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Fig. S1. Sleep-wake pattern and diurnal fluctuation of interstitial fluid (ISF) A β in the hippocampus and striatum of 3 and 9 month-old wild-type littermate mice.

Fig. S2. A β plaque deposition in female APP^{swe}/PS1 δ E9 (APP/PS1) mice at 3, 6, and 9 months of age and in wild-type littermates at 9 months of age.

Fig. S3. Correlation between wakefulness and levels of interstitial fluid (ISF) lactate.

Fig. S4. Correlation between levels of interstitial fluid (ISF) lactate and ISF A β in APP^{swe}/PS1 δ E9 mice.

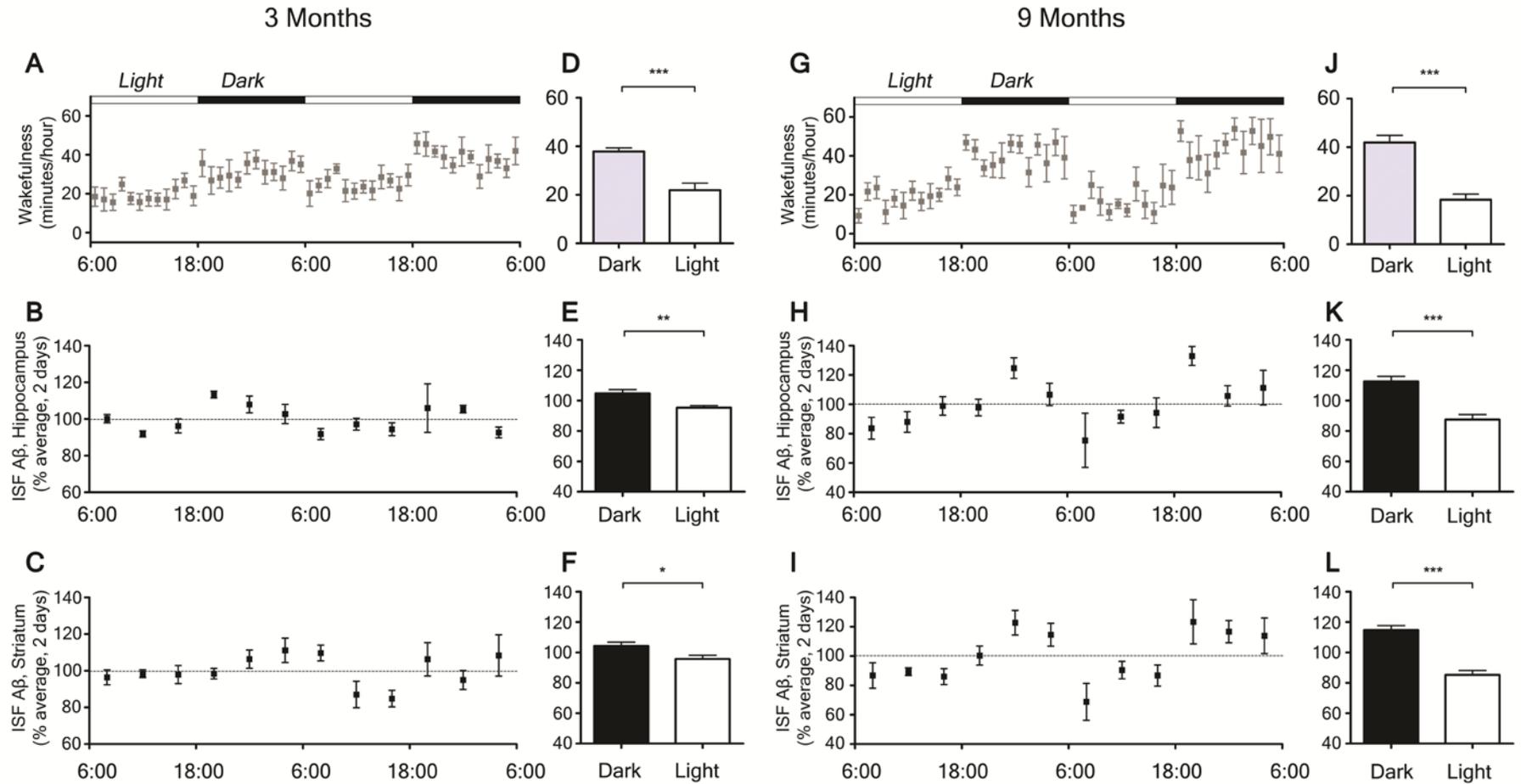
Fig. S5. Correlation between levels of interstitial fluid (ISF) lactate and ISF A β in A β 42- and phosphate buffered saline (PBS)-immunized APP^{swe}/PS1 δ E9 mice.

