HYPNOS: A New Software For EEG-Mediated Assessment Of Drug-Induced Changes In Sleep Macrostructures In The Rat

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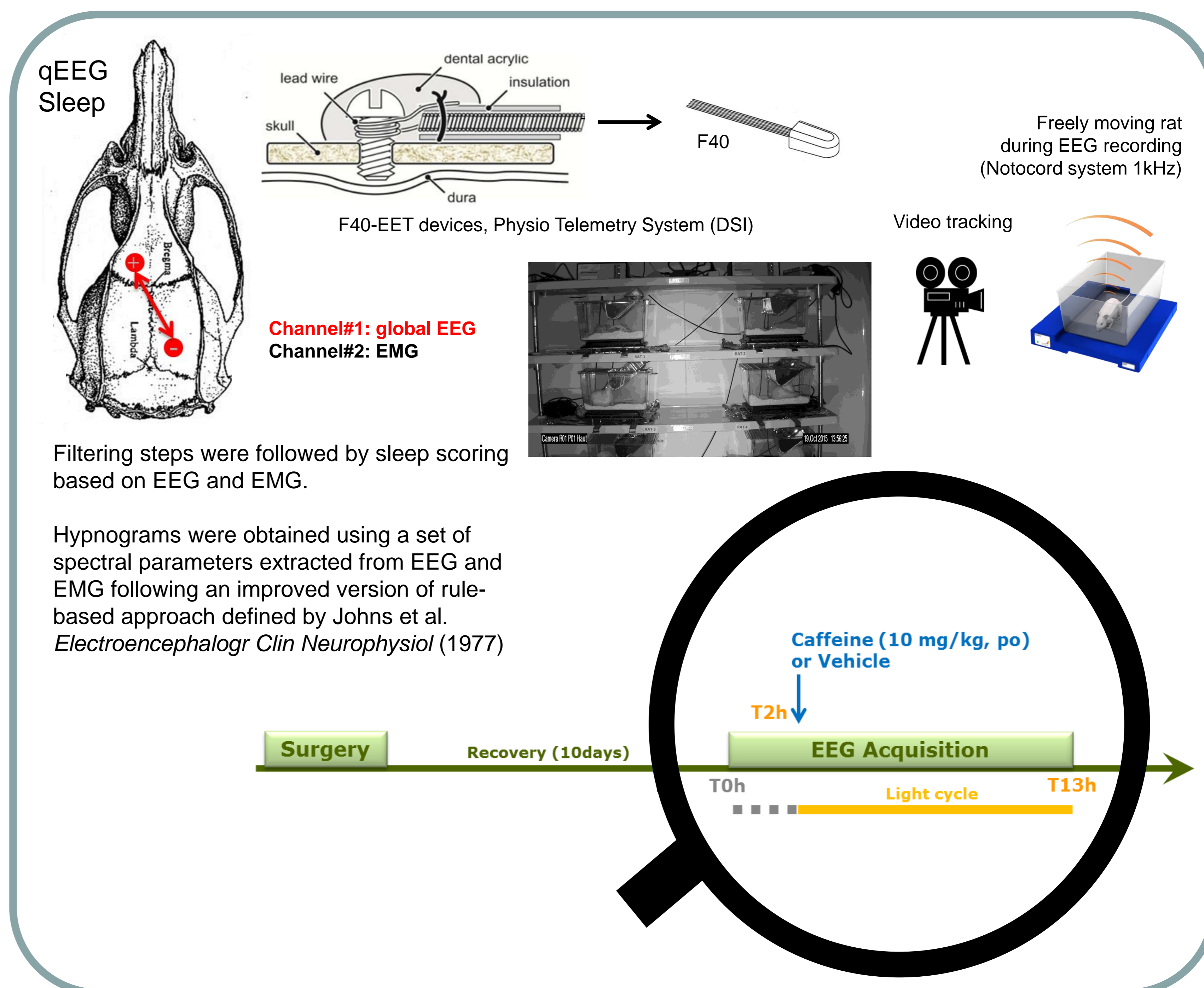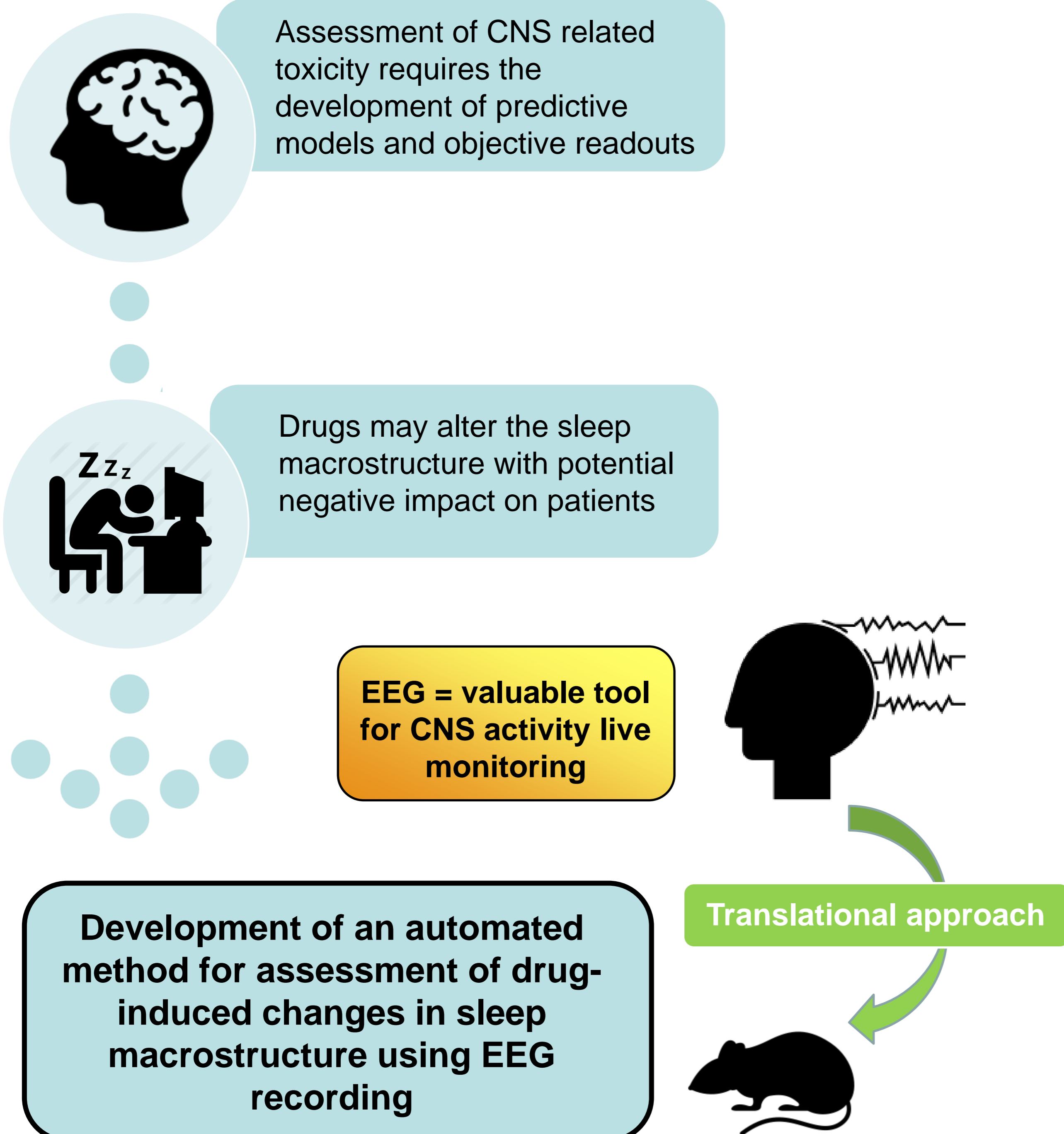
