Original Article

Subjective sleep disorders and daytime sleepiness in patients with restrictive type anorexia nervosa and effects on quality of life: a case–control study

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Abstract

To evaluate sleep disorders and daytime drowsiness in a cohort of patients affected by anorexia nervosa and their impact on health-related quality of life. We evaluated patients affected by restricting-type of anorexia nervosa (AN-R) and healthy controls by the Pittsburgh Sleep Quality Index (PSQI), Epworth Sleepiness Scale, Beck Depression Index. We also used the Short-Form Health Survey (SF-36) questionnaire to assess the quality of life in both AN-R and controls. Twenty-eight out of 34 AN-R patients (82.3%) in contrast with ten out of 34 healthy subjects (29.4%) had a pathological PSQI score compared to HC (p < 0.0001). The overall PSQI score (p < 0.001), sleep quality (p < 0.001), sleep duration (p = 0.02), sleep efficiency (p = 0.002), sleep disturbances (p = 0.03) and daytime dysfunction (p = 0.004) were significantly higher in AN-R than in controls. SF36 showed significantly reduced scores of standardized physical components (p = 0.01) and standardized mental components (p < 0.001), physical function (p < 0.001), physical role (p < 0.001) and general health (p < 0.001), vitality (p < 0.001), social functioning (p < 0.001) emotional role (p = 0.001) and mental health (p < 0.001) in AN-R. We found a significant correlation between the PSQI score and both the physical role (r = −0.35, p = 0.03) and level of education (r = 0.38, p = 0.02). Our data showed reduced overall sleep quality without excessive daytime sleepiness in AN-R. Sleep quality correlated significantly with quality of life (physical role) and level of education.

Keywords Anorexia nervosa · Restrictive type · Sleep · Sleepiness · Quality of life · SF36

Introduction

Anorexia nervosa is a severe psychiatric disorder characterized by refusal to maintain proper body weight, an intense fear of gaining weight despite being underweight due to a distorted perception of body image. Anorexia nervosa generally emerges during adolescence and adult age, and it represents the most common psychiatric disorder in young girls aged 15–19 years [1, 2]. It includes two different subtypes: the restricting-type (AN-R) and the Binge-Eating/Purging Type. In AN-R, a reduction in food intake without binge-eating or purging behaviour accomplishes weight loss [2, 3]. Sleep disorders are frequently associated with psychiatric diseases [4]. The early recognition of sleep complaints and their management may improve the outcome and prevent psychiatric illness relapse [4–7]. Anorexia nervosa is often associated with sleep impairment, even though only few studies focused on the prevalence of sleep disturbances [7]. Some authors described sleep problems as independent clinical syndromes [8]. Hypothalamic nuclei

Abbreviations

AN-R Restrictive type anorexia nervosa
BDI Beck Depression Inventory
BMI Body mass index
ESS Epworth Sleepiness Scale
HC Healthy controls
PSQI Pittsburgh Sleep Quality Index
SF36 Short-Form Health Survey

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and neuropeptides (such as hypocretin) modulate the sleep propensity, the sleep–wake cycle, feeding, and endocrinial system. Hypothalamic dysregulation might impair sleep and eating homeostasis due to anorexigenic and orexigenic hormones [7, 9–12].

However, previous studies on sleep and anorexia nervosa showed conflicting results [7, 14, 15]; in fact, polysomnographic studies showed inconsistent results. The main findings were a reduction of both slow-wave sleep and REM sleep and shorter REM sleep latency [7, 14–18], sleep microstructure impairment [19] in patients with anorexia nervosa, or no significant changes with respect to the controls [20–22]. Previous studies failed to clarify the pathogenesis of sleep disorders. Alteration of neurotransmitters (i.e. serotonin, norepinephrine, dopamine, opioids and endocannabinoids), and the close correlation between the midbrain and hypothalamic areas may be involved [9, 10, 12, 23].

The goal of our study was to evaluate sleep disturbances and daytime sleepiness by subjective scales in a homogeneous sample of patients with AN-R to assess its impact on mood and quality of life compared with a homogeneous group of healthy women matched for age, sex and education level.

