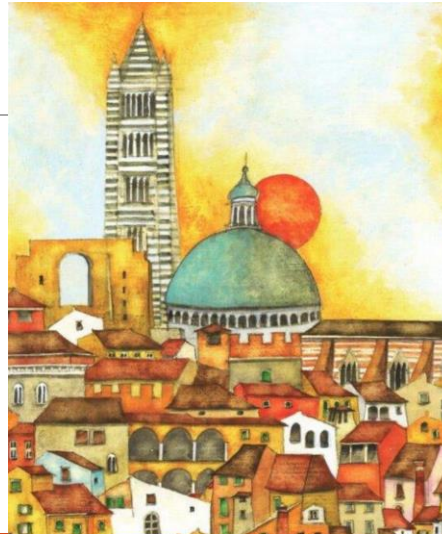




The role of K-complexes density in REM Sleep Behavior Disorder

Serena Scarpelli, F. Pietrogiacomi, M. Gorgoni, E. Fasiello, M. Camaioni, F. Reda, V. Alfonsi, F. Casoni, M. Zucconi, L. Ferini-Strambi, L. De Gennaro

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XXXI CONGRESSO NAZIONALE SIPP
Siena 9-11 novembre 2023
Museo Santa Maria della Scala

Progetto finanziato dal fondo
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Contents lists available at [ScienceDirect](#)

Sleep Medicine Reviews

journal homepage: www.elsevier.com/locate/smr



CLINICAL REVIEW

The risk of neurodegeneration in REM sleep behavior disorder: A systematic review and meta-analysis of longitudinal studies



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Luigi Ferini-Strambi ^{a, b, *}

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^c Maastricht University, Department of Neuropsychology and Psychopharmacology, Maastricht, the Netherlands

- Isolated RBD (iRBD) is a REM parasomnia characterized by vivid dream activity and dream enactment provoked by the loss of physiological REM atonia
- iRBD represents a prodromal manifestation of neurodegenerative diseases that fall under alpha-synucleinopathies, preceding their onset by many years

A growing literature suggests the importance of NREM sleep in protecting the aging brain from neurodegeneration and cognitive decline



Non-REM sleep electrophysiology in REM sleep behaviour disorder: A narrative mini-review

Maurizio Gorgoni^{a,b,*}, Andrea Galbiati^{c,d}

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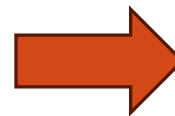
^c "Vita-Salute" San Raffaele University, Milan, Italy

^d IRCCS San Raffaele Scientific Institute, Department of Clinical Neurosciences, Neurology – Sleep Disorders Center, Milan, Italy

Recent high-density EEG studies found in RBD patients during NREM sleep:

- Alterations of slow oscillations morphology (i.e., reduced amplitude) and reduced sleep spindles power;
- Reduced overnight decline of the slow wave activity (SWA)

→ Specific NREM sleep oscillations may be disrupted in RBD: possible role in neurodegeneration?



In Parkinson's disease: Reduced regional SWA in the lower delta frequencies; a strong association of worse cognitive performance with reduced 1–2 Hz SWA with strongest association over frontal areas (Schreiner et al. 2019).

REPORT

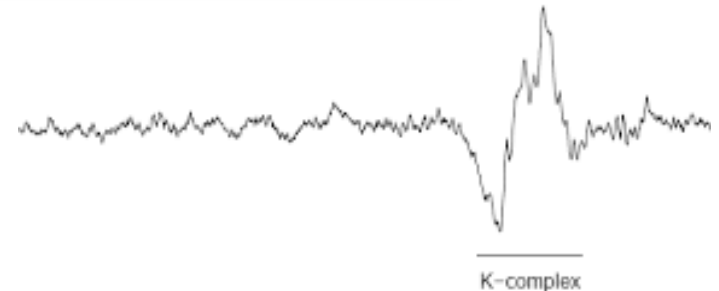
Slow wave sleep disruption increases cerebrospinal fluid amyloid- β levels

Yo-Ei S. Ju,^{1,2,*} Sharon J. Ooms,^{3,4,5,*} Courtney Sutphen,^{1,2} Shannon L. Macauley,^{1,2} Margaret A. Zangrilli,¹ Gina Jerome,^{1,2} Anne M. Fagan,^{1,2,6} Emmanuel Mignot,⁷ John M. Zempel,¹ Jurgen A.H.R. Claassen^{3,4,5} and David M. Holtzman^{1,2,6}

The potential role of a specific NREM sleep feature: the K Complex (KC)