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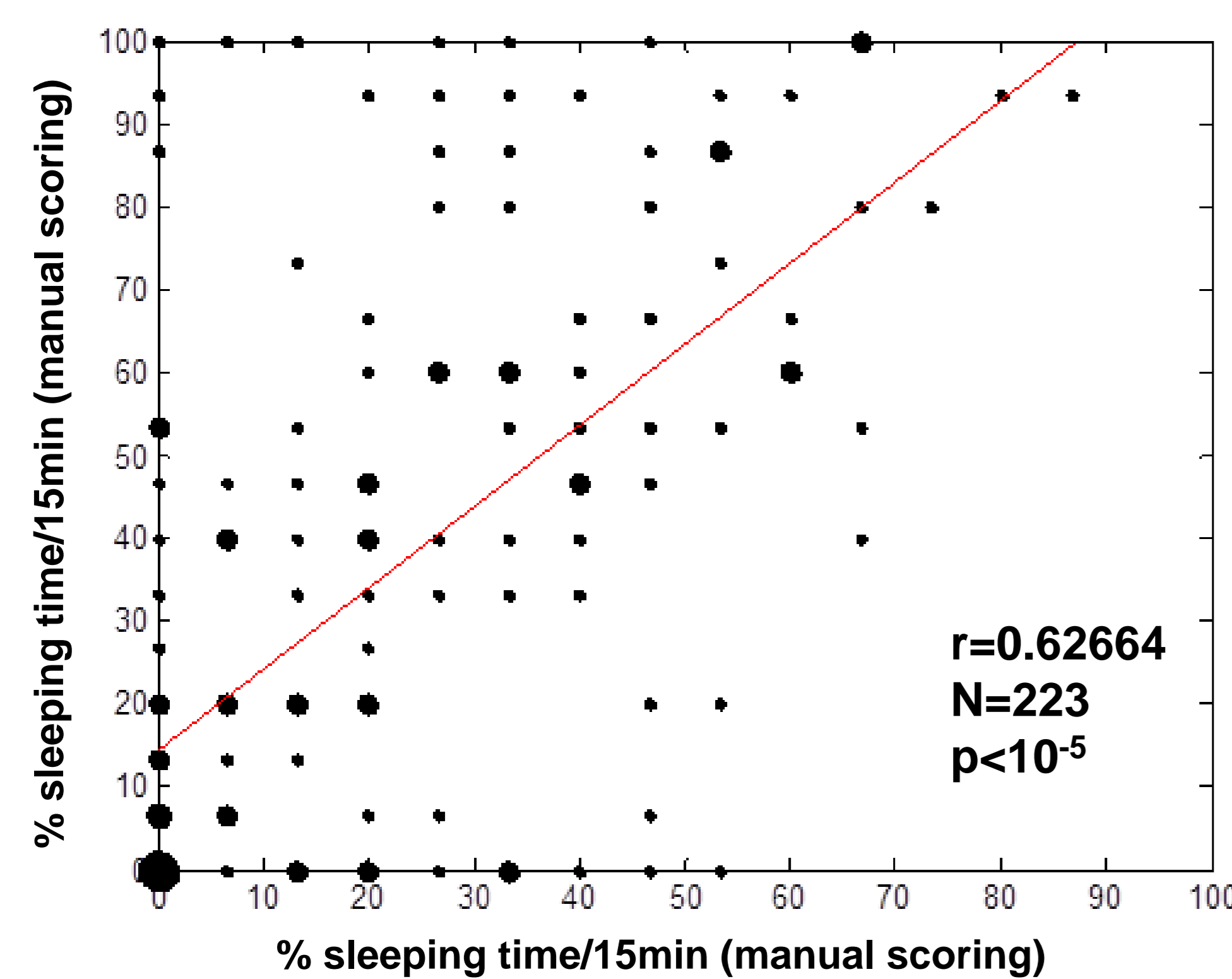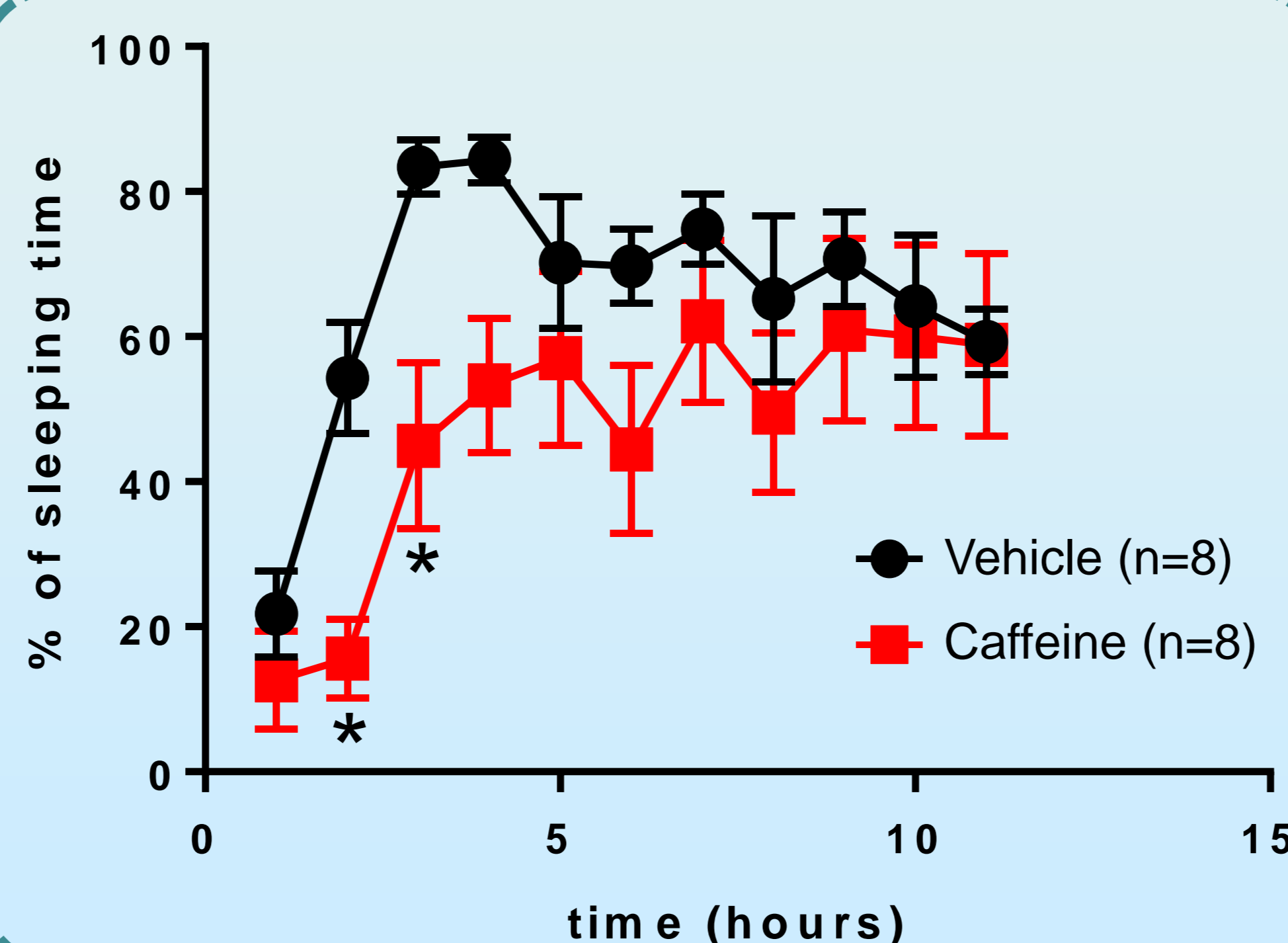