

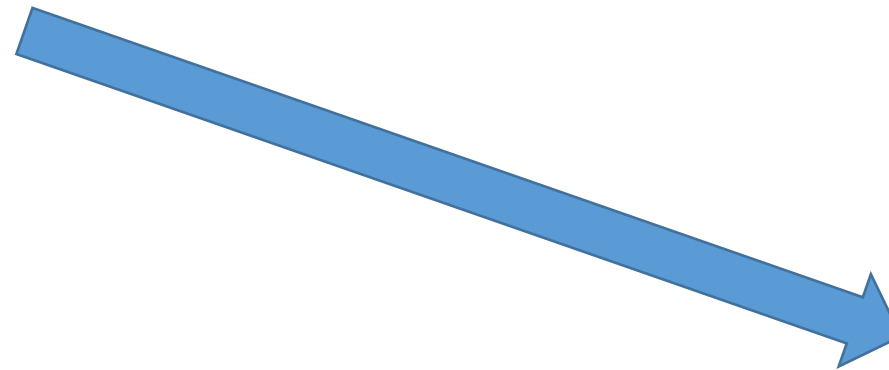
Meet ~~a the expert~~ guy with RAR research experience as evidenced by peer reviewed publications and funded projects that resulted from exposure to ... *people with expert knowledge* ...

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Assistant Professor

Department of Psychiatry, School of Medicine

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Katie Stone
Sonia Ancoli-Israel
Terri Blackwell

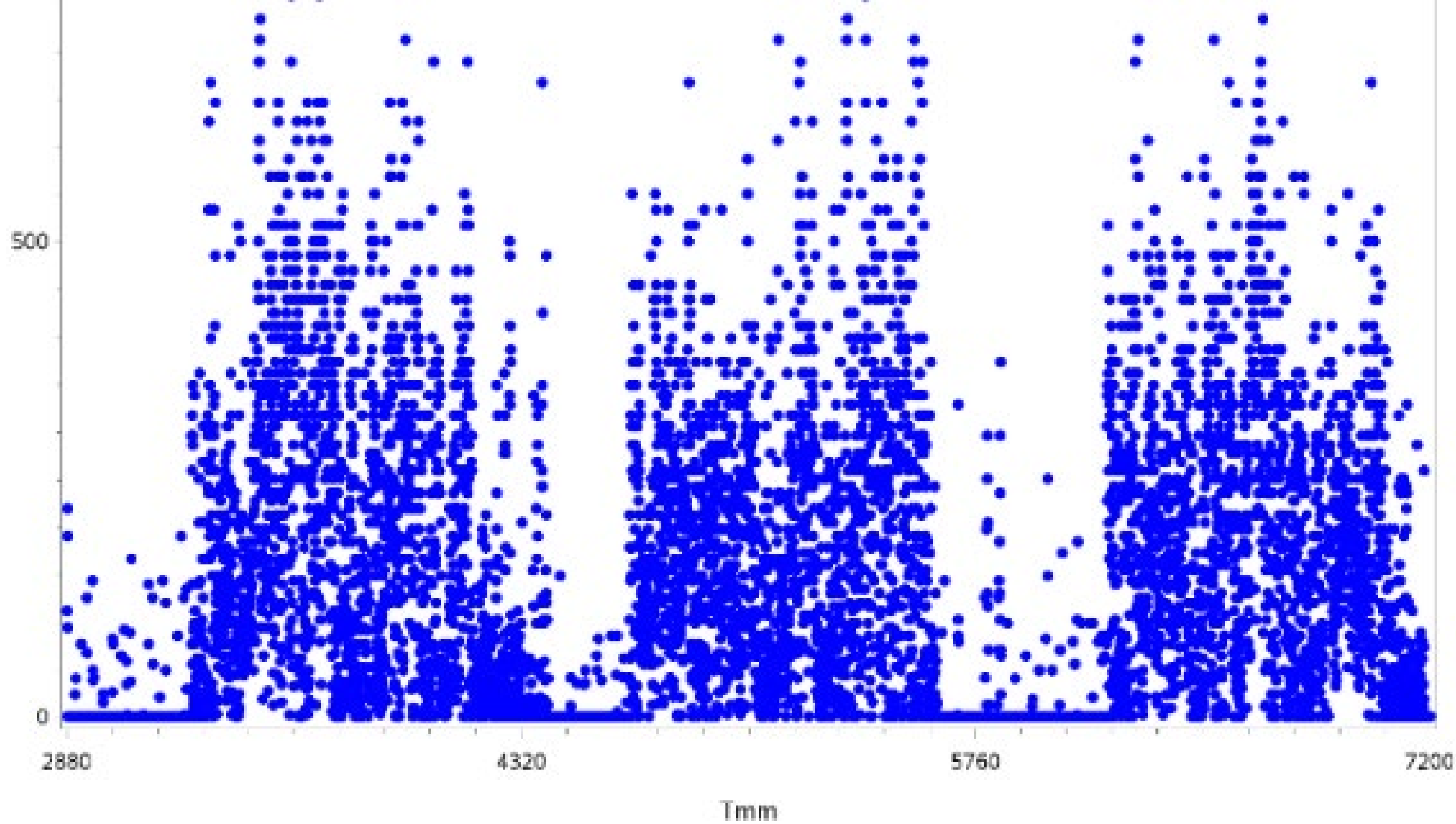
Tica Hall
Robert T. Krafty

Dan Buysse
Chris Dancy

The central box contains a list of names. It is surrounded by stars: a red star at the top, a red star at the bottom, a white star to the left, a white star to the right, and a blue star to the right.

Meet a RAR research guy

- 1) What is a rest-activity rhythm?
- 2) How do we measure rest-activity rhythms?
- 3) How can we use RAR measures in research?

