

# Sleep-Rhythm Disorder And Anarchic Eating Behaviors Impact On Adolescents' Treatment Compliance

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## Abstract

**Purpose:** Treatment compliance demands diligence and rhythmicity that not all adolescents are able to assure. Knowing adolescents' high frequencies of sleep-rhythm disorders and irregular eating habits, we hypothesized that a link exists between perturbed circadian rhythms and medication non-adherence.

**Methods:** This inquiry, with an interviewer-completed questionnaire, included 115 youths 13–20 years old, taking prescribed oral medications and consulting in a unit for adolescents with social, familial and/or school difficulties. An algorithm comprised of four scales evaluating treatment compliance was used. Associations were assessed with univariate and multivariate logistic-regression models.

**Results:** The algorithm classified 30.4 % of the participants non-adherent. After adjusting the final model, perturbed sleep rhythms and poor eating habits were significantly and independently associated with treatment non-compliance.

**Conclusions:** Although not all potential confounding factors were taken into account, the strength of the associations retained pleads for further investigations of a larger and more homogeneous population.

## INTRODUCTION

The World Health Organization declared: “Improving adherence would have the biggest impact on the health population than any improvement in medical”. Two meta-analyses (1)(2) found campaigns aimed at improving teenagers' adherence inefficient. In specific diseases, such as asthma, numerous studies showed that adherence drops drastically when comparing babies' (77 %) (3)(4) and teenagers' (30 %) (5), after which rising during adulthood (50 to 60 %) (6).

Published findings suggest that teenagers are more frequently treatment non-compliant that is to say they don't follow their treatment or do so infrequently. This could be explained by the treatments' daily load of obligations and the teenagers abilities to handle such a task. For many, juggling both treatments and their hectic everyday schedule can result in mismanaging these two departments. Moreover, they don't have the long-term perspective to appreciate a well-followed treatment's advantages. Worsening of the condition, heavy morbidity, rising health-care costs,

premature death are some consequences of non-adherence, to name a few.

The adolescent chronobiological disorder linked to circadian rhythm sleep and anarchic eating habits reflect their craving to escape parental control to be independent. Furthermore, teenagers and young adults are sensitive to disrupted circadian rhythms. The delayed-sleep-phase disorder affects approximately 7–16 % of teenagers (7). In addition to daytime drowsiness (affecting 20–40 %), are responsible for a higher rate of scholastic failures, attention problems, more accidents and affective disorders (7). However, no study has considered disturbed sleep cycles impact on treatment adherence. Concomitantly, teenagers' diets have gone from bad to worse since 2000 (8). This, alongside different types of fragmented households other a stereotypical two-parent household, contributes to the lack of limits imposed to them. Snacking has been more and more favoured with premature independence. The sleep-rhythm disorders and anarchic eating habits are markers of opposition to the social classical model (9), reflecting their desire to break free of parental

control. Qualitative studies have shown that daily drug intake could be viewed as a restriction to their freedom and a sign of addiction. We supposed that this desire for independence expressed by rhythm disorders could also influence drug compliance.

We investigated potential links between treatment compliance and two elementary circadian rhythms (disturbed sleep cycles and poor eating habits).

### **METHODS**

#### *Study design and participants*

This study was conducted in the Hôtel-Dieu Hospital Outpatient Department, dedicated to adolescents with social, familial and school difficulties, which provides free access to general practitioner, gynecologist, dermatologist and psychologist consultations. Subjects aged from 13 to 20 years old were randomly chosen in the department's waiting room from February to June 2012. To be eligible, patients had to provide verbal consent and to have been under physician-prescribed oral medication for three days or more, regardless of the indication or therapeutic regimen. Sociodemographic, lifestyle, circadian rhythm and compliance information were obtained via an investigator-completed questionnaire during an interview with an external physician. When several treatments were being taken, the investigator chose the drug with the longest prescription history or greatest clinical importance.

#### *Measures of drug compliance*

In the absence of a validated scale for adolescents, we used four different methods to assess treatment compliance: 1) Morisky Medication Adherence (10) ;2) Compliance Evaluation Test of National Health Insurance (11), validated for adults; 3) the daily journal of the preceding 72 hours(3); and 4) adolescents' "know thyself" self-identification described by Litt IF (12). Subjects who were classified as non-compliant in this study were those non-compliant in at least three of these methods.

