Prevalence of eating disorders and eating attacks in narcolepsy

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Abstract: Narcoleptic patients suffer frequently from obesity and type II diabetes. Most patients show a deficit in the energy balance regulating orexinergic system. Nevertheless, it is not known, why narcoleptic patients tend to be obese. We examined 116 narcoleptic patients and 80 controls with the structured interview for anorectic and bulimic eating disorders (SIAB) to test the hypothesis that typical or atypical eating attacks or eating disorders may be more frequent in narcoleptic patients. No difference in the current prevalence of eating disorders bulimia nervosa, binge eating disorder, or anorexia nervosa was found, nor was the frequency of eating attacks higher in the narcolepsy group. We conclude that present eating disorders and eating attacks as defined in DSM IV are not the reason for the observed differences in body composition. Additional factors, such as basal metabolic rates and lifestyle factors need to be considered.

Keywords: narcolepsy, eating disorder, SIAB, bulimia, anorexia, eating attack

Introduction

Narcolepsy is characterized by the core symptoms: excessive day time sleepiness, cataplexies, hypnopompic and hypnagogic hallucinations, sleep paralysis, and phases of automatic behavior. It was recently discovered that narcoleptic dogs have a defective receptor for the peptide orexin (Lin et al 1999) and that orexin knock out mice display behavioral anomalies reminiscent to human narcolepsy (Chemelli et al 1999). Investigations into the orexinergic system in humans revealed that most narcoleptics with cataplexies show diminished levels of orexin in the cerebrospinal fluid (CSF), typically below the detection limit of commercially available antibodies, whereas healthy controls show orexin levels above 200 pg/ml (Dauvilliers et al 2003). Orexin (hypocretin) is involved in various aspects of energy homeostasis. It stimulates feeding behavior and, in many neurons, counteracts the effects of the satiety hormone leptin (Baumann et al 2005). In addition, Orexin promotes vigilance and attention.

Narcolepsy is tightly associated with the human leukocyte antigen (HLA) system. More than 90% of the patients are positive for HLA DR2 and it is mostly the HLA DR2 patients who lack orexin in the CSF. The lack of orexin is thought to be due to a specific degeneration of orexinergic neurons located in the hypothalamus. The degenerative process is probably autoimmunological in nature (Black 2005). Nevertheless, the causes for narcolepsy remain poorly understood.

Narcoleptic patients exhibit a marked increase of body weight. In German populations, narcoleptics had 3–4 body mass index (BMI) points more than control populations and the national average (Schuld et al 2000; Dahmen et al 2001, Nishino et al 2001; Kok et al 2003). Patients anecdotally give testimony of increased appetite and altered food preferences that occur around the time of narcolepsy symptom onset. However, the issue of comorbidity with eating disorders or subsyndromal eating anomalies has never been formally studied. Peyron and colleagues (2000) described

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a juvenile narcoleptic patient with a rare genetic defect in the orexin system, who was additionally suffering from bulimic eating attacks.

We investigated 116 narcoleptic patients, 80 unrelated healthy controls with the self-report version (SIAB-S) of the structured interview for anorectic and bulimic eating disorders (SIAB) devised by Fichter and Quadflieg (2001). The study is part of a broader effort to characterize narcoleptic patients clinically, genetically, and biochemically.

