



PIA FONDAZIONE DI CULTO E RELIGIONE CARD. G. PANICO
A z i e n d a O s p e d a l i e r a



Il Ruolo delle Fluttuazioni Motorie nel Work-Up Diagnostico dei Disturbi del Sonno

Marco Filardi, PhD ^{1,2}

Ricercatore a Tempo Determinato, RTD-A

1. Università degli Studi di Bari Aldo Moro, Dipartimento di Scienze mediche di base, neuroscienze e organi di senso (DSMBNOS)
2. Centro per le Malattie Neurodegenerative e l'Invecchiamento Cerebrale dell'Università degli Studi di Bari Aldo Moro presso l'Ospedale "Card. G. Panico"

RIUNIONE ANNAUALE SIN APPULO-LUCANA

3-4 Novembre 2022 – Nicolaus Hotel, Bari



CONFLICT OF INTEREST DISCLOSURE

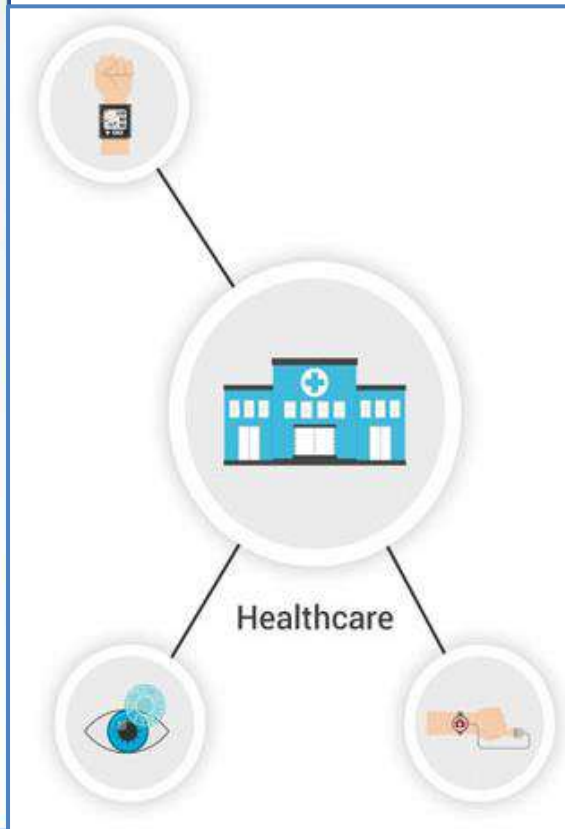
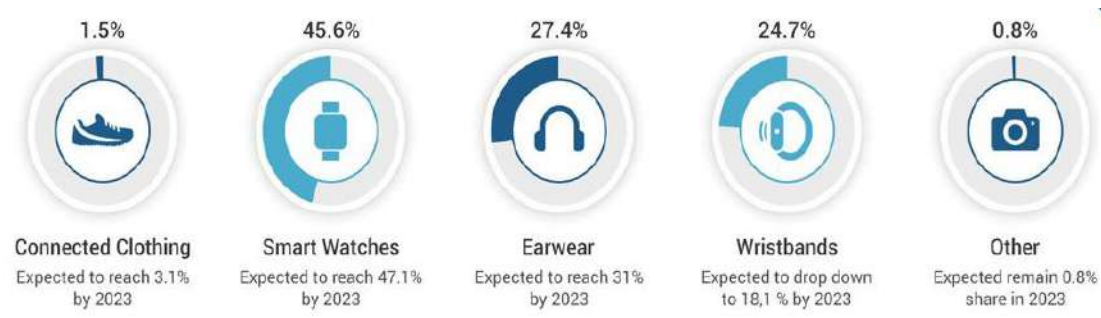
With respect to this CME activity,

No, I (nor my spouse/partner) do not have a relevant financial relationship.

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Wearable Devices



CONSUMER WEARABLE DEVICES

- **Costo ridotto**
- **Funzionamento a «Black Box»**
- **Non validati**

MEDICAL WEARABLE DEVICES

- **Costi alti**
- **Validati**
- **Software di analisi dedicati**



Wearables Pros and Cons



What Benefits Wearables Bring to Healthcare?

- 1 Better health tracking
- 2 More accurate diagnosing
- 3 Improved doctor-patient interaction
- 4 Patient identity management
- 5 Increased patient motivation
- 6 Data safety
- 7 Reduced healthcare expenses

Ecologic Assessment

Collect information on several biological signals (movement, heart rate, temperature) for extended time periods

- Elderly
- Psychiatric patient
- Patients with reduced mobility

In-field assessment of treatments effects

Monitor adherence and effectiveness

- Pharmacological treatments
- Multidomain non-pharmacological interventions (nutrition, exercise program, sleep)

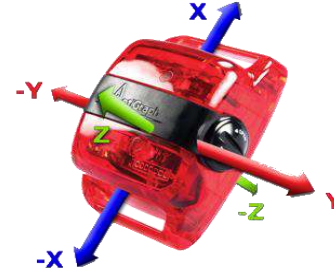


Accelerometer-based Wearables

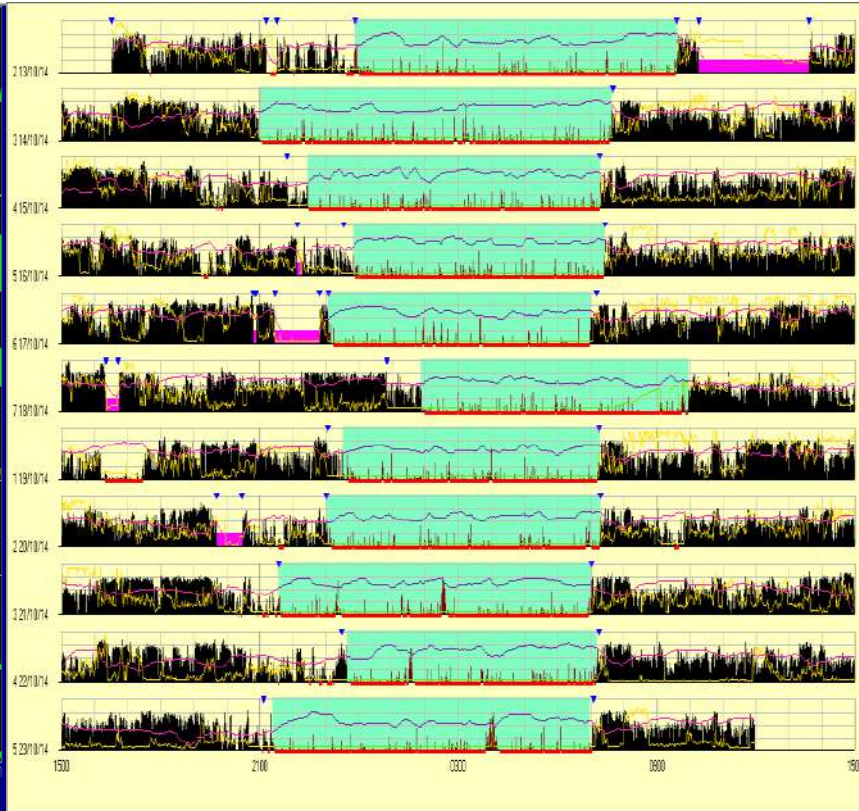
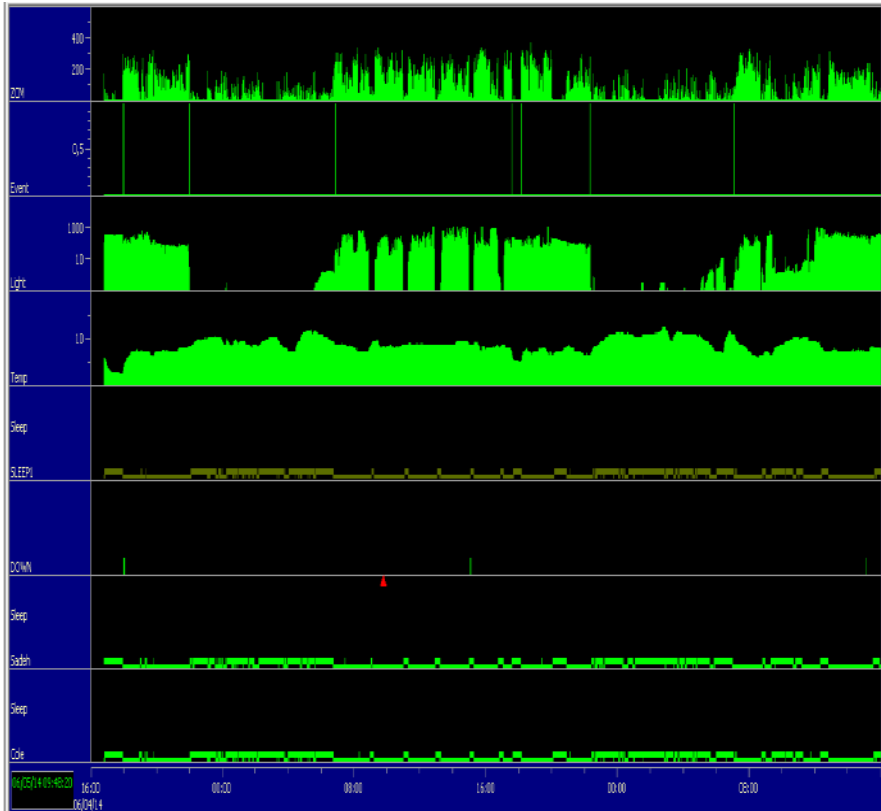
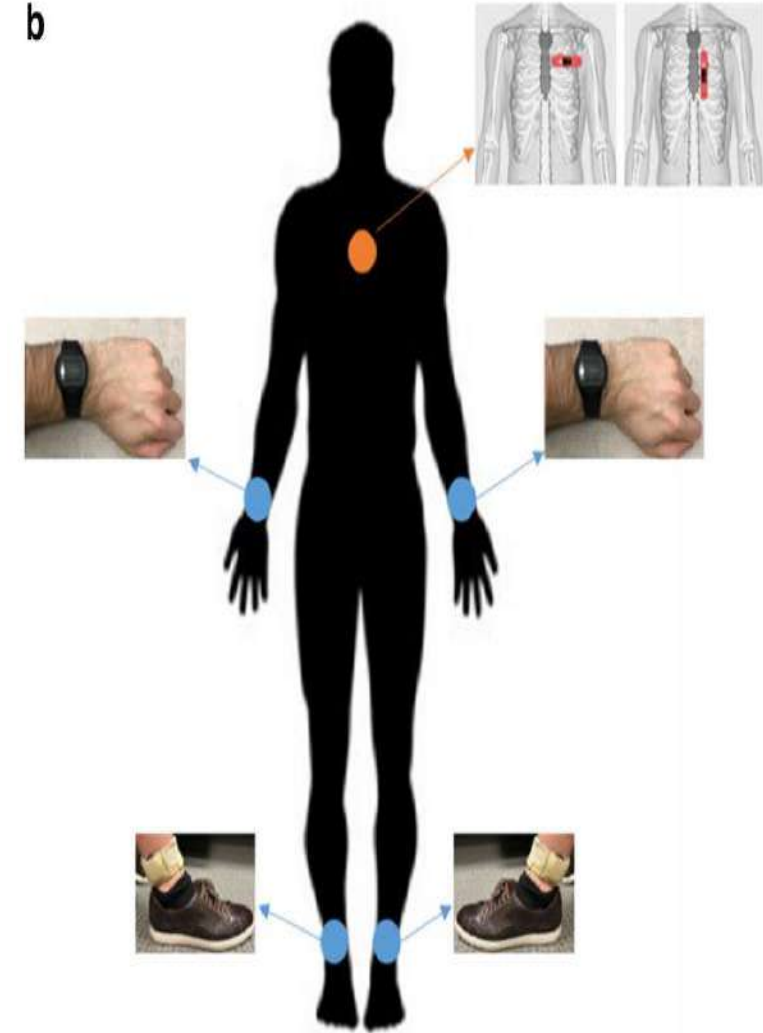