Fig. S6. Changes in diurnal fluctuation of interstitial fluid (ISF) A β _{x-42} in the hippocampus and in the striatum of 3 and 9 month old APP^{swe}/PS1 δ E9 mice.

Fig. S7. Changes in diurnal fluctuation of interstitial fluid (ISF) A β _{x-42} in the hippocampus and in the striatum of 9 month old phosphate buffered saline (PBS)-treated and A β 42-vaccinated APP^{swe}/PS1 δ E9 mice.

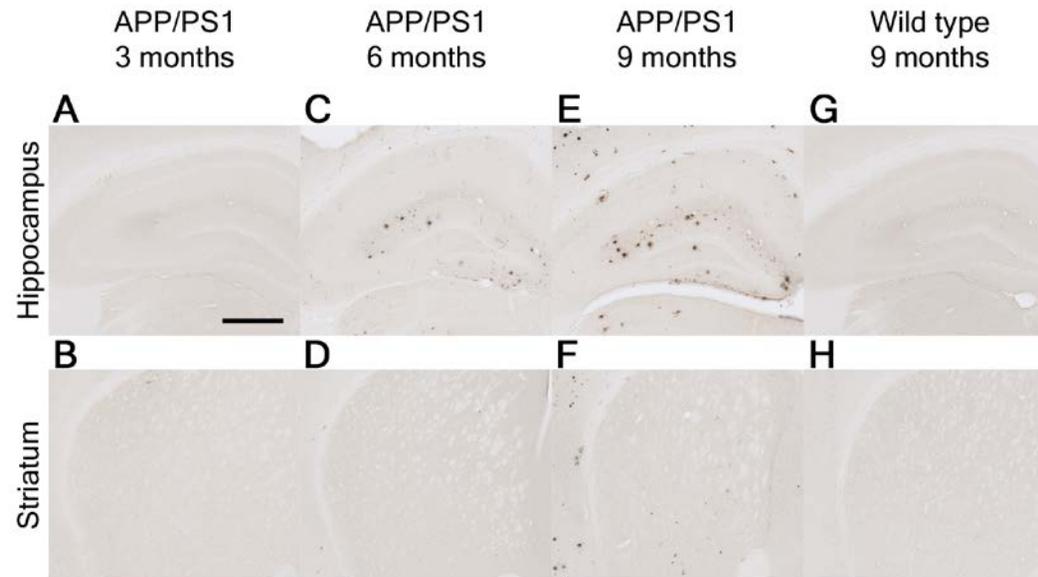
Supplementary Materials

Supplementary Figure 1



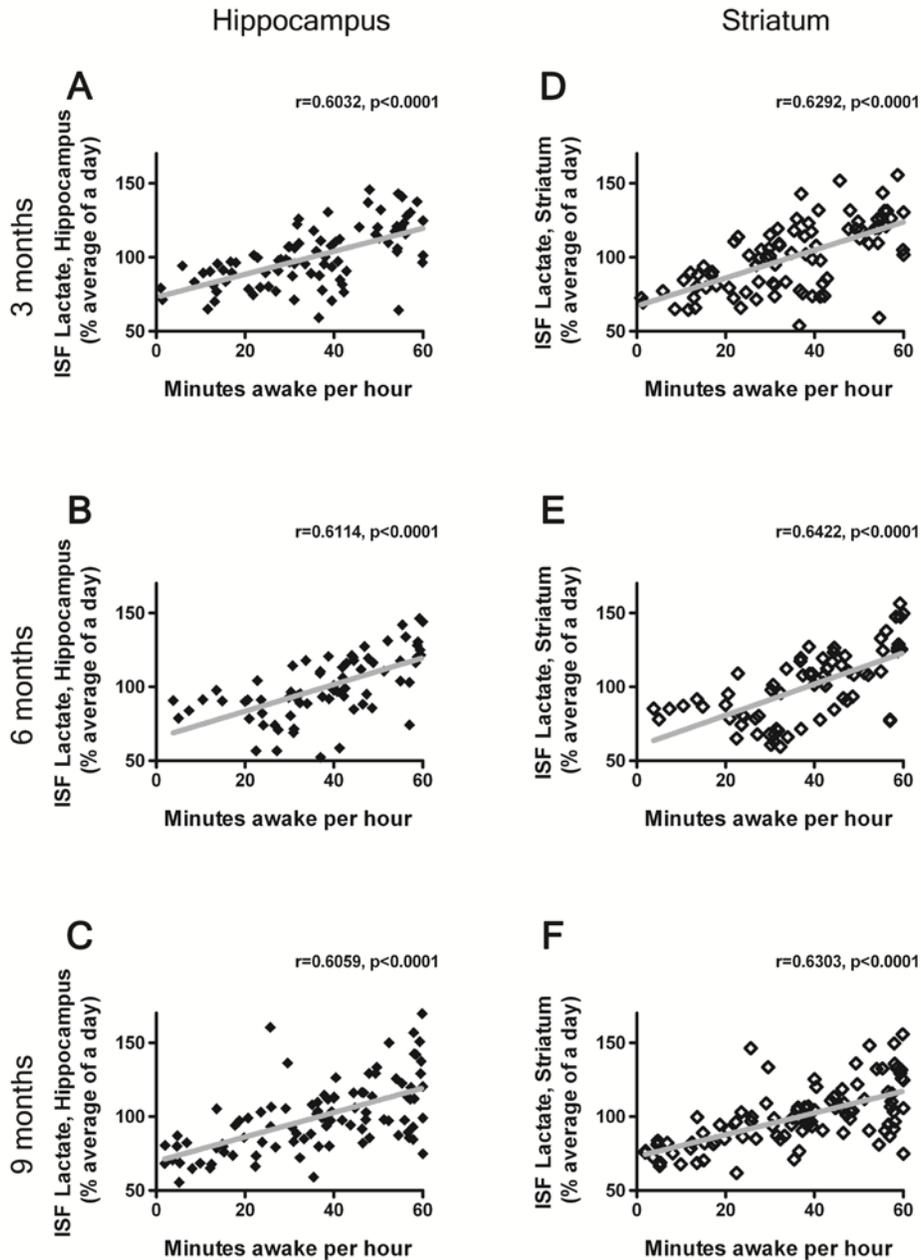
Sleep-wake pattern and diurnal fluctuation of interstitial fluid (ISF) A β in the hippocampus and striatum of 3 and 9 month-old wild-type littermate mice. **(A, G)** Sleep-wake patterns in 3 **(A)** and 9 **(G)** month-old wild-type mice across 2 days (2 light-dark periods) presented by minutes awake per hour. **(D, J)** Comparison of minutes awake per hour between the dark and light periods in each group (n = 5 per group; two tailed t-test). **(B, H)** Diurnal fluctuation of ISF A β_{x-40} in the hippocampus of 3 **(B)** and 9 **(H)** month-old wild-type littermates across 2 days presented as % average of absolute values of ISF A β_{x-40} . **(E, K)** Comparison of % average of absolute values of ISF A β_{x-40} in the hippocampus between the dark and light periods (n = 5 per group; two tailed t-test). **(C, I)** Diurnal fluctuation of ISF A β_{x-40} in the striatum of 3 **(C)** and 9 **(I)** month-old wild-type mice across 2 days. **(F, L)** Comparison of % average of absolute values of ISF A β_{x-40} in the striatum between the dark and light periods (n = 5 per group; two tailed t-test). * $P < 0.05$; ** $P < 0.01$; *** $P < 0.001$. Values represent mean \pm s.e.m.

