5th Congress of the European Academy of Neurology

Oslo, Norway, June 29 - July 2, 2019

Teaching Course 2

Treatment of adult and pediatric primary sleep disorders (Level 2)

Paediatric sleep disorders - diagnosis and treatment

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14:45 – 18:15
Room Jan Mayen 1

Teaching Course 2: Treatment of adult and paediatric primary sleep disorders – Level 2

Oslo
29 June 2019

european academy of neurology

Paediatric sleep disorders: diagnosis and treatment

Fabio Pizza

Overview

- Insomnia
- RLS
- OSAS
- Non-REM Parasomnias
- Childhood Narcolepsy

Insomnia

CLASSIFICATION OF INSOMNIA OF CHILDHOOD

- **ICSD (1990; -R, 1997)**
  - Behavioral insomnia of childhood
    - Sleep onset association disorder
    - Limit setting sleep disorder
- **ICSD-II (2005)**
  - Behavioral insomnia of childhood
    - Sleep onset association type
    - Limit setting type
    - Combined type
- **ICSD-III (2014)**
  - Chronic Insomnia disorder
    - *Because children are not expected to sleep through the night with regularity until they are 3-6 months of age,* ***6 months is a reasonable age to first consider a diagnosis of chronic insomnia disorder****, unless the sleeplessness is very marked at an earlier age.*

A related unresolved issue is whether **the current global classification promotes a generic approach to insomnia therapy that ultimately fails to benefit some insomnia subgroups**

International Classification of Sleep Disorders 3

- Pediatric insomnia may be described considering the following 3 subtypes:
  - 1) **Sleep-Onset Association Type**, which includes children who refuse to sleep because they need a specific object or person to fall asleep or get back to sleep, common in younger infants and characterized by multiple nocturnal awakenings;
  - 2) **Limit-Setting Type**, which occurs when parents lose control of the child's behavior during bedtime or awakenings from sleep. often observed in older infants, who tend to oppose their parents, especially during bedtime
  - 3) **Combined Type**, which is characterized by mixed symptoms of the 2 previous subtypes.

Sleep-Onset Association Type

Chronic Insomnia Disorder ICSD-3 Criteria
ICD-10-CM code: F51.01

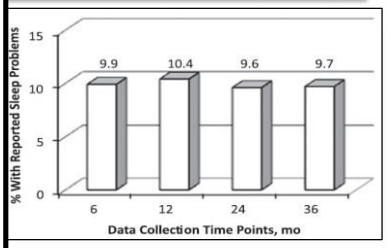
- **Parents who have unrealistic sleep expectations** (putting them in bed too early or assigning them too much time in bed each night).
- **Child insomnia is often associated with difficult temperament, as well as other comorbid medical and psychiatric conditions**.
- **Environmental factors** (unstable home situations, safety concerns, caregiver relationship and domestic abuse) **may contribute to negative sleep-onset associations or poor limit setting**
- Parents of children with a current or past history of medical problems may have difficulty setting limits, because of guilt, a sense that the child is "vulnerable," or concerns about doing psychological harm.

Prevalence of insomnia

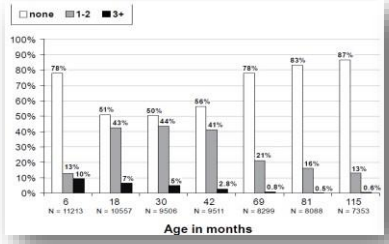
Almost all studies agree that the prevalence of insomnia is about 20-30% in the first 3 years of age and then remain stable at around 10-15%

Authors	Year	% night wakings
Moore and Ucko	1957	17% at 6 m
Bernal	1973	26% at 14 m
Richman	1981	13-24% at 12-24 m
Van Tassel	1985	27% at 4-15 m
Adair et al.	1992	28% at 9 m
Ottaviano, Bruni	1996	31.4% at 6 m, 36.1% at 1-3 y; 18.5% at 3-4y
Blader	1997	6.5% at 5-12 years
Rona	1998	20% at 5 yrs; 6% at 11 yrs
Jenni et al.	2005	33.6% at 3 m; 45% at 2 yrs; 54.2% at 4 yrs
Petit et al.	2007	36.3% at 2.5 yrs, 25.5% at 4 yrs; 13.2% at 6 yrs

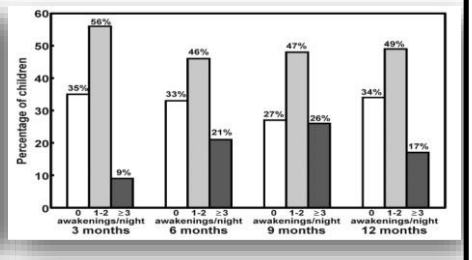
Byars et al. Prevalence, Patterns, and Persistence of Sleep Problems in the First 3 Years of life. Pediatrics 2012



Blair et al. Childhood sleep duration and associated demographic chracteristics in an english cohort. Sleep 2012



Bruni et al. Longitudinal study of sleep behavior in normal infants during the first year of life. 2014;10:1119-27



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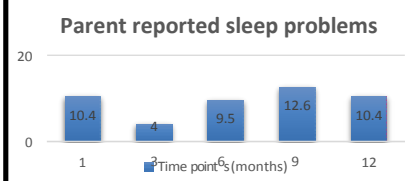


Parental perception of sleep problem:

- **awakenings**
- **difficulties falling asleep**

Table 6—Association between parental perception of an overall sleep problem and sleep variables.

	3 months	6 months	9 months	12 months
Sleep latency	0.08	0.16	0.12	0.17
Night time sleep	0.04	-0.06	-0.10	-0.15
Daytime sleep	-0.07	-0.08	-0.13	-0.12
Total sleep time	-0.04	-0.09	-0.16	-0.19
Number of naps	-0.01	-0.04	-0.06	-0.01
Bedtime	-0.08	0.00	0.01	0.06
Rise time	-0.03	-0.06	-0.09	-0.10
Nighttime awakenings	0.35*	0.41*	0.45*	0.46*
Falling asleep difficulties	0.35*	0.42*	0.37*	0.40*

*$p < 0.01$.

WHAT SLEEP DOCTORS CAN DO?
Behavioral therapy

- EXTINCTION
- GRADUATED EXTINCTION
- POSITIVE BEDTIME ROUTINES
- POSITIVE REINFORCEMENT
- SCHEDULED AWAKENINGS
- PREVENTIVE EDUCATION

* **Cognitive–behavioral treatment** for bedtime refusal and night-wakings in early childhood is has two main components:
  * modifying parental cognitions on their child's sleep behaviors and needs
  * modifying parental behaviors and responses to the child in an attempt to modify the child's learned responses, expectations and behaviors

REVIEW ARTICLES

Discussion of Extinction-Based Behavioral Sleep Interventions for Young Children and Reasons Why Parents May Find Them Difficult

Hayley Etherton, BPsychHons[1]; Sarah Blunden, PhD[1]; Yvonne Hauck, PhD[2]

J Clin Sleep Med 2016;12(11):1535–1543

- Reasons why parents may find extinction sleep interventions difficult: *enduring crying, practical considerations, fear of repercussions, misinformation, incongruence with personal beliefs, different cultural practices, and parent wellness.*

- **Parental resistance remains the largest barrier to the implementation of extinction interventions**, the majority of parents find graduated extinction too difficult and stressful to implement.

Are behavioral interventions as effective as reported?

- *Behavioral sleep techniques did not cause long-lasting harms or benefit to child and parents:* **no differences between intervention and control families for any outcome** [child's emotion and behavior, sleep problems, parent- and child psychosocial functioning] (Price et al., 2012)
- Behavioral interventions for infant sleep in the first 6 months **did not decrease infant crying, prevent sleep and behavioral problems in later childhood, or protect against postnatal depression; *instead worsened maternal anxiety and increased risk of SIDS*** (Douglas & Hill, 2013)
- **A meta-analysis of psychosocial sleep interventions** indicated impact on maternal mood and small improvements in infant nocturnal sleep time and **no evidence for reducing infant night wakes** (Kempler et al., 2016)
- Parents exposed to CBT experienced improved perceptions of infant sleep, sleep cognitions, mood, sleep quality, and fatigue, **but not infant n° of wakes measured using actigraphy.** (Hall et al., 2015)
- **A meta-analysis showed moderate-level evidence to support behavioral interventions for insomnia in young children** (Meltzer and Mindell, 2014)

Sadeh A, Mindell JA. Infant sleep interventions - Methodological and conceptual issues, Sleep Medicine Reviews (2016)

- **Parents can report reduction in night-wakings because infant sleep has actually become more consolidated or because their infant learned self-soothing and requires less attention when awake (or a combination of these two processes)?**

- This raises an important question:
  - **what are the important outcome measures?**
- Are we interested in making sure that the infant is actually sleeping better or is it enough that the *infant learned self-soothing* and requires less parental involvement?

Most sleep disturbances during early childhood are explained by common shared environmental factors; however, the influence of genetic factors could contribute to categorize insomnia

Brescianini et al. Genetic and Environmental Factors Shape Infant Sleep Patterns: A Study of 18-Month-Old Twins. Pediatrics 2011

- Heritability contributed for:
  - 30.8% on nocturnal sleep dur
  - 36.3% on diurnal sleep dur
  - **35.3% on night wakings**

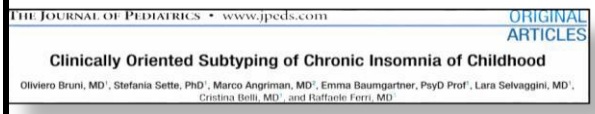
Touchette et al. Genetic and environmental influences on daytime and nighttime sleep duration in early childhood. Pediatrics. 2013

- Consolidated nighttime sleep is influenced by genetic factors
- **Heritability (71%)** observed for the **short-persistent nighttime sleep duration** trajectory

Set of questions should be based on common descriptors of insomnia by parents or caregivers

- My child is fighting against sleep
- My child wakes up every hour!!
- My child has no problem in falling asleep but wakes up in the middle of the night and wants to play!!!
- My child is like a horse in the bed!
- My child moves a lot during the night
- My child has trouble in falling asleep and wants to be rocked when waking up in the night

- *Since insomnia is a clinical diagnosis we should rely on these descriptors to categorize infants or children…*


THE JOURNAL OF PEDIATRICS • www.jpeds.com ORIGINAL ARTICLES

Clinically Oriented Subtyping of Chronic Insomnia of Childhood

Oliviero Bruni, MD[1], Stefania Sette, PhD[1], Marco Angriman, MD[2], Emma Baumgartner, PsyD Prof[1], Lara Selvaggini, MD[1], Cristina Belli, MD[1], and Raffaele Ferri, MD[1]

- **338 children (227 M)** aged 6–48 months (*mean* 21.29, *SD* 10.56) with insomnia resistant to behavioral approaches and common drug treatments.

- Insomnia characteristics based on common descriptors by parents

Table I. Descriptive statistics for the total sample

	Total sample	
Child sleep	**Mean**	**SD**
Bedtime, hour:min	9.41 p.m.	0.53
Wake-time, hour:min	7.11 a.m.	0.58
Sleep latency, min	32.0	23.0
Insomnia characteristics	**No.**	**%**
Difficulties in falling asleep	148	43.8
Difficulties in falling asleep with restlessness	62	18.3
Nocturnal restlessness	98	29.0
Early morning awakenings	72	21.3
Multiple night awakenings (≥3)	266	78.7
Family history	**No.**	**%**
Insomnia	102	30.2
Parasomnias	29	8.6
Headache/migraine	102	30.2
Depression/mood disorders	93	27.5
Anemia	80	23.7
Restless legs syndrome	42	12.4
Allergies/food intolerance	144	42.6
Child medical complaints	**No.**	**%**
Colic	161	47.6
Allergies/food intolerance	58	17.2
Dermatitis	41	12.1
Gastroesophageal reflux	89	26.3
Anemia	18	5.3

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- LCA built a **3-class model of profiles of insomnia:**

Class I: 17% (*n* = 58) **difficulties in falling asleep with nocturnal restlessness and night awakenings**
- Family history for RLS and ID anemia

Class II: 21% (*n* = 71) **early morning awakenings**
- Family history for depression and/or mood disorders or migraine

Class III: 62% (*n* = 209) **difficulties in falling asleep and night awakenings**
- Family history for allergies and/or food intolerance

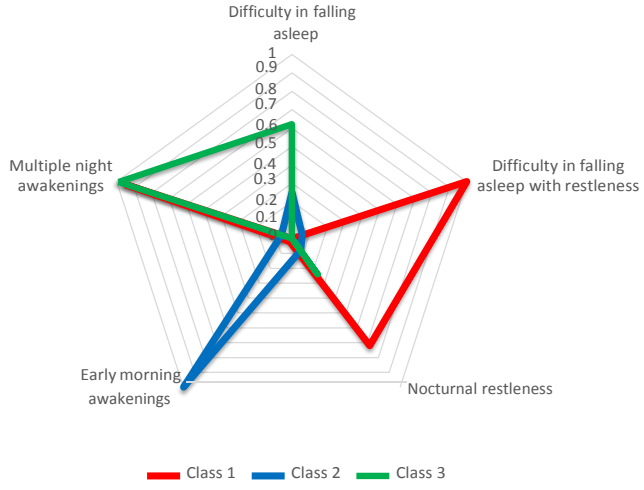

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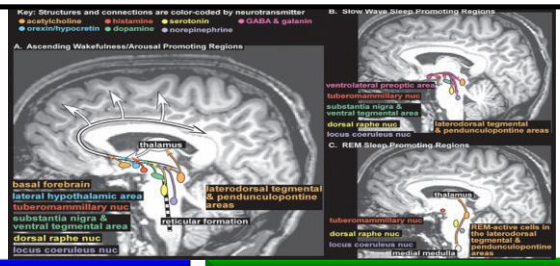
Table III. Means and SDs on child sleep variables and frequencies (percentages) of familiar history for sleep problems and child disturbances for each class