Actigraphy: Wrist-watch like devices
Monitor movements for extended periods

- *Direct Assessment* : **Motor Activity**
- *Indirect Assessment* : **Sleep** (quality, duration, timing)



b





The Role of Actigraphy in Sleep Medicine



Insomnia

“Gold Standard”

Circadian rhythm disorders

“Gold Standard”

Central Hypersomnias

Narcolepsy: “Document adequate sleep prior to the MSLT”
Idiopathic Hypersomnia: “Useful in the diagnosis of some patients with Idiopathic Hypersomnia”

Parasomnias

“iRBD is emerging as a novel potential field of application”



Wearables in Diagnostic Work-up of CDH



1995

Circadian distribution of motor activity and immobility in narcolepsy: Assessment with continuous motor activity monitoring

Psychophysiology, 32 (1995), 286-291.

HUUB A. M. MIDDELKOOP,^a GERT JAN LAMMERS,^a BOB J. VAN HILTEN,^a
CINDY RUWHOF,^a HANNO PIJL,^b AND HILBERT A. C. KAMPHUISEN^a

17 **NC** (41 ± 16y) | 14 **HC** (43 ± 16y)

- Reduced amplitude of the circadian motor activity rhythm
- Lack of significant day-to-day and night-to-night variability

2015

Actigraphic assessment of sleep/wake behavior in central disorders of hypersomnolence

Marco Filardi ^{a,*}, Fabio Pizza ^{b,c}, Monica Martoni ^d, Stefano Vandi ^{b,c}, Giuseppe Plazzi ^{b,c},
Vincenzo Natale ^a

39 **NT1** (34 ± 16y) | 24 **IH** (32 ± 16y) | 30 **HC** (29 ± 9y)

- **NT1** patients show a marked impairment of sleep quality and high representation of motor events coupled with frequent diurnal naps
- **IH** patients show a sleep quality comparable to that of controls but frequent diurnal naps and reduced daytime motor activity

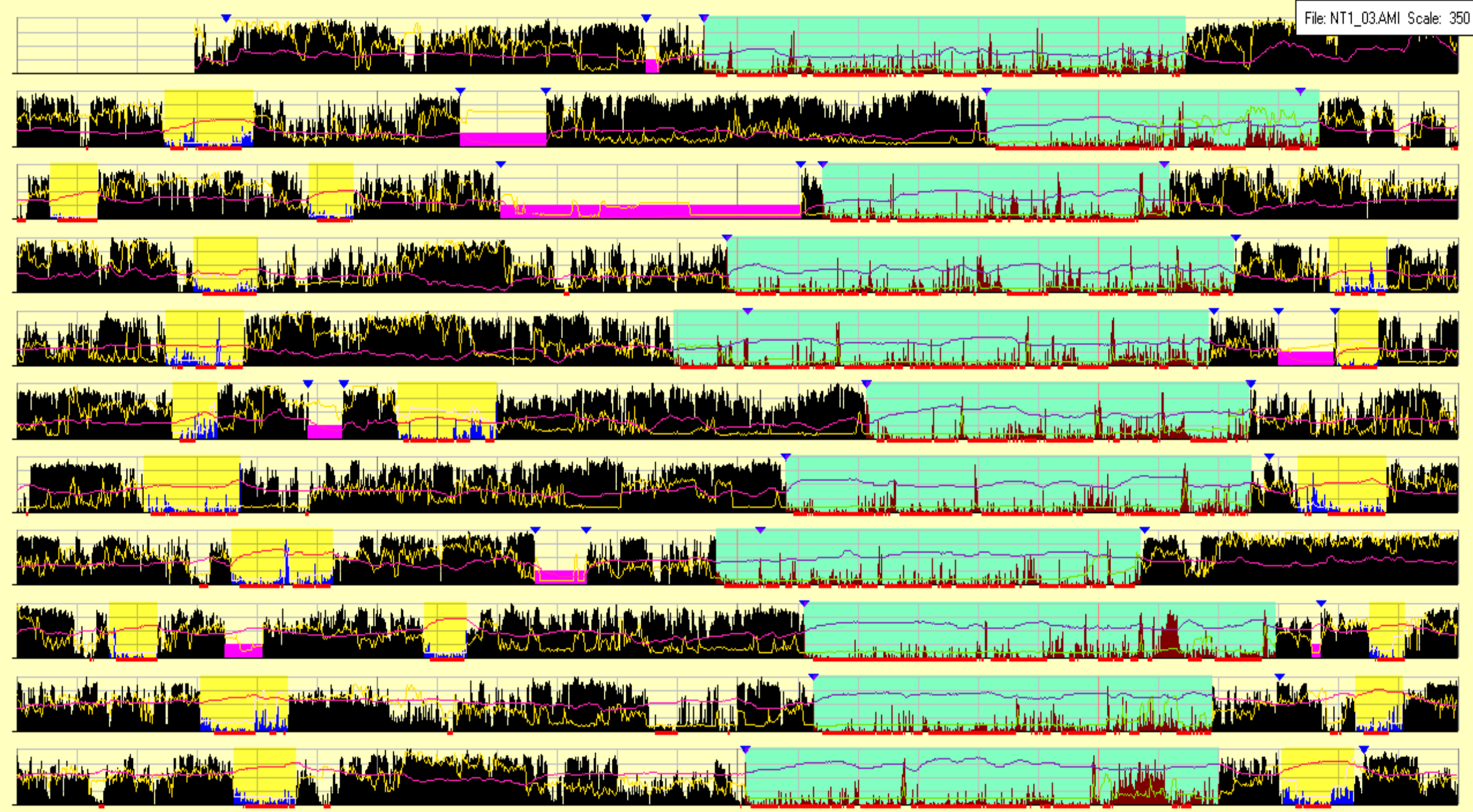
2018

Using actigraphy to assess sleep and wake rhythms of narcolepsy type 1 patients: a comparison with primary insomniacs and healthy controls

Damien Leger ^{a,*}, Caroline Gauriau ^a, Lorenzo Tonetti ^b, Michaele Lantin ^c, Marco Filardi ^d,
Pierre Philip ^e, Brice Faraut ^a, Vincenzo Natale ^b

13 **NT1** (39 ± 11y) | 13 **PI** (39 ± 11y) | 13 **HC** (38 ± 11y)

- Treated NT1 patients had poorer sleep than controls and a higher sleep fragmentation than PI patients.