**Methods**

**Subjects**

Our case–control study involved a cohort of female patients affected by AN-R and age, sex and education level matched healthy controls (HC). The participants were consecutive female outpatients, who sought treatment for their AN-R at the Clinical Nutrition and Eating Disorders Unit of University General Hospital Tor Vergata, between 1st June 2012 and 30th September 2013. All subjects were affected by AN-R at the time of the evaluation according to the Diagnostic and Statistical Manual of Mental Disorder, 4th Edition (DSM-IV-TR) criteria. We recruited HC among the high school students and university students with no medical and psychiatric diseases. Exclusion criteria for both groups were: occurrence of comorbid physical illness or any neurological disorders, psychiatric disorders other than AN-R and comorbid disorders, and intake of drugs influencing sleep and sleepiness. All patients and controls gave written informed consent; the Ethical Committee of the University of Rome Tor Vergata approved the study.

**Subjective scales**

All subjects underwent a subjective evaluation of the overall sleep quality (Pittsburgh Sleep Quality Index, PSQI) [24–26], excessive daytime sleepiness (Epworth Sleepiness Scale, ESS) [27, 28], quality of life Italian version of the Short-Form Health Survey (SF-36) questionnaire (4-week version) (SF36) [29, 30] and depressive symptoms (Beck Depression Inventory, BDI-II) [31, 32].

The PSQI is a self-rated questionnaire that assesses sleep quality and disturbance over one month. The PSQI is a 24-item scale that measures sleep disturbances according to 7 dimensions: subjective sleep quality (C1), sleep latency (C2), sleep duration (C3), habitual sleep efficiency (C4), sleep disturbances (C5), use of sleep medication (C6), and daytime dysfunction (C7). The sum of these seven areas yields the global score. The questionnaire is based on the majority of days and nights of the previous month. A global score of > 5 was an indicator of relevant sleep disturbances [25, 26].

We used the Italian version of ESS; an eight items scale investigating daytime sleep propensity in different real-life situations, referring to the previous month; each subject filled in the scale in the morning. Each item score is from zero to three with a final score from 0 to 24, and an ESS score > 10 indicates excessive daytime sleepiness [27, 28].

We evaluated health-related quality of life by the Italian version of the SF-36 questionnaire (4-week version) [29, 30]. The SF-36 is grouped in 8 multi-item scales: physical functioning (PF), role limitations due to physical problems (RP), bodily pain (BP), general health perceptions (GH), vitality (VT), social functioning (SF), role limitations due to emotional problems (RE) and mental health (MH). The score of SF-36 ranged from 0 to 100, 0 indicating extreme problems and 100 indicating no problems, higher values indicating better QoL. We obtained two global components Physical Component Summary (PCS) and Mental Component Summary (MCS) by the collapse of the eight SF-36 domains [30, 33].

The Beck Depression Inventory-II (BDI) is a validated self-administered scale consisting of 21 multiple-choice items. Each item is rated from zero (no symptoms) to three (most severe). The scores range from 0 to 63. Scores are evaluated as follows: 0 to 9, the absence of depression, 10–18, mild to moderate, 19–29, moderate to severe, 30–63, severe [31, 32].

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

**Statistical analysis**

We conducted the statistical analysis on two groups, patients with AN-R and C. We compared the demographic and clinical data of both groups (age, weight, height, BMI, and years of education) and psychometric scales BDI, PSQI, ESS, SF-36. We showed mean and standard deviation of
demographic variables, medians and interquartile ranges for psychometric variables (BDI, PSQI, ESS, SF-36).

We used nonparametric unpaired Mann–Whitney and chi-square test when required to compare demographic and psychometric variables in AN-R and HC. The patients were subdivided by the PSQI cut-off (> 5) in AN-R with sleep disorders and AN-R without the sleep disorder. We compared the subdomains of PSQI, the domains of the SF36 and the ESS score in these two groups by nonparametric unpaired Mann–Whitney test. The nonparametric correlation Spearman test was applied to test the relationship between PSQI score and education level, SF36 and BDI. Statistical analysis was performed using the Jamovi software [34, 35]. Statistical significance was set to p < 0.05. We also reported the values of effect size (r).