- K-complexes (KCs) are hallmarks of NREM 2 sleep stage
- Isolated downstate characterized by a duration >0.5 s, frequency <1 Hz, and frontal predominance
- It can occur spontaneously, or can be elicited by different kinds of stimuli

Precursors of slow waves of NREM sleep



SLEEP, 2019, 1–10

doi: 10.1093/sleep/zsz053
Advance Access Publication Date: 7 March 2019
Original Article

ORIGINAL ARTICLE

The heritability of the human K-complex: a twin study

Maurizio Gorgoni¹, Flaminia Reda¹, Aurora D'Atri¹, Serena Scarpelli¹, Michele Ferrara^{2,*} and Luigi De Gennaro^{1,*}

Genetic influence on human KC morphology

KCs as a possible endophenotype in pathological conditions.

When compared to healthy controls (HC), **Alzheimer's Disease (AD)** patients exhibit a decreased density of spontaneous KCs during Stage 2 NREM sleep, associated with a global cognitive decline evaluated by means of the Mini-Mental State Examination (MMSE)

SCIENTIFIC REPORTS

OPEN

The Fall of Sleep K-Complex in Alzheimer Disease

Luigi De Gennaro¹, Maurizio Gorgoni¹, Flaminia Reda¹, Giulia Lauri¹, Ilaria Truglia¹, Susanna Cordone¹, Serena Scarpelli¹, Anastasia Mangiaruga¹, Aurora D'Atri¹, Giordano Lucidogna², Michele Ferrara², Camillo Marra² & Paolo Maria Rossini^{2,4}

Received: 23 June 2018

Preliminary study on KCs in RBD patients


Available online at www.sciencedirect.com
ScienceDirect
Journal homepage: www.elsevier.com/locate/cortex


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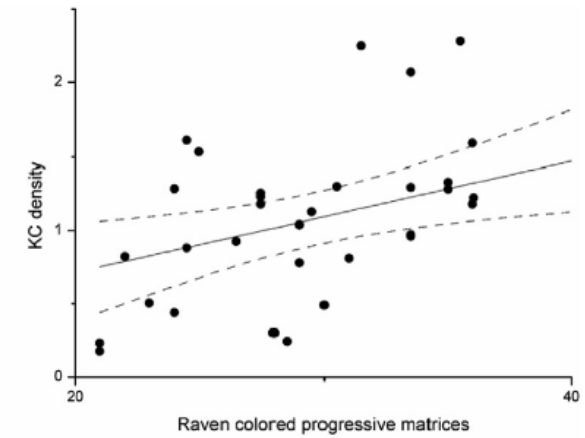
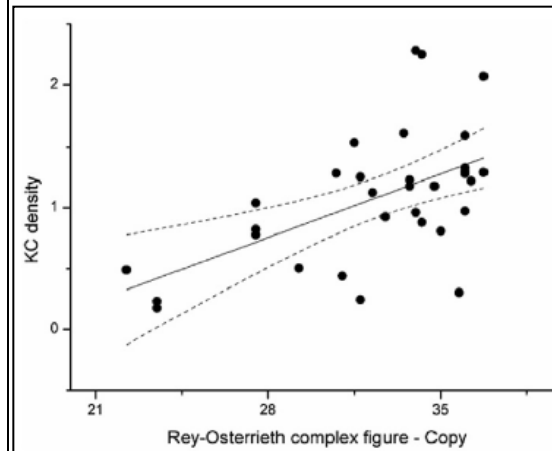
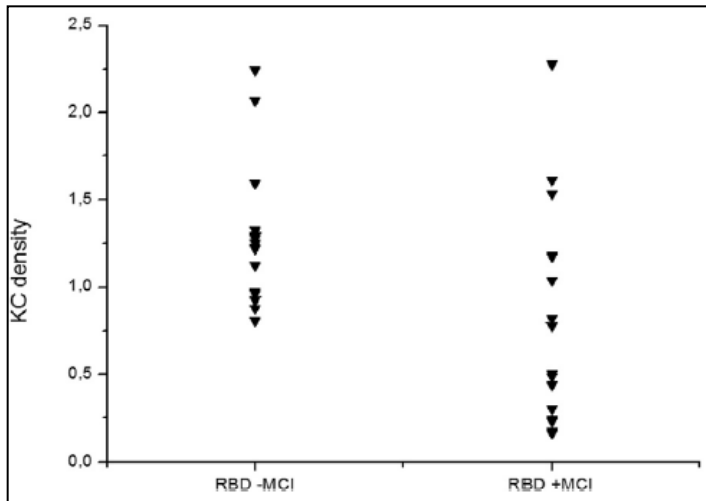
Research Report

Exploring the functional role and neural correlates of K-complexes in isolated rapid eye movement sleep behavior disorder

Andrea Galbiati ^{a,b,*}, Giulia Carli ^{a,c}, Elisabetta Fasiello ^{b,d}, Francesca Casoni ^b, Marco Zucconi ^b, Luigi De Gennaro ^d, Daniela Perani ^{a,c,e} and Luigi Ferini-Strambi ^{a,b}







- iRBD patients with cognitive decline displayed a reduced KC density in comparison with iRBD patients without cognitive impairment.
- KC density showed a significant positive correlation with global cognitive functioning, specifically with visuo-spatial and executive performances, two cognitive domains known to be relevant in predicting conversion into neurodegenerative disorders.