Supplementary Figure 2



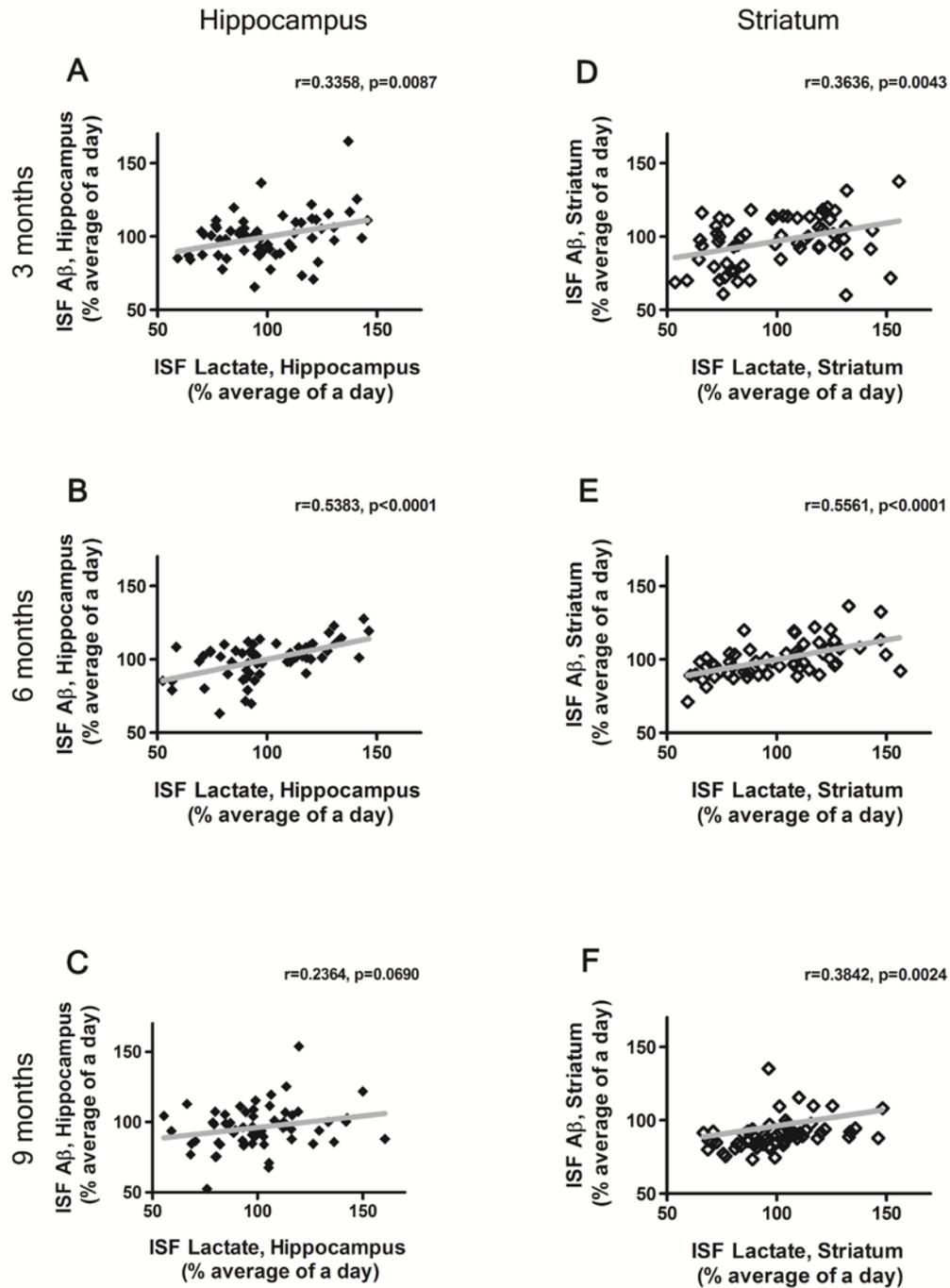
A β plaque deposition in female APP^{swE}/PS1 δ E9 (APP/PS1) mice at 3, 6, and 9 months of age and in female wild-type littermates at 9 months of age. (A-H) Representative brain sections of the hippocampus (A, C, E, G) and striatum (B, D, F, H) stained with anti-A β N-terminal antibody HJ 3.4 to visualize A β immunoreactive plaques. Scale bar in (A) is 500 μ m.