NT1 Children and Adolescents



2016

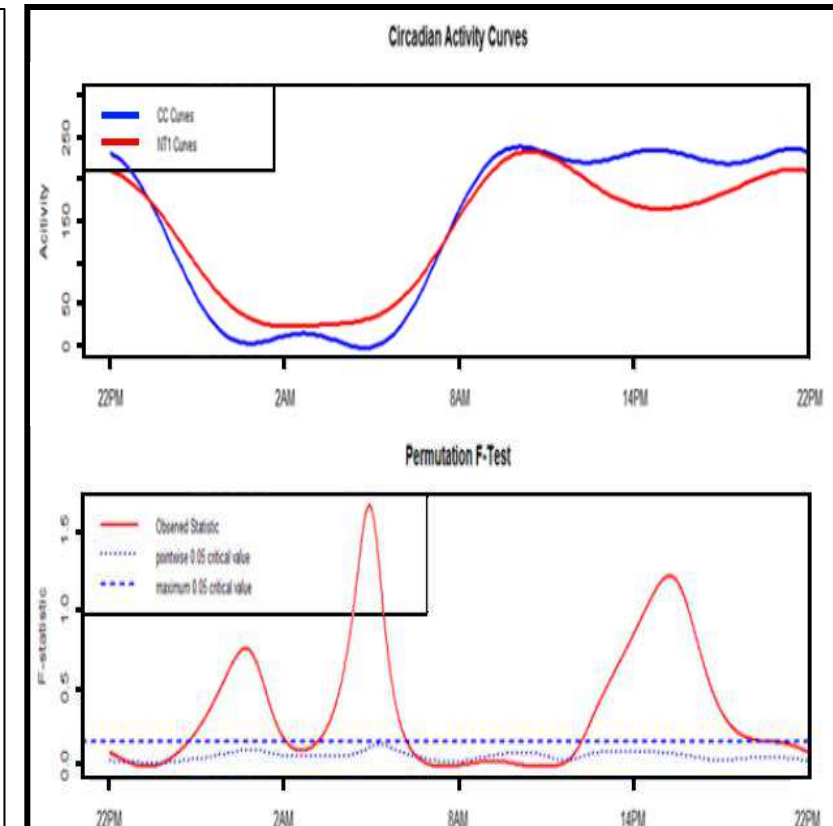
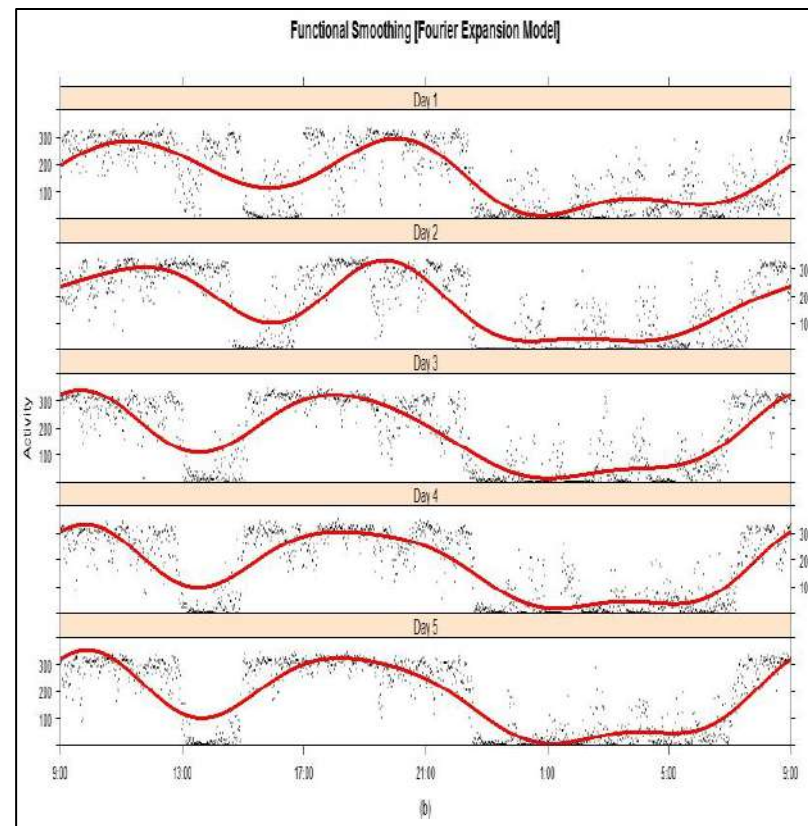
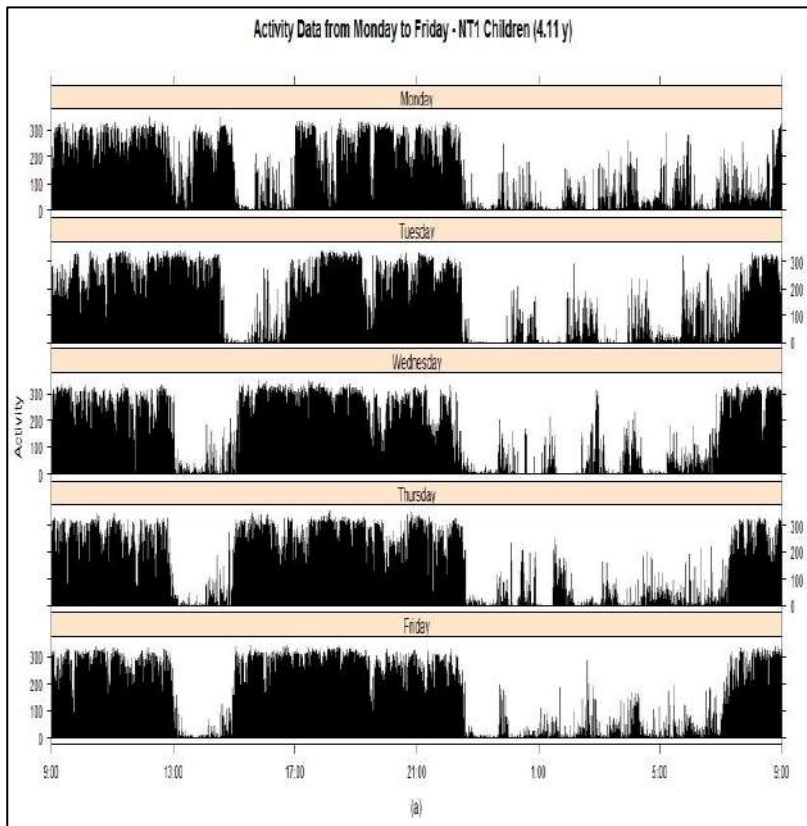
PEDIATRICS

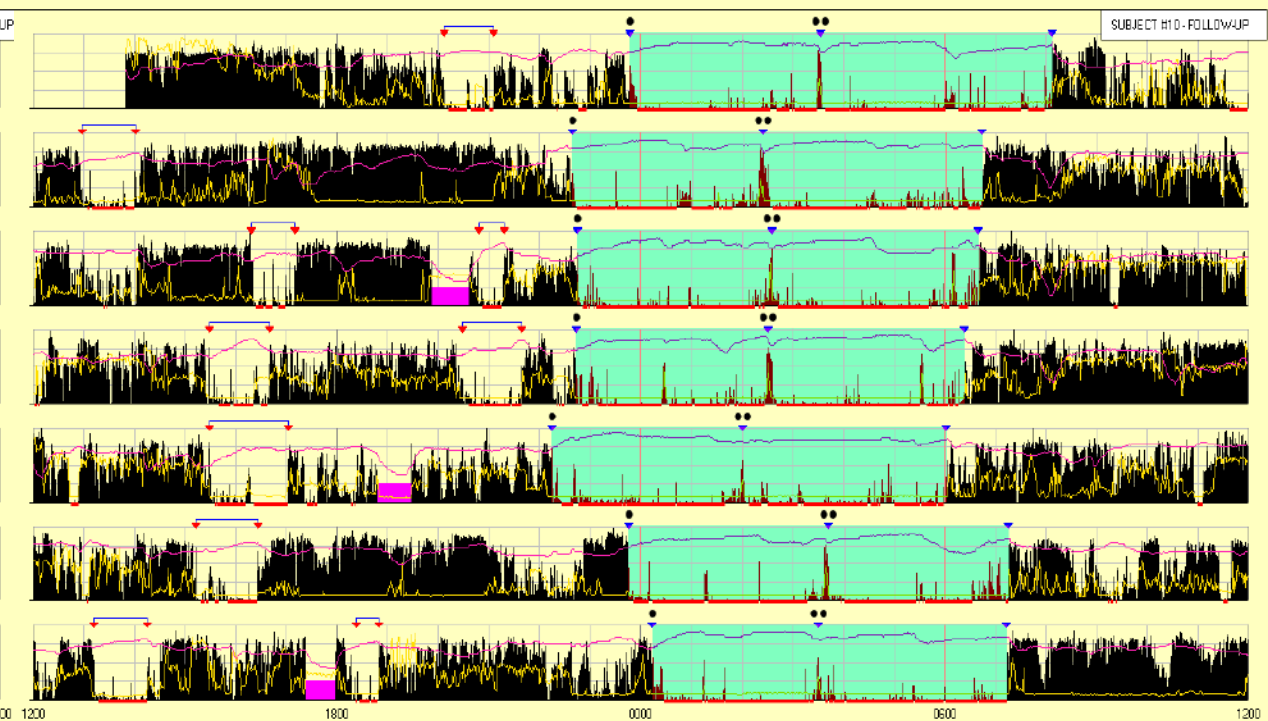
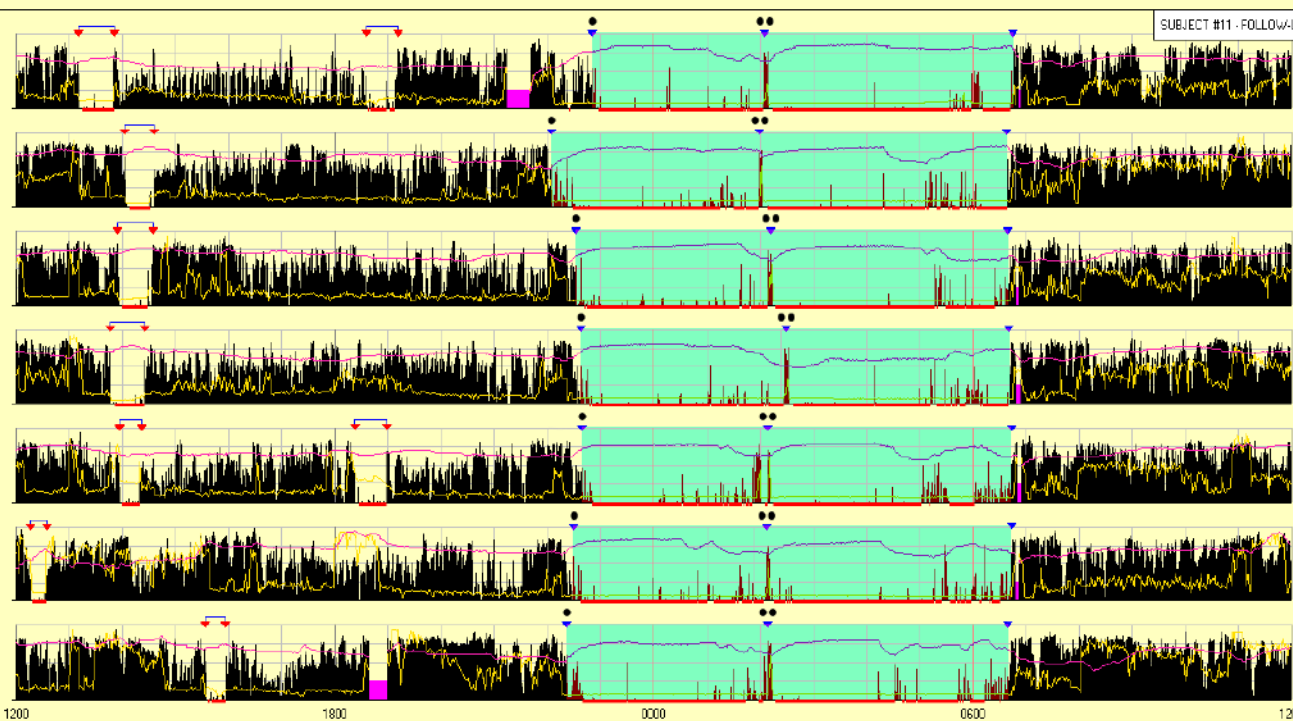
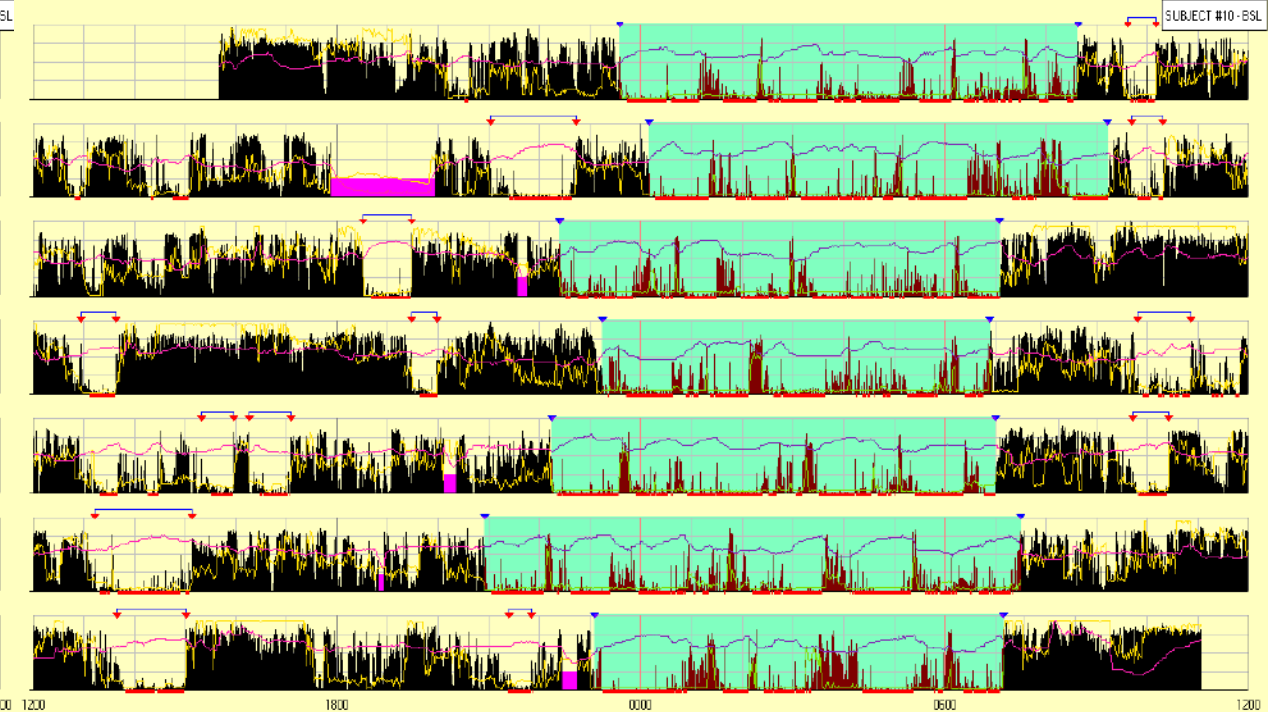
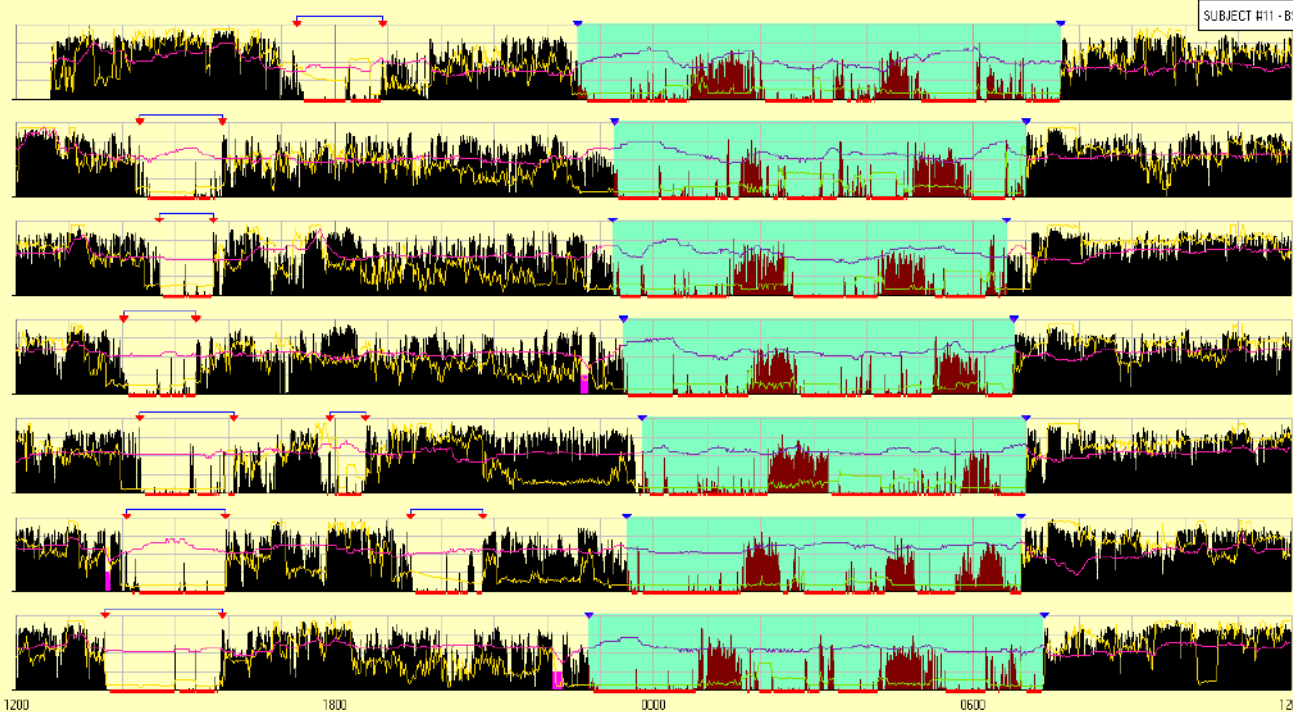
Circadian Rest-Activity Rhythm in Pediatric Type 1 Narcolepsy

