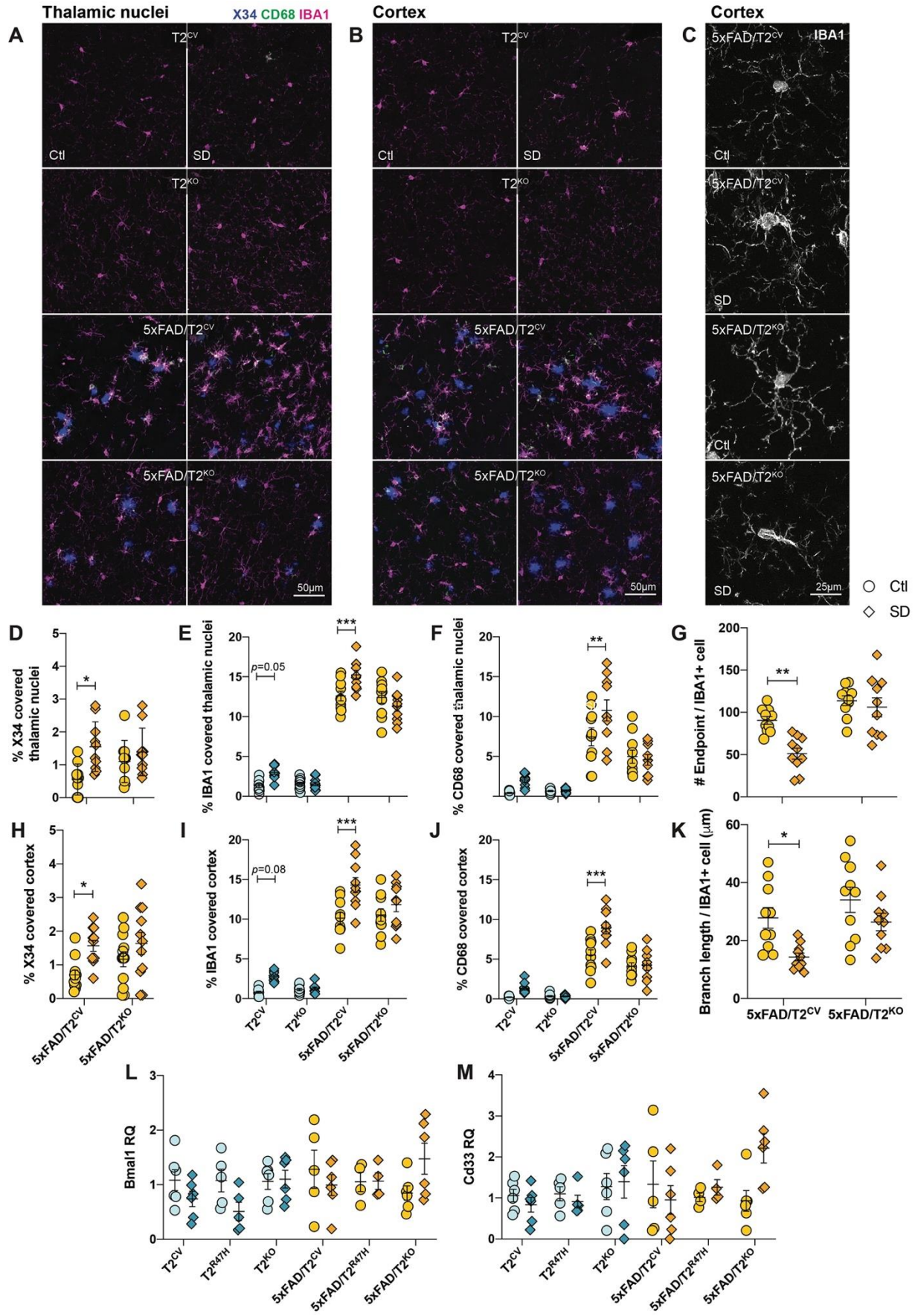
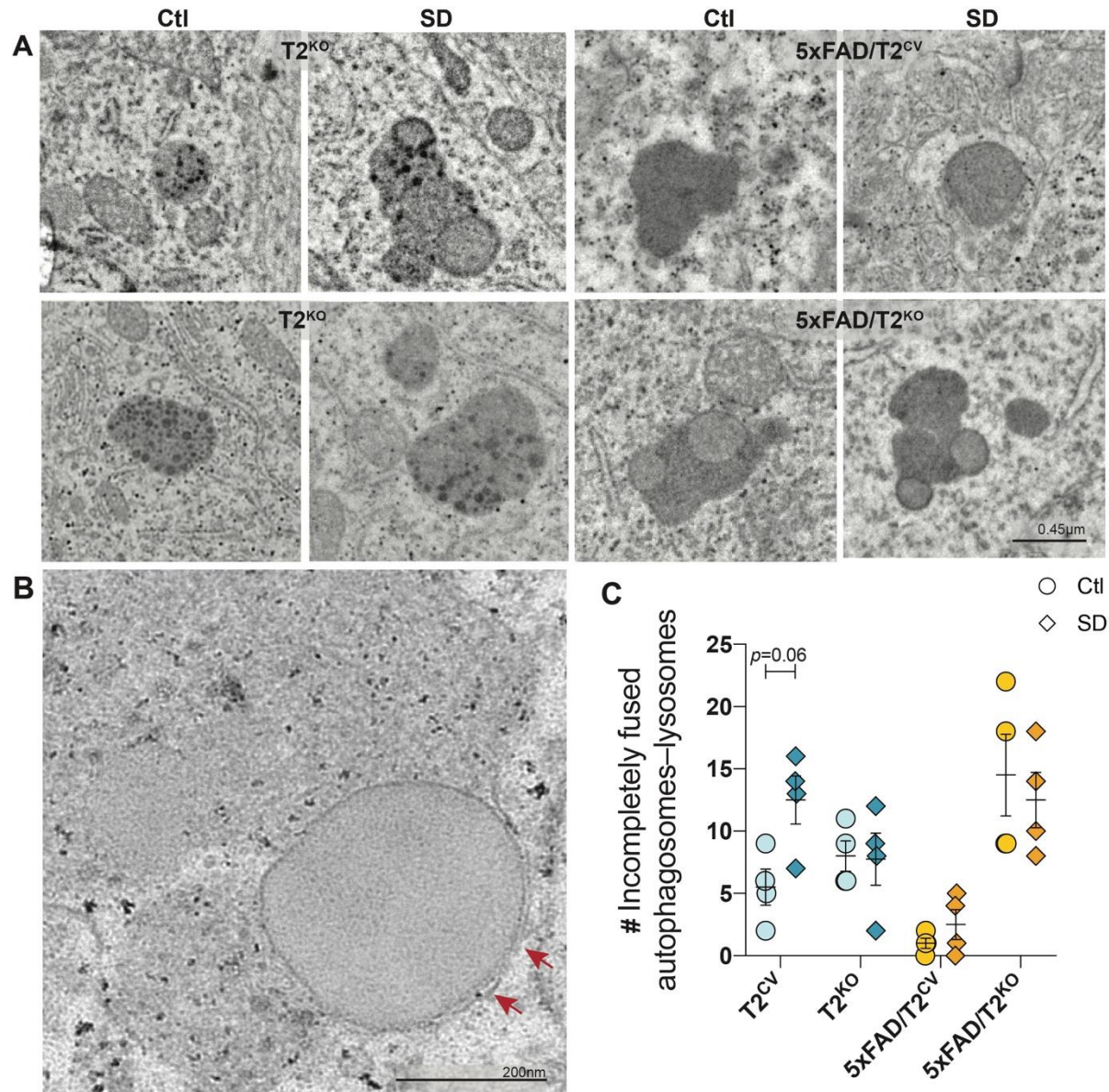


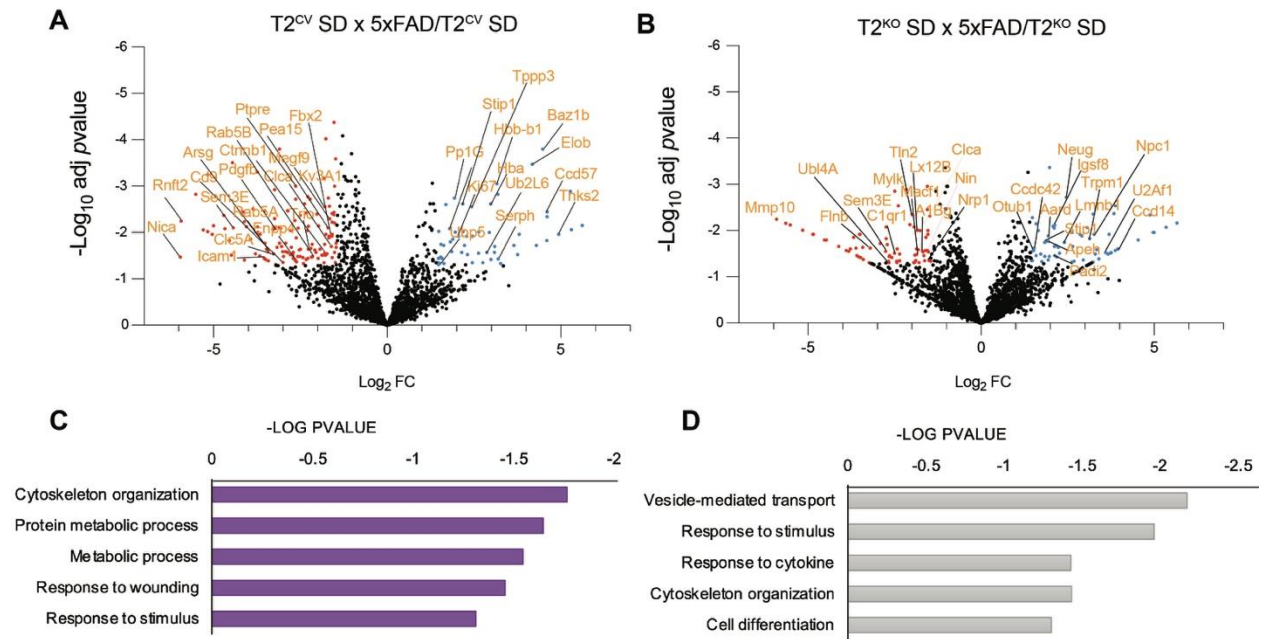
Supplementary Figure 1. Sleep deprivation reduces time spent asleep and does not influence corticosterone levels. Percentage sleep time at light and dark phase recorded from (A) T2^{CV} (n=4 mice/group) (B) 5xFAD/T2^{CV} mice (n=6-7 mice/group) during sleep deprivation or control mice. Sleep bout length at light and dark phase recorded from (C) T2^{CV} (n=4 mice/group) (D) 5xFAD/T2^{CV} mice (n=6-7 mice/group) during sleep deprivation or control mice. Data were recorded over a 24h period. (E) Electroencephalographical assessment of percentage time spent in non-rapid eye movement (NREM) sleep, REM sleep or time spent awake following sleep deprivation (SD) as a result of sleep rebound (n=4-6 mice/group). (F) Plasma corticosterone levels measured by ELISA.



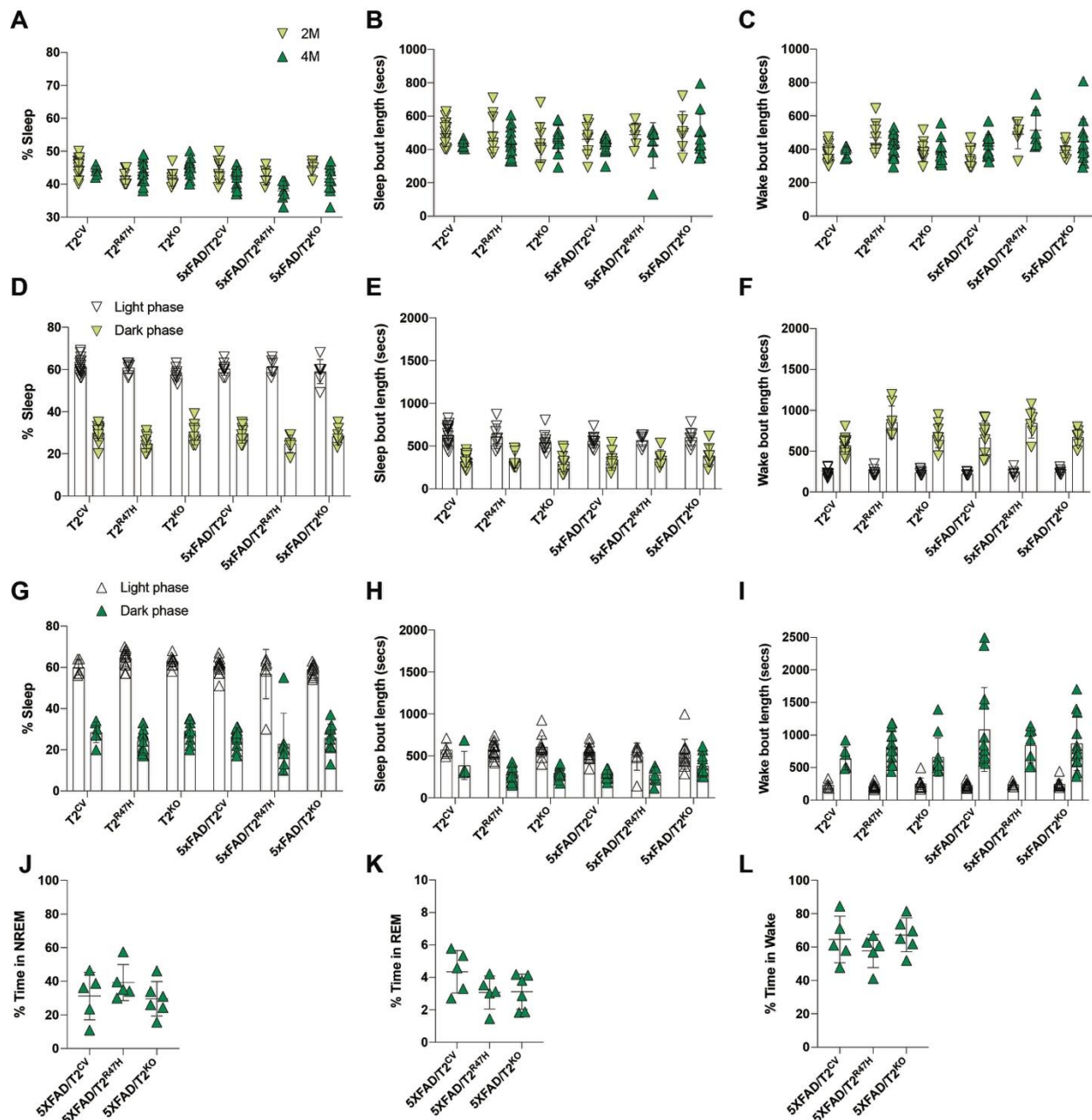
