Supporting Information

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SI Text

Sleep-Stage Stratification for Different $n:m$ Cardiorespiratory Synchronization Ratios. To identify the relative contribution of different $n:m$ synchronization ratios to the sleep-stage stratification in the degree of cardiorespiratory phase synchronization (Fig. 3 in the main text), and to test whether changes in neuroautonomic control during different sleep stages have different effect on different synchronization ratios, we analyzed the cardiorespiratory synchronization ratios $n:1$, $n:2$, and $n:3$ across all sleep stages (Fig. S1).

We find that $n:1$, $n:2$, and $n:3$ synchronization ratios exhibit a similar sleep-stage stratification pattern (Fig. S1), which is consistent with the pattern shown Fig. 3 in the main text. However, there is a significant difference in the relative contribution of $n:1$, $n:2$, and $n:3$ ratios to the total $n:m$ phase synchronization shown in Fig. 3 (main text). Specifically, we find that $n:1$ synchronization dominates in all sleep stages (Fig. S1*A*), with a significant reduction of approximately 300% in the degree of $n:2$ type synchronization (Wilcoxon Signed Rank Test yields $p < 10^{-3}$ for all within-sleep-stage comparisons, i.e., comparing $n:1$–REM (rapid eye movement) with $n:2$–REM, $n:1$–wake with $n:2$–wake, etc.) (Fig. S1 *A* and *B*), and approximately 15% reduction for the $n:3$ type synchronization (Wilcoxon Signed Rank Tests: $p = 0.030$ comparing $n:1$–REM with $n:3$–REM; $p = 0.809$ comparing $n:1$–wake with $n:3$–wake; $p < 10^{-3}$ for $n:1$–LS (light sleep) vs. $n:3$–LS; $p = 0.040$ for $n:1$–DS (deep sleep) vs. $n:3$–DS) (Fig. S1 *A* and *C*).

Applying a one-way ANOVA with repeated measures separately for each synchronization ratio, we obtain a significant difference across sleep stages with $p < 10^{-3}$ for each of the three synchronization ratios. Further, for all $n:1$, $n:2$, and $n:3$ ratios we find a similar approximate 400% increase from REM to DS in the degree of phase synchronization.

Results from a surrogate test (right bars in red color in Fig. S1 *A*–*C*) based on Fourier phase randomization indicate statistical significance of the observed cardiorespiratory synchronization in each sleep stage. Error bars represent the standard error. All comparisons between real and surrogate data for each sleep stage and synchronization ratio yield $p < 10^{-3}$ (Mann–Whitney Rank Sum Test).

Age Dependence of Cardiorespiratory Phase Synchronization for Different $n:m$ Synchronization Ratios. To further probe the mechanism of cardiorespiratory coupling and whether particular $n:m$ phase-synchronization ratios contribute more to the decline of this coupling with age (Fig. 4, main text), we analyze different ratios of cardiorespiratory phase synchronization separately for each age group (Fig. S2). We find that different synchronization ratios exhibit very different age dependence. Whereas both $n:1$ and $n:2$ show a significant decline with healthy aging (Fig. S2 *A* and *B*), which is consistently more pronounced across all age groups for the $n:1$ ratio with approximately 50% difference between the youngest and the oldest groups (Mann–Whitney Rank Sum Test, $p = 0.036$), the $n:3$ ratio has a maximum for the middle-aged groups (Mann–Whitney Rank Sum Test yields $p = 0.375$ comparing the age groups 20–34 and 35–49 y) followed by a pronounced, however, statistically not significant decline for the oldest group (Mann–Whitney Rank Sum Test, $p = 0.254$ comparing the age groups 50–64 and ≥80 y) (Fig. S2*C*).

Comparing the frequency of occurrence of different synchronization ratios within each age group, we find that $n:1$ synchronization is dominant in all age groups: approximately 300% higher than $n:2$ synchronization (comparing Fig. S2 *A* and *B*), and approximately 30% higher than $n:3$ synchronization (comparing Fig. S2 *A* and *C*).