Marco Filardi, MSc¹; Fabio Pizza, PhD^{2,3}; Oliviero Bruni, MD⁴; Vincenzo Natale, PhD¹; Giuseppe Plazzi, PhD^{2,3}

22 **NT1** (12 ± 2y) | 21 **HC** (11 ± 2y)

- No alteration of Sleep Timing
- Marked impairment of sleep quality, overrepresentation of motor events. Naps longer than in adults NT1.
- NT1 children have a characteristic circadian activity profile.







Isolated rapid eye movement sleep behavior disorder



PIA FONDAZIONE DI CULTO E RELIGIONE CARD. G. PANICO
A z i e n d a O s

2018

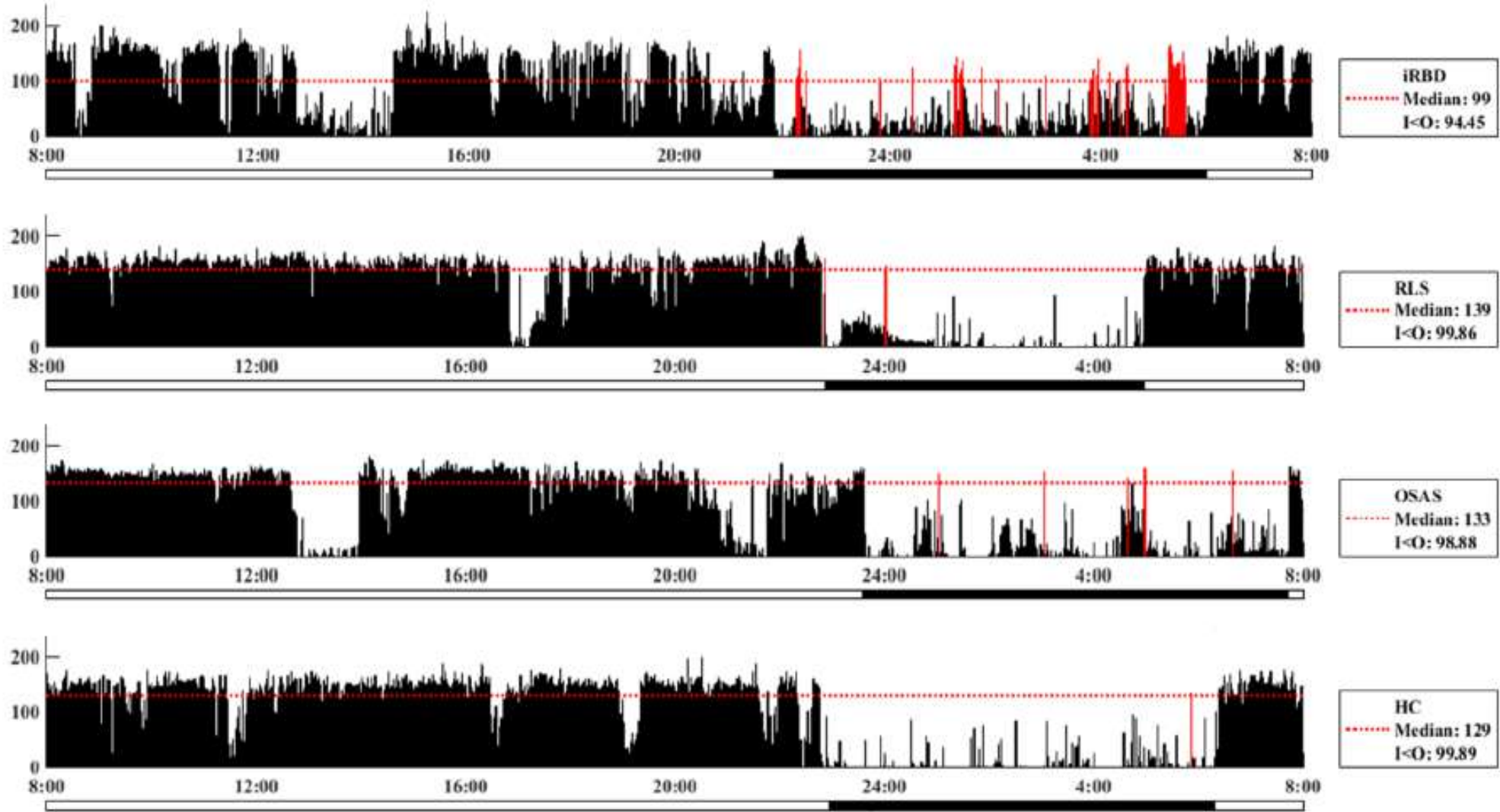
Screening for actigraphy

Ambra Stefani¹, An
Thomas Mitterling
Claudia Trenkwald
Werner Poewe¹, Os

2020

Objective res

M. Filardi^a



HC (37)

iRBD
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SA and

Figure 2 Activity data of four representative participants. Red bars indicate epochs with motor activity higher than the median of diurnal motor activity. HC, healthy controls; iRBD, isolated rapid eye movement sleep behavior disorder; RLS, restless leg syndrome; SAS, sleep apnea syndrome.