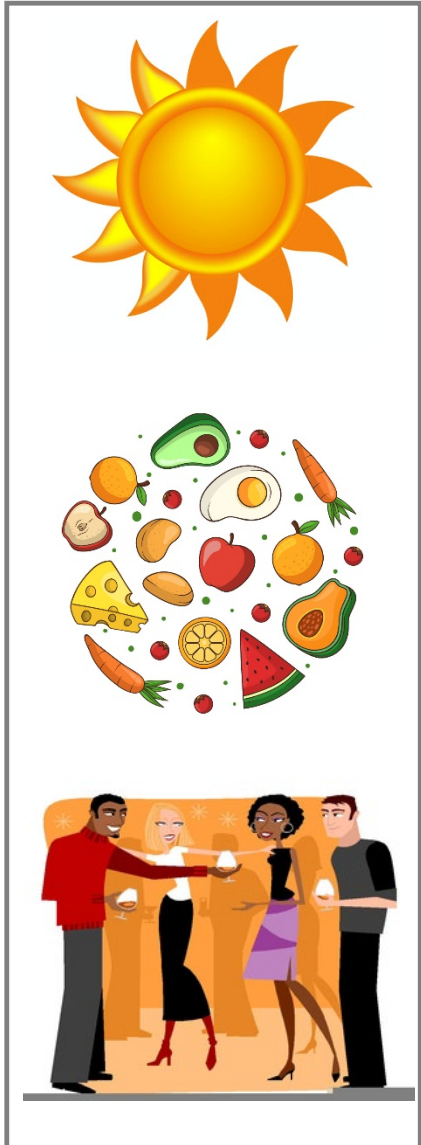


What is a rest-activity rhythms (RAR)?

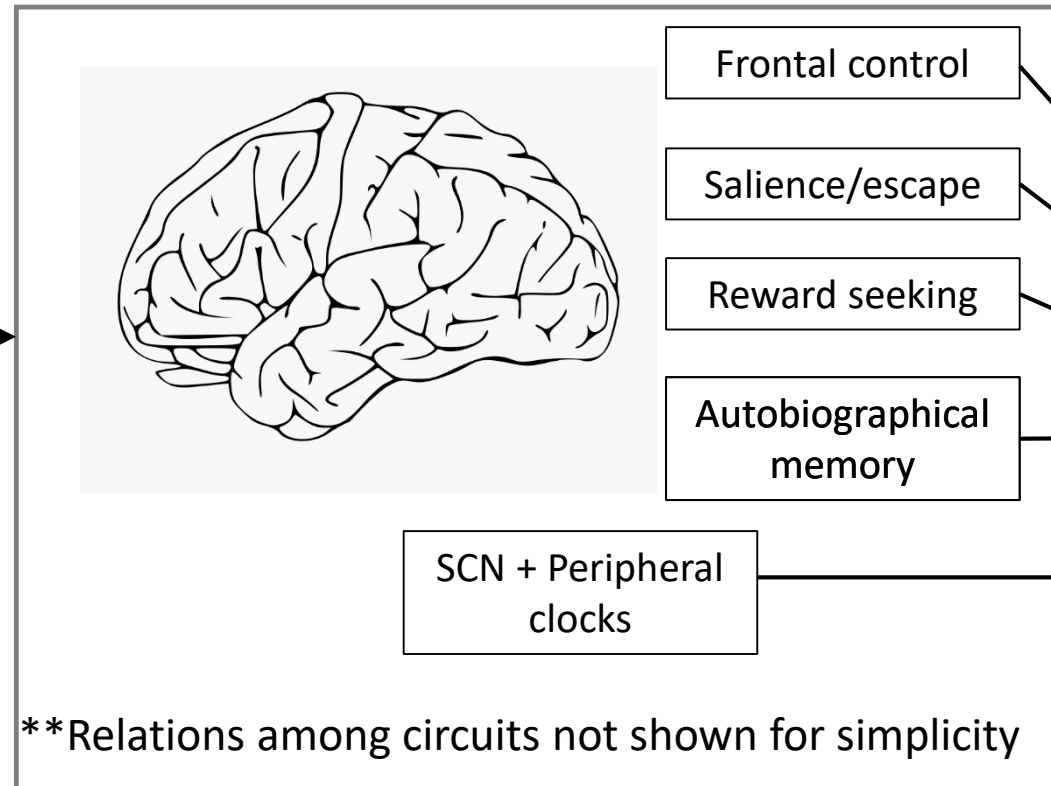
Pattern of psychomotor behavior, and the absence of psychomotor behavior, usually occurring in 24-hour cycles and useful to infer sleep-wake states.

Hypothetical behavioral control mechanism

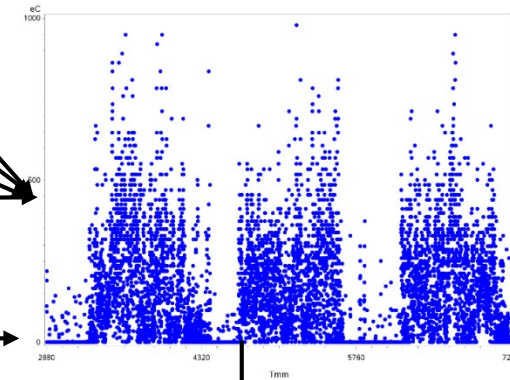
Environmental Input



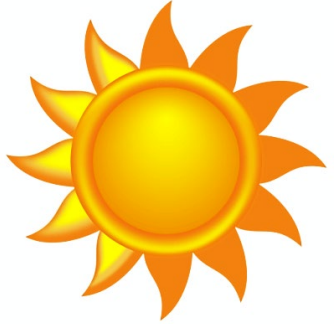
Internal computation



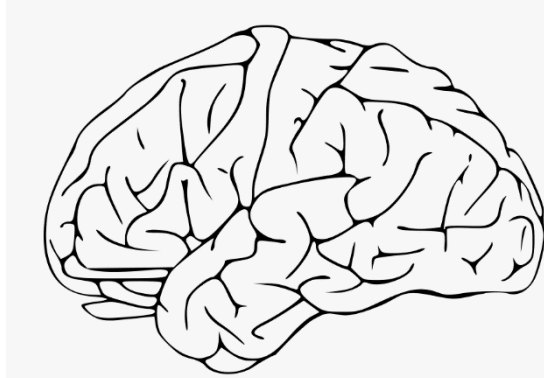
Behavior



Environmental Inputs



Internal computation (voluntary and involuntary)