	Class 1 n = 58		Class 2 n = 71		Class 3 n = 209				
Sleep variables	**Mean**	**SD**	**Mean**	**SD**	**M**	**SD**	**F**	***P***	**Partial η^2**
Bedtime, hour:min	9:40 p.m.	1:04	9:47 p.m.	0:49	9:38 p.m.	0:52	0.600	.55	
Wake-time, hour:min	6:59 a.m.	0:53	7:14 a.m.	1:01	7:13 a.m.	0:54	1.305	.27	.01
		24	33[b]	29	28[b]	20	12.608	<.001	.09
	n (%)		**n (%)**		**n (%)**		**χ^2**	***P***	**χ^2 post-hoc analysis**
Family history									
Insomnia	12 (20.7)		20 (28.2)		70 (33.5)		3.799	.15	
Parasomnias	8 (13.8)		6 (8.5)		15 (7.2)		2.501	.29	
Headache/migraine	14 (24.1)		28 (39.4)		60 (28.7)		4.060	.13	
Depression/mood disorders	7 (12.1)		45 (63.4)		41 (19.6)		58.972	<.001	Class 2 > 1 and 3
Anemia	32 (55.2)		11 (15.5)		37 (17.7)		38.390	<.001	Class 1 > 3
Restless legs syndrome	24 (41.4)		6 (8.5)		12 (5.7)		55.356	<.001	Class 1 > 3
Allergies/food intolerance	22 (37.9)		16 (22.5)		106 (50.7)		18.138	<.001	Class 3 > 2
Child medical complaints									
Colic	30 (51.7)		29 (40.8)		102 (48.8)		1.816	.40	
Allergies/food intolerance	14 (24.1)		11 (15.5)		33 (15.8)		2.402	.30	
Dermatitis	12 (20.7)		9 (12.7)		20 (9.6)		5.292	.07	
Gastroesophageal reflux	19 (32.8)		13 (18.3)		57 (27.3)		3.686	.16	
Anemia	9 (15.5)		5 (7.0)		4 (1.9)		17.189	<.001	Class 1 > 3

- Combining the 3 groups with personal and family history, we hypothesize that these 3 insomnia subtypes may have different underlying mechanistic causes and pathophysiology.

Genetic predisposition to insomnia as sign of neurotransmitter dysfunction



Importance of family history

Dopaminergic dysfunction

- Anemia
- RLS
- PLM
- Growing pains
- Breath-holding spells

- ***Difficulty in falling asleep (kicking legs)***
- ***Noct. hyperactivity (horse in bed)***

Serotonergic dysfunction

- Insomnia
- Parasomnias
- Headache/migraine
- Depression
- Mood disorders

- ***No difficulties in falling asleep***
- ***Mid-night awakenings***

Histaminergic dysfunction

- Atopic dermatitis
- Milk intolerance
- Cow's milk allergy
- GER?

- ***Difficulty in falling asleep***
- ***Several night awakenings (all night)***

Dopaminergic dysfunction

Child referred at 2 years of age for resistant insomnia

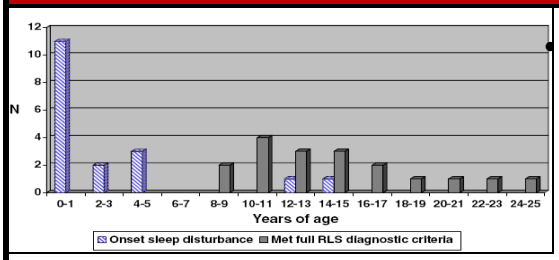
From 1 month of age prolonged (several hours) crying episodes during the night followed by afinalistic movements of upper and lower limbs with spontaneous resolution

Ferritin 19 ng/ml

Diagnostic hypothesis: *periodic syndrome of infancy, benign paroxysmal torticollis*

Courtesy O.Bruni

Early insomnia as precursor of RLS



In children and adolescents, clinical sleep disturbance preceded a diagnosis of definite RLS by an average of 11.6 yrs (Picchietti, 2009; Kotagal 2004)

RLS in children

- age-related description of leg discomfort (oowies, tickle, spiders, boo-boos, and energy in my legs)
- sleep disturbance for age
- biologic parent or sibling has definite RLS
- PLMI>5 at PSG

Dopaminerigc dysfunction	Serotonergic dysfunction	Histaminergic dysfunction
▪ Anemia ▪ RLS ▪ PLM ▪ Growing pains ▪ Breath-holding spells	▪ Insomnia ▪ Parasomnias ▪ Headache/migrain ▪ Depression/Mood disorders	▪ Atopic dermatitis ▪ Milk intolerance ▪ Cow's milk allergy ▪ GER?
▪ ***Difficulty in falling asleep (kicking legs)*** ▪ ***Noct. hyperactivity (a horse in the bed)***	▪ *No difficulties in falling asleep* ▪ *Mid-night awakenings*	▪ ***Difficulty in falling asleep*** ▪ ***Several night awakenings (all night)***
▪ ***Iron*** ▪ ***Gabapentin, DA***	▪ ***L-5-HTP***	▪ ***Antihistaminics*** ▪ ***MLT***

RLS

Restless legs syndrome (RLS)
Diagnostic Criteria

1. ***An urge to move the legs*** usually but **not always accompanied by uncomfortable and unpleasant sensations in the legs.**
2. **begin or worsen during periods of rest or inactivity** such as lying down or sitting.
3. **are partially or totally relieved by movement** such as walking or stretching, as long as the activity continue
4. **occur or worsen in evening or night than in day.**
5. The occurrence of the above features are **not solely accounted for as symptoms primary to another medical or a behavioral condition** (e.g., myalgia, venous stasis, leg cramps, positional discomfort, habitual foot tapping.)

Restless Legs Syndrome in children

- The knowledge of RLS in children is **limited**
- The presence of RLS may be unrecognized in infants and preschool children because of the **mild and intermittent nature of the symptoms**
- The diagnosis of RLS relies **on subjective complaints difficult to obtain in children**
- Symptoms of RLS in children younger than 5 years **may appear as sleep disturbances**, and the underlying diagnosis can be easily missed.

Childhood-Onset Restless Legs Syndrome

Suresh Kotagal, MD,[1–3] and Michael H. Silber, MD[2,3]

Ann Neurol. 2004;56:803-7.

- Sleep onset or maintenance insomnia common symptoms (87.5%)
- Leg discomfort/"growing pains"
- Inattentiveness/ADHD in 25%.
- Serum ferritin levels below 50g/L in 83%
- PLMS on PSG
- A family history of RLS present in 72%, with mothers 3 times more than fathers
- Often do not meet all essential adult criteria - especially circadian component

How prevalent is RLS in children?

- RLS in **1.9%** of children and **2%** of adolescents in the US and UK, [Picchietti, 2007].
- RLS prevalence in clinical populations was **1.3%** in 12 pediatric practices [Kinkelburg, 2003], and **5.9%** at a Pediatric Sleep Disorders Clinic [Kotagal, 2004].
- RLS prevalence in ADHD and in uremic children reach 20-30% (Kothare, 2011)

Prevalence of OSA about 2%; prevalence of epilepsy about 0.5%

Pediatric restless legs syndrome diagnostic criteria: an update by the International Restless Legs Syndrome Study Group ☆

Daniel L. Picchietti [a,*], Oliviero Bruni [b], Al de Weerd [c], Jeffrey S. Durmer [d], Suresh Kotagal [e], Judith A. Owens [f], Narong Simakajornboon [g],
On behalf of the International Restless Legs Syndrome Study Group (IRLSSG)

Sleep Medicine 14 (2013) 1253–1259

Table 2
Special considerations for the diagnosis of pediatric restless legs syndrome.

- The child must describe the RLS symptoms in his or her own words
- The diagnostician should be aware of the typical words children and adolescents use to describe RLS
- Language and cognitive development determine the applicability of the RLS diagnostic criteria, rather than age
- It is not known if the adult specifiers for clinical course apply to pediatric RLS
- As in adults, a significant impact on sleep, mood, cognition, and function is found. However, impairment is manifest more often in behavioral and educational domains
- Simplified and updated research criteria for *probable* and *possible* pediatric RLS are available (Table 5)
- Periodic limb movement disorder may precede the diagnosis of RLS in some cases

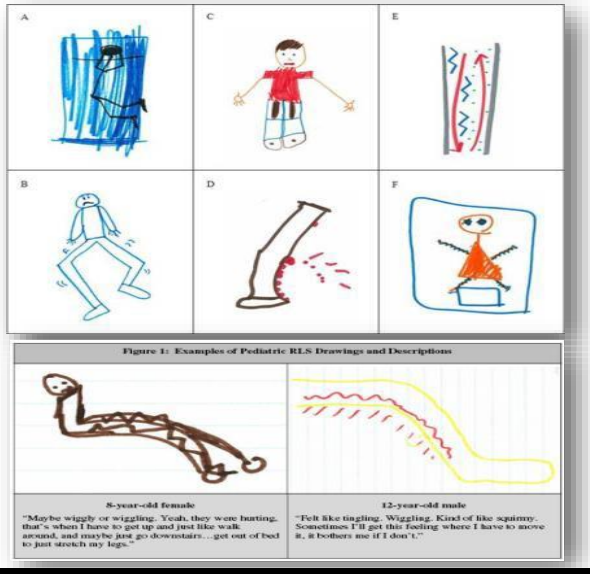
Differential diagnosis of pediatric restless legs syndrome.

Common mimics
- Positional discomfort
- Sore leg muscles
- Ligament sprain/tendon strain
- Positional ischemia (numbness)
- Dermatitis
- Bruises
- Growing pains

Less common mimics
- Leg cramps
- Arthritis
- Other orthopedic disorders
- Peripheral neuropathy
- Radiculopathy
- Myelopathy
- Myopathy
- Fibromyalgia
- Complex regional pain syndrome
- Drug-induced akathisia
- Sickle cell disease

Picchietti DL, Arbuckle RA, Abetz L, Durmer JS, Ivanenko A, Owens JA, Croenlein J, Allen RP, Walters AS. Pediatric restless legs syndrome: analysis of symptom descriptions and drawings. J Child Neurol. 2011;26(11):1365-76

- The RLS sensations described: *have to move, need to kick, pain/hurts, 'like bugs crawling, weird/funny feelings, and tingling.*
- Two main descriptors:
  - **Need to Move/Kick.**
  - **Pain as a description of RLS Sensations**



Journal of the Neurological Sciences 336 (2014) 232–236

Daytime dysfunction in children with restless legs syndrome

Naomichi Furudate [a,b], Yoko Komada [a,c], Mina Kobayashi [a,b,c], Shun Nakajima [a,b,c], Yuichi Inoue [a,b,c,*]

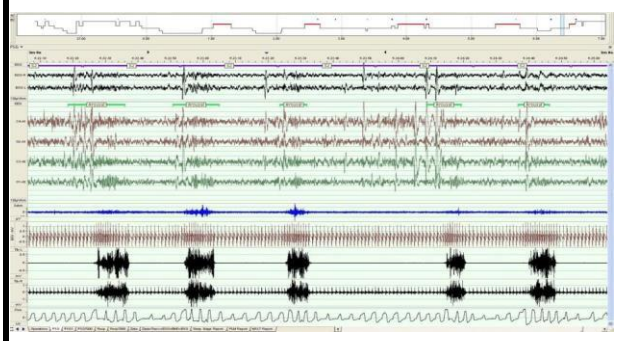
- Prospective study to investigate daytime dysfunction in children with RLS and the effects of iron supplements
- 25 children with RLS (M:F=6:19, mean age 12.3 yrs) vs. 28 controls
- Instruments: *ADHD Rating Scale IV (ADHD-RS-IV), the Pediatric Symptom Checklist (PSC), and the Pediatric Quality of Life Inventory (PedsQL).*
- The mean serum ferritin level was 29.7 ± 19.1 ng/mL
- **Before treatment, ADHD-RS-IV and PSC scores were significantly higher and PedsQL scores significantly lower in the RLS group than in the control group.**
- **Following treatment, daytime function had improved to levels similar to those of controls**.