#### *Measures rhythm*

A review of recent worldwide sleep patterns and problems during adolescence describes with evidence that sleep-rhythm disorders affect social and school-life if bedtimes are after 11.30pm on weekdays (7). We asked the patient: " At what time do you go to bed on average on weekdays, excluding holidays?". This continuous variable was dichotomized as  $\leq 11:30$  pm or  $> 11:30$  pm. Eating habits

were evaluated with the following item (community dimension of meals) asking the subject to indicate the most precise answer describing his/her habits: "About your eating habits, you eat your meals: 1) at regular hours with a group; 2) at irregular hours, sometimes alone; 3) rarely a real meal with frequent snacking."

#### *Statistical analysis*

Treatment compliance, the dependent variable, was scored as a binary response. First, a univariate logistic-regression model tested its relationship with the different parameters and those achieving  $p < .2$  were included in the multivariate analysis. Age and number of pills taken daily were deemed continuous variables because of their non-significant deviation-from-linearity tests ( $p = .09$  and  $.12$ , respectively). All other parameters with more than two classes were considered categorical. Analyses were computed with STATA v11® software;  $p < .05$  defined significance. The study was approved by the Ethics Committee in the Health Research section of the Children's Hospital in Paris.

### **RESULTS**

There were 125 subjects who were eligible to participate at the study. Eight refused to participate and two did not speak English or French. Most of the 115 youths included (mean  $\pm$  standard deviation age:  $17.8 \pm 1.92$  years) were girls, mainly because of contraceptive use. Treatment and disease heterogeneities reflected the department's multidisciplinary (Table 2).

**Table 2**

The odds ratios (OR) describe the relationship between the characteristic and non-compliance, results of univariate and multivariate logistic models.

Characteristics	Univariate model		Multivariate model	
	OR [95% CI]	p-value	Adjusted OR [95% CI]	p-value
Sex				
male	1 (ref)		.	
female	0.85 [0.36–1.99]	0.71	.	
Age years (continuous variables)				
one additional years	1.03 [0.84–1.27]	0.754	.	
Highest education level				
Middle school	1 (ref)		.	
High school	0.74 [0.3–1.82]	0.519	.	
University	0.35 [0.06–1.87]	0.218	.	
Socioeconomic level				
high and middle	1 (ref)		1 (ref)	
low	4.37 [1.64–11.68]	0.003	7.1 [1.9–26.53]	0.004
Smoker				
no	1 (ref)		.	
yes	1.65 [0.73–3.71]	0.22	.	
Marijuana user				
no	1 (ref)		1 (ref)	
yes	2.6 [1.01–6.66]	0.047	1.22 [0.29–5.1]	0.787
duration of the prescription drug				
<3 months	1 (ref)			
>3 months	1.32 [0.59–2.96]	0.503		
Pills/day (continuous variables)				
one additional pill	1.17 [1.01–1.38]	0.05	1.43 [1.06–1.93]	0.02
Adverse event(s)				
absent	1 (ref)		1 (ref)	
present	2.79 [1.22–6.37]	0.015	4.28 [1.38–13.28]	0.012
Therapeutic class c				
Antiretroviral	1 (ref)		1 (ref)	
Antibiotic	1 [0.22–4.56]	1	3.09 [0.37–25.76]	0.298
Antiasthmatic	1.26 [0.32–5.17]	0.724	2.31 [0.31–17.26]	0.416
Contraceptive	1 [0.19–5.22]	1	5.49 [0.57–53.22]	0.142
Psychotropic agent	1.23 [0.34–4.39]	0.753	1.86 [0.32–11.01]	0.491
Diverse others	3 [0.73–12.27]	0.126	10.01 [1.22–82.36]	0.032
Average weekday bedtime				
< 11:30 pm	1 (ref)		1 (ref)	
> 11:30 pm	6.12 [2.51–14.93]	<.001	5.85 [1.7–20.09]	0.005
Meals				
At fixed times	1 (ref)		1 (ref)	
Irregular	1.57 [0.57–4.32]	0.384	1.25 [0.35–4.43]	0.728
No meals, snacking	6.19 [1.9–20.21]	0.003	4.59 [1.01–20.77]	0.048

The odds ratios (OR) describe the relationship between the characteristic and non-adherence to treatment.

<sup>a</sup> The variables included in the multivariate model are those that achieved  $p < .2$  in the univariate analysis.