Frontal control

Salience/escape

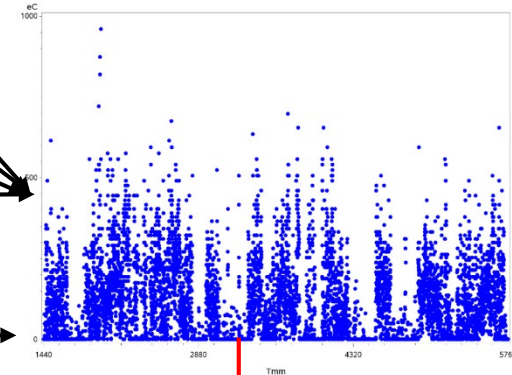
Reward seeking

Autobiographical memory

SCN + Peripheral clocks

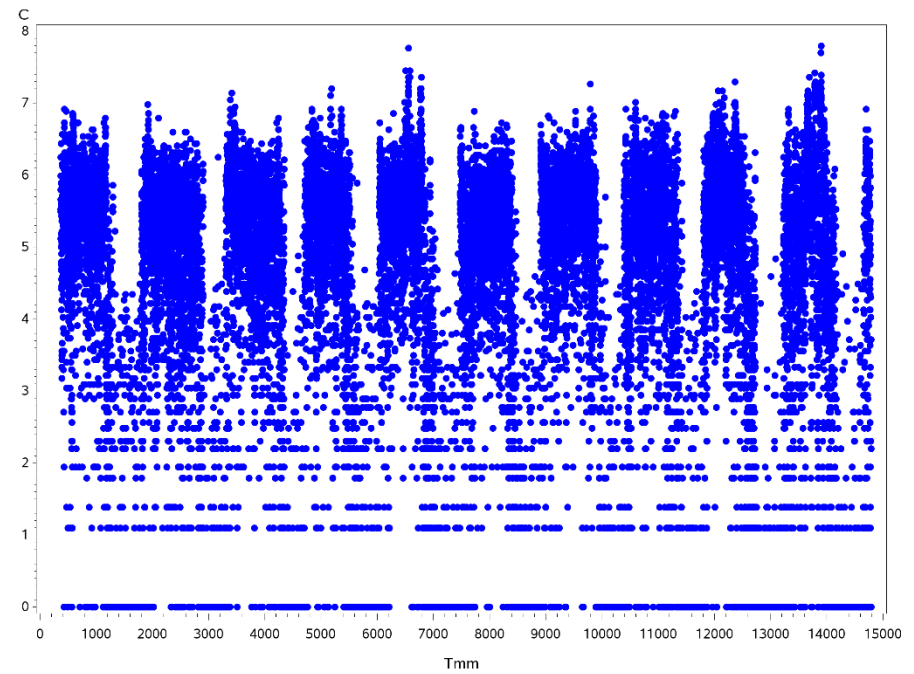
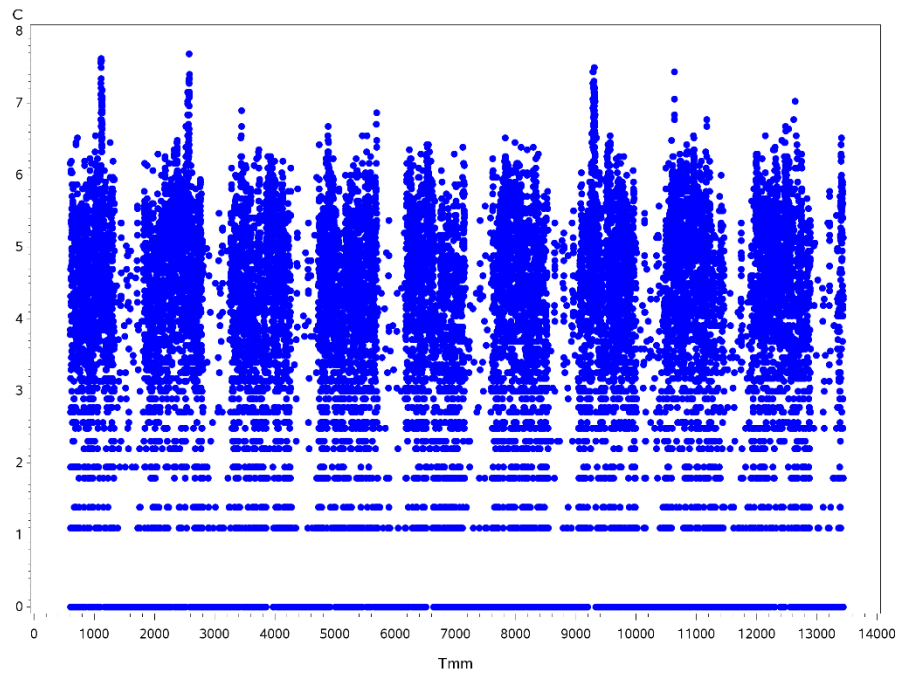
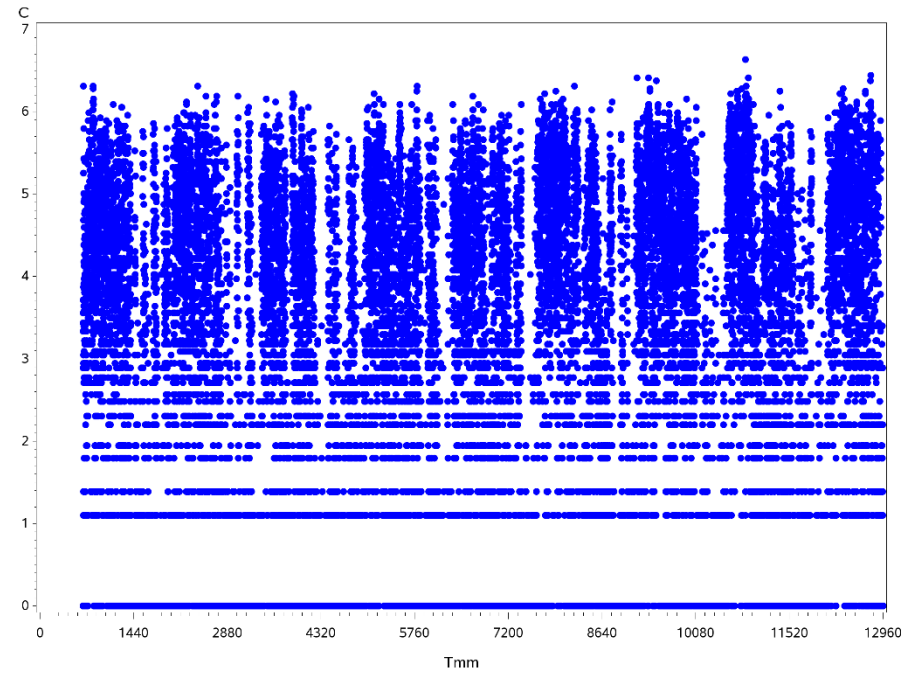
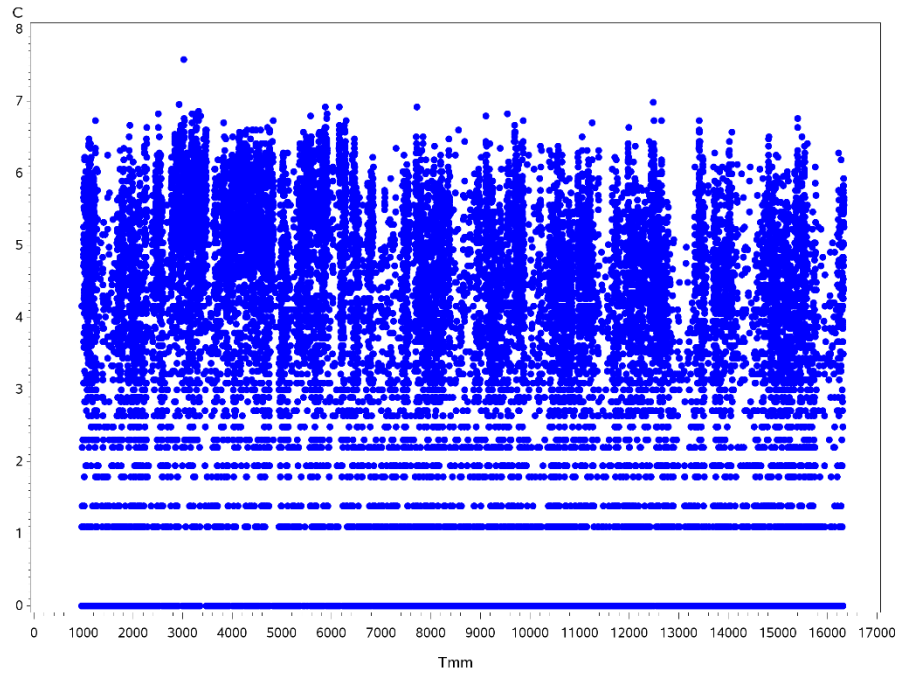
**Relations among circuits not shown for simplicity