Actigraphy in Neurodegenerative Diseases

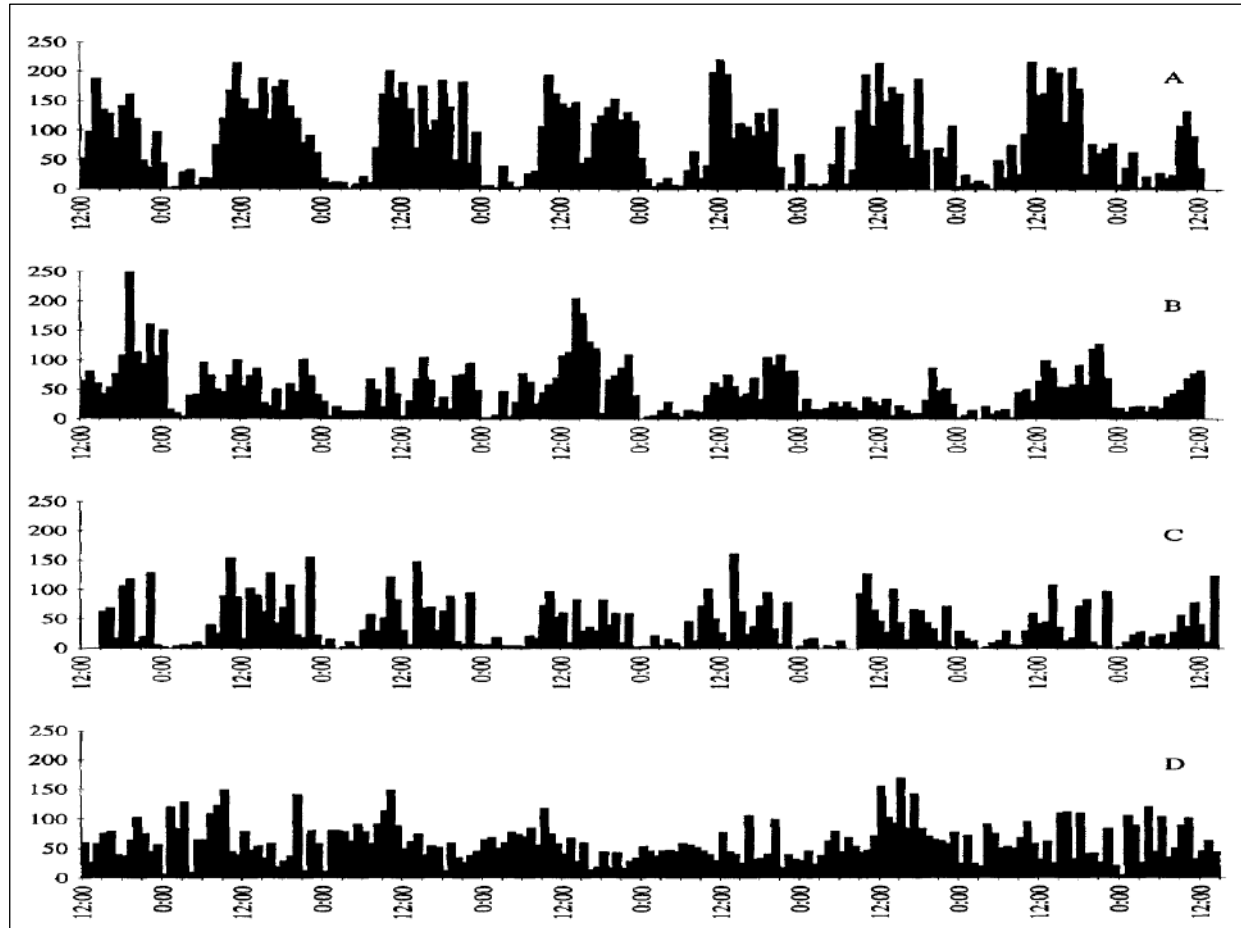


Biological Psychiatry
A Journal of Psychiatric Neuroscience and Therapeutics

ORIGINAL ARTICLE | VOLUME 40, ISSUE 4, P259-270, AUGUST 15, 1996

Circadian rest—activity rhythm disturbances in alzheimer's disease

Eus J.W. van Someren ^{1,2} • Eveline E.O. Hagebeuk ¹ • Cees Lijzenga ¹ • ... Anne-Margriet Pot ¹ • Majid Mirmiran ¹ • Dick F. Swaab ¹ • Show all authors



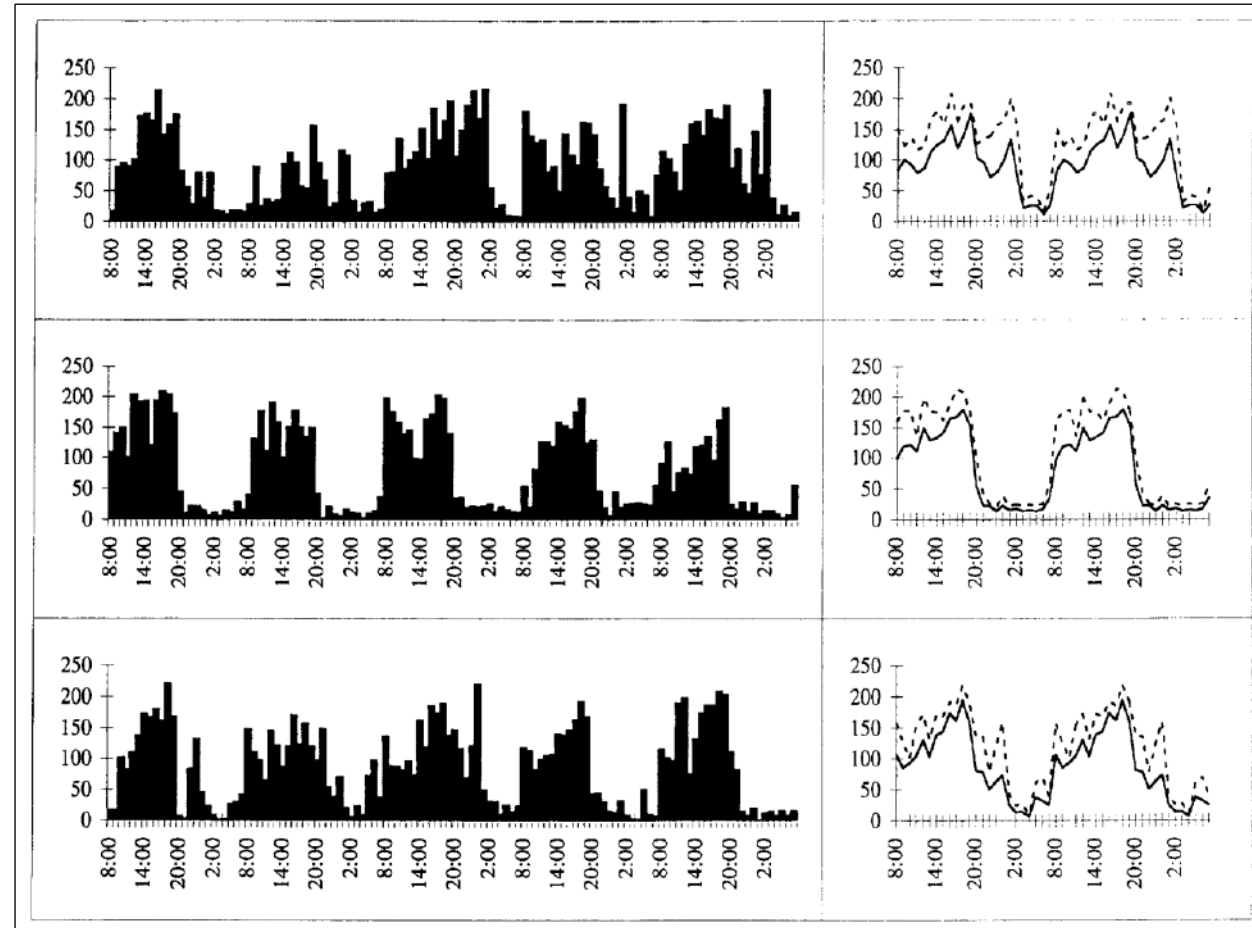
Biological Psychiatry
A Journal of Psychiatric Neuroscience and Therapeutics

ORIGINAL ARTICLE | VOLUME 41, ISSUE 9, P955-983, MAY 01, 1997

Indirect bright light improves circadian rest-activity rhythm disturbances in demented patients

Eus J.W. Van Someren ^{1,2} • Annemarijke Kessler ¹ • Majid Mirmiran ¹ • Dick F. Swaab ¹

DOI: [https://doi.org/10.1016/S0006-3223\(97\)89928-3](https://doi.org/10.1016/S0006-3223(97)89928-3)