<sup>b</sup> The low socioeconomic level corresponds to adolescents in single-parent families or when at least one parent has been unemployed for >1 year.

<sup>c</sup> The reference therapeutic class is that corresponding to the highest number of subjects, herein antiretrovirals.

<sup>d</sup> According to the mean bedtime on week nights.

The algorithm classified 30.4 % of the subjects as non-compliant. Our univariate analysis selected seven parameters, including the two targeted. The final multivariate model retained weekday bedtime after 11:30 pm, snacking-type eating habits, the parents' low socioeconomic level, treatment's adverse events and therapeutic class of oligo-elements as being significantly associated with treatment non-compliance (Table 1).

**Table 1**

Characteristics of the 115 patients (Paris 2012)

Characteristic	Total sample (N=115) n (%)
Sex	
male	39 (33.9)
female	76 (66.1)
Age years (mean $\pm$ SD = 17.8 $\pm$ 1.92)	
13–14	14 (12.2)
15–16	39 (33.9)
17–18	33 (28.7)
19–20	29 (25.2)
Highest education level	
Middle school	30 (26.1)
High school	73 (63.5)
University	12 (10.4)
Socioeconomic level	
high and middle	44 (38.3)
low	71 (61.7)
Smoker	
no	72 (62.6)
yes	43 (37.4)
Marijuana user	
no	92 (80)
yes	23 (20)
duration of the prescription drug	
<3 months	71 (61.7)
>3 months	44 (38.3)
Pills/day (mean $\pm$ SD = 2.9 $\pm$ 2.4)	
1	43 (37.4)
2	19 (16.5)
3	21 (18.3)
$\geq 4$	32 (27.8)
Adverse event(s)	
absent	
present	40 (34.8)
Therapeutic class c	
Antiretroviral	20 (17.4)
Antibiotic	20 (17.4)
Antiasthmatic	16 (13.9)
Contraceptive	12 (10.4)
Psychotropic agent	31 (27)
Diverse others	16 (13.9)
Average weekday bedtime	
< 11:30 pm	75 (65.2)
> 11:30 pm	40 (34.8)
Meals	
At fixed times	37 (32.2)
Irregular	56 (48.7)
No meals, snacking	22 (19.1)

<sup>b</sup> The low socioeconomic level corresponds to adolescents in single-parent families or when at least one parent has been unemployed for >1 year.

<sup>d</sup> According to the mean bedtime on week nights.

## DISCUSSION

The multivariate analysis retained weekday bedtime after 11:30 pm or snacking-type eating habits as significantly associated with treatment non-compliance, apparently considering perturbed elementary circadian rhythms as a risk factor of non-compliance. These associations have multifactorial and interwoven origins(5). In neurobiological terms, attention disorders linked to sleep-cycle disturbance also impact compliance. From a psychological point of view treatment intake can be viewed as a parental-imposed rules, most of which are met by teenagers' objections. Taking their treatment is then regarded as following one such rule, which goes against their desire for freedom.

Our study's main strengths include the rigor and plurality of our treatment-compliance evaluation that limited classification bias. Having an external interviewer avoided the guilt associated with admitting non-compliance, thereby limiting non-participation and missing data.

The weak external validity, reflecting the single-center

recruitment and atypical population, is the main limitation. Due to the sample used, these data are not generalizable. Participants had more frequent conflicting family relationships and school difficulties than normal French adolescents. We know that higher rhythm-disturbance frequencies than those previously reported(13), which supports our analytical findings. The population size prevents further subgroup analyses of disease chronicity or treatment duration, and explains the large size of the confidence intervals proposed by the model. These confidence intervals greatly limit the accurate assessment of the link between our interests variables and compliance.

## CONCLUSION

Our findings encourage new therapeutic strategies, enabling any physician, as an outsider, to establish simple benchmarks for adolescents, emphasizing the importance of stable rhythmicity, and adaptating the prescriptions according to their schedules as much as possible. It is now important to prove these collaborations on a larger scale and foresee specific lectures fitted to a teen audience about circadian rhythms. Parental support favours proper adherence(14). The doctor can serve as the mediator and provide the necessary information. Chronobiology is currently one of the main focuses of the European debate on the reorganization of school hours. It is fundamental to seize this opportunity to assess its impact on the importance of following circadian rhythms (15) and, thus, teenagers' health and their academic achievements.

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