RLS and PLMS in children

- PLMS >5/h found in 80% of adults with RLS on a single-night study (Montplaisir et al., 1997) but in 91% when five nights are sampled (Trotti et al., 2009)
- Similarly, **children with RLS demonstrate PLMS >5/h in 74%, 67%, and 63% of case series with single-night sampling** (Picchietti and Picchietti, 2010)
- 38% - 45% of adults with RLS recall onset of symptoms before the age of 20y (Montplaisir 1997); 18% by age 10y, 25% 11-20 y (Walters 1996)
- *A diagnosis of PLMD can precede an RLS diagnosis in children, especially in young children who do not have the verbal ability to describe the sensory symptoms of RLS (Picchietti, Stevens, 2008)*

PLMS

leg movements or jerks occurring every 20 to 40 s. during sleep



Dorsiflexion of the big toe and ankle, sometimes flexion of the leg and thigh

Courtesy Prof Bruni

World Association of Sleep Medicine (WASM) 2016 standards for recording and scoring leg movements in polysomnograms developed by a joint task force from the International and the European Restless Legs Syndrome Study Groups (IRLSSG and EURLSSG)

R. Ferri [a,*], S. Fulda [b], R.P. Allen [c], M. Zucconi [d], O. Bruni [e], S. Chokroverty [f], L. Ferini-Strambi [d], B. Frauscher [g], D. Garcia-Borreguero [h], M. Hirshkowitz [i], B. Högl [j], Y. Inoue [k], A. Jahangir [l], M. Manconi [b], C.L. Marcus [m], D.L. Picchietti [n], G. Plazzi [o], J.W. Winkelman [p], R.S. Zak [q] on behalf of the International and European Restless Legs Syndrome Study Groups (IRLSSG and EURLSSG)

Sleep Medicine 26 (2016) 86–95

2.6. Special considerations for pediatric studies (rules in 3.5)

- **In absence of adequate data in a pediatric population, the adult criteria should be used for children.**

a) **Total LM and PLMS appear to be higher in younger than older children** *[Pennestri et al., 2006; Scholle et al, 2014; Marcus et al., 2015].*

b) **Notable night-to-night variability of PLMS in children** *[Picchietti et al., 2009].*

c) **Analysis of IMI showed short and variable intervals, often <10 s** *[Ferri et al., 2008, 2009, 2013]* higher in younger than in older children and therefore the minimum IMI of 10 s may not be appropriate for children.

d) **It is strongly recommended that total LMS counts and LMS indices be reported in pediatric cases, in addition to PLMS counts and indices**.

Treatment of childhood-onset restless legs syndrome and periodic limb movement disorder using intravenous iron sucrose

Kendra Grim, Bernard Lee, Alan Y. Sung, Suresh Kotagal *

Sleep Medicine 14 (2013) 1100–1104

- Some children with RLS/PLMD are unable to tolerate oral iron
- Intravenous iron sucrose to 16 patients at 3.6 mg/kg infused over 2 h.
- Baseline serum ferritin 16.4 ± 6.6 ng/mL → after infusion 45.7 ± 22.4 ng/mL

- **Improved sleep in 62.5%** of subjects and no improvement in 12.5% of subjects. No follow-up information for 25% of subjects.
- **Minor adverse events** occurred in 25% (n = 4) of subjects— two subjects experienced difficulty with peripheral intravenous catheter placement, while two had transient GI symptoms

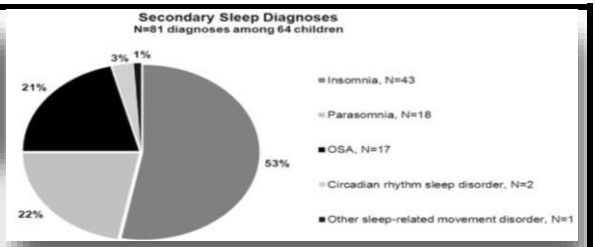
Treatment of Pediatric Restless Legs Syndrome

Clinical Pediatrics
2014, Vol. 53(4) 331–336

DOI: 10.1177/0009922813507997
cpj.sagepub.com
SAGE

Louella B. Amos, MD[1], Megan L. Grekowicz, APN[1], Evelyn M. Kuhn, PhD[2], Jenna D. Olstad, BA[2], Maureen M. Collins, MS, RD[2], Nan A. Norins, MD[1], and Lynn A. D'Andrea, MD[1]

- 97 children with RLS
- 65% received iron as monotherapy or with other treatments.
- Median baseline ferritin level was 22.7 ng/mL
- **80% had improvement** or resolution of symptoms.
- **The median time to improvement or resolution of symptoms was 3.8 mths**



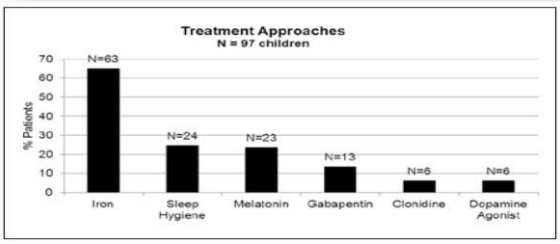


Figure 2. Distribution of the various treatment approaches in this study. Some children required more than 1 treatment.

Treatment in Children: medication

- **Dopaminergics**
  - pramipexole, ropinirole (Konofal., 2005; Cortese, 2009)
  - levodopa/carbidopa (Walters, 2000; Picchietti and Walters, 1999)
- **Clonazepam** (Shinno et al., 2010)
- **Gabapentin** (Kotagal & Silber, 2004)
- **Levetiracetam** (Gagliano, 2011)
- **Clonidine** (Amos et al., 2013)
- **Vit. D** (Wali et al.,2017)

Drug	Total No.	Max. dose	Min. age
Pergolide	3	1 mg	4 yrs ?
Ropinirole	4	0.5 mg	6 yrs.
Pramipexole	24/3	0.375 mg	5 yrs ?
L-dopa	22/7	– 210 mg	4 yrs ?
Iron	18/39		2 yrs.
Gabapentin	11	n.r.	5 yrs ?
Levetiracetam	6	60 mg/kg	5 yrs.
Clonazepam	2	n.r.	5 yrs ?

OPEN QUESTIONS

- How to clinically define RLS in non verbal children?
- What is the relation between RLS and PLMS in children?
- Does exist PLMS in children?
- What is periodicity in children?
- Should we count total LMS?
- Since children moves more during the night the “periodic” pattern is only related to this increase of movements?
- The Periodicity Index could be helpful to characterize RLS/PLM in children?

OSAS

ICSD-3

Criteria A (symptoms) and B (PSG) must be met

A. The presence of one or more of the following:
1. Snoring.
2. Labored, paradoxical, or obstructed breathing during the child's sleep.
3. Sleepiness, hyperactivity, behavioral problems, or learning problems.

B. PSG demonstrates one or both of the following:
1. *One or more obstructive apneas, mixed apneas, or hypopneas, per hour of sleep.*

2. *A pattern of obstructive hypoventilation*, defined as at least 25% of total sleep time with hypercapnia ($PaCO_2$ > 50 mm Hg) in association with one or more of the following:
   a. Snoring.
   b. Flattening of the inspiratory nasal pressure waveform.
   c. Paradoxical thoraco-abdominal motion.

The sleepy child

Inattention, Hyperactivity, and Symptoms of Sleep-Disordered Breathing

Ronald D. Chervin, MD, MS*; Kristen Hedger Archbold, PhD*; James E. Dillon, MD‡; Parviz Panahi, MD§; Kenneth J. Pituch, MD§; Ronald E. Dahl, MD‖; and Christian Guilleminault, MD¶

Pediatrics 2002

- 866 Children (7±3 y.o.)
- Pediatric sleep questionnaire
  - Snoring
  - SDB Risk
- Parents' Questionanire on
  - Inattention
  - Hyperactivity
  - Hyperactivity Index

Results. Habitual snoring was reported in 16% (95% confidence interval [CI]: 13, 19) of the participants. High HI scores (>60) were found in 13% (95% CI: 11, 16) of all participants, 22% (95% CI: 15, 29) of habitual snorers, and 12% (95% CI: 9, 14) of nonsnorers. Odds ratios between HI >60 and each of the following were: habitual snoring, 2.2 (95% CI: 1.4, 3.6); 1 additional positive symptom-item on the snoring scale, 1.3 (95% CI: 1.1, 1.5); 1 additional positive item on the sleepiness scale, 1.6 (95% CI: 1.4, 2.0); and a 1-standard deviation increase in the overall SDB score, 1.7 (95% CI: 1.4, 2.0; all odds ratios age- and sex-adjusted). Results were similar for high IHS scores (>1.25). Stratification by age and sex showed that most of the association with snoring (but not sleepiness) derived from boys <8 years old.

Conclusions. Inattention and hyperactivity among general pediatric patients are associated with increased daytime sleepiness and—especially in young boys—snoring and other symptoms of SDB. If sleepiness and SDB do influence daytime behavior, the current results suggest a major public health impact. *Pediatrics* 2002;109:

American Academy of Pediatrics

TECHNICAL REPORT

Diagnosis and Management of Childhood Obstructive Sleep Apnea Syndrome

Prevalence

TABLE 6 Prevalence of OSAS on the Basis of Ambulatory Monitoring

Source	Year	No.	No. Undergoing Ambulatory Monitoring	Country	Age, y	OSAS Prevalence, %	HS Prevalence	OSAS Criteria and Comments
Castronovo et al[14]	2003	595	265	Italy	3–6	12	34.5% "Often" or "Always"	OAI ≥5
Goodwin et al[15]	2005	480	All	United States	6–11	24	10.5% "Frequently"	RDI ≥1 ↑ in male Not ↑ in obese
Hultcrantz and Löfstrand Tideström[205]	2009	393	26	Sweden	12	0.8	6.9% "Regularly"	AHI ≥1 and/ or OAI ≥1
Rosen et al[19]	2003	850	All	United States	8–11	2.2		AHI ≥5 or OAI ≥1 ↑ in AA ↑ in premature infants
Sánchez-Armengol et al[18]	2001	101	All	Spain	12–16	1.9	14.8%	Based on RDI ≥10 and snoring witnessed apneas, and/or excessive daytime sleepiness.
Urschitz et al[206]	2010	1144	183	Germany	7.3–12.4	2.8	"Often"	Girls = boys AHI ≥1

OAI, obstructive apnea index; AA, African American.

American Academy of Pediatrics

TECHNICAL REPORT

Diagnosis and Management of Childhood Obstructive Sleep Apnea Syndrome

Prevalence

TABLE 5 Prevalence of OSAS on the Basis of Laboratory PSG

Source	Year	No.	No. Undergoing PSG	Country	Age, y	OSASPrevalence	HSPrevalence
Anuntaseree et al[201]	2001	1005	8	Thailand	6–13	0.69%	8.5%
Anuntaseree et al[202]	2005	755	Unclear, possibly 10			1.3%	6.9% "most nights"
Beebe et al[21]	2007	60 obese 22 control	All	United States	10–16.9	0% normal 13% obese	
Bixler et al[11]	2009	5740	700	United States	5–12	1.2%	
Brunetti et al[203]	2001	895	34 home monitoring	Italy	3–11	1%–1.8%	4.9%
Brunetti et al[23]	2010		12 PSG				5.4% "always"
Li et al[172]	2010	6447	619	China	5–13	4.8%	7.2%
Li et al[12]	2010						"frequently"
Ng et al[204]	2002	200	16	Hong Kong	6.4 ± 4	1%	14.5%
O'Brien et al[13]	2003	5728	110	United States	5–7	5.7%	11.7% "frequent and loud"
Sogut et al[16]	2005	1198 total	28	Turkey	3–11	0.9%–1.3%	3.3% >3 times/week
Wing et al[17]	2003	46 obese, 44 control	All	China	7–15	2.3%–4.5% control; 26% to 32.6% obese	
Xu et al[22]	2008	99 obese, 99 control	All	China	Elementary school	0 if not obese and no ATH	

ATH, adenotonsillar hypertrophy; ICSD, International Classification of Sleep Disorders; OAI, obstructive apnea index.

Differences in Overnight Polysomnography Scores Using the Adult and Pediatric Criteria for Respiratory Events in Adolescents

SLEEP 2010;33(10):1333-1339.