These results indicate that the effect of sleep regulation on cardiorespiratory synchronization is very different compared to the effect of healthy aging. Indeed, although the sleep-stage stratification pattern for different $n:m$ synchronization ratios remains the same (Fig. S1), the process of aging has different impact on different $n:m$ ratios (Fig. S2).

We find that the decrease in synchronization with age (Fig. 4, main text) is due to a significant reduction during DS and LS—approximately 50% drop comparing the youngest to the oldest group (Fig. 5, main text). This reduction is most pronounced for the $n:1$ synchronization ratio with approximately 70% decline for DS (Fig. S3*A*) and 60% for LS (Fig. S3*B*). In contrast, the $n:1$ synchronization during REM and wake does not change with age (Fig. S3 *C* and *D*). These results indicate that the decline in cardiorespiratory phase-synchronization with age is primarily mediated through the neuroautonomic mechanisms regulating DS and LS. In contrast to $n:1$ synchronization, the $n:2$ ratio exhibits much weaker decline with age (Fig. S3*E*), whereas $n:3$ is not significantly different for all sleep stages across age groups (Fig. S3*F*).

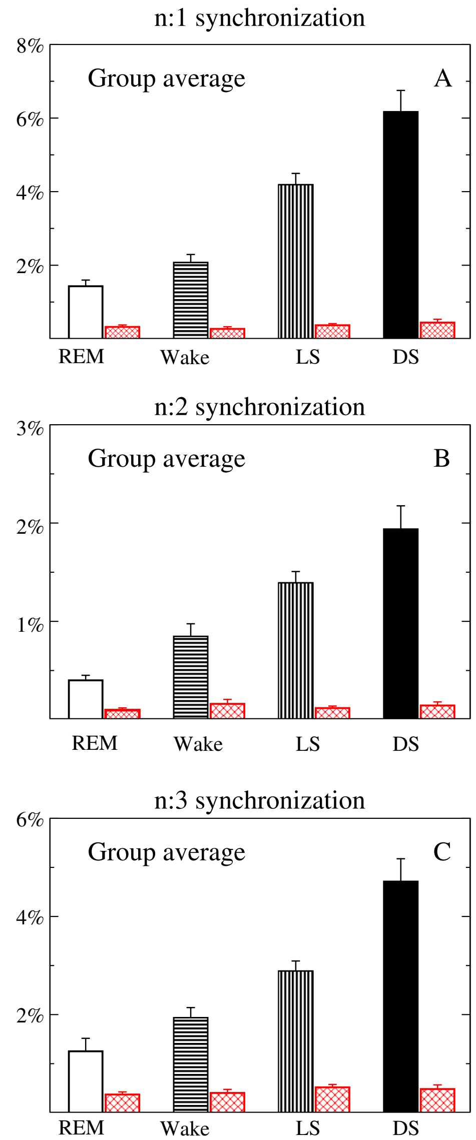

Fig. S1. Robust stratification pattern of cardiorespiratory phase synchronization across sleep stages. The same pattern is consistently observed for $n:1$ (*A*), $n:2$ (*B*), and $n:3$ (*C*) synchronization ratios, indicating a similar effect of sleep-stage regulation on cardiorespiratory synchronization. Remarkably, for each ratio, there is an approximately 400% increase in the degree of phase synchronization with transition from REM to DS.