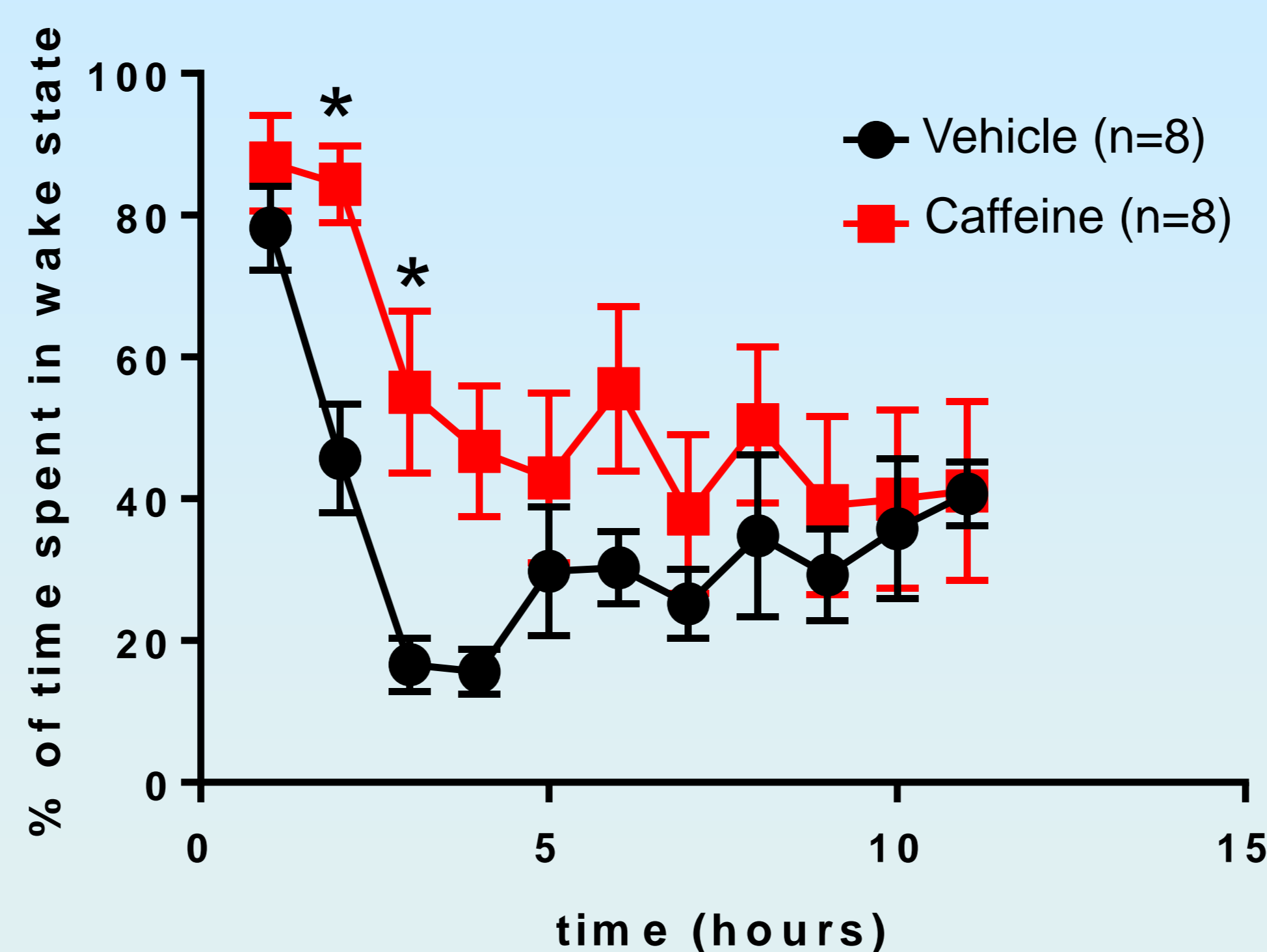
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BIOTRIAL
DRUG EVALUATION AND PHARMACOLOGY RESEARCH