Jennifer A. Accardo, MD[1]; Justine Shults, PhD[2]; Mary B. Leonard, MD, MSCE[2,3]; Joel Traylor[1]; Carole L. Marcus, MBBCh[1,4]

	Pediatric	Adult
Obstructive apnea	• Drop in thermal sensor amplitude by ≥ 90% baseline • Duration ≥ 2 missed breaths • ≥ 90% duration meets amplitude reduction criteria • Continued or increased inspiratory effort during reduced airflow	• Drop in thermal sensor amplitude by ≥ 90% baseline • Duration ≥ 10 sec • ≥ 90% duration meets amplitude criteria • Continued or increased inspiratory effort during absent airflow
Central apnea	• Drop in thermal sensor amplitude by ≥ 90% baseline • **EITHER** duration ≥ 20 sec **OR** ≥ 2 missed breaths and associated with arousal, awakening or ≥ 3% desaturation • Absent inspiratory effort	• Drop in thermal sensor amplitude by ≥ 90% baseline • Duration ≥ 10 sec • ≥ 90% duration meets amplitude criteria • Absent inspiratory effort during absent airflow
Mixed apnea	• Drop in thermal sensor amplitude by ≥ 90% baseline • Duration ≥ 2 missed breaths • ≥ 90% duration meets amplitude reduction criteria • Absent inspiratory effort initially, then resumption of effort during latter part of event	• Drop in thermal sensor amplitude by ≥ 90% baseline • Duration ≥ 10 sec • ≥ 90% duration meets amplitude criteria • Absent inspiratory effort initially, then resumption of effort during latter part of event
Hypopnea	• Drop in nasal air pressure transducer amplitude by ≥ 50% • Duration ≥ 2 missed breaths • ≥ 90% of duration meets amplitude criteria • Associated with arousal, awakening or ≥ 3% desaturation	**HYPOPNEA A** • Drop in nasal air pressure transducer amplitude by ≥ 30% baseline • Duration ≥ 10 sec • Associated with ≥ 4% desaturation • ≥ 90% of duration meets amplitude criteria **HYPOPNEA B** • Drop in nasal air pressure transducer amplitude by ≥ 50% baseline • Duration ≥ 10 sec • Associated with ≥ 3% desaturation or arousal • ≥ 90% of duration meets amplitude criteria

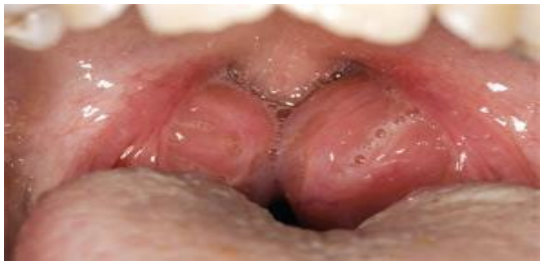
Common Predisposing Factors

- *Adenotonsillar hypertrophy*
- *Obesity*
- *Gastroesophageal reflux (upper airway edema or laryngospasm)*

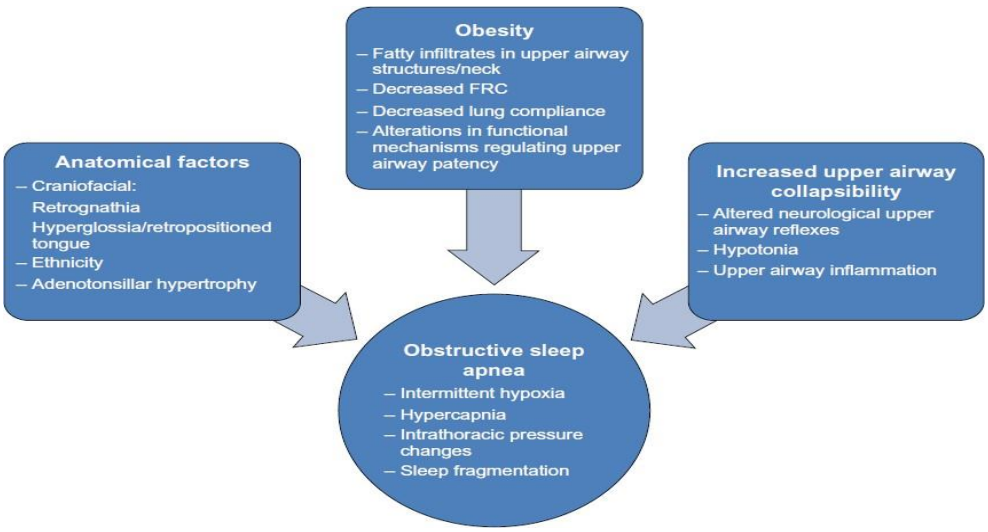
- *Craniofacial abnormalities* (micrognathia, midfacial hypoplasia)

- Down syndrome
- Neuromuscular diseases (weakness)
- Cerebral palsy (spasticity, weakness, or incoordination)

- Mucopolysaccharidosis, cleft palate surgery, environmental tobacco smoke exposure



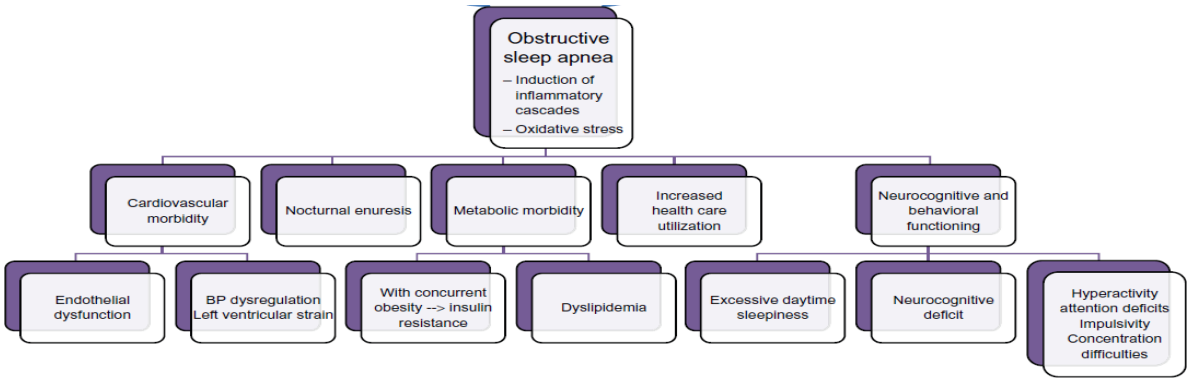
Pathophysiology



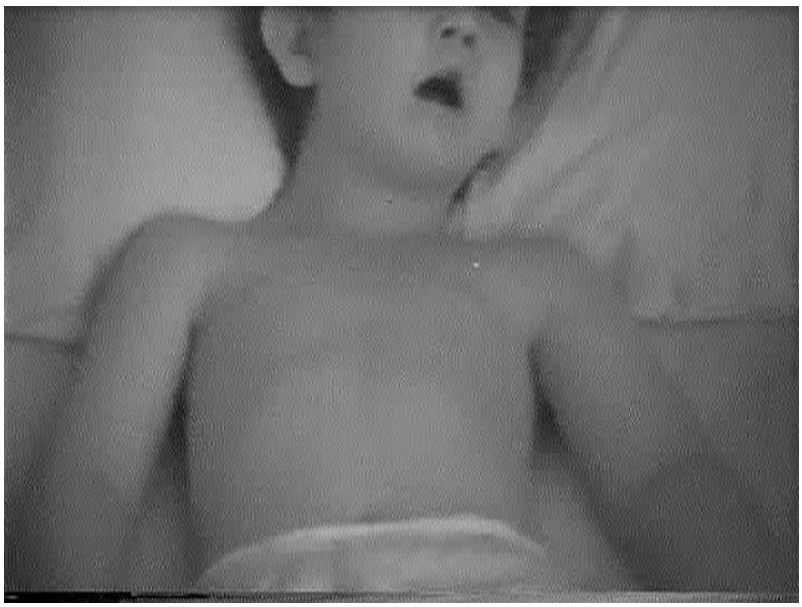
Complications

- *Cognitive*
  - Poor school performance
  - Developmental delay
- *Behavioral*
  - ADHD
  - Inattention
  - Impaired concentration
  - Aggressivity
- *Medical*
  - Asphyxial brain damage
  - Seizures
  - Coma
- *Cardiovascular*
  - Pulmonary hypertension
  - Cor pulmonale
  - Systemic hypertension

Complications



Impact on cardiovascular system



Differential Diagnosis

- Isolated snoring (PSG required)
- Central sleep apnea
- Fixed airway obstruction (also during wakefulness, stridor-like)
- Non-Obstructive Lung/Chest disorders (desaturate during sleep)
- Other causes of sleepiness:
  - **Narcolepsy,**
  - Idiopathic Hypersomnia,
  - Insufficient sleep
- Sleep related epilepsy

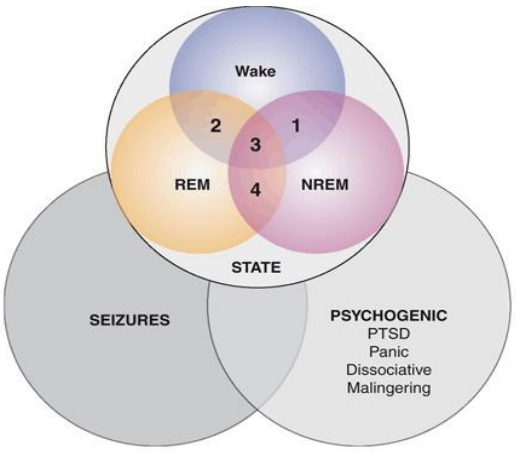
- Treatment Decision:
  - Should be based on the magnitude of symptoms, on predisposing and aetiological factors, not only on PSG findings!
  - **Adenotonsillar Hypertrophy** → surgery, steroids (mild forms)
  - Surgery Failure: African-American, Obese, Asthma, Craniofacial anomalies, Chromosomal defects, and neuromuscular disease.
  - *Residual OSA after surgery* → **CPAP/BiPAP**, (high flow nasal cannula oxygen therapy ?), steroids, leukotriene antagonists, orthodontic procedures, UPPP, tongue-base suspension

Non REM Parasomnias

Parasomnias

Parasomnias encompass abnormal sleep related complex movements, behaviors, emotions, perceptions, dreams, and autonomic nervous system activity. Parasomnias are clinical disorders because of the resulting injuries, sleep disruption, adverse health effects, and untoward psychosocial effects. The clinical consequences of the parasomnias can affect the patient, the bed partner, or both.

Human consciousness consists of three essential states: Wake, NREM sleep, and REM sleep. However, as the sleep-wake cycle oscillates, the normally distinct states of consciousness may be rendered into a state that is not fully declared, resulting in a temporary unstable state of dissociation



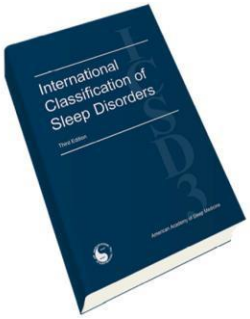
1. Disorders of arousal (NREM)
Confusional arousals
Sleep-related abnormal sexual behaviors
Sleepwalking
Sleep terrors
Sleep-related eating disorders

2. Narcolepsy Triad
Hypnagogic Hallucinations
Sleep Paralysis, and Cataplexy

REM Sleep Behavior Disorder (RBD)
Lucid dreaming
Out-of-body experiences

3. Status Dissociatus
Parasomnia overlap syndrome

4. Asymptomatic
(no conscious awareness)



NREM-Related Parasomnias

Disorders of Arousal
- Confusional Arousals
- Sleepwalking
- Sleep Terrors

Sleep Related Eating Disorder

Arousal Disorders (ICSD)

Criteria A-E must be met

- A. Recurrent episodes of *incomplete awakening* from sleep.
- B. *Inappropriate or absent responsiveness* to efforts of others to intervene or redirect the person during the episode.
- C. *Limited* (e.g., a single visual scene) or *no associated cognition* or dream imagery.
- D. Partial or complete *amnesia* for the episode.
- E. The disturbance is not better explained by another sleep disorder, mental disorder, medical condition, medication, or substance use.

Notes

- 1. The events usually occur during the first third of the major sleep episode.
- 2. The individual may continue to appear confused and disoriented for several minutes or longer following the episode.

Objective Findings

- PSG not indicated in typical uncomplicated A.D.

- PSG findings:
  - Motor episode occurring with arousal from SWS, most often from first or second SWS period, rare from N2, with persistent delta activity
  - Hypersynchronous delta activity, frequent arousals (not diagnostic)
  - Rare documentation in the sleep laboratory, use of acoustic stimuli/sleep deprivation
  - Documentation of triggers (e.g. OSA)
  - Useful for differential diagnosis (RBD, Epilepsy, Dissociative disorders, etc…)
  - SWS fragmentation as proposed marker

Arousal Disorders

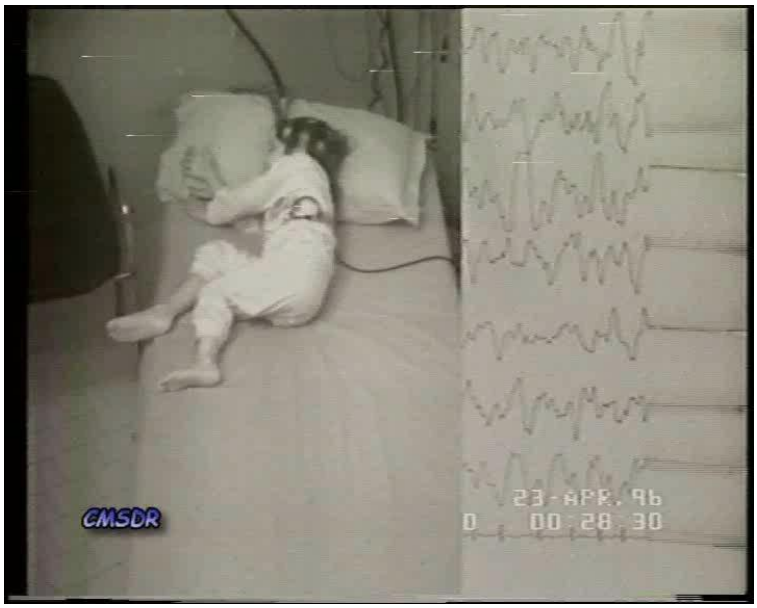
- **Prevalence**
  - 17.3% in children 3-13 y.o.
  - 18.5% lifetime
  - 2.9-4.2% above 15 y.o.