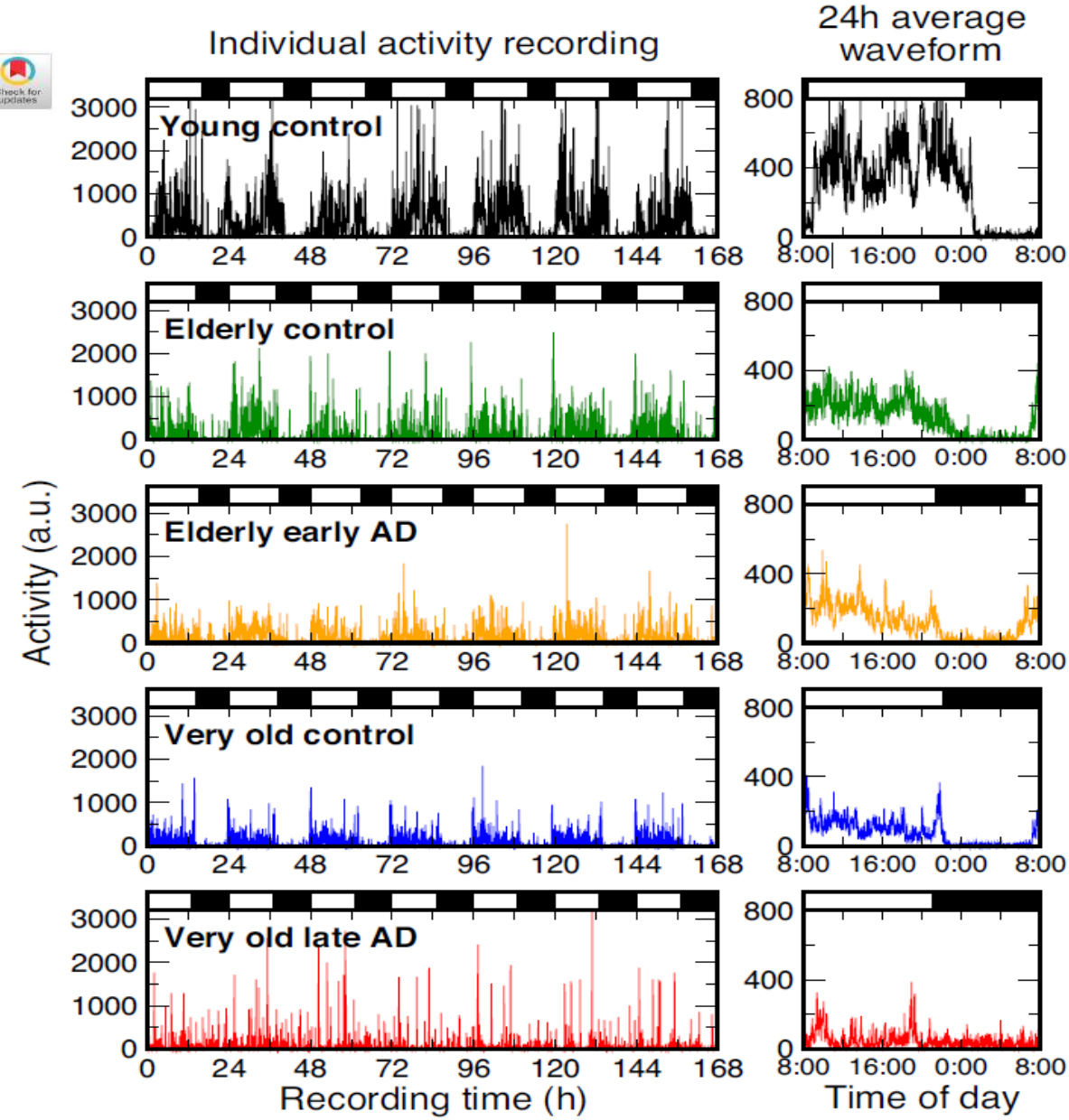
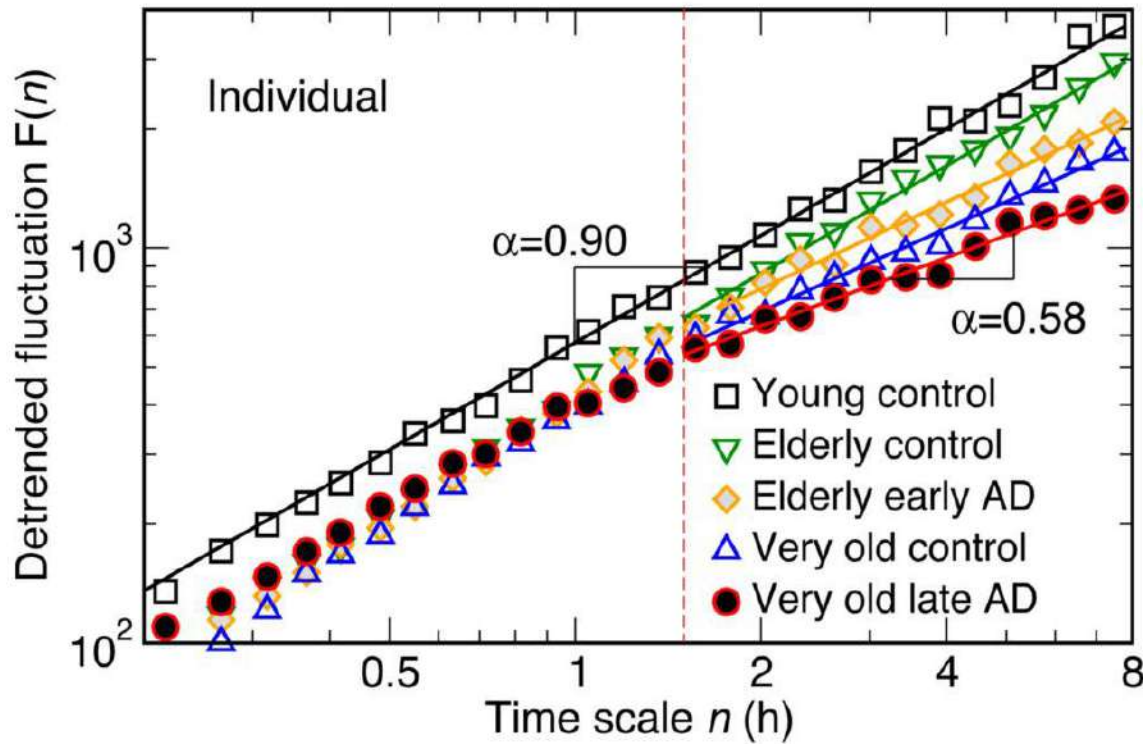


Motor activity Fluctuations in AD



Reduction of scale invariance of activity fluctuations with aging and Alzheimer's disease: Involvement of the circadian pacemaker

Kun Hu^{a,1}, Eus J. W. Van Someren^{b,c}, Steven A. Shea^a, and Frank A. J. L. Scheer^a





Motor activity fluctuations: frailty, disability, and mortality



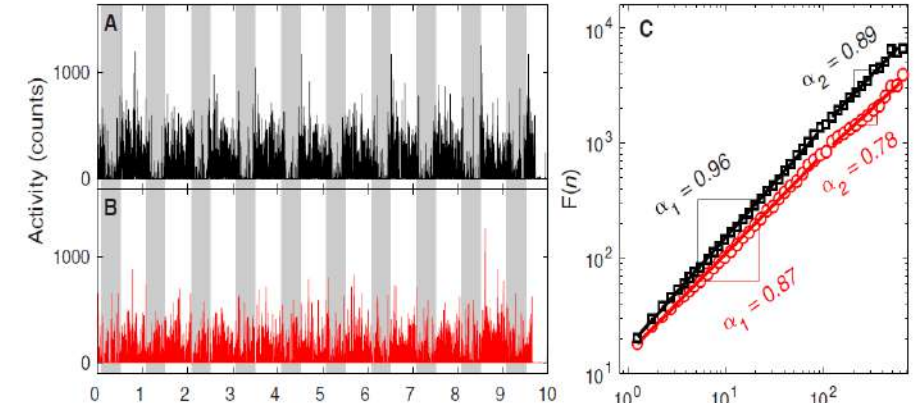
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Azienda Ospedaliera

SCIENCE TRANSLATIONAL MEDICINE | RESEARCH ARTICLE

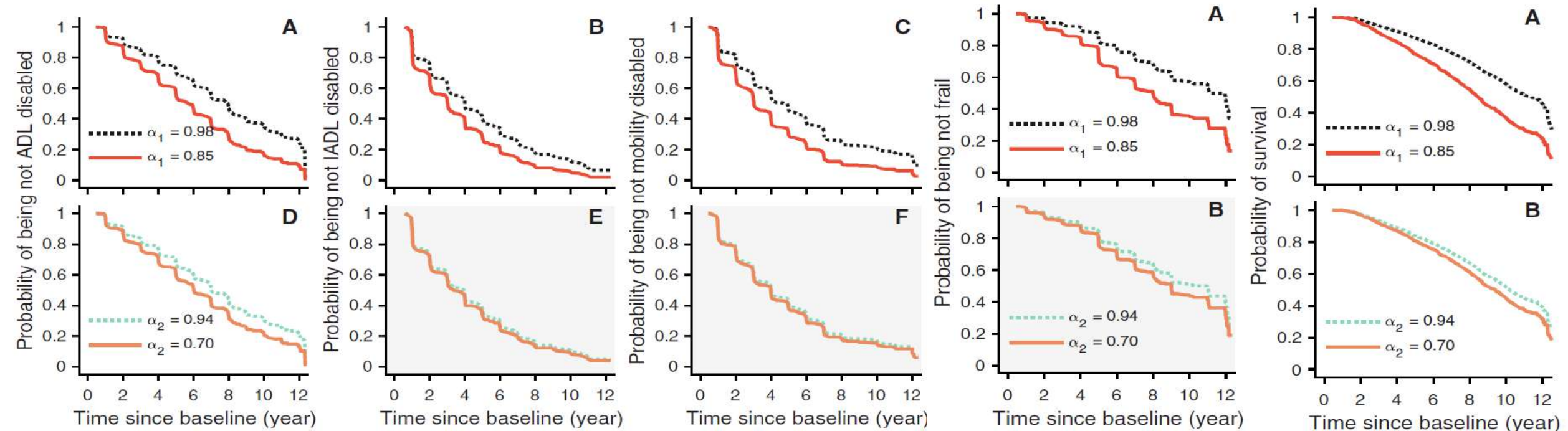
PHYSIOLOGY

More random motor activity fluctuations predict incident frailty, disability, and mortality

Peng Li^{1,2*}, Andrew S. P. Lim³, Lei Gao^{1,4}, Chelsea Hu¹, Lei Yu⁵, David A. Bennett⁵,
Aron S. Buchman⁵, Kun Hu^{1,2*}



SCIENCE TRANSLATIONAL MEDICINE | RESEARCH ARTICLE





Sleep-Wake Behavior and Circadian Rest-Activity Pattern in bvFTD



Sleep (M Thorpy and M Billiard, Section Editors) | [Published: 02 August 2016](#)

Sleep Disturbances in Frontotemporal Dementia

[Stuart J. McCarter](#) , [Erik K. St. Louis](#) & [Bradley F. Boeve](#)

[Current Neurology and Neuroscience Reports](#) **16**, Article number: 85 (2016) | [Cite this article](#)

2152 Accesses | **35** Citations | **4** Altmetric | [Metrics](#)

Differential Circadian Rhythm Disturbances in Men with Alzheimer Disease and Frontotemporal Degeneration

David G. Harper, PhD; Edward G. Stopa, MD; Ann C. McKee, MD; [et al](#)

NREM sleep transient events in fronto-temporal dementia: beyond sleep stage architecture

