compared to boys, a result that is expected.

	Underweight	Normal weight
N (%)	145 (15%)	7499 (79.8%)
Age, mean (SD)	17.4 (0.8)	17.4 (0.8)*
BMI, mean (SD)	16.0 (0.6)	21.0 (1.9)*
Gender		
Girls, % (n)	8.3% (421)	77.1% (3915)*
Boys, % (n)	5.0% (216)	76.7% (3348)

Figure 12. Weight in adolescents associated with gender. Modified from Sivertsen et al. 2014.

It was also found that underweight participants were significantly more likely to be short sleepers compared to those participants with normal weight as visible in figure 13. On top of that underweight participants displayed shorter sleep durations during both weekends and weekdays compared to normal weight participants and were more likely to suffer from insomnia than these participants, a result that is backed up by research discussed earlier.

	Underweight	Normal weight
Sleep duration category (weekdays)		
Short sleeper (<1SD: 5 hours), % (n)	27.3% (39)	13.2%(972)*
Normal Sleeper, (5–8 hours) % (n)	65.7% (94)	76.4% (5636)
Long sleeper (1 > SD: 8 hours), % (n)	7.0% (10)	10.4% (769)
Sleep duration weekdays, mean (SD)	5:48 (1:51)	6:29 (1:36)*
Sleep duration weekends, mean (SD)	8:28 (2:09)	8:41 (1:47)*
Insomnia	19.3% (28)	12.6% (943)*
OSA symptoms, % (n)	1.6% (2)	3.2% (194)*

Figure 13. Sleep characteristics in adolescents associated with BMI. Modified from Sivertsen et al. 2014.

Figure 14 shows data on sleep duration divided by gender. While both genders display a decrease in sleep duration associated with underweight the decrease in sleep duration in underweight girls is far more drastic than that in underweight boys.

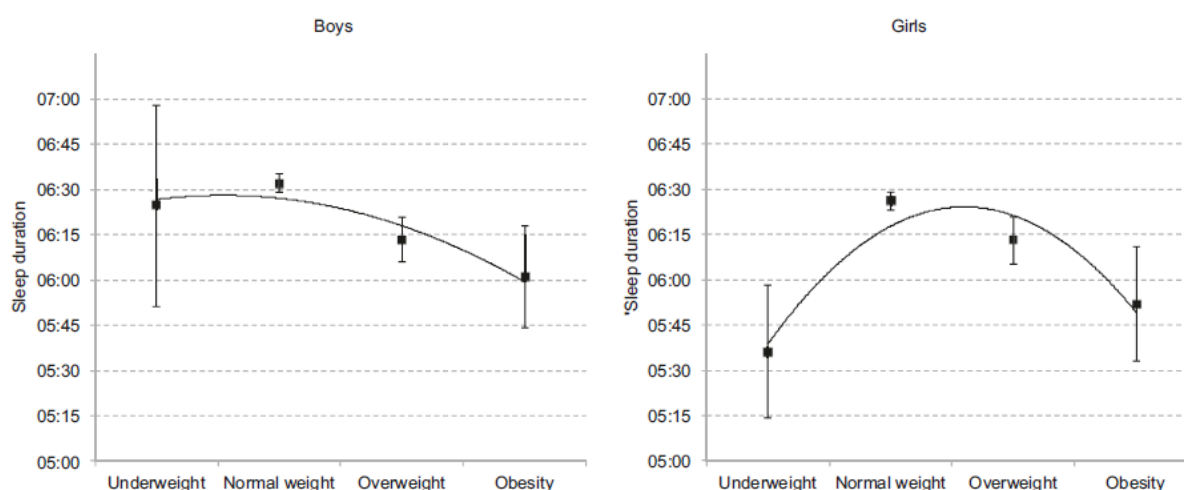


Figure 14. Sleep duration associated with BMI in adolescent boys and girls. Sivertsen et al. 2014.

Discussion

The present paper sought to answer the question: *Are the cognitive problems found in AN patients a consequence of the sleeping problems AN patients are found to experience?* As well as the question: *Are the sleeping problems observed in AN patients caused by AN itself or could they be a consequence of a low body weight?*

Evidence has shown that AN patients do in fact suffer from several sleeping problems, mainly a decrease in total sleep time, a decrease in REM sleep, a decrease in SWS sleep and an increase in time spent awake after sleep onset. Furthermore, evidence from the same studies has shown that sleep

improved after weight restoration in AN patients, though what aspect of sleep improved after weight restoration was different among the three weight restoration studies discussed. If only the significant results of the three studies are taken into account it can be concluded that weight restoration in AN patients leads to an increase in REM sleep, an increase in total sleep duration and a decrease in time spent awake after sleep onset. Lacey & Krieg (1992) also found a significant increase in stage 3 sleep in AN patients compared to controls at baseline, a result that directly contradicts other literature. This odd result is likely by chance because of the composition of the sample in the study, given its low sample size of only 10. When also taking into account non-significant findings an increase in SWS sleep after weight restoration is also observed.

Evidence has also shown that sleep problems associated with AN patients are found in people with a low BMI in the absence of an eating disorder, both in adults and adolescents. From the studies discussed it can be concluded the older adults as well as females are more likely to suffer from insomnia compared to younger adults and males. Underweight adults were also found to be significantly more likely to suffer from insomnia compared to those of normal weight. Underweight was found to have the second highest association with prevalence of insomnia out of all the factors found to have an influence on insomnia, only being just behind fatigue. Ade et al. (2021) did report way higher odds of insomnia associated with age, sex and BMI compared to Awadalla & Al-musa (2019), this difference is likely due to the significantly lower sample size in the study conducted by Ade et al. (2021). In adolescents it was found that girls are more likely to suffer from insomnia compared to boys. It was also found that underweight adolescents are more likely to be short sleepers and have a decreased sleep duration on both weekdays and weekends compared to adolescents with normal weight. Finally, it was found that underweight girls have significantly lower sleep duration compared to underweight boys. The results for both adults and adolescents fit what was expected from other literature.

The clear presence of sleeping problems found in AN patients combined with the observation that the cognitive problems observed in AN patients are largely the same as the cognitive problems associated with sleep deprivation suggests that these cognitive problems could very well be caused by a lack of sleep rather than by AN itself. Furthermore, the observation that sleeping problems in AN patients largely disappear when weight is restored suggests that sleeping problems and the cognitive problems that come with it could be caused by underweight rather than by AN. The observation that underweight causes sleeping problems on its own in absence of AN supports this even further.

Future prospects

If we could restore AN patients BMI to a healthy level and sustain this BMI it is likely that both the sleeping and cognitive issues observed in these patients would disappear. However, given the nature of AN as a disorder, this has been proven to be very difficult. Now, with the observation that the cognitive problems in AN could very well stem from the sleeping problems in AN caused by a low body weight but not from low body weight in general. Curing or at the very least alleviating cognitive problems in AN through curing of the sleeping problems in AN could prove to be a very promising solution. Cognitive behavioural therapy as a cure for insomnia is already widely used and often leads to great results (Riemann et al., 2017). Investigating the effect of curing sleeping problems through cognitive behavioural therapy on the cognitive problems observed in AN would make for a great future study that would not only serve to confirm the observations made in the present study but could also lead to a potential cure for the cognitive problems in AN.

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