- **Predisposing Factors**: variale genetic patterns
- **Precipitating Factors**
  - Sleep Deprivation
  - Situational stress
  - Sleep disordered breathing
  - Environmental triggers
  - Travel, Unfamiliar sorroundings, Fever, Psychotropic medications, Alcohol

Sleep Terrors

- Sleep terrors differ from other disorders of arousal in that the events are often accompanied by a *cry or piercing scream*, accompanied by autonomic nervous system and behavioral manifestations of intense fear.
- There is often *intense autonomic discharge*, with tachycardia, tachypnea, flushing of the skin, diaphoresis, mydriasis, and increased muscle tone.
- The person usually sits up in bed; is unresponsive to external stimuli; and, if awakened, is confused and disoriented.
- However, bolting out of bed and running is not uncommon in adults

SLEEP TERRORS

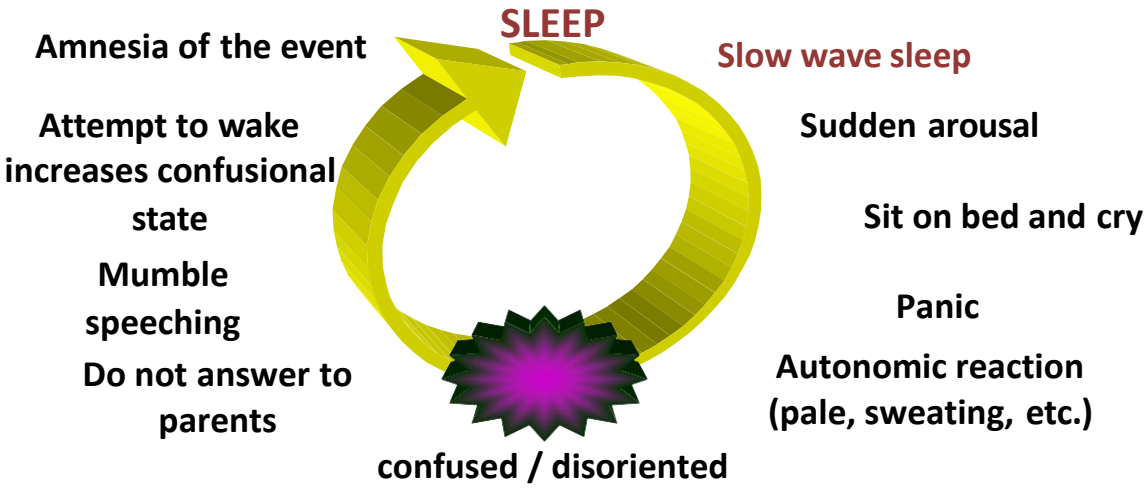


SLEEP TERRORS

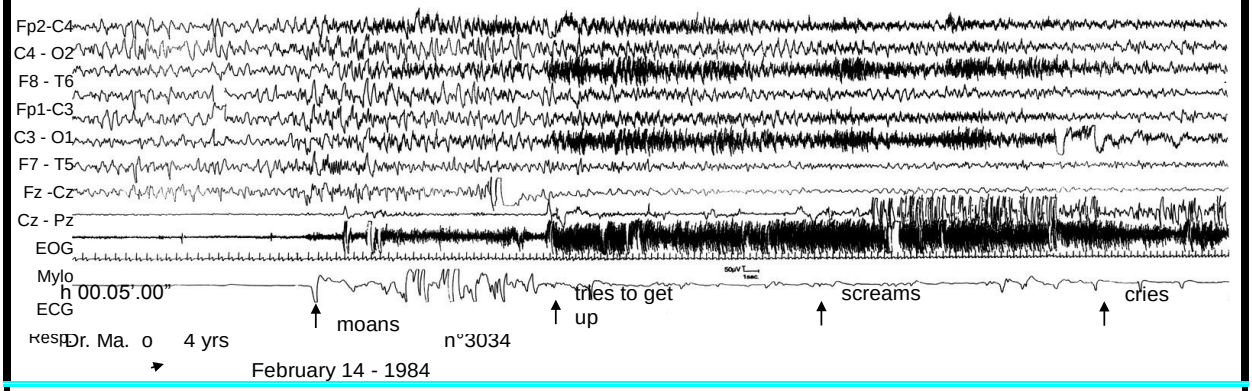
Courtesy Prof.Bruni

Typical pattern of sleep terrors

Duration 30 sec -5 mins



SLEEP TERRORS



Confusional Arousals

Criteria A-C must be met

A. The disorder meets general criteria for NREM disorders of arousal.

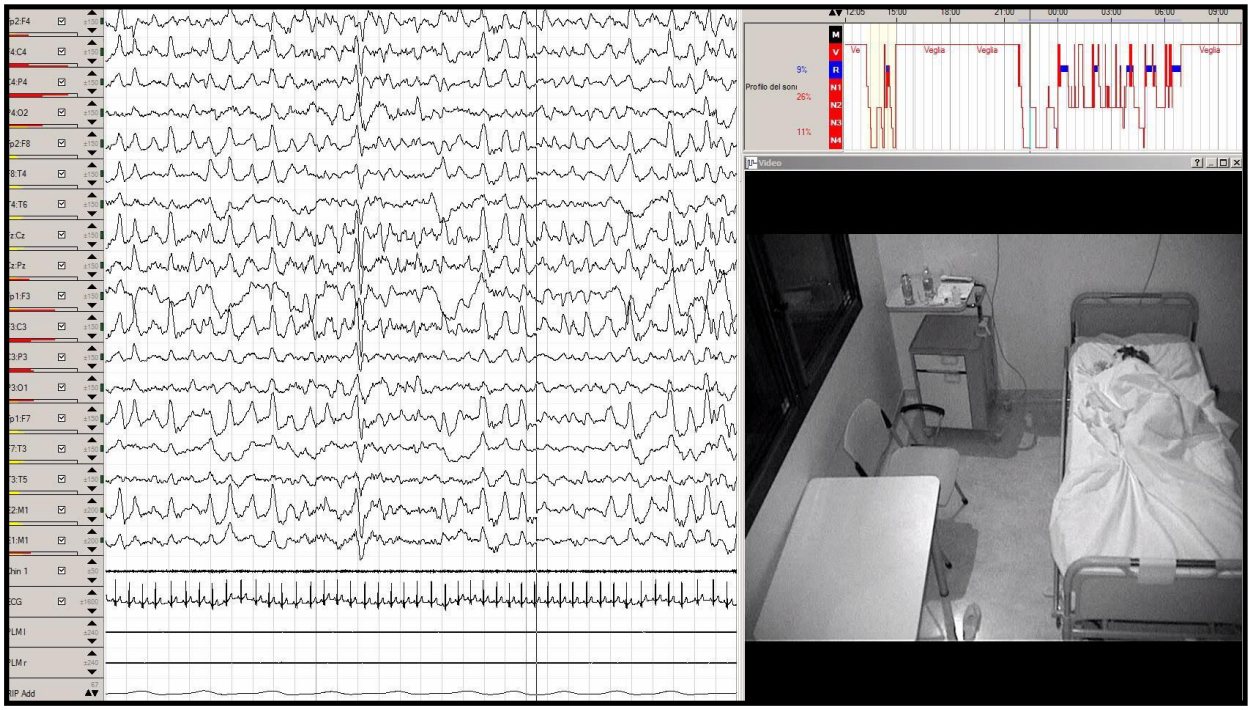
B. The episodes are characterized by mental confusion or confused behavior that occurs while the patient is in bed.

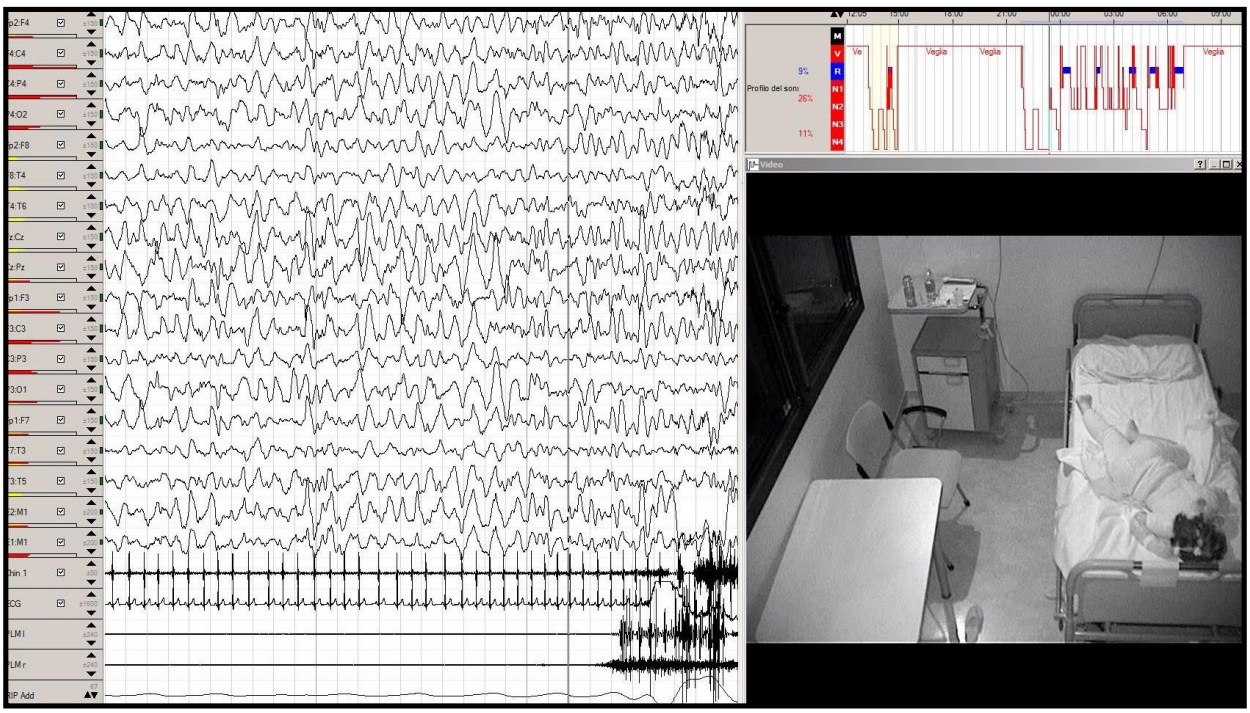
C. There is an absence of terror or ambulation outside of the bed.

Notes

1. There is typically a lack of autonomic arousal such as mydriasis, tachycardia, tachypnea, and diaphoresis during an episode.

- Confusional arousals often <u>start with the individual sitting up in bed and looking around in a confused manner.</u>


Profilo del sonno
Veglia
Video

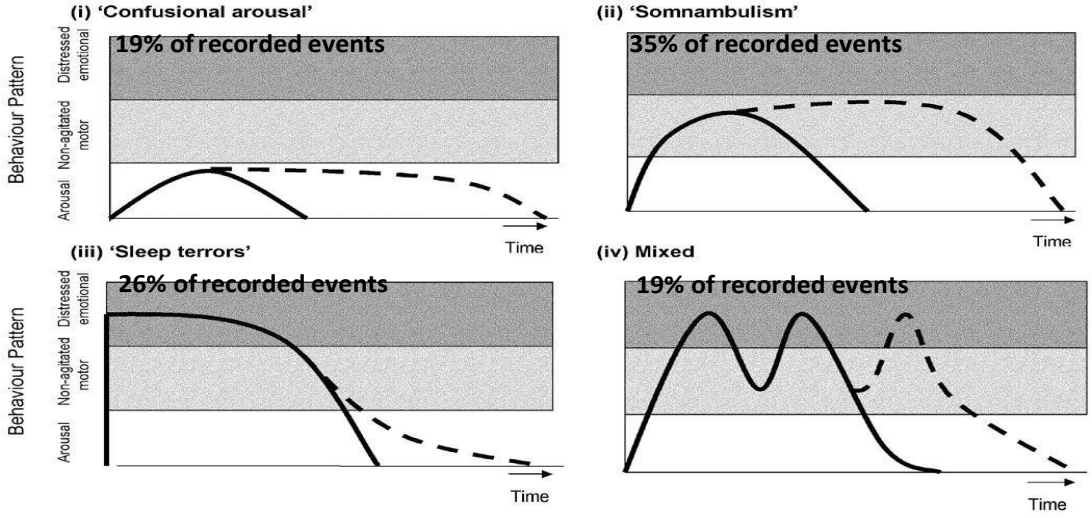

Profilo del sonno
Veglia
Video

Sleepwalking

- Sleepwalking episodes typically begin as confusional arousals.
- Sleepwalking episodes can also begin with the individual immediately leaving the bed and walking or even "bolting" from the bed and running. Highly inappropriate, agitated, resistive, belligerent, or violent behavior can also occur.
- Behaviors can be simple and non–goal-directed, or complex and protracted, and may involve inappropriate sexual activity with oneself or an individual in close proximity such as a bed partner. The ambulation may terminate spontaneously, at times in inappropriate places, or the sleepwalker may return to bed, lie down, and continue to sleep without reaching conscious awareness at any point.
- The sleepwalking individual is disoriented in time and place, with slow speech, with severely diminished mentation, and blunted response to questions or requests. There is often prominent anterograde and retrograde memory impairment. Despite diminished external perception as a result of blockade of sensory input, the individual may appear to be awake during some or most of a disorder of arousal with reduced vigilance and impaired cognitive response.