Results

Demographic characteristics

We recruited a total of 34 women affected by AN-R (mean age 23.3, SD 6.53 range 14–39). Mean BMI was 16.4 (SD 1.47 range 12.6 to 18.7). The control group consisted of 34 women matched for age (mean age 23.3 SD 6.53 range 14–39), sex and education to the AN group. In particular, the group of patients showed a significantly lower BMI compared with controls (p < 0.0001), whereas age, sex and education were similar as required by the study design. Demographic data are summarized in Table 1.

Psychometric variables

All patients with AN-R (n = 34) and all healthy subjects (C) have been evaluated by psychometric scales described above. BDI-II presented significantly more severe scores in patients (median 15; interquartile range 7–24) than in HC (p = 0.0001). The data are summarized in Table 1.

Nocturnal sleep quality (PSQI)

Patients with AN-R experienced a significant presence of sleep disorders. Twenty-eight of the 34 subjects with AN (82.3%) compared to ten out of 34 healthy subjects (29.4%) had a pathological PSQI score (> 5) (χ² = 17.2, p < 0.0001).

The overall PSQI score was significantly higher in the affected group (AN-R) than in the controls (p < 0.001). As for the individual components, the C1 sleep quality (p < 0.001), C3 sleep duration (p = 0.02), C4 sleep efficiency (p = 0.002), sleep disturbances C5 (0.003) and daytime dysfunction C7 (p = 0.004) were higher in AN-R than in HC. These data are presented in Table 2. Patients with sleep complaints (PSQI > 5, n = 28) and without sleep complaints (PSQI ≤ 5, n = 6) showed no significant differences in ESS score (p = 0.96), in individual components of SF-36 and in the physical (p = 0.27) and mental (p = 0.94) standardized components. The values are shown in Table 3.

Daytime sleepiness (Epworth Sleepiness Scale ESS)

Patients affected by AN-R did not experience significant daytime drowsiness as assessed by ESS. Eight of the 34 AN-R patients (23%) compared to three out of 34 HC (8%) reported a pathological ESS score (> 10) (χ² = 2.7, p = 0.09). The total ESS score was not statistically different in the two groups (AN-R vs HC, p = 0.7) (see Table 2).

Quality of life (SF-36)

AN-R patients presented significantly reduced physical component summary scores (p = 0.01) and mental component summary scores (p < 0.001). Considering the single components, physical functioning (p = 0.001), role limitations due to physical problems (p < 0.001) and general health perceptions (p < 0.001), vitality (p < 0.001), social functioning (p < 0.001), role limitations due to emotional problems (p = 0.001) and mental health (p < 0.0001) were significantly lower than in HC. The data are presented in Table 2.

Comparison between patients with or without sleep complaints

No significant differences were found between sleep complaints and no sleep complaints regarding ESS, BDI-II and SF36 (see Table 3).

Table 1 Demographic characteristics of AN and healthy controls

| Variable                  | AN-R (N=34) | HC (n=34) | p   |
|---------------------------|-------------|-----------|-----|
| Age (mean ± SD)           | 23.3 ± 6.53 | 23.3 ± 6.53 | NS  |
| Gender                    | 34 F        | 34 F      | NS  |
| Education (y)             | 13 (13–17)  | 13 (13–17) | 0.37|
| BMI                       | 16.5 (15.3–17.6) | 20.98 (19.8–23.3) | <0.0001*|
| BDI-II                    | 15 (7–24)   | 6.5 (3–7)  | 0.0001*|

AN-R anorexia nervosa restricting type, C controls, BMI body mass index, BDI-II Beck Depression Inventory-II

*Values expressed as median and interquartile ranges

*p < 0.05 is considered statistically significant
The correlations between the PSQI and SF36, BMI, education and BDI score, are shown in Table 4. A significant negative correlation between the PSQI score and the role physical in SF36 was found ($r = -0.35, p = 0.03$ see Table 3 and Fig. 1A). A significant positive correlation between PSQI score and years of education ($r = 0.38, p = 0.02$ Table 4 and Fig. 1B) was also evident.

