New vistas on how stress affects sleep: prenososologic issues

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The slow (<1 Hz) rhythm of non-REM sleep
a dialogue between three cardinal oscillators

Crunelli & Hughes, 2010
Cortical mapping of sleep slow oscillations
Structure and spatial distribution

Menicucci et al., PLoS one 2009;
Piarulli et al., on IEEE Trans BioMed Eng, 2010
How stress modulates the spatial and dynamics features of Sleep Slow Oscillations

Wake

SWS

Physiologic Synaptic Downscaling

↑ Signal/noise

W = 100

W = 120

W = 130

W = 80

Wake SWS wake SWS

Synaptic homeostasis

Slow oscillation
Our experimental model of acute stress
(the “ironmen” model)
Experimental design – flow chart

BDC

- Cardiac MRI
- Echocardiography
- EKG
- Blood pressure

Swimming
3.8 Km

Synch (GBF, PBF, RA, EKG)
Tilt test

RDC

- Cerebral MRI
- Sleep HiDe EEG

- Spirometry
- Gas Exchange (Diffusion, Alveolar gradients)
- MIP-MEP
- Comet tails

- Routinely BS
- ILKs
- Hormones
- Heat Shock Proteins
- …..
Sleep Slow Oscillation Spatial Features

Acute stress effect

Piarulli et al., 2010, IEEE TBME
Gemignani et al., in prep
Sleep Slow Oscillation Mapping

Acute stress effect

Baseline

Psychophysical stress

Baseline

Psychophysical stress

Cortisol

IL-6

Piarulli et al., 2010, IEEE TBME
Gemignani et al., in prep
Hippocampal connectivity

*Acute stress effect*

Baseline

Huge psychophysical stress
Our experimental model of chronic stress

(the MARS 500 model)
Long lasting manned mission in space

*General aim of the research project*

**ARES**

[Astronauts Resistance Enhancement to Stress]
Flow chart of the research project
(for each astronaut)

"pre-flight" Baseline (BDC)

during "flight"

"post-flight" Recovery (RDC)

- Neuropsychologic evaluation of cognitive & emotional functions
- Psychometric evaluation of stress levels
- Autonomic and hormonal monitoring of stress levels
- Sleep Slow Oscillation monitoring
Sleep Slow Oscillation Mapping

Stress effect

Correlation maps

SWS

ORIGINS

DETECTIONS

Correlation maps

SWS

R= -0.49, p<.03

R= -0.55, p<.01

Event rate (event/min)

Detection rate (waves/min)

Cortisol pre-sleep (µg/24hours)
Sleep Slow Oscillation Detection Mapping

Stress effect

R = -0.53, p < .02

Gemignani et al., 2010
Open issue

What do we expect in the case of a long lasting stress-related SSO changes?
Prediction is difficult, especially of the future

Niels Bohr
Synaptic homeostasis
(Tononi & Cirelli, 2003)

Physiologic Synaptic Downscaling

↑Signal/noise

Wake
SWS

Synaptic Weight

W = 100

W = 110

Synaptic homeostasis

Slow oscillation

1 sec
↓ or altered Synaptic Downscaling

Saturation

wake SWS wake SWS

Practice Points

... Sleep-disordered patients show cognitive dysfunctions. Major dysfunctions appear in the areas of attention, vigilance ...

Beyond Diathesis Stress: Differential Susceptibility to Environmental Influences

Jay Belsky and Michael Pluess
Birkbeck University of London

Evolutionary-biological reasoning suggests that individuals should be differentially susceptible to environmental influences, with some people being not just more vulnerable than others to the negative effects of adversity, as the prevailing diathesis-stress view of psychopathology (and of many environmental influences) maintains, but also disproportionately susceptible to the beneficial effects of supportive and enriching experiences (or just the absence of adversity). Evidence consistent with the proposition that individuals differ in plasticity is reviewed. The authors document multiple instances in which (a) phenotypic temperamental characteristics, (b) endophenotypic attributes, and (c) specific gene function less like “vulnerability factors” and more like “plasticity factors,” thereby rendering some individuals more malleable or susceptible than others to both negative and positive environmental influences. Discussion focuses upon limits of the evidence, statistical criteria for distinguishing differential susceptibility from diathesis stress, potential mechanisms of influence, and unknowns in the differential-susceptibility equation.

Keywords: parenting, differential susceptibility, diathesis stress, GxE, psychopathology
Conclusion

How can the Sleep Slow Oscillation study be used to functionally map brain responses to stressful conditions?

- Index of local cortical activity
- Index of learning-related cellular and molecular phenomena
- Index of functional connectivity
- Marker of STRESS VULNERABILITY

In psycho-physiologic conditions

In pathophysiologic conditions (including psychiatry!!!)

To be continued …
Future researches

1. Study of learning effects related to SSO
2. Study of countermeasures of negative effect of stress on SSO (tDCS)
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Our experimental clinical models
(the “FFI” model)
• REM sleep alteration
• Slow Wave Sleep alteration
Familial and sporadic fatal insomnia
Pasquale Montagna, Pierluigi Gambetti, Pietro Cortelli, and Elio Lugaresi


FFI

CJD

Codon 178

Codon 129

Methionine

Valine
FFI pt: hypnogram
FFI pt: PSD during NREM sleep

Fz

db

Hz

FFI pt

δ  θ  σ  β

Ctrls
Cortical mapping of sleep slow oscillations spatial distribution: FFI pt vs healthy controls

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FFI pt

Origins

Detections

Ctrls
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W/min

W/min
Altered SSO grouping effect in FFI

Menicucci et al., Submitted; Gemignani et al., in prep
GROUPING OF BRAIN RHYTHMS IN CORTICOTHALAMIC SYSTEMS
Mircea Steriade, Neuroscience, 2005

Slow + spindle

Cx

RE (spindle sequence)

CTP

TCP

TC

Slow + gamma

Depth EEG

Intra-cell
How can the Sleep Slow Oscillation study be used to functionally map brain functions/dysfunctions in physiologic and pathophysiologic conditions?

- Index of local cortical activity
- Index of learning-related cellular and molecular phenomena
- Index of functional or anatomical disconnectivity (CC or TC or CTC) ???
- Marker of stress vulnerability ???
- Marker of neural loss ???

In physiologic conditions

In pathophysiologic conditions

To be continued ...
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Sleep Slow Oscillation: Open issues

Marker of group fingerprint?

Controls
(No 10, 1 recording for each subject)

Astronauts
(No 4, 5 recordings for each subject)

Menicucci et al., PLoS one 2009;
Material & Methods

Brain
*Wake-Sleep EEG*

Heart
*Echo & Dynamic ECG*

Lung
*MIP-MEP*

Brain-Heart-Lung axis
*Autonomic rhythms synchronization*