Methods

Patients

Patients were recruited with the help of the German Narcolepsy Association (Deutsche Narkolepsie Gesellschaft), a nationwide self-help group that promotes the exchange of information between affected members and whose members have been participated in many scientific studies in narcolepsy. The diagnosis of narcolepsy was based on the unambiguous presence of cataplexies (95%) and severe day-time sleepiness (100%). Patients without cataplexies were only admitted when other rapid eye movement (REM)-associated symptoms and results of polysomnographic investigations were demonstrating the diagnosis. Most patients exhibited additional symptoms such as automatic behavior, hallucinations, and sleep paralysis. The Stanford Centre for Narcolepsy Sleep Inventory was used to quantify symptoms. The Stanford Centre for Narcolepsy Sleep Inventory consists of 146 questions organized in eight sections that assess all typical symptoms of narcolepsy patients. Sections one and two collect general and sociodemographic information. Section three is the Epworth Sleepiness Scale (ESS). Section four asks for sleep quality and medication. Sections five, six, seven, and eight are concerned with cataplexies, hallucinations, sleep paralysis, and automatic behavior, respectively. The core section on cataplexies section has been validated in 983 sleep-disorders patients (Anic-Labat et al 1999). Patients were investigated in respect to HLA status as described by Olerup and Zetterquist (1992). Patients and controls are depicted in Table 1

Controls

Controls were recruited by advertisements and postings within the local community. All controls were free of narcolepsy symptoms. Neither controls nor patients were suffering from acute psychiatric disorders such as acute depression that could influence eating behavior or food choice (Harris et al 1986; Pijl et al 1994). All participants gave informed consent. The study was approved by the local ethics committee.

SIAB-S-Questionnaire

The SIAB-S Questionnaire consists of 81 items and is specifically designed to assess pathological eating patterns as well as related symptoms such as depressed mood, impaired social integration, and dysfunctional self images and body perceptions. In contrast to most other eating questionnaires, the SIAB-S allows also for a diagnostic evaluation according to ICD10 and DSM IV since 20 of the items are formulated in a way to assess diagnostic criteria. Since its inception, the SIAB has been validated in several clinical populations and in addition in a number of scientific studies, among which are several large multicenter studies into the genetics of eating disorders.

In addition the SIAB allows to define subsyndromal categories. Bulimia nervosa binge was defined as binge-eating disorder without DSM IV criterion C (more than two eating attacks per week). Bulimic syndrome was defined as bulimia nervosa with eating attacks (criterion A) and either recurrent inappropriate compensatory behavior or a frequency of at least twice weekly (criteria B or C) but without undue influence of self-evaluation (criterion D). Atypical bulimic behavior is characterized by the steady consumption of sweet or otherwise high caloric food throughout the day.

The anorectic syndrome was defined as refusal to maintain body weight above minimal normal weight (criterion A) and either intense fear of gaining weight or disturbance in the way in which the body weight or shape is experienced (criteria B or C).

Regular (inappropiate) compensatory behavior is the disproportionate and undue effort to counteract food intake either

Table 1 Characteristics of patients and controls

	Narcoleptics	Controls	
Number (n)			
All	116	80	
Females	81 (69.8%)	44 (55%)	
Males	35 (30.2%)	36 (45%)	0.0359
Age (years)			
All	50.7 ± 16.0	40.8 ± 15.2	<0.0001
Females	47.9 ± 16.7	45.4 ± 15.7	ns
Males	57.3 ± 12.2	35.1 ± 12.5	<0.0001
BMI			
All	28.3 ± 5.5	25.1 ± 5.3	<0.0001
Females	28.2 ± 6.1	25.0 ± 5.4	0.0042
Males	28.6 ± 4.0	25.2 ± 5.3	0.0033
Age of onset	22.4 ± 10.7	na	
Epworth sleepiness scale	18.4 ± 4.5	na	
HLA DR2 (n = 92)	86 (93%)	na	

Abbreviations: BMI, body mass index; HLA, human leukocyte antigen; na, not available; ns, not significant.

through laxative medication, diuretics, or excessive sport. Spitting is chewing and spitting of foodstuff without swallowing. Regurgitation is self-induced vomiting after eating.

Patients and controls filled out the questionnaires after the diagnosis was checked by an experienced physician (ND). All participants had additional opportunities to ask questions concerning the correct interpretation of questions. To assure data quality, questionnaires were reviewed in the presence of participants and gaps were filled.

Primary outcome parameters were the frequencies of typical and atypical eating attacks as well as eating disorder diagnoses.