Background & Purpose

Assessment of CNS related toxicity requires the development of predictive models and objective readouts

Drugs may alter the sleep macrostructure with potential negative impact on patients

EEG = valuable tool for CNS activity live monitoring

Translational approach

Development of an automated method for assessment of drug-induced changes in sleep macrostructure using EEG recording

Material & Methods

qEEG Sleep

lead wire   dental acrylic   insulation
skull   →   F40
dura

F40-EET devices, Physio Telemetry System (DSI)

Channel#1: global EEG
Channel#2: EMG

Freely moving rat during EEG recording (Notocord system 1kHz)

Video tracking

Filtering steps were followed by sleep scoring based on EEG and EMG.

Hypnograms were obtained using a set of spectral parameters extracted from EEG and EMG following an improved version of rule-based approach defined by Johns et al. *Electroencephalogr Clin Neurophysiol* (1977)

Caffeine (10 mg/kg, po) or Vehicle

T2h

Surgery   Recovery (10days)   EEG Acquisition
T0h   Light cycle   T13h

Results

Correlation between automatic scoring (HYPNOS) and manual scoring (video) of sleeping time

% sleeping time/15min (manual scoring)
% sleeping time/15min (manual scoring)

r=0.62664
N=223
p<10^{-5}

Dot size is proportional to log(number of overlapping points)

Significant correlation

Effect of caffeine on sleeping time

% of time spent in wake state
Vehicle (n=8)
Caffeine (n=8)
time (hours)

% of sleeping time
Vehicle (n=8)
Caffeine (n=8)
time (hours)

Effect of caffeine on sleep macrostructure

Vehicle
Wake / NREM / REM
Pourcentage of each stage [%]
Time [hours]