Supplementary Figure 3



Correlation between wakefulness and [concentrations levels](#) of interstitial fluid (ISF) lactate. (A-F) Correlation presented as minutes awake per hour and % average of 24 hours of absolute values of ISF lactate in the hippocampus (A-C) and striatum (D-F) of APP^{swe}/PS1 δ E9 mice at 3, 6, and 9 months (n = 72-96 paired measurement per group; Pearson's correlation test).

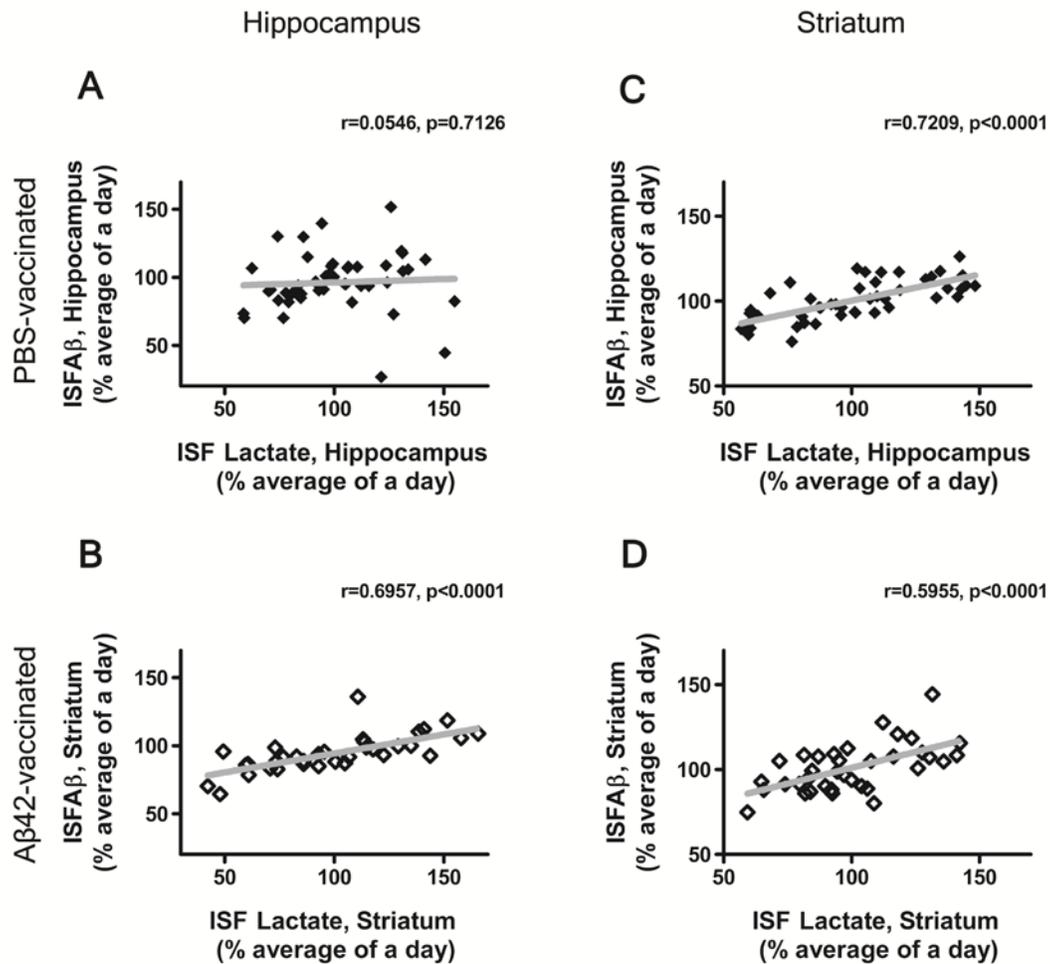
Supplementary Figure 4



Correlation between [concentrations/levels](#) of interstitial fluid (ISF) lactate and ISF A β in APPswe/PS1 Δ E9 mice. (A-F) Correlation presented as % average of 24 hours of absolute values