Statistics

All statistical calculations were done with the help of a commercial statistics package (SPSS). Exploratory statistics and, where appropriate, the comparison of mean values (t-tests) and distributions (Chi-square tests) were calculated. No corrections were made for multiple testing, because we sought to increase the likelihood to generate hypotheses, rather then to confirm pre-established relations.

Results

No difference in the present prevalences of DSM IV eating disorders bulimia disorder, binge-eating disorder, and anorexia nervosa was found. As with the formal eating disorders, none of the subsyndromal categories was significantly different between narcoleptics and controls (Table 2)

Next, we assessed the frequency of eating attacks without regard to specific diagnoses (Table 3). Again, no difference was apparent between narcoleptics and controls.

Finally, we were interested in the effect of hyperphagic behavior on the actual BMI. Persons with hyperphagic traits (any hyperphagic diagnosis, see Table 2) have a higher BMI (narcoleptics: 30.3 ± 6.3; controls: 27.7 ± 5.8) than persons without (narcoleptics: 28.0 ± 5.4; controls: 25.4 ± 4.7), regardless of the narcolepsy diagnosis.

Discussion

The first result of this study was that eating disorders as defined in DSM and ICD 10 were not more prevalent in narcoleptic patients than in controls. Disorders associated with hyperphagic behavior (bulimia nervosa, binge-eating disorder, and the subsyndromal entities bulimic syndrome, atypical bulimia and bulimia nervosa "binge") were of particular interest, because narcoleptic patients generally show increased BMIs. In addition, no differences between narcoleptic patients and controls were noted for the frequency of typical and atypical eating attacks. Hyperphagic behavior, when present, was associated with an increase in BMI for both narcoleptics and controls.

Taken together, the results indicate that overt anomalies in eating behavior are not the reason for the higher BMI of narcoleptic patients and that other mechanisms need to be explored. The narcoleptic sample consisted of slightly more women than the control sample. One could argue that both samples are not perfectly matched and thus not comparable. However, eating disorders are more frequent in women, than in men. Therefore, the study group composition was, if at all, biased towards a higher incidence of eating anomalies in the narcolepsy group that still was not detectable. In addition, the age of the men in the control sample was younger

Table 2 Frequencies of current eating disorders in narcoleptic patients and controls: no significant differences were detected (Chi-square tests)

Disorder	Narcoleptic	[Male/Female]	Controls	[Male/Female]
Hyperphag				
Any hyperphag diagnosis	15 (13%)	[6/9]	14 (18%)	[7/7]
Bulimia nervosa	2 (2%)	[0/2]	0 (0%)	[0/0]
Binge eating disorder	3 (3%)	[1/2]	1 (1%)	[0/1]
Bulimia nervosa binge	6 (5%)	[3/3]	1 (1%)	[0/1]
Bulimic syndrome	10 (9%)	[5/5]	11 (14%)	[4/7]
Atypical bulimic	8 (7%)	[3/5]	7 (9%)	[5/2]
Hypophag				
Anorexia nervosa	0 (0%)	[0/0]	0 (0%)	[0/0]
Anorectic syndrome	0 (0%)	[0/0]	0 (0%)	[0/0]
Other				
Regular compensatory	9 (8%)	[1/8]	2 (3%)	[0/2]
Spitting	0 (0%)	[0/0]	0 (0%)	[0/0]
Regurgitation	0 (0%)	[0/0]	0 (0%)	[0/0]

Table 3 Frequency of current eating attacks in narcoleptic patients and controls: no significant differences were detected (Chi-sqare tests)