Supplementary Figure 2. Sleep deprivation promotes amyloid deposition and microglial reactivity. (A) Representative images of thalamic nuclei co-stained with X34 (blue), IBA1 (magenta) and CD68 (green). (B) Representative images of cortex co-stained X34, IBA1 and CD68. (C) Representative confocal images of IBA1+ microglia in cortex. Quantifications of (D) percentage X34, (E) percentage IBA1, and (F) percentage CD68 covered thalamic nuclei. (G) Quantification of number of endpoints per IBA1+ cell. Quantifications of (H) percentage X34, (I) percentage IBA1, and (J) percentage CD68 covered cortex. (K) Quantification of branch length per IBA1+ cell. n=8-12 mice/genotype. Quantitative PCR of (L) Bmal1 and (M) Cd33 normalized to geometric mean of two housekeeping genes. n=4-6 mice/genotype Ctl – Control, SD – Sleep deprived. Data represent mean \pm S.E.M. Two-way ANOVA, Sidak's multiple comparison test; *P<0.05; **P<0.01; ***P<0.001.



Supplementary Figure 3. Sleep deprivation impairs autophagosome-lysosome fusion TREM2 dependently. (A) Representative transmission electron microscopy images of autolysosomes from subiculum. (B) Higher magnification of an unfused autolysosome. Arrows point to the double membrane. (C) Number of incompletely fused autophago-lysosomes quantified in the subiculum. Data represent mean \pm S.E.M. Two-way ANOVA, Sidak's multiple comparison test.



Supplementary Figure 4. Sleep deprivation induces metabolic dysregulation in cerebrospinal fluid proteome. (A) Volcano plots of SD T2^{CV} versus SD 5xFAD/T2^{CV} and (B) SD T2^{KO} and SD 5xFAD/T2^{KO} mice. (C) Gene ontology functional pathways of SD T2^{CV} versus SD 5xFAD/T2^{CV} and (B) SD T2^{KO} and SD 5xFAD/T2^{KO} mice. n=9-11 mice/genotype. Significantly downregulated proteins are noted in blue and upregulated ones in red dots. Ctl – Control, SD – Sleep deprived. Significance for volcano plots was marked at p<0.05 with a 1.5-fold change in Log₂.



Supplementary Figure 5. TREM2 genotype does not influence sleep/wake states. (A) Piezosleep recordings illustrating percentage time spent asleep, (B) sleep bout length, and (C) wake bout length in 2- and 4-months old mice of each genotype. (D) Piezosleep recordings illustrating percentage time spent asleep, (E) sleep bout length, and (F) wake bout length in 2-months old mice separated by light and dark phase. (G) Piezosleep recordings of 4 months old mice demonstrating percentage time spent asleep, (H), sleep bout length, and (I) wake bout length separated by light and dark phase. $n=7-10$ /genotype. (J) Electroencephalography analyses of percentage time spent in NREM sleep, (K) REM sleep, or (I) awake. $n=4-6$ /genotype. Ctl – Control, SD – Sleep deprived. Data represent mean \pm S.E.M. Two-way ANOVA, Tukey’s multiple comparison test; * $P<0.05$; ** $P<0.01$; *** $P<0.001$.

Data File Supplementary Figure 1. Primary data from Figures 1-5; Supplementary Figures 1-S3, S5. Excel file provided.