### Discussion

Sleep research in anorexia nervosa addressed two crucial issues: (1) the effects of forced fasting in the anorexia nervosa and rapid food fluctuations in bulimia nervosa on the regulatory processes of the sleep–wake cycle and (2) the search for a significant relationship between the neurobiology of anorexia nervosa and major depression. At present, the second question seems to have found some answers, since most of the available evidence underlines the idea...
that anorexia nervosa and mood disorders are two distinct entities, even if it has several psychiatric comorbidities (i.e. mood and anxiety disorders, personality disorders, suicidality, substance use disorders) [36]. On the other hand, for what regards the effects of forced fasting on sleep regulation, recent research on animal models and humans seems to show that anorexia nervosa produces substantial sleep fragmentation and deep sleep reduction [14]. It has been recently suggested an involvement of the hypothalamus in the pathogenesis of anorexia nervosa. Hypothalamus is involved in appetite control, hunger, satiety, and energy balance, but also in the regulation of sleep–wake cycle [37]. Orexin is a neuropeptide synthesized in the hypothalamus that modulates complex behaviors, such as sleep and vigilance, reward, food intake, and cognition [37–39]. It is still unclear how abnormal activity of hypothalamic neuropeptides (i.e. orexin) or their receptors may play a role in the mechanisms of hyperactivity, disturbed control of appetite, hormonal dysfunction and sleep fragmentation in patients with anorexia nervosa [40–42]. In our controlled study, we confirm a significant tendency to low sleep quality as shown by the significantly higher overall PSQI score in the patient group than in the controls. Sleep disorders are significantly represented, affecting approximately 83% of AN-R compared to 29.4% of the healthy subjects. In addition, PSQI seems to be a useful tool documenting the presence of disturbed sleep in the AN-R. It is well known that patients with AN-R rarely report sleep disorders as part of the clinical picture. It is probably due to AN-R patients’ common belief that a shortened sleep period and time in bed may allow being longer active and, therefore, increase caloric expenditure. On the other hand, patients affected by bulimia nervosa may delay sleep onset time of one hour or more because of compulsive eating episodes in the late evening or early morning [7, 14, 15, 21]. These different sleep profiles could account for conflicting results obtained in several studies conducted in heterogeneous patient groups that included both restrictive and binge-eating type [14, 15, 43]. The paucity of studies conducted in patients with AN-R confirmed the sleep fragmentation (mainly due to early awakening), lower sleep efficiency and total sleep time and a reduction of slow-wave sleep (SWS) and REM sleep, higher REM sleep latency [14, 16, 22, 44]. Reduction of slow-wave activity (a quantitative measure of deep sleep) correlated with weight and BMI [16, 44]. Regarding PSQI, we found a significant impairment of the overall sleep quality component (C1), sleep duration (C3), sleep efficiency (C4) and sleep disorders (C5) in our AN-R sample. These findings are closely associated with the sleep profile of AN-R. In fact, the patients prolong the active time and consequently reduce total sleep time and time in bed to increase caloric expenditure. The consequences of prolonged sleep deprivation and poor sleep quality may induce daytime dysfunction as confirmed by the higher daytime dysfunction in PSQI. Moreover, diurnal sleepiness is not affected.