ABSENCE OF A CONTROL GROUP!

AIM AND STUDY DESIGN

To assess spontaneous KC density alterations during Stage 2 NREM sleep in iRBD patients and their possible relationship with cognitive functioning

Participants

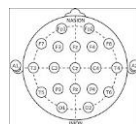
31 iRBD patients vs. 31 age-matched healthy controls (HC)

MMSE
(All)



Neuropsychological/Clinical
Evaluation
(iRBDs)

EEG montage 19-
ch. (All)

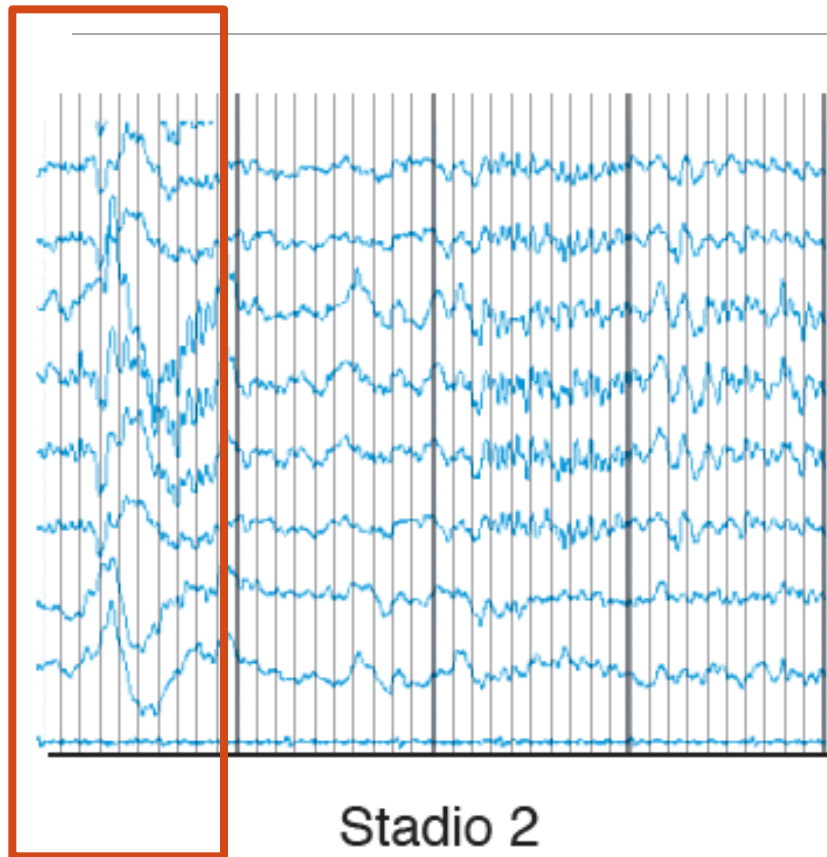


Night PSG (All)



Sleep and
dream diary
(All)

DATA ANALYSES



K-Complexes

- Offline detection by a blind scorer during Stage 2 NREM on the derivations F3, F4, C3, C4, Cz, P3, P4
- Nonstationary event with (a) a marked and well-delineated sharp wave initially negative in polarity, immediately followed by a positive polarity component; (b) maximum amplitude at frontocentral derivations; (c) duration 0.5-3 s.
- KC density: number of KCs divided by Stage 2 NREM sleep minutes

RESULTS

Demographic and clinical variables

Chi-squared (gender) and Student's t-test

	RBD Mean (SD) N=31	HC Mean (SD) N=31	<i>p</i>
Gender, M/F	27/4	23/8	0.20
Age, y	68.64 (6.67)	69.03 (6.12)	0.81
Education, y	9.90 (3.46)	11.03 (4.19)	0.25
MMSE	27.64 (2.03)	29.10 (1.35)	*0.002