SLEEPWALKING

Derry CP; Harvey AS; Walker MC; Duncan JS; Berkovic SF. NREM arousal parasomnias and their distinction from nocturnal frontal lobe epilepsy: a video eeg analysis. *SLEEP 2009;32(12):1637-1644*

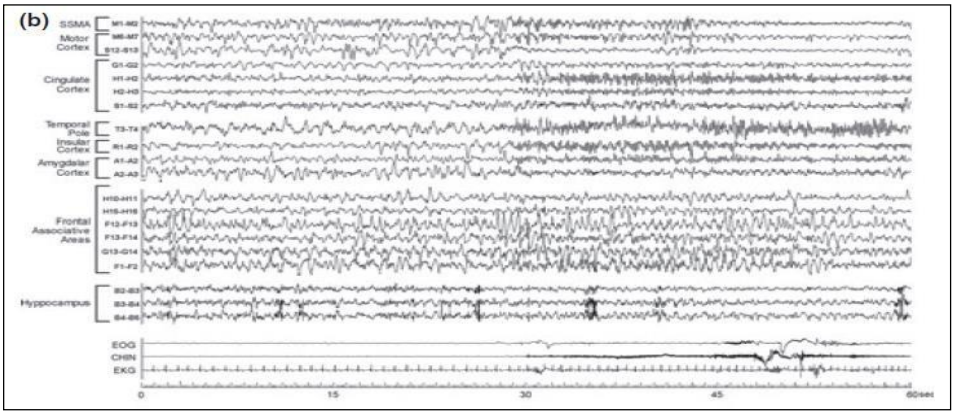


J. Sleep Res. (2012) 21, 502–506

Local sleep and parasomnia

Dissociated local arousal states underlying essential clinical features of non-rapid eye movement arousal parasomnia: an intracerebral stereo-electroencephalographic study

MICHELE TERZAGHI[1], IVANA SARTORI[2], LAURA TASSI[2], VALTER RUSTIONI[1], PAOLA PROSERPIO[2], GIORGIO LORUSSO[2], RAFFAELE MANNI[1] and LINO NOBILI[2]



NREM sleep parasomnias as disorders of sleep-state dissociation

Anna Castelnovo[1,2,6], Régis Lopez[3,6], Paola Proserpio[4], Lino Nobili[4,5,6] and Yves Dauvilliers[3,6]**

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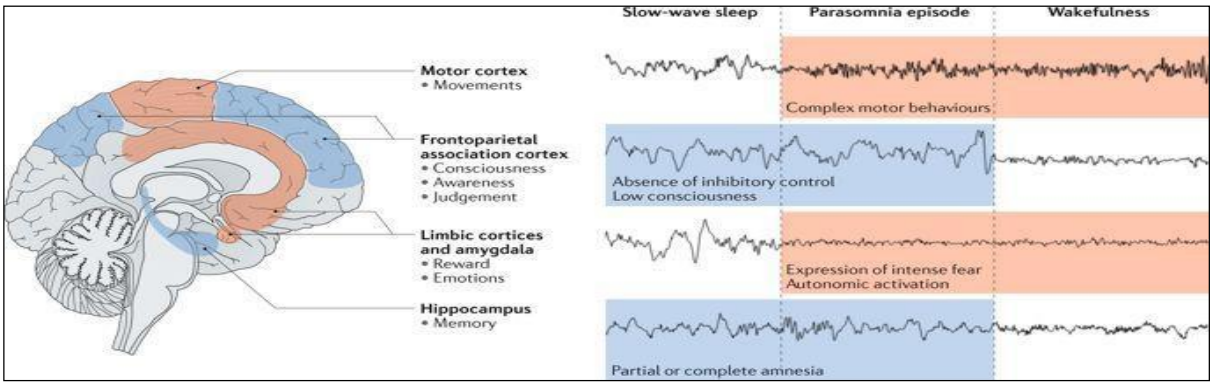
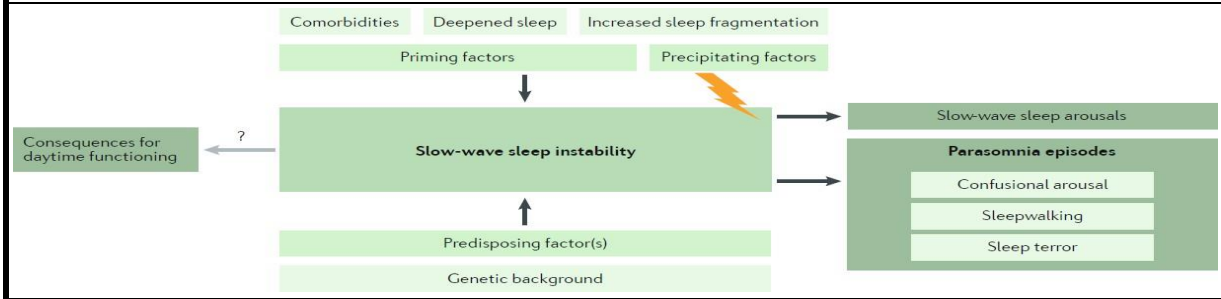


NREM sleep parasomnias as disorders of sleep-state dissociation

Anna Castelnovo[1,2,6], Régis Lopez[3,6], Paola Proserpio[4], Lino Nobili[4,5,6] and Yves Dauvilliers[3,6]**



DISORDERS OF AROUSAL (DOA)
Non pharmacological approach

- Reassure parents on the benign nature
- Safety measure at home
- Remove predisposing factors (OSA, PLM, drugs with CNS-related adverse effects)
- Avoid sleep deprivation [Ohayon et al., 1999]
- Avoid interrupting the event [will increase agitation and prolong the event] (Galbiati et al., 2015)
- Behavioral methods: psychotherapy [Kales et al., 1982], relaxation therapy [Kellerman, 1979], and autogenic training or hypnosis [Hurwitz et al., 1991].
- Scheduled awakening [Owens et al., 1999; Lask, 1988]

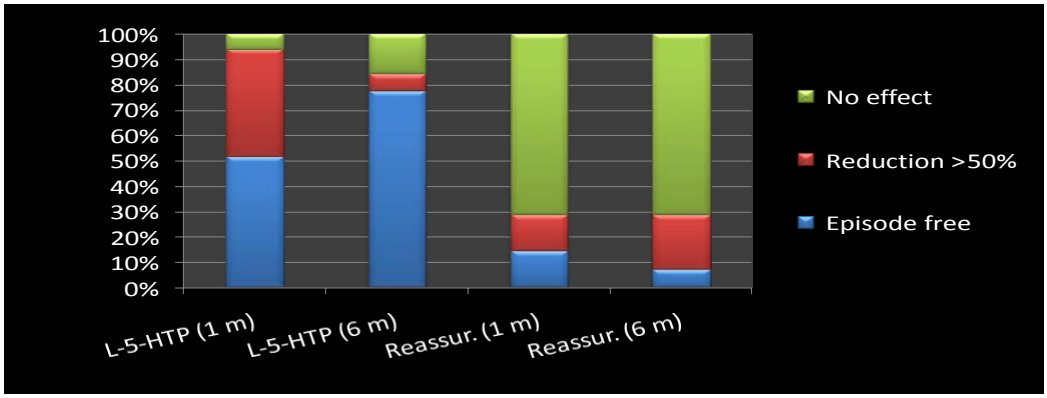
Pharmacological treatment of parasomnias

- When parasomnias become frequent, cause extreme anxiety or there is potential for harm to the person or household members.
- The use of medicines to treat parasomnias is complex, rarely evidence based and recommended for children
- *Commonly if episodes >1/week*
  - clonazepam (0,25-2 mg) → decrease SWS
  - carbamazepine (100-200 mg) → not known
  - tricyclics (imipramine 10 mg), trazodone, paroxetine (*they can trigger parasomnias!!!!*) → stabilize or fragment SWS
  - **L-5-hydroxytriptophan: 5HT precursor (2-5 mg/kg)**

Oliviero Bruni · Raffaele Ferri · Silvia Miano
Elisabetta Verrillo

Eur J Pediatr (2004) 163: 402–407

L -5-Hydroxytryptophan treatment of sleep terrors in children



Group L-5-HTP: 31 (22 M,9 F; 6.7 y)
Group reassurance: 14 (12 M, 2 F; 7.3 y)

Narcolepsy

First descriptions

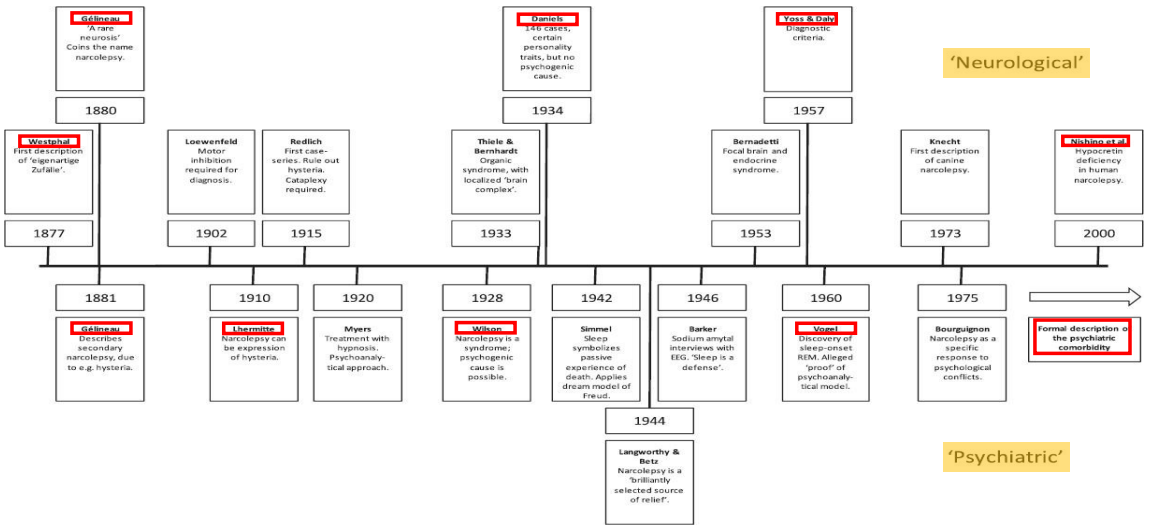
Westphal K. Eigentümliche mit Einschlafen verbundene Anfälle. Archiv für Psychiatrie und Nervenkrankheiten **1877**;7:631-5.

Gélineau JBE. De la narcolepsie. Gazette des Hôpitaux **1880**;53:626-8;54:635-7.

Historical Issues in Sleep Medicine — Sleep Medicine 12 (2011) 714–719

Narcolepsy and psychiatry: An evolving association of increasing interest

H.A. Droogleever Fortuyn [a,*], P.C. Mulders [a], W.O. Renier [b], J.K. Buitelaar [a], S. Overeem [b,c]



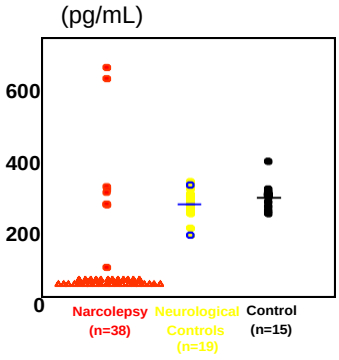
Human narcolepsy is genetically complex

Human Leukocyte Antigen (HLA)

- Tight (99.9%) association with **HLA DQB1*06:02** (*vs*.12-38%)
- Minor effects of other DQA1 and DQB1 alleles
- Increased familial risk (1-4%, λ˜10-40), thus likely other genes are also involved
- Environmentally influenced (17-25% twin concordance)

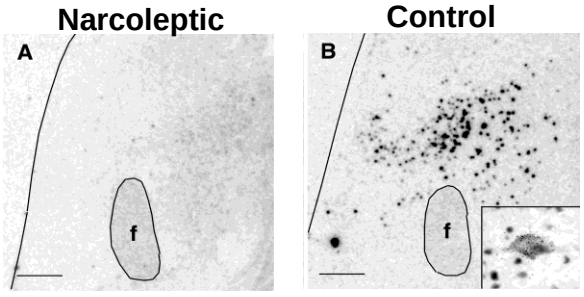
Hypocretin deficiency in sporadic, HLA positive narcolepsy cases

Cerebrospinal fluid

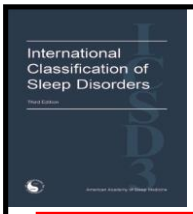


Lateral hypothalamic brain tisSUE

mRNA in situ Hybridization



Adapted from Nishino et al. *Ann Neurol* 2001;50:381; Peyron et al. *Nat Med* 2000;6:991.