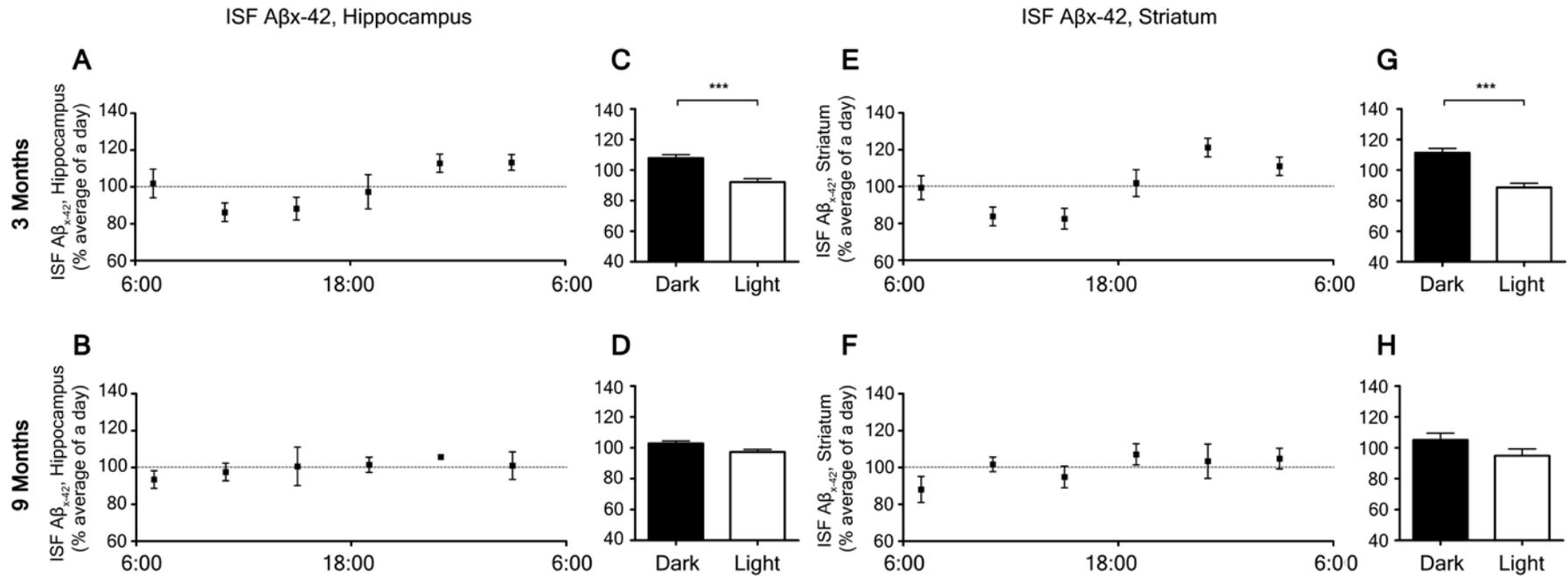
of ISF lactate and % average of 24 hours of absolute values of ISF $A\beta_{1-x}$ in the hippocampus (**A-C**) and striatum (**D-F**) of APP^{swe}/PS1 δ E9 mice at 3, 6, and 9 months of age (n = 60 paired measurement per group; Pearson's correlation test).

Supplementary Figure 5



Correlation between [concentrations/levels](#) of interstitial fluid (ISF) lactate and ISF Aβ in Aβ42- and phosphate buffered saline (PBS)-immunized APP^{swe}/PS1^{ΔE9} mice. (A-D) Correlation presented as % average of 24 hours of absolute values of ISF lactate and % average of 24 hours of absolute values of ISF Aβ_{1-x} in the hippocampus and striatum of PBS-treated APP^{swe}/PS1^{ΔE9} mice (A, C) and Aβ₄₂-vaccinated APP^{swe}/PS1^{ΔE9} mice (B, D) in 9 months of age (n = 36-48 paired measurement per group; Pearson's correlation test).