Table 3 Comparison in PSQI, ESS, BDI and SF-36 scores between AN with sleep disorders (ANSD, PSQI > 5,) and AN without sleep disorders (ANwSD, PSQI ≤ 5)

|                      | ANSD (n = 28) | ANwSD (n = 6) | p       | Effect size (r) |
|----------------------|--------------|---------------|---------|-----------------|
| PSQI                 |              |               |         |                 |
| Global Score         | 9 (8–13)     | 4 (3–5)       | 0.0001  | 1               |
| ESS                  | 7 (3–10.5)   | 6 (4–8)       | 0.96    | 0.01            |
| BDI-II               | 13 (8–22.5)  | 9.5 (8–12)    | 0.35    | 0.13            |
| Health-related quality of life SF-36 | | | | |
| PF                   | 87.5 (72.5–97.5) | 90 (85–95) | 0.96    | 0.01            |
| RP                   | 50 (0–100)   | 100 (50–100)  | 0.17    | 0.34            |
| BP                   | 68 (51.5–100)| 87 (60–100)   | 0.52    | 0.16            |
| GH                   | 54.5 (43.5–63.5) | 64.5 (27–72) | 0.45    | 0.19            |
| VT                   | 50 (30–60)   | 47.5 (35–65)  | 0.76    | 0.07            |
| SF                   | 56.25 (31.2–65)| 50 (50–50) | 0.66    | 0.11            |
| RE                   | 33.3 (0–100) | 50 (0–100)    | 0.69    | 0.10            |
| MH                   | 48 (28–60)   | 44 (20–60)    | 0.92    | 0.03            |
| PCS                  | 49.1 (45.1–55.9) | 55.5 (49.1–58.8) | 0.27    | 0.28            |
| MCS                  | 51.6 (44.5–54.7) | 50.61 (45–56.6) | 0.94    | 0.01            |

ANSD anorexia nervosa with sleep disorders (PSQI > 5), ANwSD anorexia nervosa in the absence of sleep disorders (PSQI ≤ 5), PSQI Pittsburgh Sleep Quality Index, ESS Epworth Sleepiness Scale, SF-36 domain PF physical operation, RP role limitations due to physical problems, BP bodily pain, GH general health, VT vitality, SF social functioning, RE role limitations due to emotional problems, MH mental health, MCS mental component summary, PCS physical component summary

Values expressed as median (interquartile range). Non-parametric statistical test Mann–Whitney for independent samples. p < 0.05 considered statistically significant. Effect size (r) rank biserial correlation
in AN-R compared to controls as shown by the Epworth Sleepiness Scale. Animal models confirmed that the induction of ‘feeling full’ (i.e. intake of food, CCK applications, bombesin and leptin) prompts an increase in excessive diurnal somnolence and deep sleep (short sleep onset latency, an increase of SWS, decrease in REM sleep). On the other hand prolonged food deprivation and the application of orexin (induction of ‘hunger’) result in an increased wake time and light sleep, in particular, a decrease in slow-wave sleep [14, 45]. Therefore, prolonged fasting in AN-R may increase vigilance. This condition may explain the lack of excessive daytime somnolence in our sample of anorectic patients.

Furthermore, we found a significant and widespread reduction in quality of life measures in all five mental dimensions (vitality, general health, social functioning, role emotional and mental health) and 4 out of 5 physical components (physical functioning, physical role and vitality and general health) and in both Physical and Mental components summaries in AN-R compared to HC. The SF-36 represents a widely validated and accepted quality of life assessment scale in different clinical areas [30, 33, 46]. Anorexia nervosa is a chronic and often severe disorder, which significantly impacts different areas of life. AN may impair mental, physical, behavioral and socio-professional abilities. Therefore, the quality of life in patients is often worse than in the healthy population. Quality of life can be a key factor in measuring the severity of the disease and the effectiveness of the treatment carried out. Mental health components are more often affected than physical ones in anorexia nervosa [46]. AN-R patients may perceive fewer limitations than subjects with other eating disorders. This finding is consistent with previous reports of better SF-36 emotional well-being in those with restrictive eating behaviors. However, this result should be interpreted with caution, as it may be due to intrinsic limitations of the instruments used and/or an "artefact" produced by the psychopathological condition itself, obesity and other correlated condition rather than by a real better condition of AN [47, 48]. We divided AN-R into two groups with or without sleep impairment by PSQI cut-off > 5. No significant differences were found concerning daytime drowsiness (ESS), the severity of depression (BDI-II), and quality of life (SF-36) even if the small sample

| SF-36 domain | AN-R (N=34) |
|--------------|-------------|
| PF           | 0.03        |
| RP           | 0.35        |
| BP           | 0.14        |
| GH           | 0.10        |
| PCS          | 0.21        |
| VT           | 0.01        |
| SF           | 0.07        |
| RE           | 0.03        |
| MH           | 0.12        |
| MCS          | 0.07        |
| BMI          | 0.19        |
| Education (y)| 0.38        |
| BDI-II       | 0.1         |