International Classification of Sleep Disorders 3°edition, 2014

Narcolepsy Type 1

- A) Excessive daytime sleepiness
- B)
  1. Cataplexy & MSLT +

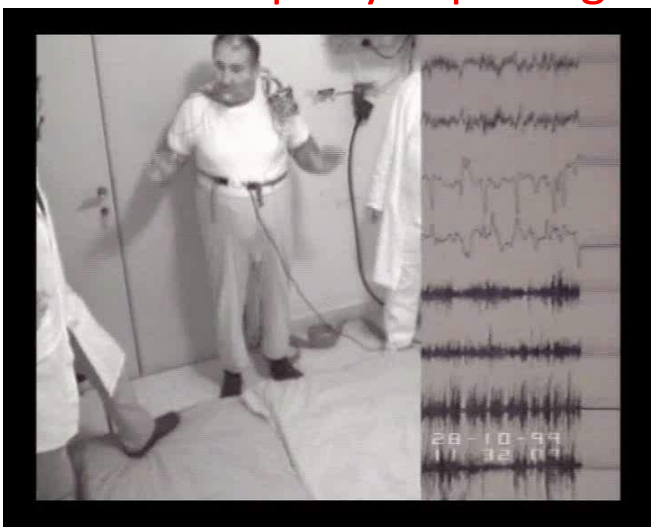
and/or

  2. CSF Hcrt-1 <110pg/ml

Narcolepsy Type 2

- A) Excessive daytime sleepiness
- B) Cataplexy absent
- C) MSLT +
- D) CSF Hcrt-1 >110pg/ml, if known

Human Narcolepsy-Cataplexy
Cataplexy: a pathognomonic symptom



- Excessive daytime sleepiness
- Sleep Onset REM periods
- Cataplexy
- Sleep paralysis
- Hypnagogic hallucinations
- Disturbed nocturnal sleep

Contents lists available at ScienceDirect
Sleep Medicine
journal homepage: www.elsevier.com/locate/sleep

Review Article

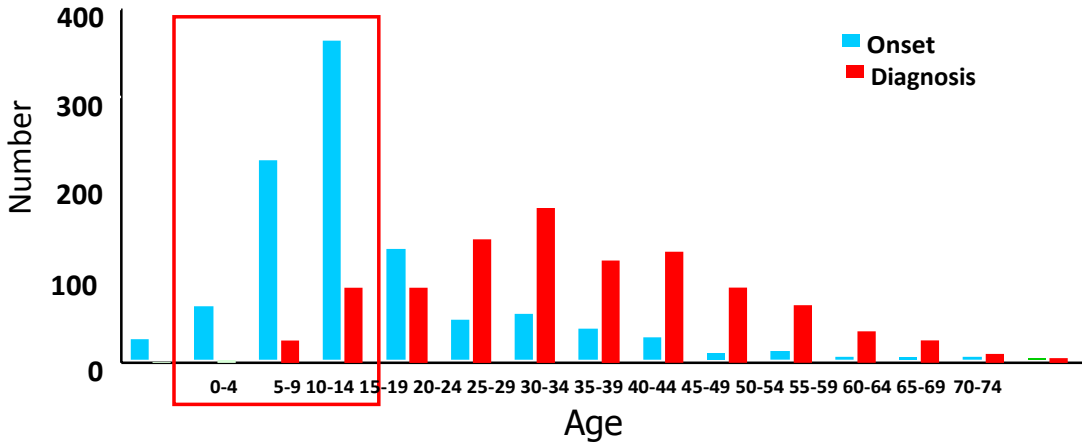
Delayed diagnosis of narcolepsy: characterization and impact

Michael J. Thorpy[a,b,*], Ana C. Krieger[c,d,e]

Contents lists available at SciVerse ScienceDirect
Sleep Medicine
journal homepage: www.elsevier.com/locate/sleep

Editorial

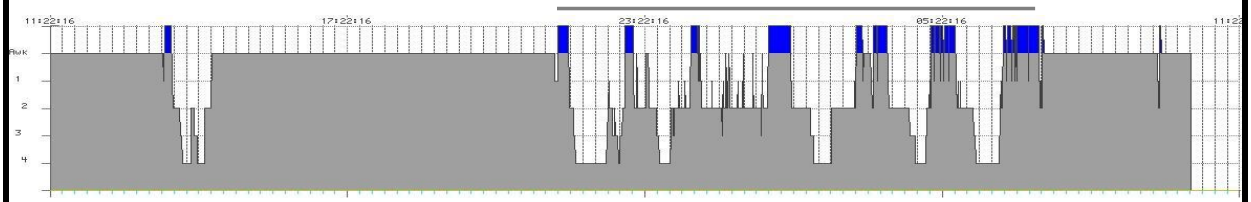
Childhood narcolepsy with cataplexy: a newly reported phenotype of an old disease?



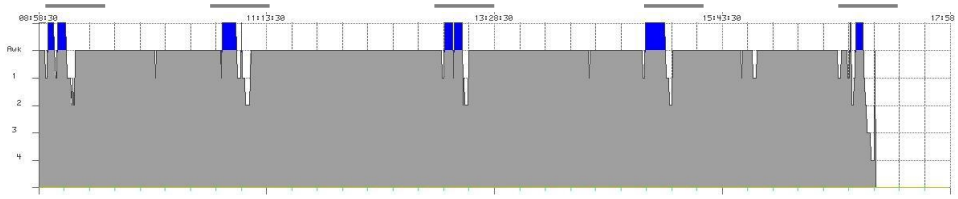
EDS presentation in childhood NT1 - 1

Increased need for nighttime and daytime sleep

24-hour-PSG



MSLT



Neuropediatrics
Journal of Pediatric Neurobiology, Neurology and Neurogenetics

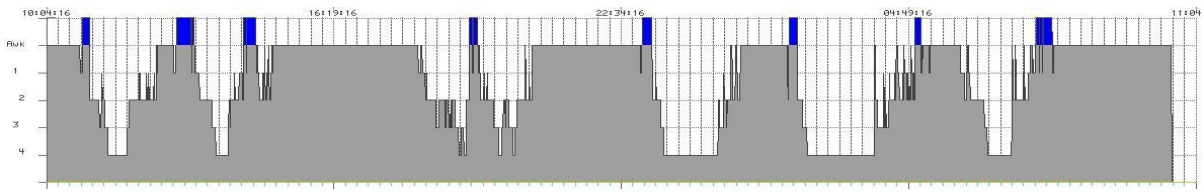
Narcolepsy during Childhood: An Update

Francesca Letizia Rocca[1,2] Fabio Pizza[2,3] Emilia Ricci[4] Giuseppe Plazzi[2,3]

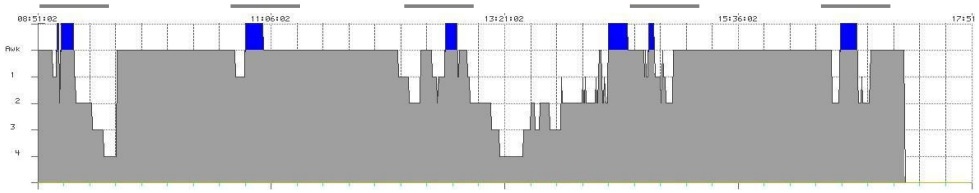
EDS presentation in childhood NT1 - 2

Inability to stay awake during the daytime & to maintain continuous sleep at night

24-hour-PSG



MSLT



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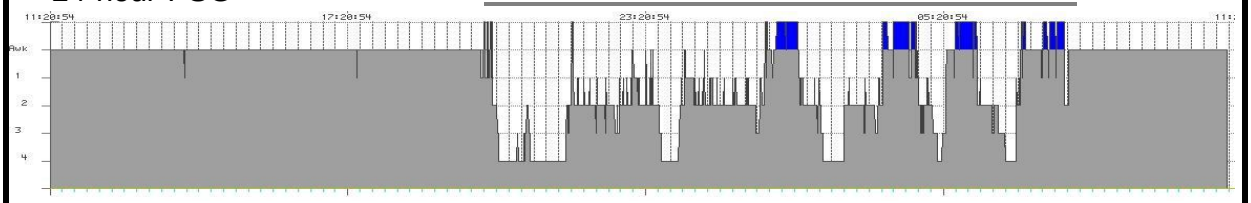
Narcolepsy during Childhood: An Update

Francesca Letizia Rocca[1,2] Fabio Pizza[2,3] Emilia Ricci[4] Giuseppe Plazzi[2,3]

EDS presentation in childhood NT1 - 3

Absence (irritability) of sleep attacks/spontaneous daytime sleep

24-hour-PSG



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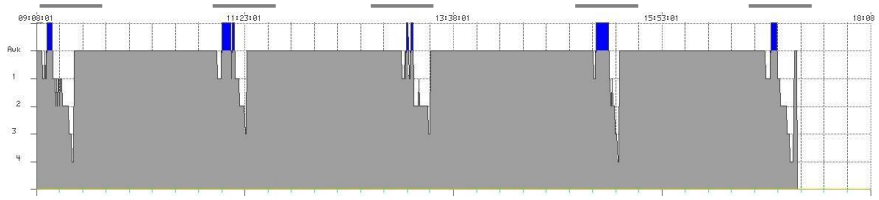

Neuropediatrics
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Narcolepsy during Childhood: An Update

Francesca Letizia Rocca[1,2] Fabio Pizza[2,3] Emilia Ricci[4] Giuseppe Plazzi[2,3]

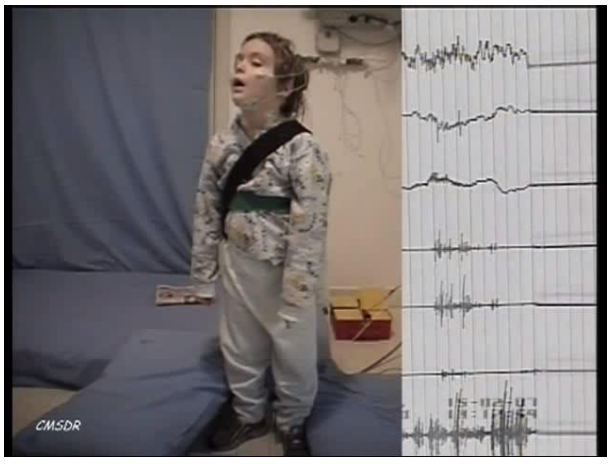
Movement Disorders
Vol. 23, No. 6, 2008, pp. 858–865
© 2008 Movement Disorder Society

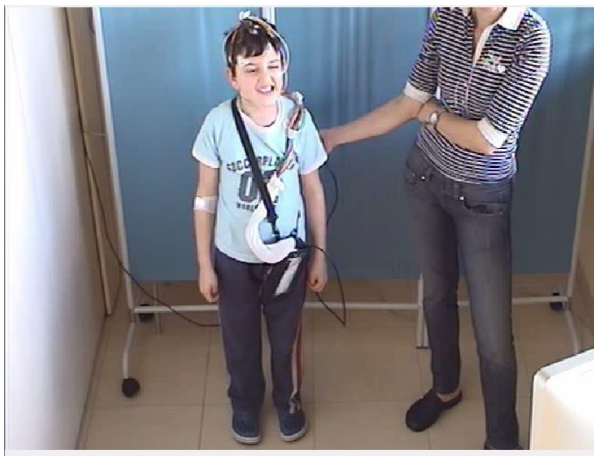
Cataplexy Features in Childhood Narcolepsy

Leonardo Serra, MD,[1,2] Pasquale Montagna, MD,[1] Emmanuel Mignot, MD, PhD,[3] Elio Lugaresi, MD,[1] and Giuseppe Plazzi, MD[1]*

- childhood cataplexy is characterized by generalized hypotonia and prominent facial involvement ("*cataplecticfacies*")
- abnormal neurological examination: fluctuating hypotonia, ptosis, wide based gait (ataxia)
- cataplexy can be spontaneous (acute onset movement disorder): while walking or eating
- cataplexy can go unrecognized, though easily elicited by funny videos

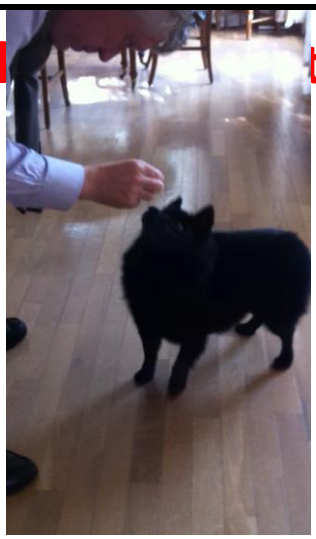
Fluctating Hypotonia, Ptosis, Wide Based Gait, elicited by funny videos…





Cataplexy not reported…

exy el ting



Courtesy Prof. Mignot

doi:10.1093/brain/awr244 Brain 2011: 134; 3480–3492 | 3480

BRAIN
A JOURNAL OF NEUROLOGY

Complex movement disorders at disease onset in childhood narcolepsy with cataplexy