*p<0.05 relative to vehicle

Caffeine
Wake / NREM / REM
Pourcentage of each stage [%]
Time [hours]
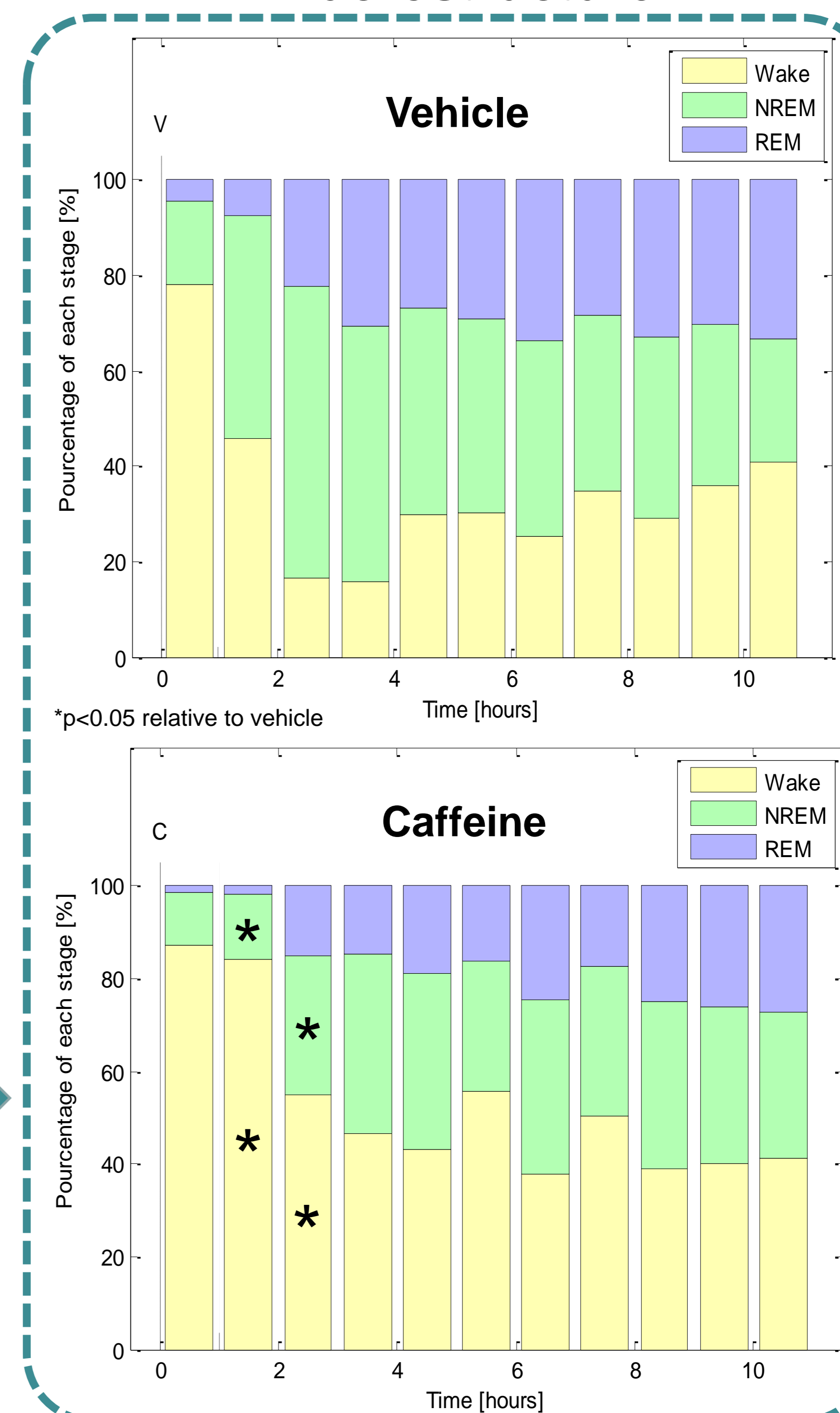
Conclusion

We were able to highlight the stimulant effect of caffeine using "HYPNOS" supporting the validity of our model for polysomnography studies. Additional experimentations aiming at highlighting the effect of a CNS depressant are currently ongoing. We propose our automated method as a valuable tool for assessment of drug-induced changes in sleep patterns in the framework of CNS safety pharmacology studies.