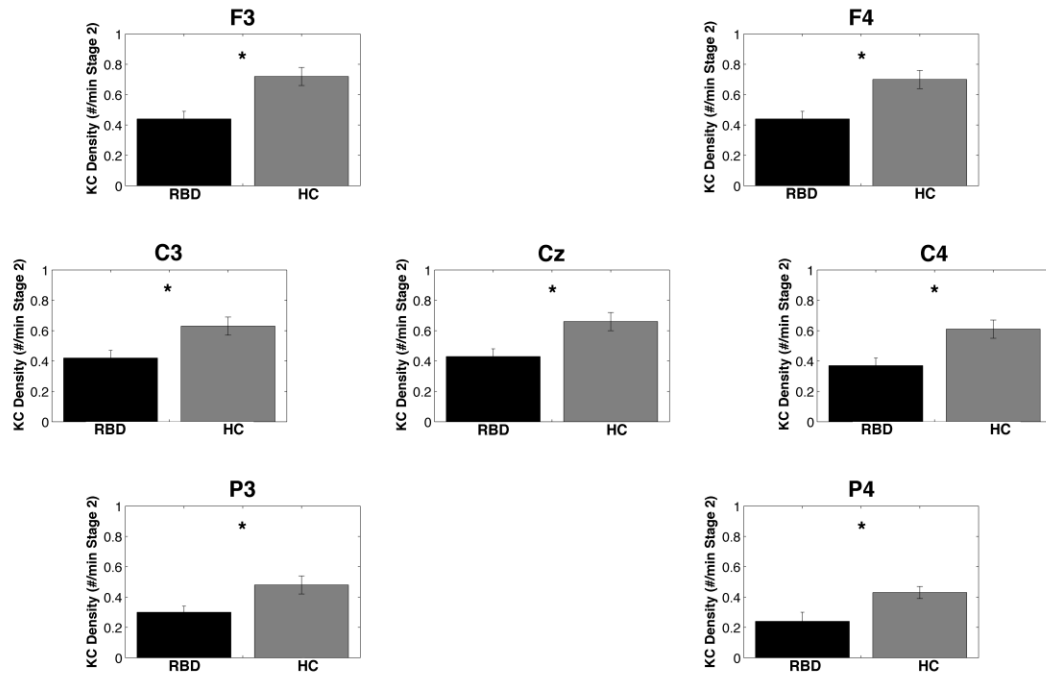
- Absence of significant differences between iRBD and HC concerning demographic variables
- Significantly reduced MMSE scores in iRBD patients compared to HC

RESULTS

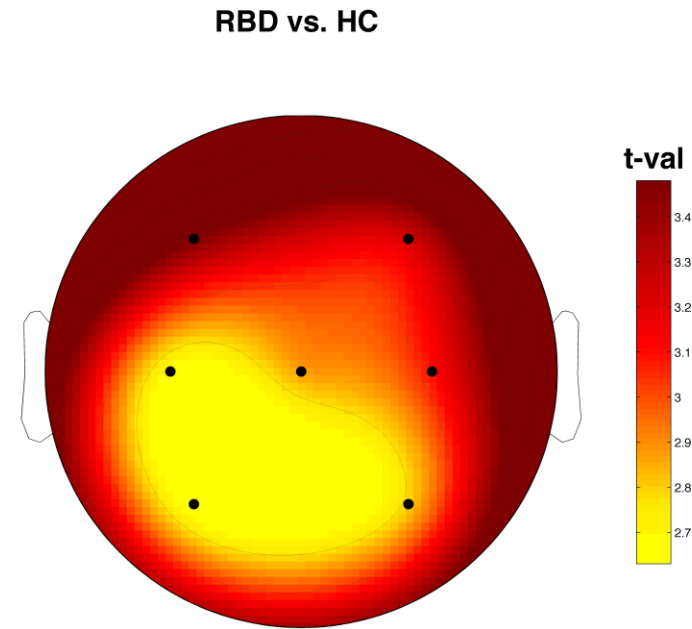
KC Density

Student's t-test (iRBD vs. HC)

A



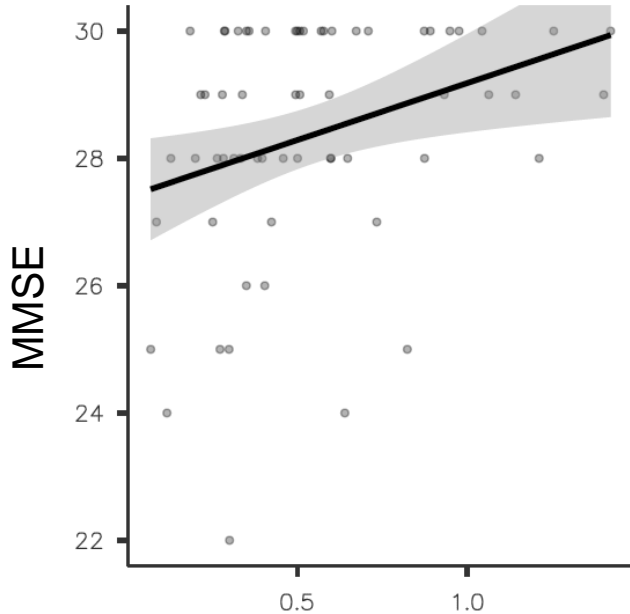
B



Compared to HC, iRBD patients showed a significantly reduced KC density in frontal, central, and parietal derivations