Behavior



Physiological stress

Selecting behavioral inputs



Measurement

Cosine-based RAR measures

STATISTICS IN MEDICINE

Statist. Med. 2006; **25**:3893–3904

Published online 28 December 2005 in Wiley InterScience (www.interscience.wiley.com). DOI: 10.1002/sim.2466

Standard cosine

$$r(t) = \text{mes} + \text{amp} \cdot \cos([t - \phi]2\pi/24)$$

The sigmoidally transformed cosine curve: A mathematical model for circadian rhythms with symmetric non-sinusoidal shapes

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and Sonia Ancoli-Israel^{1,2}

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³Department of Social Sciences, University of the Sciences in Philadelphia, PA, U.S.A.

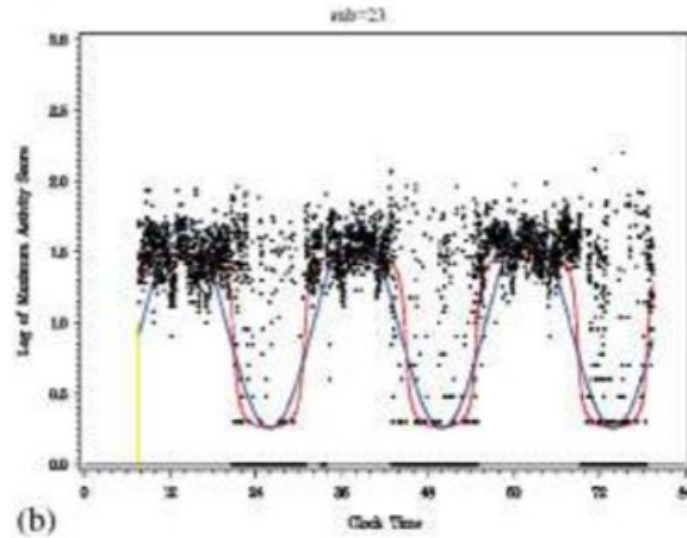
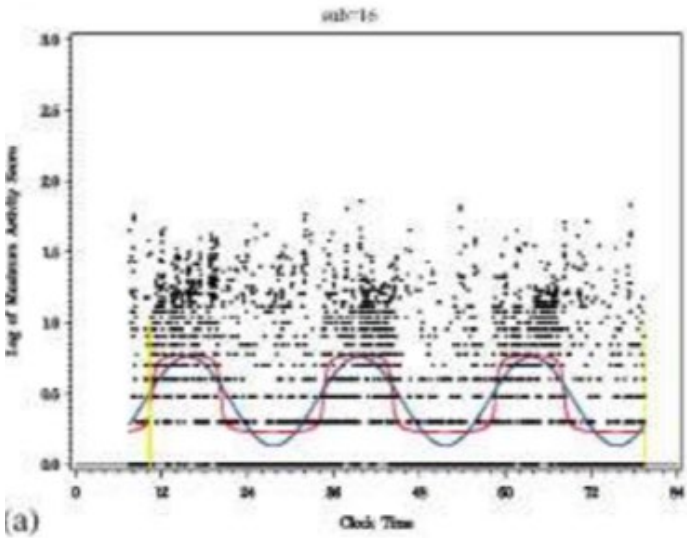
⁴Department of Medicine, University of California, Los Angeles, U.S.A.

⁵VA Sepulveda Ambulatory Care Center and Nursing Home, CA, U.S.A.