Frequency of eating attacks	Narcoleptics	Controls
All (n = 114 + 80)		
Never	88 (77%)	63 (79%)
<1–4x/month	11 (10%)	12 (15%)
<2x/week	4 (4%)	4 (5%)
<1x/day	7 (6%)	1 (1%)
>1x/day	4 (4%)	0 (0%)
Women (n = 80 + 44)		
Never	61 (76%)	36 (82%)
1–4x/month	8 (10%)	3 (7%)
<2x/week	2 (3%)	4 (9%)
<1x/day	6 (8%)	0 (0%)
>1x/day	3 (4%)	1 (2%)
Men (n = 34 + 36)		
Never	27 (79%)	27 (75%)
1–4x/month	3 (9%)	9 (25%)
<2x/week	2 (6%)	0 (0%)
<1x/day	1 (3%)	0 (0%)
>1x/day	1 (3%)	0 (0%)

than in the narcoleptic sample, possibly reflecting the lower inclination of older male controles to detail on eating habits. Medications such as antidepressants or stimulants can stimulate (eg, tricyclics) or suppress (eg, stimulants) appetite and thus modify eating behavior. However, as we have shown in a previous paper, narcolepsy medication status had no demonstrable association with the BMI of obese narcoleptics (Dahmen et al 2001). All prevalences are well within the range commonly reported for eating disorders in Western countries (Hoek and Hoeken 2003; Makino et al 2004).

A clear limitation of the study is that the SIAB questionnaire is suited only to detect rather gross anomalies of feeding behavior. Discrete changes in food preference or eating habits could be physiologically relevant but undetectable within our study design. It is well known that rather small imbalances in energy homoeostasis can, over time, lead to remarkable changes in body shape. Moreover, we investigated only symptoms that were present during the time of interview (last three months). Thus it can not be ruled out that eating disorders or eating anomalies might manifest at some point in the life of narcoleptic patients, eg, at the time of onset and then ameliorate or disappear. In addition, the (parasomnic) sleep related eating disorder (Schenck et al 1991) and the night eating syndrome are not covered by the SIAB, so that the potential contribution to increased BMIs of these disorders could not be evaluated. Both traits are not known to be necessarily associated with obesity or increased BMIs in general (Schenck et al 1993; Striegel-Moore et al 2006) but may play a role in subsets of obese persons or under specific circumstances such as in narcolepsy.

There are no data in the literature in respect to metabolic basal or resting rates of narcoleptic patients. Orexin neuron-deficient transgenic mice, however, have been reported to show lower rates of basal metabolism and also to display higher body weight, when caged under identical conditions, than control animals (Hara et al 2005). Another reason for narcoleptic patients to be more obese may be found in the lifestyle usually associated with narcolepsy. Patients tend to be less active in sports and other activities and thus could be prone to obesity because of a imbalance between "normal" calorie intake and reduced consumption after the onset of symptoms. In line with this suggestion, Pollak and Green (1990) showed that the degree of "postprandial deactivation" was much larger in narcoleptics than in controls.

The relation between reduced or absence of orexin and increase of body weight is a complex one, because typically reduced orexin would be expected to lead to a reduction of food intake and hence to a lower, not higher body weight. In fact, in a study of 12 narcoleptic patients, Lammers and colleagues (1996) showed that the caloric intake and particularly the carbohydrate intake were reduced in comparison to controls.

One of the additional factors worth to be considered might be the leptin-signaling system. Leptin levels have been reported to be reduced in narcoleptic patients (Schuld et al 2000; Kok et al 2002). Because leptin is produced by fat cells as part of a signaling pathway to maintain long term energy balance, the incapacitation of this signaling could indeed contribute to a positive energy balance. However, newer reports have not replicated the finding of lowered leptin levels (Arnulf et al 2006; Dahmen et al 2007).

Conclusion

Narcoleptic patients do not show increased prevalences of eating disorders and present eating symptomatology may not explain the increased BMI of narcoleptic patients. Therefore studies covering past symptoms and studies with more precise instruments, including those measuring satiety after standardized meals and assessing sleep-related eating disorders seem worthwhile. In addition the attempt to measure basal metabolic rates in narcoleptic patients by indirect calorimetry may be a way to gain additional insights.

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