Giuseppe Plazzi,[1] Fabio Pizza,[1] Vincenzo Palaia,[1] Christian Franceschini,[1] Francesca Poli,[1] Keivan K. Moghadam,[1] Pietro Cortelli,[1] Lino Nobili,[2] Oliviero Bruni,[3] Yves Dauvilliers,[4] Ling Lin,[5] Mark J. Edwards,[6] Emmanuel Mignot[5] and Kailash P. Bhatia[6]

rhapsodic 'negative" and 'active" movements

dissection and scoring of elementary motor phenomena: **"Negative" vs "Active"**

"Negative"

paroxysmal head drops and falls

persistent eyelid narrowing and tongue protrusion

facial hypotonia

generalized hypotonia:
wide-based gait
squatting
unsteady gait

BRAIN A JOURNAL OF NEUROLOGY

Plazzi G. et al Brain. 2011

"Active"

raising of the eyebrows

perioral and tongue movements

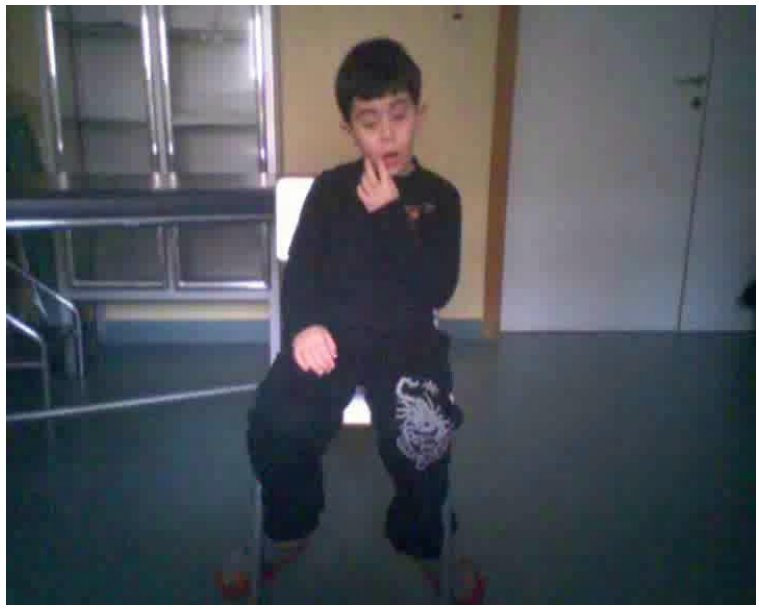
facial grimaces

swaying of the head and/or trunk

stereotyped motor behaviour

dyskinetic or dystonic movements

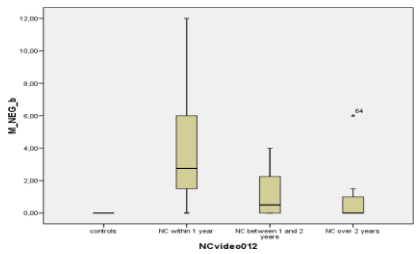
Plazzi G. et al Brain. 2011

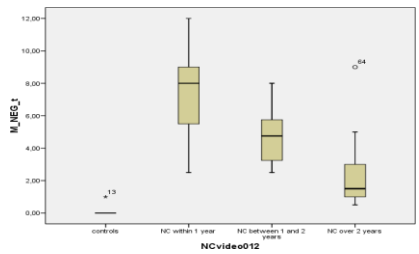


"Negative" and "Active" motor phenomena: severity & time from onset

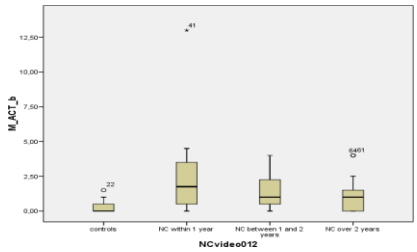
Baseline | Emotionally triggered

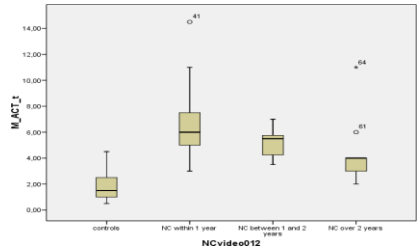
negative





active





doi:10.1093/brain/awt277 Brain 2013: Page 1 of 9 | 1

BRAIN
A JOURNAL OF NEUROLOGY

Clinical and polysomnographic course of childhood narcolepsy with cataplexy

Fabio Pizza,[1,2] Christian Franceschini,[1,2,3] Hanna Peltola,[4] Stefano Vandi,[1,2] Elena Finotti,[1,2] Francesca Ingravallo,[5] Lino Nobili,[6] Oliviero Bruni,[7] Ling Lin,[8] Mark J. Edwards,[9] Markku Partinen,[4] Yves Dauvilliers,[10] Emmanuel Mignot,[8] Kailash P. Bhatia[9] and Plazzi Giuseppe[1,2]

21 NC children (70% Males)

Baseline:

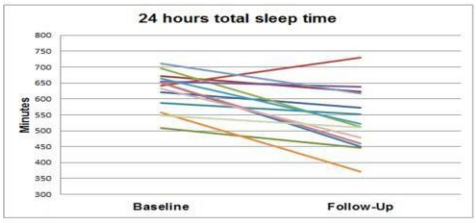
age=10±3 y.o.

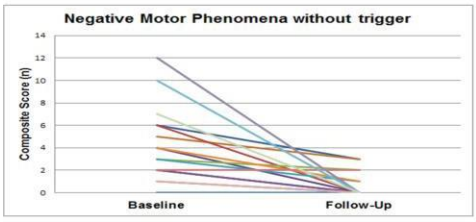
1±1 y. from NC onset

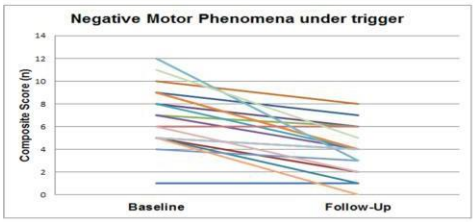
Follow-Up (median=3y):

age=12±4 y.o.

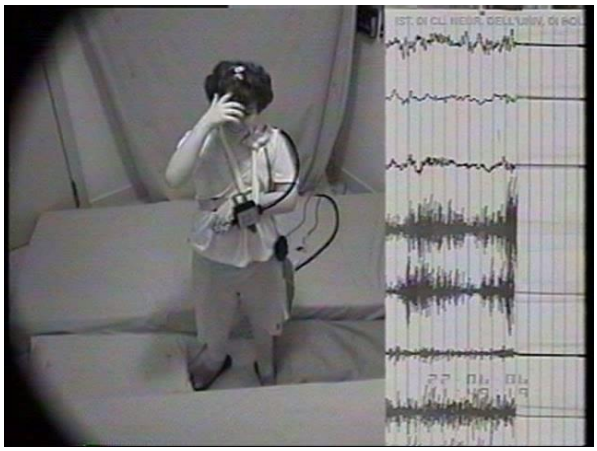
3±2 y. from NC onset





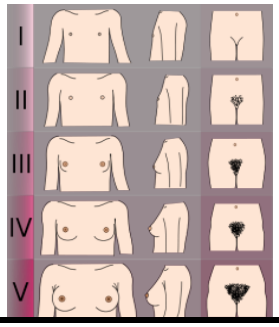


childhood cataplexy turns into typical phenotype

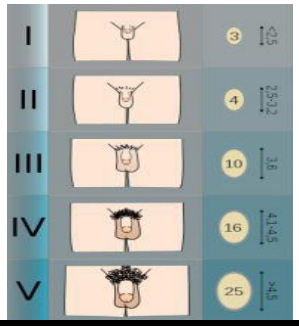


overweight and/or obesity

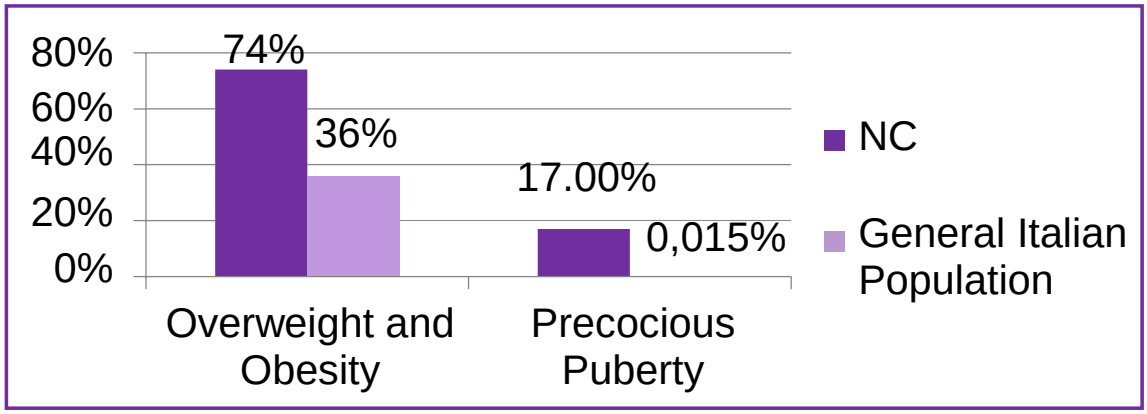
NT1 discordant twins



Precocious puberty



metabolic and puberal dysfunction severity and age at onset



VIDEO

Narcolepsy–cataplexy associated with precocious puberty

Plazzi G, et al. 2006

NEUROLOGY

PRECOCIOUS PUBERTY AND OBESITY IN CHILDHOOD NARCOLEPSY WITH CATAPLEXY

http://dx.doi.org/xxxxxxxxxxxxxx

High Prevalence of Precocious Puberty and Obesity in Childhood Narcolepsy with Cataplexy

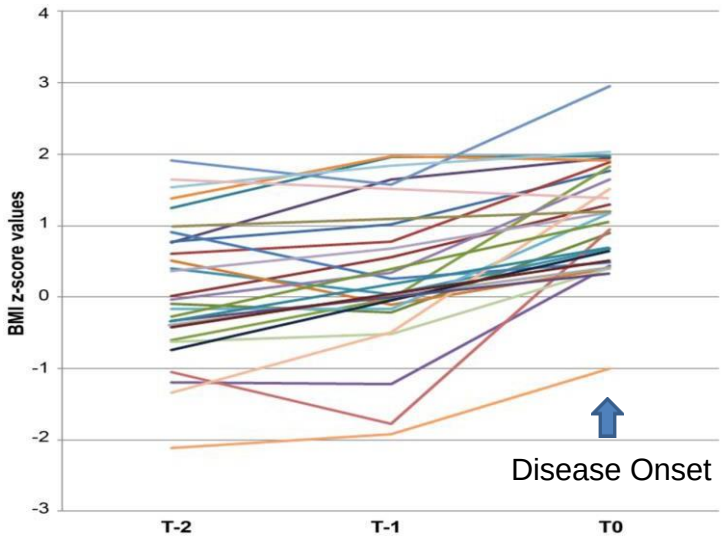
Francesca Poli, MD, PhD[1]; Fabio Pizza, MD, PhD[1]; Emmanuel Mignot, MD, PhD[2]; Raffaele Ferri, MD[3]; Uberto Pagotto, MD, PhD[4]; Shahrad Taheri, MB, BS, PhD, FRCP[5]; Elena Finotti, MD[1]; Filippo Bernardi, MD[6]; Piero Pirazzoli, MD[6]; Alessandro Cicognani, MD[6]; Antonio Balsamo, MD[6]; Lino Nobili, MD, PhD[7]; Oliviero Bruni, MD[8]; Giuseppe Plazzi, MD, PhD[1]

Growing Up with Type 1 Narcolepsy: Its Anthropometric and Endocrine Features

J Clin Sleep Med 2016;12(12):1649–1657.

Virginia Ponziani, MD[1]; Monia Gennari, MD, PhD[1]; Fabio Pizza, MD, PhD[2,3]; Antonio Balsamo, MD, PhD[4]; Filippo Bernardi, MD[1]; Giuseppe Plazzi, MD, PhD[2,3]

Pediatricians anthropometric data collectd in the two years before disease onset (T0)



Childhood phenotype

when the onset of NT1 occurs at an early age

- development of symptoms is frequently abrupt and partially remits (cataplexy may follow the detection of a low CSF hcrt-1 level)
- misdiagnosis or no diagnosis at all at NT1 onset are common
- cataplexy is an early sign (cataplecic facies), easy to document, acute-onset (complex movement disorder), changes with the disease progress
- hallucinations and disturbed nocturnal sleep are common
- possible concomitant obesity and precocious puberty

Neuropediatrics
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Narcolepsy during Childhood: An Update

Francesca Letizia Rocca[1,2] Fabio Pizza[2,3] Emilia Ricci[4] Giuseppe Plazzi[2,3]

Treatment

- Behavioral treatment
- Off-Label Pharmacological approaches
  - Sodium Oxybate
  - Stimulants
- Recent pharmacological trials in children (S.O., Pitolisant)

Thanks for your attention and to

- Giuseppe Plazzi
- Stefano Vandi
- Marco Filardi
- Keivan Kaveh Moghadam
- Christian Franceschini
- Elena Finotti
- Vincenzo Donadio
- Rocco Liguori
- Monica Moresco
- Giulia Neccia
- Alice Mazzoni
- Elena Antelmi
- Elio Lugaresi†
- Carlo Cipolli
- Francesca Ingravallo
- Anna Govi
- Marco Menchetti
- Uberto Pagotto
- Filippo Bernardi
- Monia Gennari
- Raffaele Lodi
- Caterina Tonon
- Stefano Meletti
- Anna Vaudano
- Emmanuel Mignot
- Yves Dauvilliers and the Montpellier Group
- Birgitte R. Kornum
- Poul Jennum and the Copenaghen Group
- Kailash Bhatia, Mark J. Edwards
- Luigi Ferini Strambi
- Oliviero Bruni
- Raffaele Ferri
- Lino Nobili