Extended cosine:

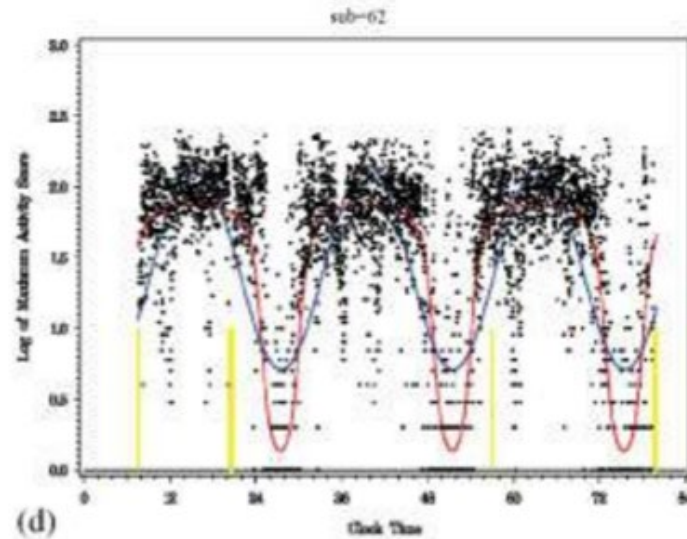
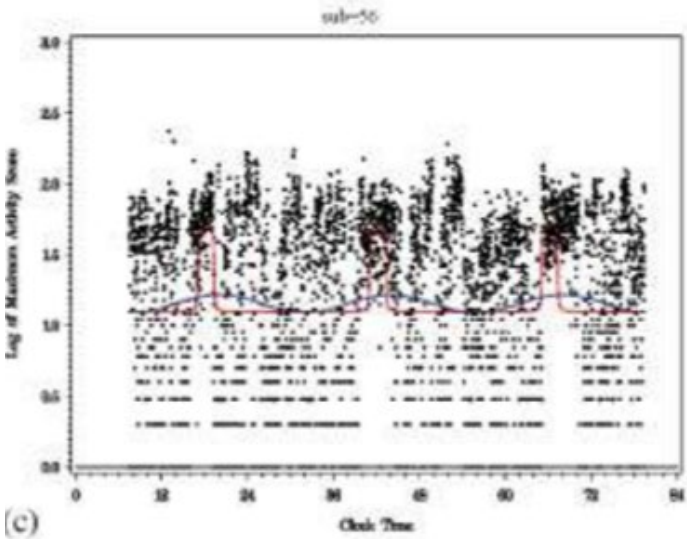
$$c(t) = \cos([t - \phi]2\pi/24).$$

$$\ell(c(t)) = \exp(\beta[c(t) - \alpha]) / \{1 + \exp(\beta[c(t) - \alpha])\};$$



Standard cosine

$$r(t) = \text{mes} + \text{amp} \cdot \cos([t - \phi]2\pi/24)$$

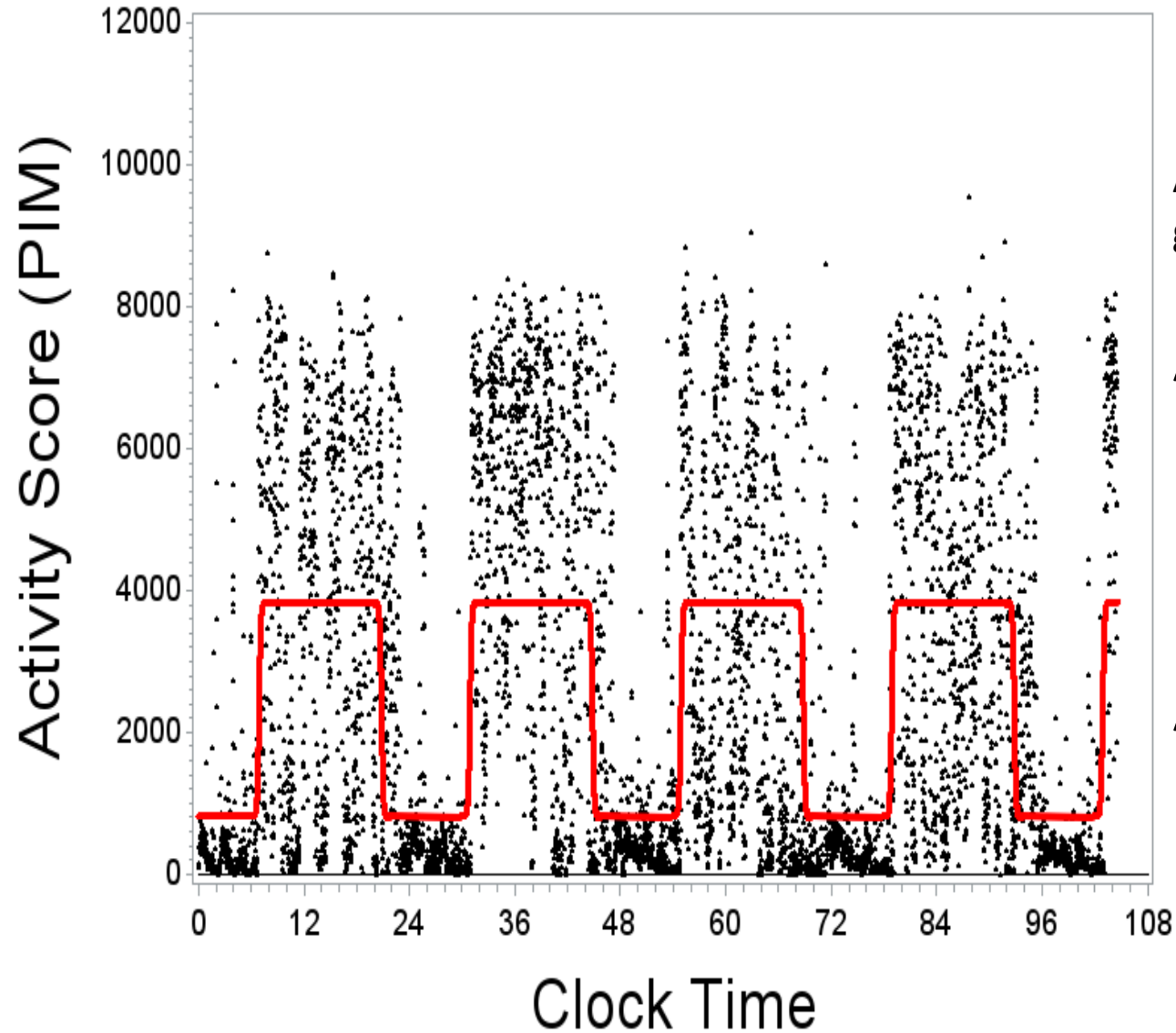


Extended cosine:

$$c(t) = \cos([t - \phi]2\pi/24).$$

$$\ell(c(t)) = \exp(\beta[c(t) - \alpha]) / \{1 + \exp(\beta[c(t) - \alpha])\};$$

Normal CAR



Average parameters for this group:

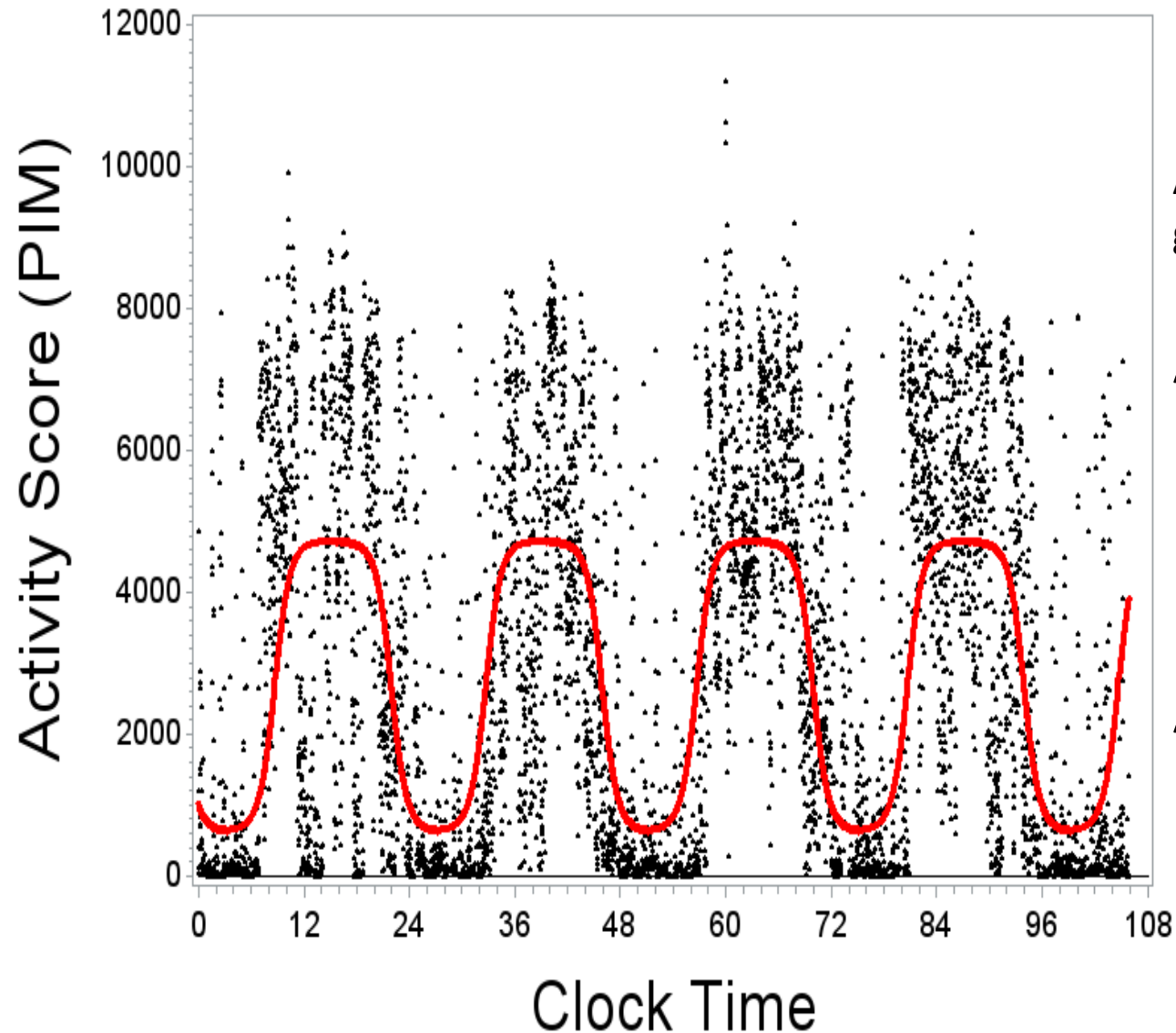
Amplitude: 3953.75
(counts/minute)

Up-mesor: 6.45 am

Acrophase: 2.30 pm

Down-mesor: 9.52 pm

Short Active Period



Average parameters for this group:

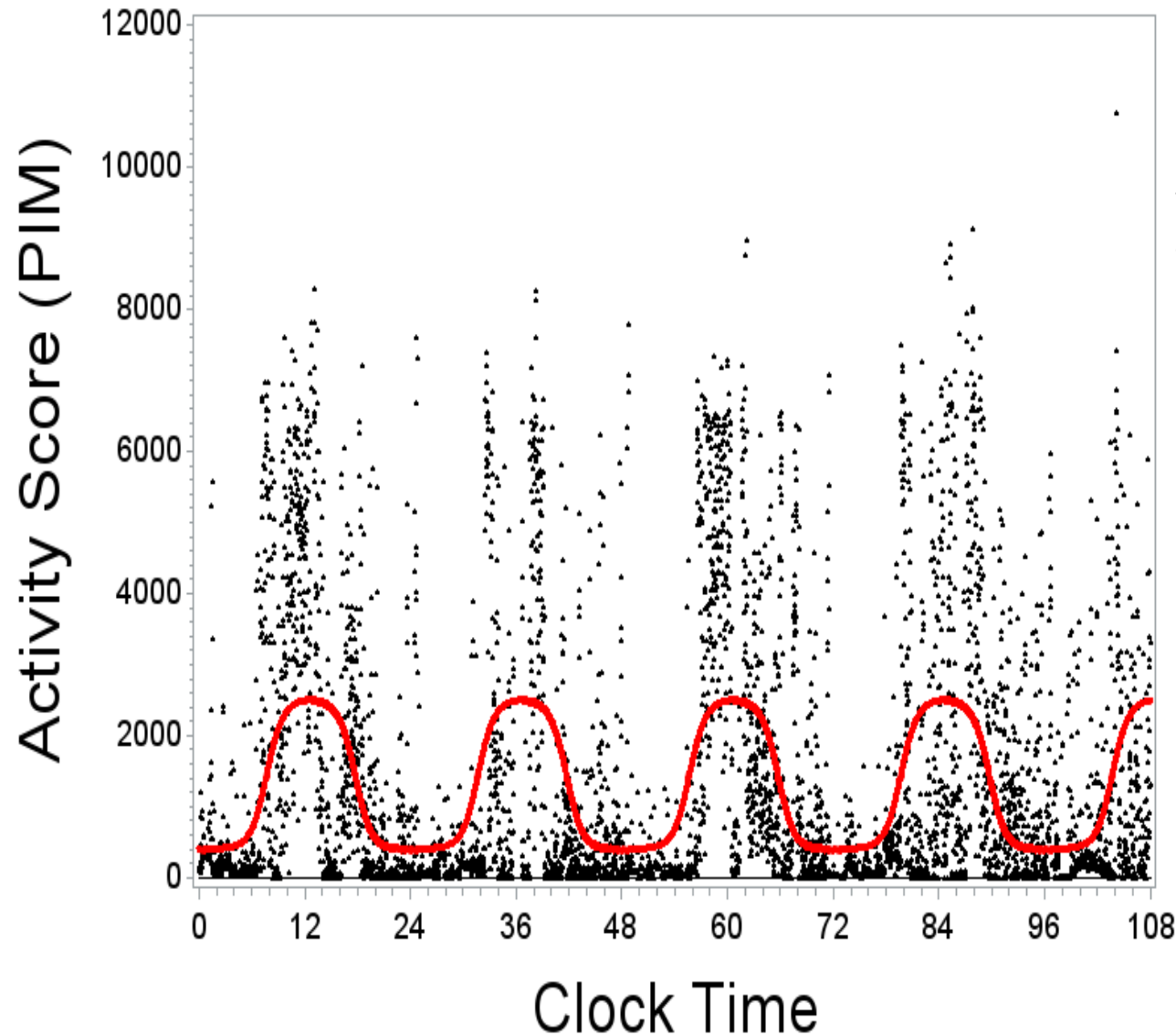
Amplitude: 4275.28
(counts/minute)

