Supplementary Data

METHODS

Signal preprocessing

EKG. For each wake epoch, the EKG was filtered via Chebyshev II filter (low-frequency stop = 0.3Hz, low-frequency pass = 0.5 Hz, high-frequency pass = 150 Hz, high-frequency stop = 151 Hz. The filtering produced no attenuation at pass-band, and -60 dB at the both low and high stop-band sides). Filtering was performed in both forward and reverse directions to avoid any time lag bias between EKG and EEG signals. Heartbeat events were then detected from the EKG using the Pan-Tompkins detection algorithm [1]. Artefactual R peaks as well as ectopic beats were identified and corrected using a second algorithm, based on the point-process modelling[2].

Theta wave detection

The theta wave recognition was carried out following the approach proposed and validated by Ferrarelli and colleagues for sleep spindles[3], with some adaptations:

1) EEG for all wake epochs were filtered in the 4-7Hz band via Chebyshev II filter (low-frequency stop = 3Hz, low-frequency pass = 4 Hz, high-frequency pass = 7 Hz, high-frequency stop = 8 Hz. The filtering procedure produced no attenuation at passband, and -60 dB at the both low and high stop-band sides). Filtering was performed in both forward and reverse directions to avoid any time lag bias between EKG and EEG signals.

2) The envelope of the filtered signal was derived from the magnitude of its analytic signal obtained using Hilbert transform (Marple, S. L. ""Computing the Discrete-Time Analytic Signal via FFT"." IEEE® Transactions on Signal Processing. Vol. 47,

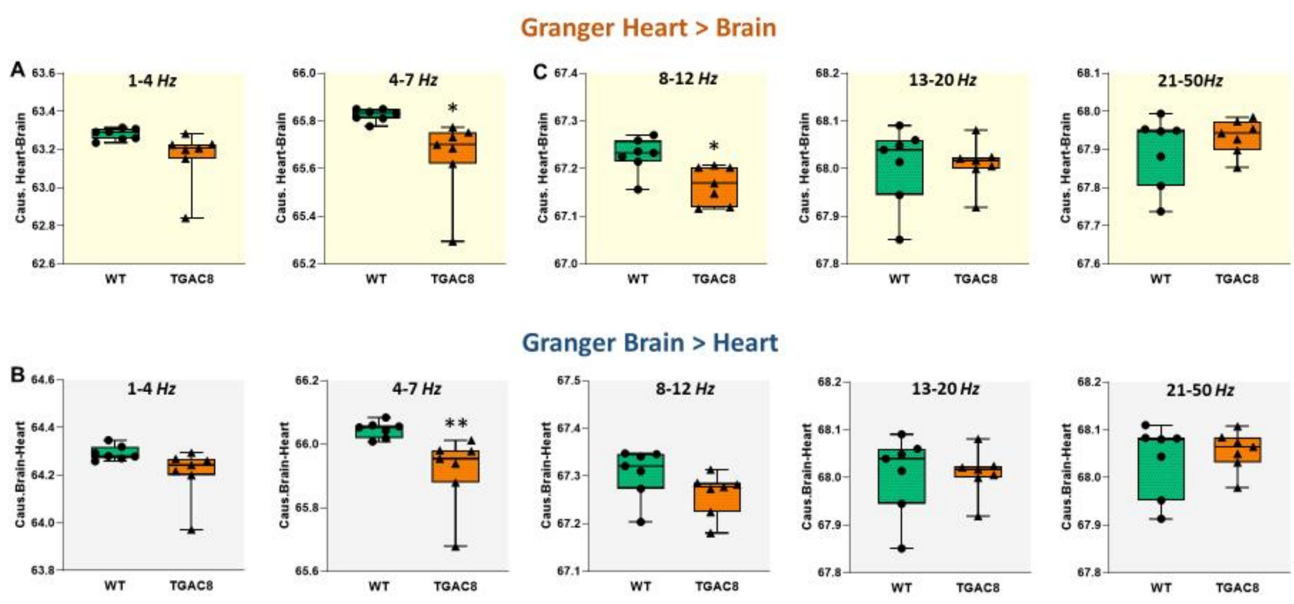
1999, pp. 2600–2603) and the amplitude of the envelope was used as a new time series.

3) A threshold value for detecting theta waves was derived as the median amplitude of the envelope (median calculated over all epochs for each animal).

4) A theta wave event was identified as the signal segment whose envelope had an amplitude exceeding four times the threshold.

From all detected events three parameters were derived: the rate, peak amplitude and dominant frequency. The rate corresponded to the number of events per time unit, the peak amplitude was defined as the local maximum of each theta wave event, the dominant frequency as the average of 4-7Hz frequencies weighted by the associated squared coefficients of the discrete Fourier transform. The measures characterizing each animal were derived as the average over all theta wave events detected during its wake epochs.

RESULTS



Sup. Figure. 1 *Dispersion within groups of GC estimates in different frequencies windows, both for heart->brain (A) and brain->heart (B) directions. Results are shown as box and whiskers plot, N=7, unpaired t-test has been performed between WT and TGAC8 groups, *p<0.05, **p<0.01.*

(1) Pan, J.; Tompkins, W. J. A real-time QRS detection algorithm. *IEEE Trans Biomed Eng* **1985,** *32* (3), 230.
(2) Citi, L.; Brown, E. N.; Barbieri, R. A real-time automated point-process method for the detection and correction of erroneous and ectopic heartbeats. *IEEE Trans Biomed Eng* **2012,** *59* (10), 2828.
(3) Ferrarelli, F.; Huber, R.; Peterson, M. J.; Massimini, M.; Murphy, M.; Riedner, B. A.; Watson, A.; Bria, P.; Tononi, G. Reduced sleep spindle activity in schizophrenia patients. *Am J Psychiatry* **2007,** *164* (3), 483.