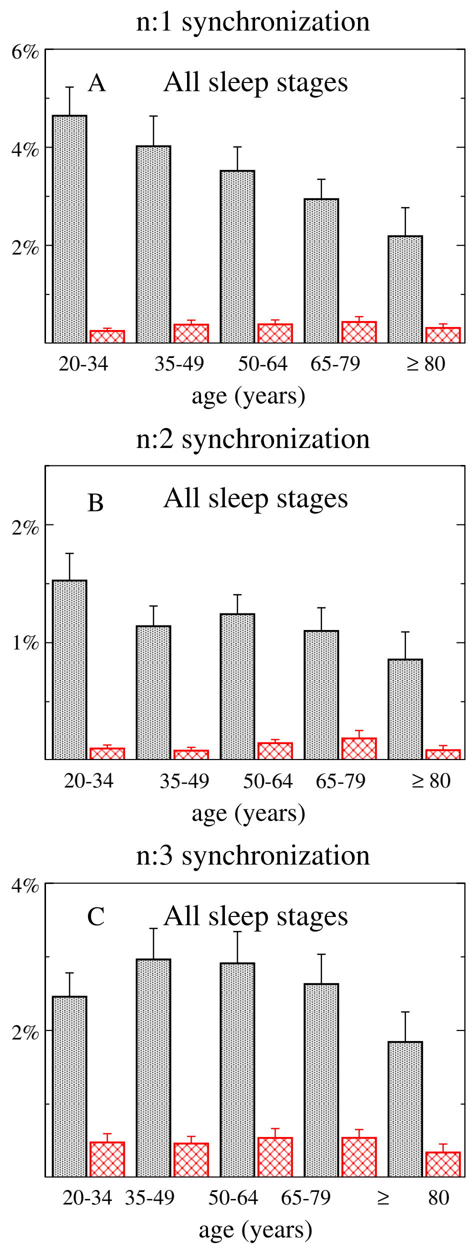

Fig. S2. Cardiorespiratory phase synchronization in different age groups for $n:1$ (*A*), $n:2$ (*B*), and $n:3$ (*C*) synchronization ratios. Although for all ratios there is a relative decrease in the synchronization for the oldest subjects, the most pronounced age effect is observed for the $n:1$ synchronization ratio, which monotonously decreases by approximately 50%— the main contributor to the reduction in $n:m$ synchronization with increasing age, shown in Fig. 4 in the main text. Right bars in red color show results from the same surrogate test as in Fig. S1 and indicate significance of the results for all age groups and all synchronization ratios (Mann–Whitney Rank Sum Test for all age groups and synchronization ratios, $p < 10^{-2}$). Error bars represent the standard error.

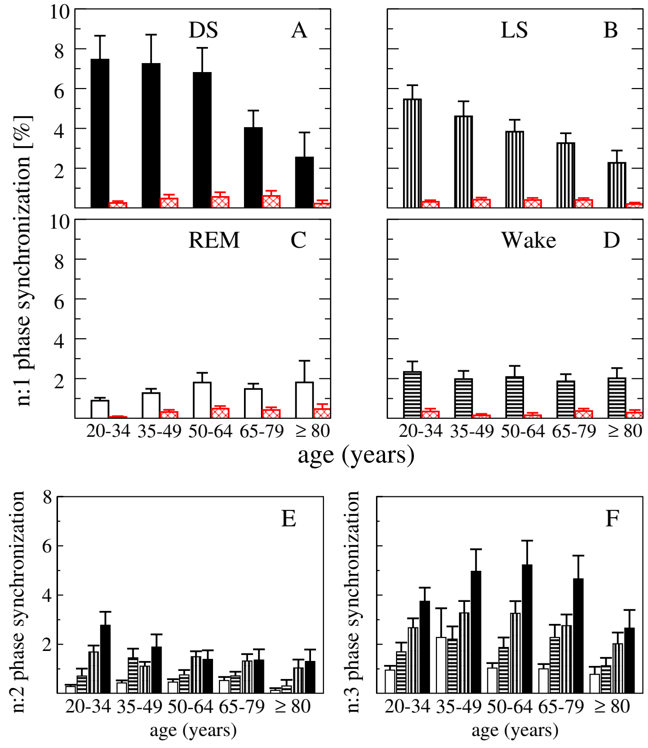

Fig. S3. Sleep-stage stratification pattern in cardiorespiratory phase synchronization for different synchronization ratios across age groups. (*A*–*D*) Relative contribution of $n:1$ synchronization across sleep stages for different age groups. A significant approximate 70% reduction of $n:1$ synchronization with age is observed for DS and LS, in contrast to REM and wake where there is no age dependence. Right bars in red show synchronization from a surrogate test as in Figs. S1 and S2, indicating significance of the results for all sleep stages and age groups. (*E* and *F*) The same sleep-stage stratification pattern is observed in all age groups for $n:2$ and $n:3$ synchronization ratios, although with a lower percent synchronization compared to $n:1$. Error bars in all panels show the standard error.