Up-mesor: 8.49 am

Acrophase: 2.40 pm

Down-mesor: 8.29 pm

Early and Dampened w/ Short Active Period



Average parameters for this group:

Amplitude: 2296.71
(counts/minute)

Up-mesor: 6.49 am

Acrophase: 12.43 pm

Down-mesor: 6.36 pm

Non-parametric analysis of RARs

$$RA = \frac{(M10 - L5)}{(M10 + L5)}$$

Relative amplitude (RA)

Relative difference between active and rest period counts standardized to overall activity levels

Inter-daily stability (IS)

How much activity varies across days

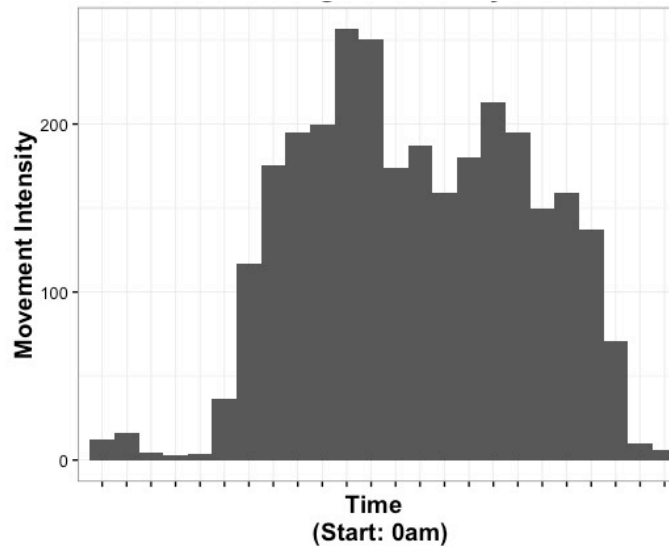
$$IS = \frac{n \sum_{h=1}^p (\bar{X}_h - \bar{X})^2}{p \sum_{i=1}^n (X_i - \bar{X})^2}$$

Intra-daily variability (IV)

How much activity varies hour-to-hour relative to how much activity varies overall

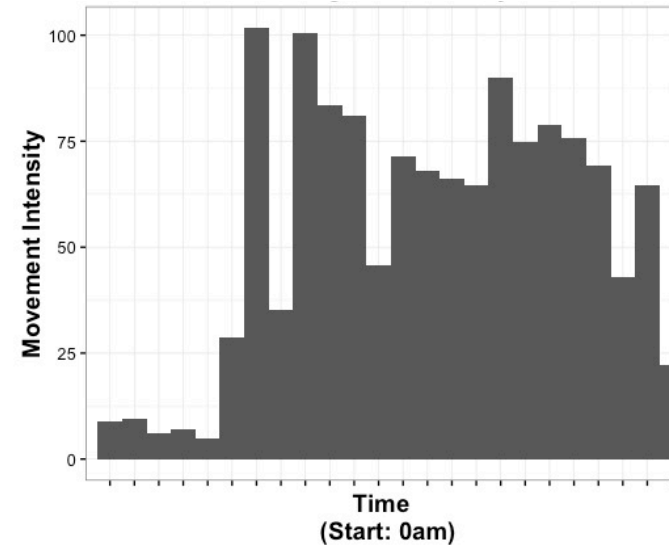
$$IV = \frac{n \sum_{i=2}^n (X_i - X_{i-1})^2}{(n-1) \sum_{i=1}^n (X_i - \bar{X})^2}$$