Non parametric Spearman correlation test was performed

$p < 0.05$ was considered statistically significant

### Table 4

| SF-36 domain | AN-R (N=34) |
|--------------|-------------|
| PF           | 0.03        |
| RP           | 0.35        |
| BP           | 0.14        |
| GH           | 0.10        |
| PCS          | 0.21        |
| VT           | 0.01        |
| SF           | 0.07        |
| RE           | 0.03        |
| MH           | 0.12        |
| MCS          | 0.07        |
| BMI          | 0.19        |
| Education (y)| 0.38        |
| BDI-II       | 0.1         |

Fig. 1 A Correlation between PSQI global score and Physical Role of SF36 in AN-R (Spearman nonparametric correlation test, $r = -0.35$, $p=0.03$). B Correlation between PSQI global score and Education level (years) in AN (Spearman nonparametric correlation test, $r=0.38$, $p=0.02$)
limits this analysis. Finally, we found an interesting correlation between the severity of sleep disturbances (PSQI global score) score and a physical domain of the SF-36 (role physical) and education. We stated that the SF36 physical components seemed to be less affected in the AN-R or perhaps less easily assessable either because of intrinsic limitations of the quality of life measurement instruments and the specific aspects of the disease itself. We did not find studies correlating QoL and sleep quality in AN. In our sample, we found a negative correlation between role physical and PSQI scores, demonstrating that poor sleep quality may directly impact the physical component of the quality of life. The physical role may quantify work problems and other daily activities due to physical health [30, 33]. Sleep impairment due to sleep fragmentation and sleep loss could negatively affect the quality of life and diurnal function, as demonstrated by PSQI scores. Regarding the positive correlation between education level and severity of PSQI, previous studies report significant interactions between the social environment and the development of eating disorders. However, the results are mixed, and the social context’s role in the etiology of anorexia nervosa is unclear [49]. Some authors found higher parental education related to eating disorders severity [49, 50]. However, these findings may represent a selection bias, linked to increased attention in this type of family context [49, 50]. On the other hand, a negative effect of higher education for memory and cognitive flexibility was very recently described in a recent meta-analysis in anorexia nervosa [51]. Although education is usually associated with a positive influence on neuropsychological performance [52], sleep fragmentation, low total sleep time and sleep efficiency may play a role in the cognitive dysfunction of anorectic patients.

Conclusions

About 50% of ED patients with AN have sleep problems [15, 43]. Insomnia seems to be a central clinical symptom of anorexia nervosa [53]. Nevertheless, limited sleep studies and little is known regarding the real influence of sleep complaints on outcomes [53].

To our knowledge, this is the first study examining the link between sleep disturbances, sleepiness and QoL in AN-R. We found impaired sleep quality without daytime sleepiness in AN. Subjective sleep quality correlated significantly with quality of life (physical role) and level of education. The main limitation of the study is the small sample and the lack of polysomnographic data. Nevertheless, our study evaluated the relationship between sleep disorders and AN in a sample of homogenous patients with AN-R. We found significant impairment of sleep and daytime function without EDS. Both the physical and mental components of QoL are profoundly affected in anorexia nervosa. Sleep impairment correlated significantly with a worse quality of physical role (negative correlation) and a higher education level (positive correlation). Future studies should evaluate sleep disorders in a larger sample, by subjective and objective evaluation (i.e. actigraphic and/or polysomnographic methods).

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Declarations

Conflict of interest The authors have no conflicts of interest to report.

Ethical approval The Ethical Committee of the University of Rome Tor Vergata approved this study. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent All eligible participants completed an informed consent form prior to participation in the study.

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