Supplementary Figure 6

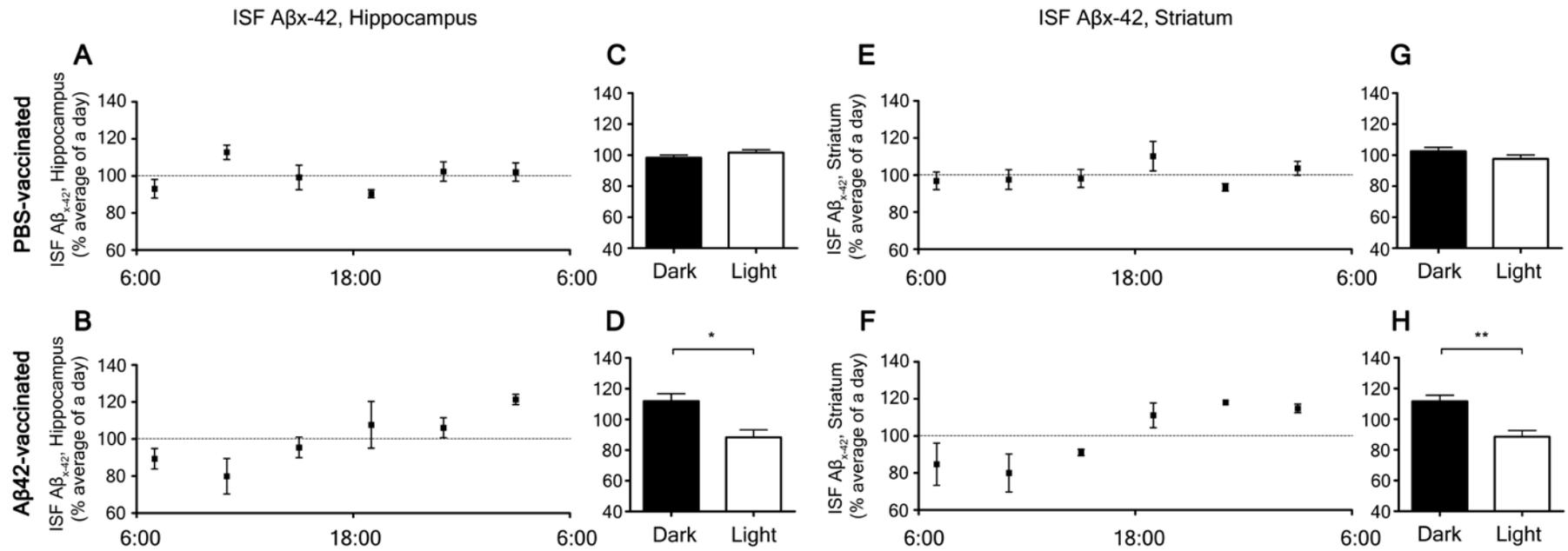


Changes in diurnal fluctuation of interstitial fluid (ISF) Aβ_{x-42} in the hippocampus and in the striatum of 3 and 9 month old

APPswe/PS1δE9 mice. (A, B, E, F) Diurnal fluctuation of ISF Aβ_{x-42} in the hippocampus (A, B) and in the striatum (E, F) of 3 and 9 month old APPswe/PS1δE9 mice across 24 hours (one light-dark period) presented as % average of absolute values of ISF Aβ_{x-42}.

(C, D, G, H) Comparison of % average of 24 hours of absolute values of ISF Aβ_{x-42} in the hippocampus (C, D) and in the striatum (G, H) between the dark and light periods (n = 5 per group; two tailed t-test). ****P* < 0.001. Values represent mean ± s.e.m.

