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Supplemental information

Sleep-wake dynamics pre- and post-exposure

to chronic social stress

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Supplementary Material

1 Supplementary Figures



Figure S1. Related to all Figures.

Timeline of the sleep EEG recordings pre- and post-exposure to CSD stress. Mice are habituated for 48-h in the sleep chambers before EEG and EMG recording.



Figure S2. Related to Figure 1 and Figure 2.

Majority of transitions between sleep and wake bouts. There are transitions between NREM and Wake or from NREM to REM to Wake.



Figure S3. Related to Figure 1.

A histogram representation of the exponential and power law distributions of sleep and wake bouts respectively in NREM↔Wake.



Figure S4. Related to Figure 2.

A histogram representation of the exponential and power law distributions of sleep and wake bouts respectively in NREM->REM->Wake.



Figure S5. Related to Figure 2.

REM bouts filtered either as REM bouts transitioning to wake or REM bouts transitioning from NREM (Figure 2) are essentially the same, due to the rare occurrence of REM bouts transitioning to NREM in our case. *Pre-CSD:* Susceptible exhibit shorter REM bouts compared to resilient and stress-naïve mice in the light and dark (p<0.05 for both). *Post-CSD: Light:* Susceptible mice exhibit shorter REM bouts compared to stress-naïve mice (p<0.05). *Dark:* Resilient mice exhibit shorter REM bouts compared to stress-naïve mice (p<0.05).



Figure S6. Related to Figure 3.

Lower stability of NREM bouts in Susceptible mice <u>pre-CSD</u> in the light. (A) A three-state discrete Markov was used to model the transition between NREM, REM and wake states. (B) Markov transition matrix computed for all phenotypes in the light and the dark which encompasses the probability of transition of the state to itself and the probability of transition of the state to another. (C) In the light, NREM stability of susceptible mice was lower relative to resilient and stress-naïve mice (p<0.05 for both). The probability of transition of NREM to wake was higher in susceptible relative to resilient mice and a trend of being higher relative to control mice (p<0.01 and p=0.05). (D) In the dark, there was a trend of lower stability of NREM states in susceptible compared to resilient mice (p<0.05 for both), and wake stability was lower in susceptible mice compared to resilient mice (p<0.05). The transition from wake to NREM was higher in susceptible compared to resilient mice, while the transition from REM to wake was higher in susceptible compared to resilient mice, while the transition from REM to wake was higher in susceptible compared to resilient mice, while the transition from REM to wake was higher in susceptible compared to resilient and stress-naïve mice (p<0.05). The transition from REM to wake was higher in susceptible compared to resilient mice, while the transition from REM to wake was higher in susceptible compared to resilient and stress-naïve mice (p<0.05 for all comparisons). * denotes, p < 0.05. One-way ANOVAs followed by post hoc Tukey tests were performed for multiple comparisons.



Figure S7. Related to Figure 3.

No difference was detected in the stability and probability of transitions of states <u>post-CSD.</u> (A) A three-state discrete Markov was used to model the transition between NREM, REM and Wake states. (B) Markov transition matrix computed for all phenotypes in the light and the dark which encompasses the probability of transition of the state to itself and the probability of transition of the state to another. (C) and (D) No significant difference in the stability and probability of transitions of states was detected.



B. Pre-CSD



C. Post-CSD



Figure S8. Related to Figure 3.

A four-state discrete Markov was used to model the transition between NREM, REM and Wake states in NREM \leftrightarrow Wake and NREM \rightarrow REM \rightarrow Wake separately. Specifically, the Markov Model was used to model the transitions between **NREM** \rightarrow Wake (N-W), **Wake** \rightarrow NREM(W-N) in NREM \leftrightarrow Wake and **NREM** \rightarrow REM (N-R), **REM** \rightarrow Wake (R-W) and **Wake** \rightarrow NREM (W-N) in NREM \rightarrow REM \rightarrow Wake transitions. Both paths of transitions converge on wake bouts (W-N) that transition to either **NREM** \rightarrow Wake (N-W) or **NREM** \rightarrow REM (N-R) (**A**)Pre-CSD: Markov transition matrix computed for all phenotypes in the light and the dark which encompasses the probability of transition of the state to itself and the probability of transition of the dark which encompasses the probability of transition of the state to another. (**B**) Post-CSD: Markov transition matrix computed for all phenotypes in the light and the probability of transition of the state to itself and the probability of transition of the state to itself and the state to itself and the probability of transition of the state to another. (**B**) Post-CSD: Markov transition matrix computed for all phenotypes in the light and the probability of transition of the state to another.



Figure S9. Related to Figure 4.

A model summarizing the change in sleep wake dynamics post exposure to chronic social stress. Post-CSD, the mice resilient to stress exhibited shorter NREM duration in NREM↔Wake in the light relative to stress-naïve mice, while all the sleep and wake bouts were shorter in the dark relative to stress-naïve. This suggests that the NREM in the light in NREM↔Wake are more sensitive to the effects of chronic stress.



adopted from Luthi, 2016

Figure S10. Related to Figure 4.

A simple model that summarizes the findings of shorter sleep bout duration, no change in wake bout duration except in the dark, lower stability of sleep bouts specifically NREM and increased switching between NREM and wake bouts as a greater pull toward the wake state leading to early termination of the sleep bouts.



Figure S11. Related to Figure 4.

Modeling the sleep states in **NREM** \leftrightarrow Wake and **NREM** \rightarrow REM \rightarrow Wake as 'short sleep' and 'long sleep' global states respectively transitioning to wake.





Pre-CSD, susceptible mice spent less time in 'long sleep' in the light, and more time in 'short sleep' in the dark relative to resilient mice. (A) Pre-CSD: In the light, susceptible mice spent less time in NREM and REM state in **NREM**→**REM**→Wake, inferring shorter time in 'long sleep' relative to resilient mice. In the dark, susceptible mice spent more time in 'short sleep 'since they spent more time in NREM state in **NREM**↔Wake relative to resilient mice. (B) Post-CSD: Susceptible mice spent more in wake state in NREM↔Wake relative to resilient mice. * denotes, p < 0.05. One-way ANOVAs followed by post hoc Tukey tests were performed for multiple comparisons.

2 Supplementary Tables

Phenotype	Condition	Phase	Average- number
Control	Pre	Light	4.72
		Dark	5.49
	Post	Light	4.56
		Dark	5.43
Resilient	Pre	Light	3.74
		Dark	4.76
	Post	Light	3.57
		Dark	6.49
Susceptible	Pre	Light	5.9
		Dark	5.89
	Post	Light	4.75
		Dark	7.49

Table S1. Related to Figure 4.

A summary of average number of 'Short Sleep'/ **NREM**↔Wake occurrences before 'Long Sleep' / **NREM→REM**→Wake occurrences.