Low IV

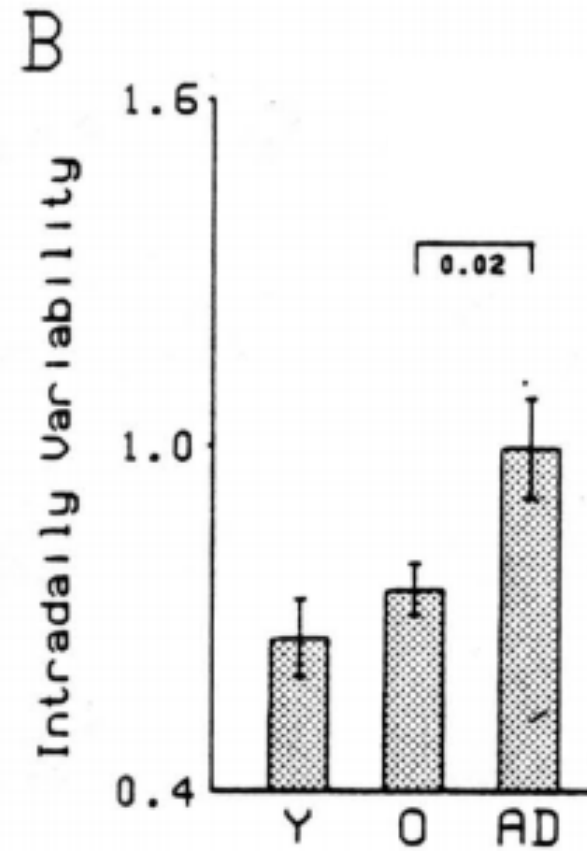
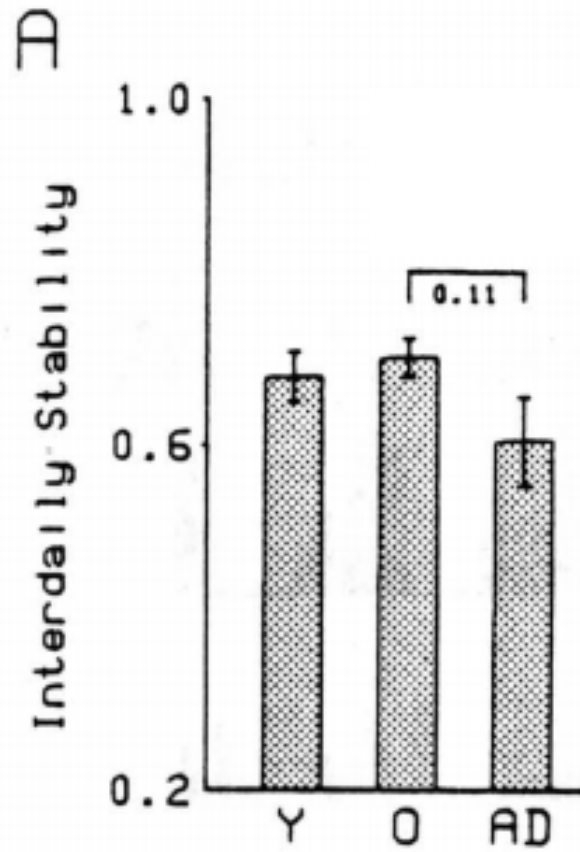


← Consistent within days

High IV

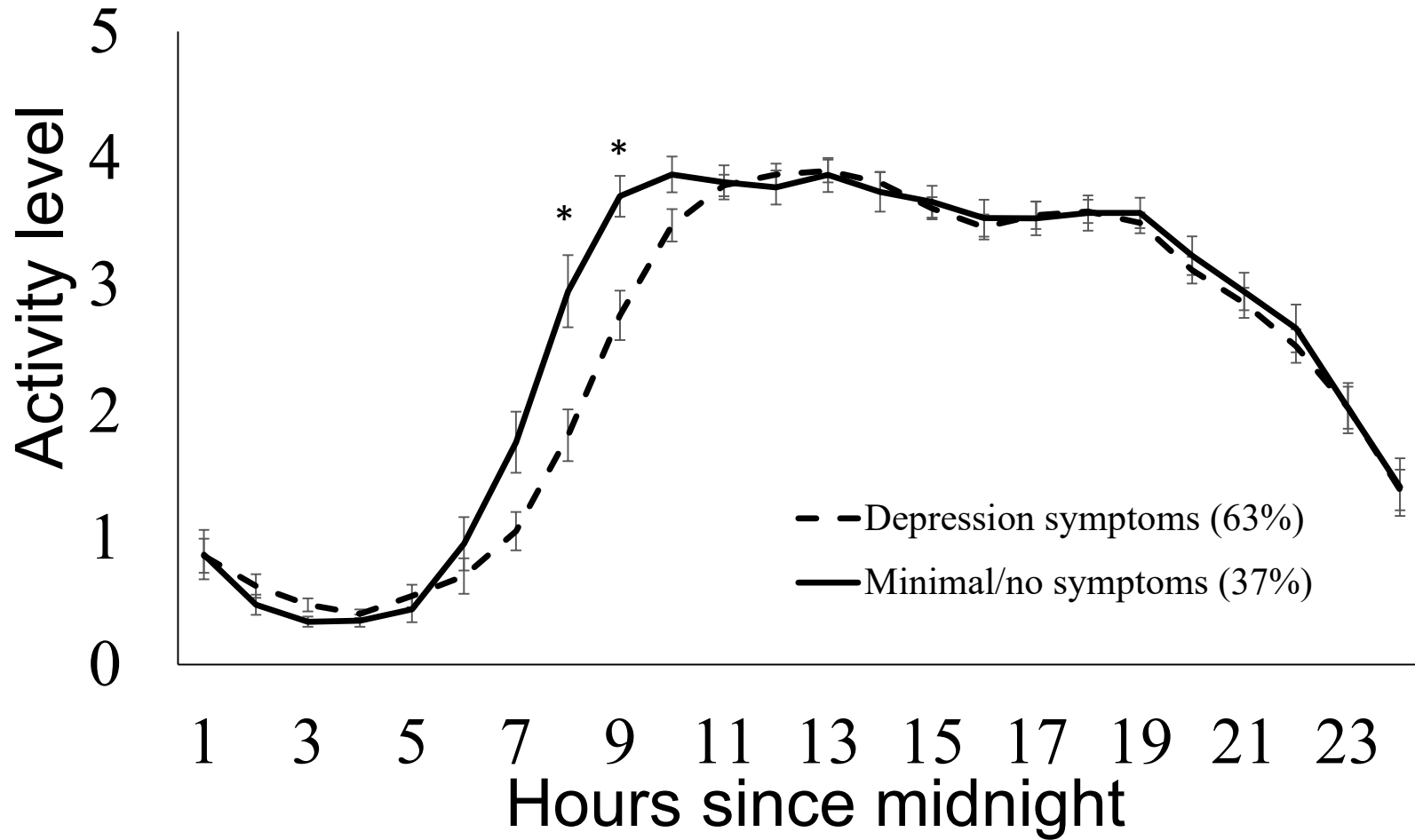


Inconsistent within days →



Witting W, Kwa IH, Eikelenboom P, Mirmiran M, Swaab DF. (1990). Alterations in the circadian rest-activity rhythm in aging and Alzheimer's disease. *Biol Psychiatry*. 1990 Mar 15;27(6):563-72.

Timing Localization



Means and standard errors shown

*Indicates local Benjamini-Hochberg False Discovery Rate $q < 0.05$.

International Psychogeriatrics. (2019)

Research applications

1) Cross-sectional studies:

- Majority of published research
- Great at finding differences related to disease states

2) Prospective studies

- Only a few studies and little (nothing) with RARs at outcome
- Shows RARs can influence future health

3) Clinical trials

- Targeting RARs: Can you change RARs? Does doing so influence health?
- Targeting other things: does changes in RARs signal health?

Thank you

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