[Michelangelo Maestri](#) ¹, [Luca Carnicelli](#), [Nicholas-Tiberio Economou](#), [Anastasios Bonakis](#), [Thomas Paparrigopoulos](#), [Sokratis T Papageorgiou](#), [Filippo Sean Giorgi](#), [Elisa Di Coscio](#), [Gloria Tognoni](#), [Raffaele Ferri](#), [Ubaldo Bonuccelli](#), [Enrica Bonanni](#)

- **Insomnia** and **EDS** common in patients with FTD.
- Sleep is severely fragmented, **likely secondary to behavioral disturbances, other primary sleep disorders and neurodegeneration of nuclei involved in sleep and wakefulness**

- Rest-Activity rhythm of FTD patients was **highly fragmented, phase-advanced** in comparison with controls and **uncoupled from the rhythm of CBT**

- **Sleep** in FTD patients is **altered at different levels**, involving **not only the conventional sleep stage architecture parameters** (total sleep time, single stage percentage, NREM/REM cycle organization), but also **microstructure (CAP and Arousal Index)**



Material and Methods



Sample

- Thirty patients with probable bvFTD (Rascovsky, 2011)
- Twenty-three age- and sex- matched healthy controls recruited from the local community

Assessment

- Neurological evaluation
- Neuropsychological evaluation
- Nutritional/Geriatric evaluation
- High-field (3-Tesla) brain MRI
- CSF biomarkers of neurodegeneration assay

Analysis

QAC, NPCRA, TSA

	bvFTD (<i>n</i> = 30) Mean ± SD	HC (<i>n</i> = 23) Mean ± SD	<i>p</i>
Male/Female	19/11	9/14	<i>ns</i>
Age, <i>y</i>	68.43 ± 9.68	66.35 ± 6.93	<i>ns</i>
Education, <i>y</i>	8.83 ± 4.19	13.36 ± 4.25	<0.0005
ASRS	34.20 ± 12.22	16.41 ± 12.23	<0.0001
ASRS – Inattention	18.67 ± 7.49	8.45 ± 7.24	<0.0001
ASRS – Hyperactivity/Impulsivity	15.53 ± 7.05	7.95 ± 5.92	<0.0005
DAS	43.38 ± 10.09	19 ± 7.30	<0.0001
DAS – Executive	15 ± 4.54	6.30 ± 5.83	<0.0001
DAS – Emotional	10.34 ± 3.31	5.91 ± 2.52	<0.0001
DAS – Initiation	18.03 ± 5.96	6.78 ± 3.70	<0.0001
CDR	1 ± 0.66		
CDR – Sum of Boxes	4.58 ± 3.08	NA	
CDR – <u>Comportamento</u>	1.52 ± 0.68		
CDR – <u>Linguaggio</u>	0.71 ± 0.62		
A β	956.57 ± 400.93		
Tau	425.52 ± 197.34	NA	
Phospho-tau	48.81 ± 32.53		



Sleep Diary



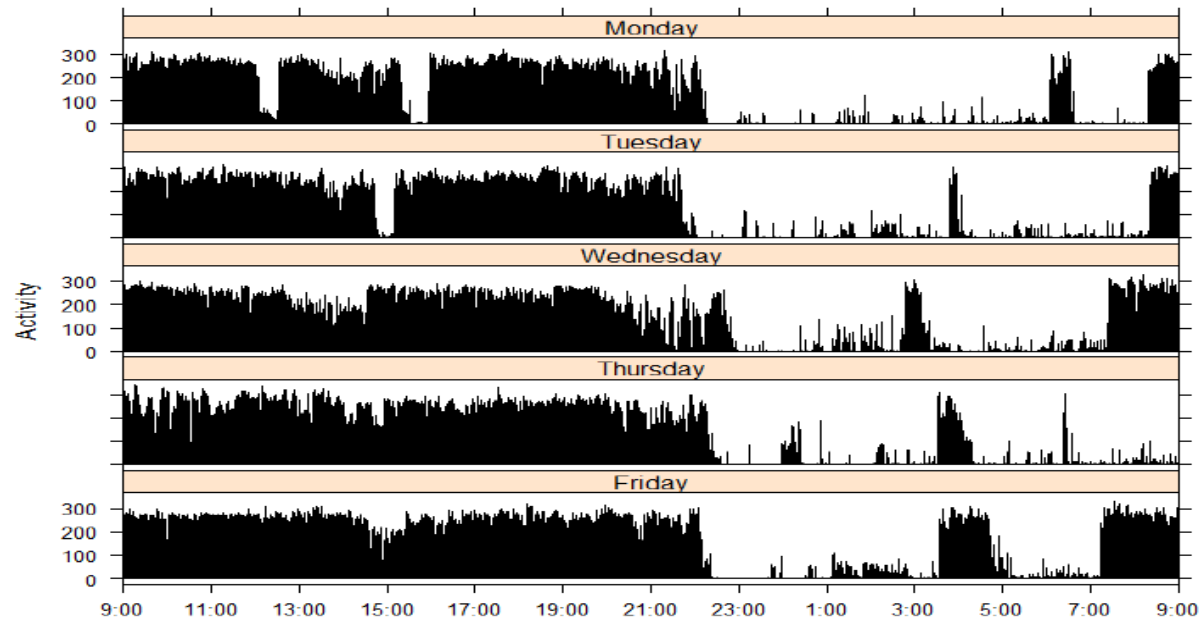
	bvFTD (<i>n</i> = 27) Mean ± SD	HC (<i>n</i> = 23) Mean ± SD	<i>t</i> ₍₄₈₎	<i>p</i>
<i>Sleep Timing</i>				
BT, <u>hr:m</u>	22:24 ± 1:12	23:36 ± 00:44	-4.168	<0.0005
GUT, <u>hr:m</u>	7:59 ± 01:21	6:46 ± 00:30	4.126	<0.0005
TIB, min	576.75 ± 105.92	425.16 ± 52.66	6.232	<0.0001
<i>Nighttime period</i>				
TST, min	504.34 ± 98.35	343.88 ± 67.26	6.612	<0.0001
SOL, min	17.38 ± 12.51	22.66 ± 22.43	-1.049	<i>ns</i>
WASO, min	23.74 ± 21.01	33.03 ± 45.28	-0.953	<i>ns</i>
SE, %	87.76 ± 8.27	81.27 ± 15.39	1.896	<i>ns</i>
NWAK, n	1.53 ± 1.15	1.56 ± 1.30	-0.107	<i>ns</i>
TWAK, min	32.43 ± 40.86	25.59 ± 20.02	0.730	<i>ns</i>
<i>Daytime period</i>				
<u>Nap</u> , n	7.22 ± 6.61	6.13 ± 5.50	0.628101	<i>ns</i>
<u>NapD</u> , n	83.99 ± 53.26	72.54 ± 36.54	0.721899	<i>ns</i>