RESULTS

Correlational Analyses (Pearson's r)

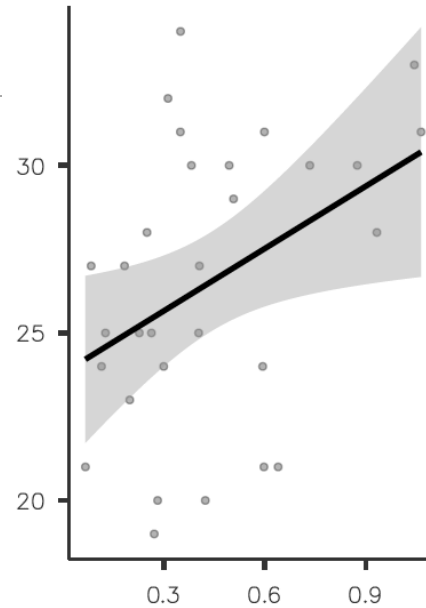


KC Density (Cz)

$r = 0.32$

$p = 0.01^*$

Raven's Progressive Matrices

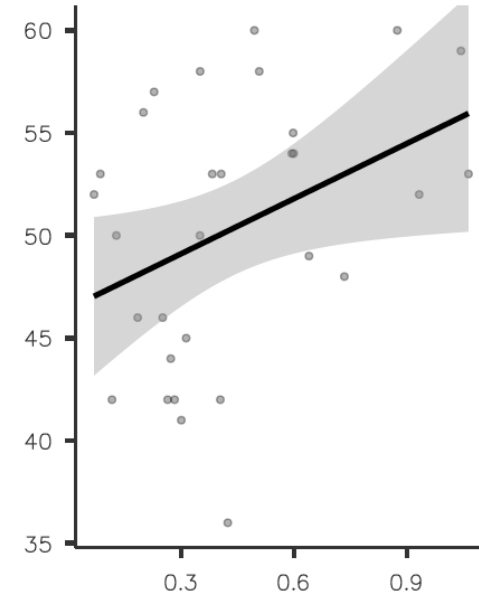


KC Density (Cz)

$r = 0.40$

$p = 0.03^*$

Attentional Matrices



KC Density (Cz)

$r = 0.38$

$p = 0.04^*$

KC density at Cz was positively correlated to MMSE scores (whole sample)

In iRBD patients, KC density at Cz was positively correlated to attention and executive functions performance

CONCLUSIONS

- iRBD patients are characterized by a generalized reduction of KC density compared to HC
- Such reduction was associated with cognitive functioning, particularly in specific cognitive domains (i.e., attention and executive functions) considered relevant for the prediction of conversion into α -synucleinopathies (Galbiati et al., 2019)
- KC alteration as a possible marker of neurodegeneration in iRBD?
 - A further characterization of the KC features (i.e., quantitative, morphological) in iRBD and their possible relationship with cognitive functioning is needed



- Absence of neuropsychological measures (only MMSE) for control subjects
- Absence of adaptation nights
- Absence of longitudinal measures



SAPIENZA
UNIVERSITÀ DI ROMA



I.R.C.C.S. Ospedale
San Raffaele



***THANKS
FOR YOUR ATTENTION!***

Neuropsychological Assessment

RBD+HC

MMSE

11 items evaluating:

- orientation to time and place
- registration/encoding
- attention
- calculation
- spontaneous recall
- language (naming, repetition, reading, and spontaneous writing)
- visual construction

RBD

Evaluation of:

- **Language:** The Token test
- **Verbal Learning:** The immediate and delayed recall of Rey Auditory Verbal Learning test
- **Verbal and Visuo-Spatial memory:** the Rey–Osterrieth complex figure recall, the digit span forward and the Corsi block tapping test
- **Visuo-Spatial abilities:** the Rey–Osterrieth complex figure Copy
- **Executive functions:** The Attentional Matrices, the Raven Colored Progressive Matrices and the digit span backward
- **Verbal fluency:** The phonemic and semantic cues