Supplementary Figure 7

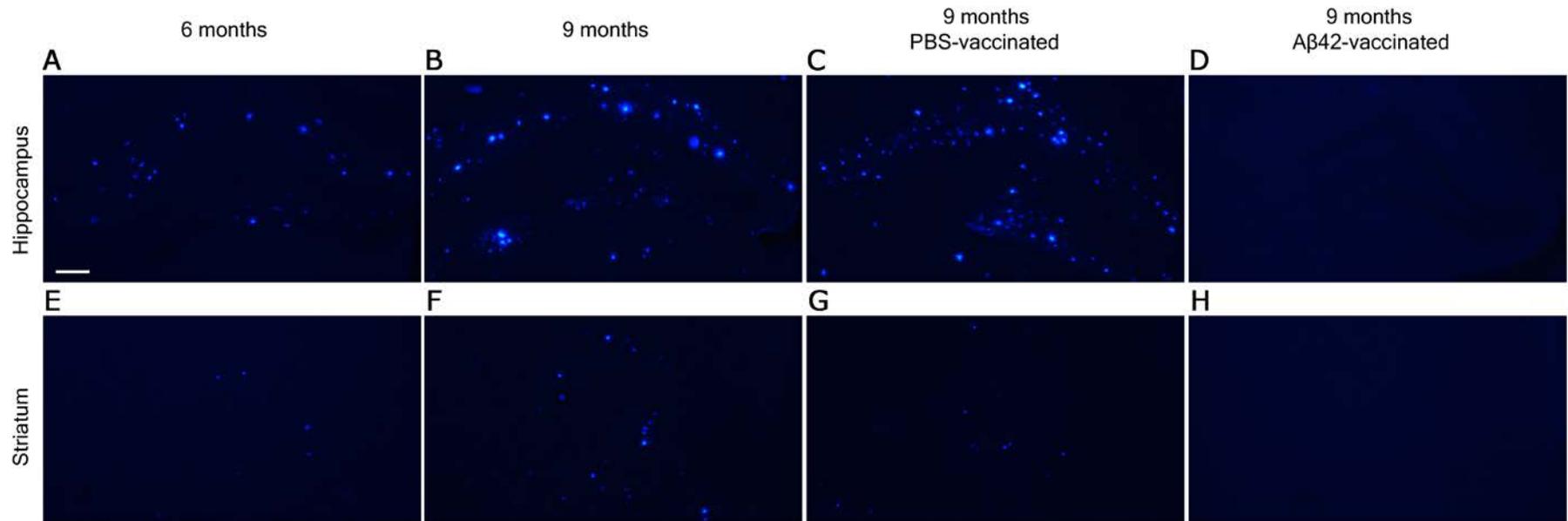


Changes in diurnal fluctuation of interstitial fluid (ISF) Aβ_{x-42} in the hippocampus and in the striatum of 9 month old phosphate buffered saline (PBS)-treated and Aβ₄₂-vaccinated APPsw/PS1δE9 mice. (**A, B, E, F**) Diurnal fluctuation of ISF Aβ_{x-42} in the hippocampus of PBS-treated (**A**) and Aβ₄₂-vaccinated (**B**) APPsw/PS1δE9 mice and diurnal fluctuation of ISF Aβ_{x-42} in the striatum of PBS-vaccinated (**E**) and Aβ₄₂-vaccinated (**F**) APPsw/PS1δE9 mice. Data represents % average of 24 hours of absolute values of ISF Aβ_{x-42} across 24 hours (1 light-dark period). (**C, D, G, H**) Comparison of % average of absolute values of ISF Aβ_{x-42} in the

hippocampus (**C, D**) and in the striatum (**G, H**) between the dark and light periods (n = 5-6 per group; two tailed t-test). * $P < 0.05$;

** $P < 0.01$. Values represent mean \pm s.e.m.

Supplementary Figure 8



X-34 positive amyloid plaque deposition in the hippocampus and striatum of 6 and 9 months old APP_{swe}/PS1 δ E9 mice and 9 months old phosphate buffered saline (PBS)-vaccinated and A β ₄₂-vaccinated APP_{swe}/PS1 δ E9 mice. (A-H) Representative images of hippocampus (A-D) and striatum (E-H) stained by amyloid-binding dye X-34 to visualize fibrillar amyloid plaques in 6 and 9 month old APP_{swe}/PS1 δ E9 mice (A, E, B, F), PBS-treated mice (C, G) and A β ₄₂-vaccinated mice (D, H) at 9 months. Scale bar in (A) is 50 μ m.