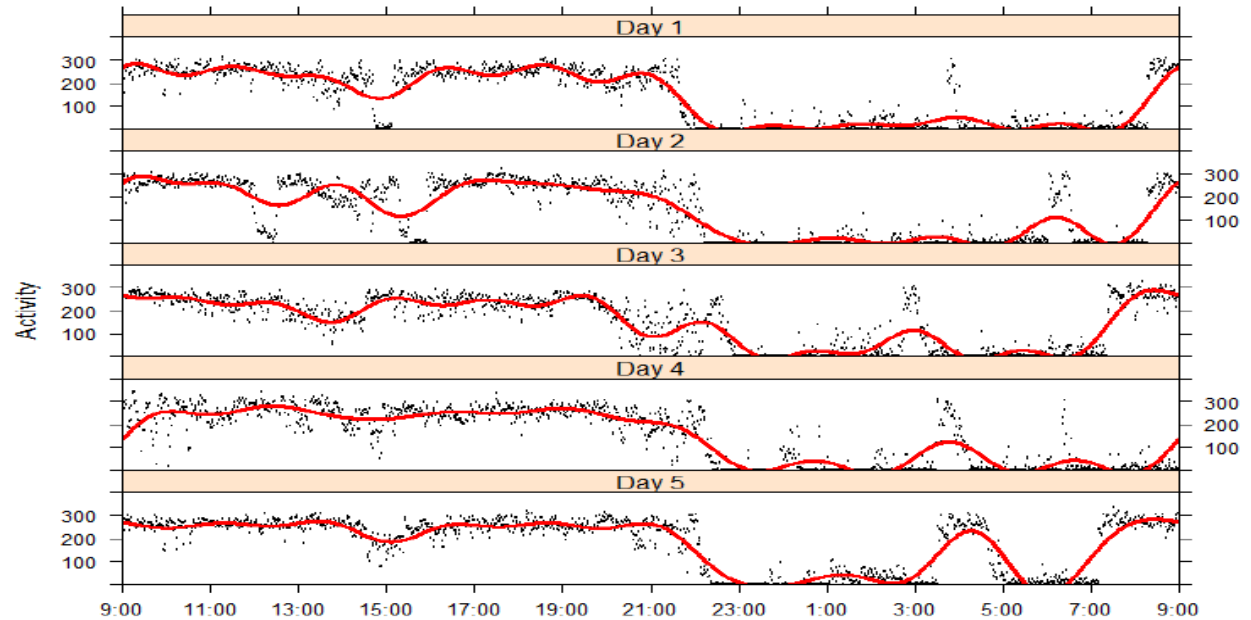
Actigraphy



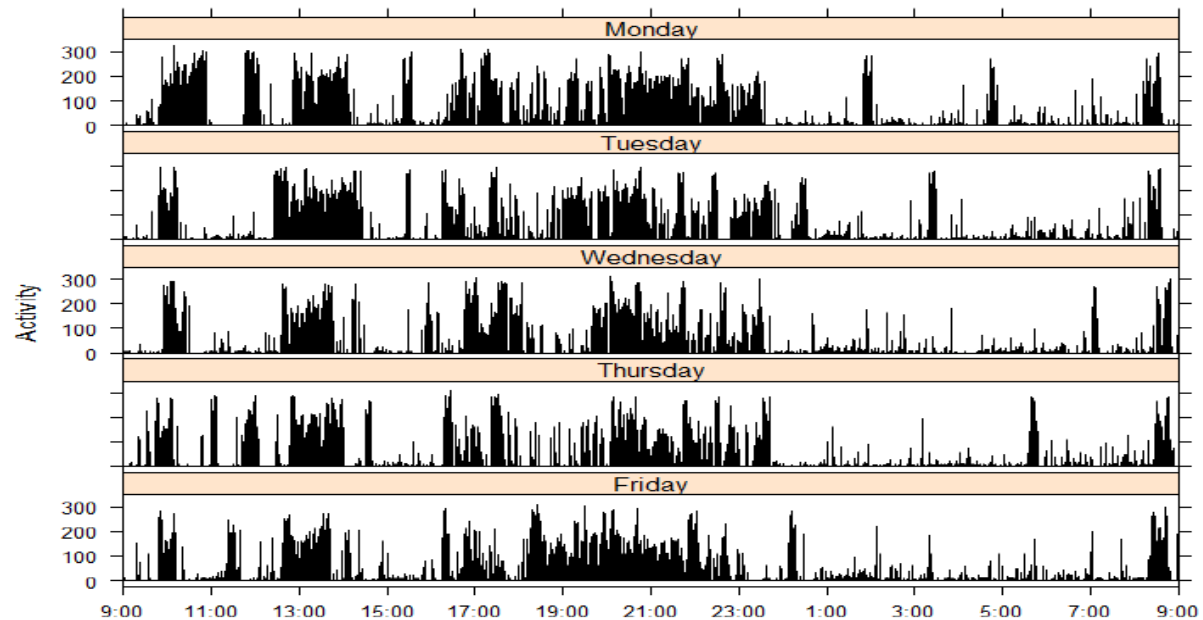
	bvFTD (n = 30) Mean ± SD	HC (n = 23) Mean ± SD	t(51)	p
<i>Sleep Timing</i>				
BT, hr:m	22:23 ± 1:20	23:18 ± 00:55	-2.819	<0.01
GUT, hr:m	7:46 ± 01:06	6:41 ± 00:25	4.497	<0.0001
MS, hr:m	3:06 ± 00:59	2:59 ± 00:29	0.504	ns
TIB, min	563.85 ± 88.38	443.14 ± 63.71	5.535	<0.0001
<i>Nighttime period</i>				
eTST, min	460.80 ± 100.11	391.40 ± 53.98	3.002	<0.005
eSOL, min	31.27 ± 26.07	24.84 ± 18.73	0.999	ns
eSE, %	81.83 ± 12.49	88.63 ± 6.39	-2.377	<0.05
eWASO, min	69.11 ± 53.91	28.60 ± 20.84	3.407	<0.005
eNWAK, n°	14.05 ± 5.42	9 ± 4.10	3.723	<0.0005
eProlonged NWAK, n°	4.29 ± 2.54	2.24 ± 1.97	3.200	<0.005
eLongest sleep, min	149.38 ± 58.08	157.87 ± 55.44	-0.538	ns
SMA, counts	25.76 ± 13.41	17.04 ± 5.87	2.907	<0.01
<i>Daytime period</i>				
DMA	197.06 ± 34.71	192.57 ± 23.33	0.533	ns
eDTST, min	70.35 ± 66.14	86.52 ± 57.47	-0.932	ns
eNap, n°	9.83 ± 9.16	8.04 ± 7.52	0.760	ns
eNapD, min	33.24 ± 25.53	40.96 ± 25.56	-1.090	ns
24hr TST, min	533.65 ± 133.04	477.24 ± 66.89	1.858	ns
<i>Non-Parametric Circadian Rhythm Measures</i>				
IS	0.78 ± 0.11	0.80 ± 0.05	-1.055	ns
IV	0.53 ± 0.17	0.54 ± 0.11	-0.215	ns
RA	0.81 ± 0.11	0.87 ± 0.06	-2.088	<0.05
I<O	97.80 ± 1.73	98.96 ± 0.74	-3.018	<0.005

Activity Data from Monday to Friday - bvFTD (64.09 y)

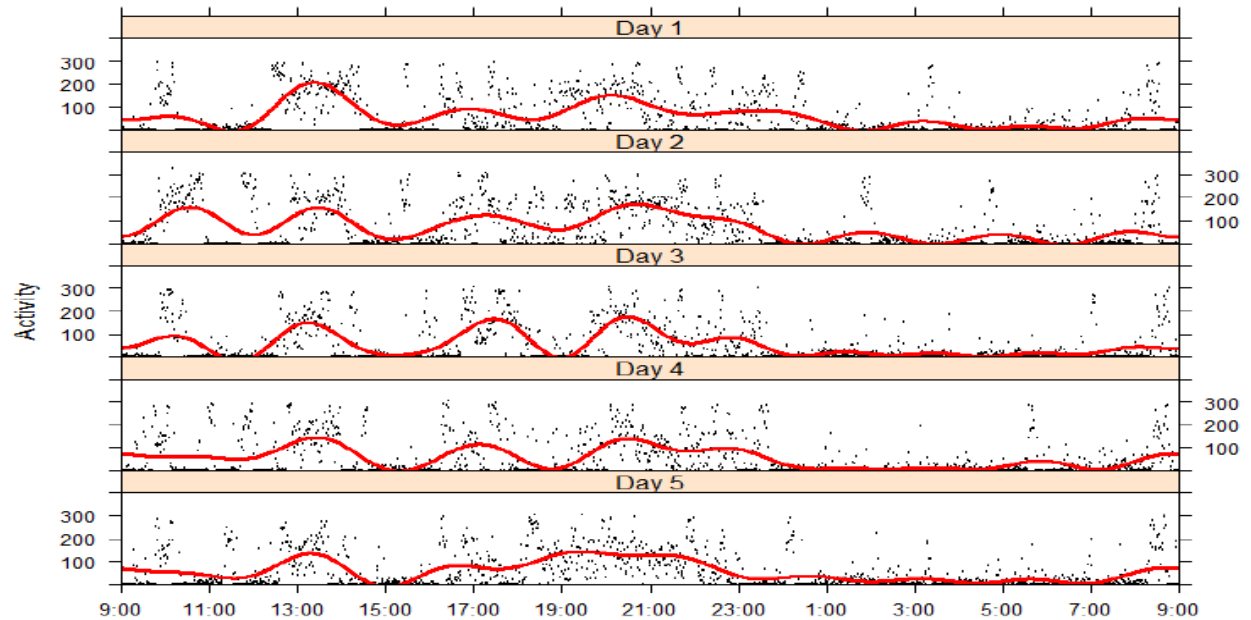
(a)

Fourier Expansion Model [nbasis=21]

(a)

Activity Data from Monday to Friday - bvFTD (61.09 y)

(b)

Fourier Expansion Model [nbasis=21]

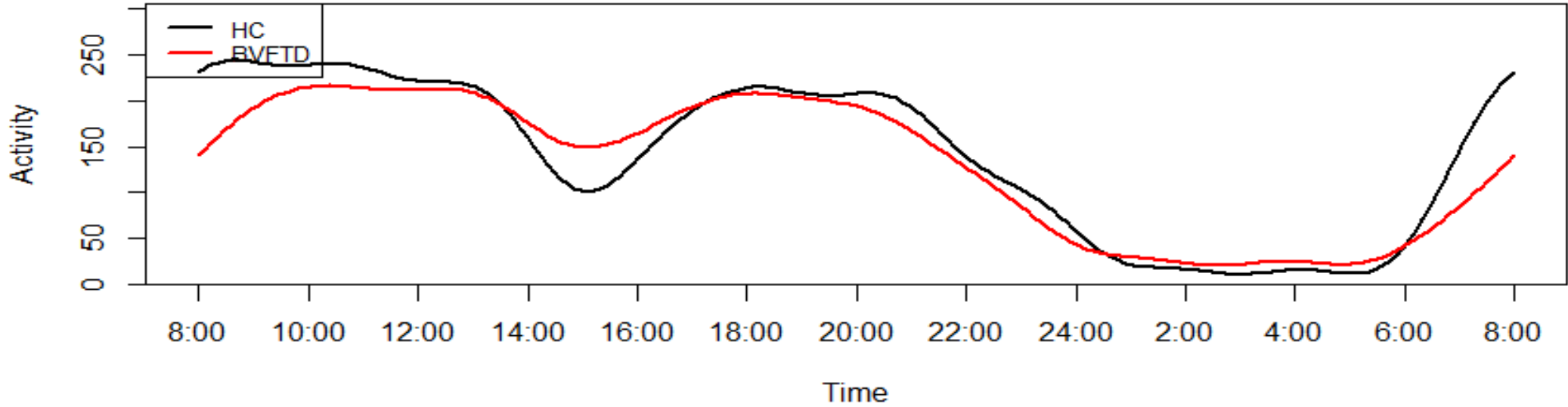
(b)



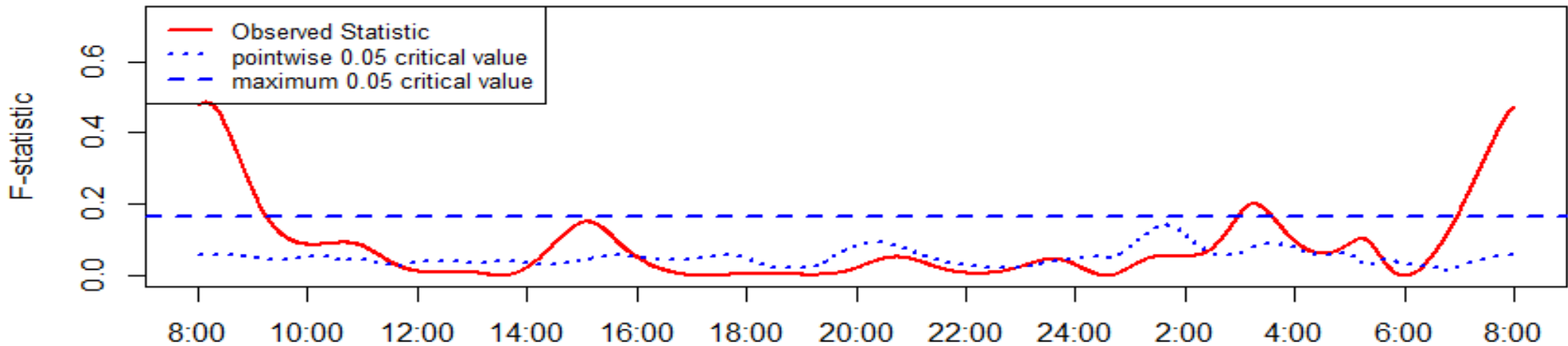
Times Series Analysis



Activity~Diagnosis



Permutation F-Test





Grazie per L'attenzione



Direttore: Prof. Giancarlo Logroscino

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MARIA ELISA FRISULLO

MARIA ROSARIA BARULLI