Supplementary materials

Disassortative network structure improves the synchronization between neurons in the suprachiasmatic nucleus

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I Effect of lag in the method of transfer entropy

We also check the case of *lag* =2 in Eq. (1). The results for *lag* =2 shown in Fig. S1 is consistent with Fig. 2 (*lag* =1) in the main text.

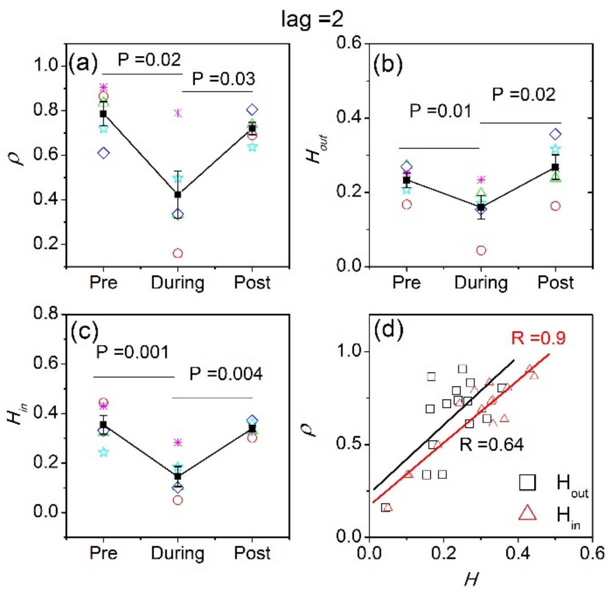

Fig. S1The results of *lag* =2. This figure corresponds to Fig. 2.

II Distribution of out-degree

The heterogeneity can be explained by the distribution of the node degree, i.e., if the distribution satisfies a power-law form, the network is considered to be heterogeneous. Figure S2 shows the distribution of out-degree in log-log plot for all derived networks. It is evident that the range of out-degree is from 1 to ~100, almost across two scales for each stage, and a power-law form is observed in the distribution of out-degree in each network in (a-e) for pre-TTX, in (f-j) for during-TTX and in (k-o) for post-TTX. The scaling exponent *b* differs between the stages. In particular, the exponent of during-TTX -1.50 ± 0.12 (mean$\pm$se) is significantly smaller than pre-TTX -1.36 ± 0.11 (paired t-test, P =0.05) or post-TTX 1.31 ± 0.06 (paired t-test, P =0.01).

Based on the method of Ref.[1], we calculate the Log-likelihood ratio L_R for the out-degrees within each network. If L_R >0, the out-degrees are more likely in the power-law distribution, and if L_R <0, the out-degrees are more likely in the exponential distribution. Table S1 shows that the out-degrees of most the networks examined in this paper more likely satisfy a power-law distribution, with the exception of SCN3 or SCN5 in the stage of post-TTX.

Table S1 Log-likelihood ratio L_R between power-law distribution and exponential distribution for out-degrees. If L_R >0, the out-degrees are more likely in the power-law distribution, and if L_R <0, the out-degrees are more likely in the exponential distribution. P is the significance value for that direction (the value of p >0.05 corresponds to significant result).

L_R, P	SCN1	SCN2	SCN3	SCN4	SCN5
pre-TTX	0.82, 0.41	0.63, 0.53	0.05, 0.96	1.43, 0.15	0.97, 0.33
dur-TTX	1.09, 0.27	0.56, 0.58	1.11, 0.27	0.95, 0.34	3.02, 0.00
post-TTX	5.47, 0.00	1.30, 0.19	0.00,1.00	1.05, 0.29	-0.24, 0.81

III Distribution of in-degree

Figure S3 shows the distribution of in-degree in log-log plot for all derived networks. It is evident that the range of in-degree is from 1 to ~100, almost across two scales for each stage, and a power-law form is observed in the distribution of in-degree in each network in (a-e) for pre-TTX, in (f-j) for during-TTX and in (k-o) for post-TTX. The scaling exponent *b* differs between the stages. In particular, the exponent of during-TTX -1.92 ± 0.21 (mean$\pm$se) is significantly smaller than pre-TTX -1.45 ± 0.14 (paired t-test, P =0.01) or post-TTX 1.41 ± 0.09 (paired t-test, P =0.02).

Based on the method of Ref.[1], we also calculate the Log-likelihood ratio L_R for the in-degrees within each network. Table S2 shows that the in-degrees of nine of the networks examined in this paper more likely satisfy a power-law distribution, and the in-degrees of the other six networks more likely satisfy in an exponential distribution.

Table S2 Log-likelihood ratio L_R between power-law distribution and exponential distribution for in-degrees. If L_R >0, the in-degrees are more likely in the power-law distribution, and if L_R <0, the in-degrees are more likely in the exponential distribution. P is the significance value for that direction (the value of p >0.05 corresponds to significant result).

L_R, P	SCN1	SCN2	SCN3	SCN4	SCN5
pre-TTX	5.76, 0.00	-1.10, 0.27	-0.49, 0.62	0.32, 0.75	-0.61, 0.54
dur-TTX	-0.33, 0.74	0.93, 0.35	-3.16, 0.00	0.67, 0.50	1.34, 0.18
post-TTX	-0.48, 0.00	5.10, 0.00	5.32, 0.00	6.22, 0.00	0.41, 0.68

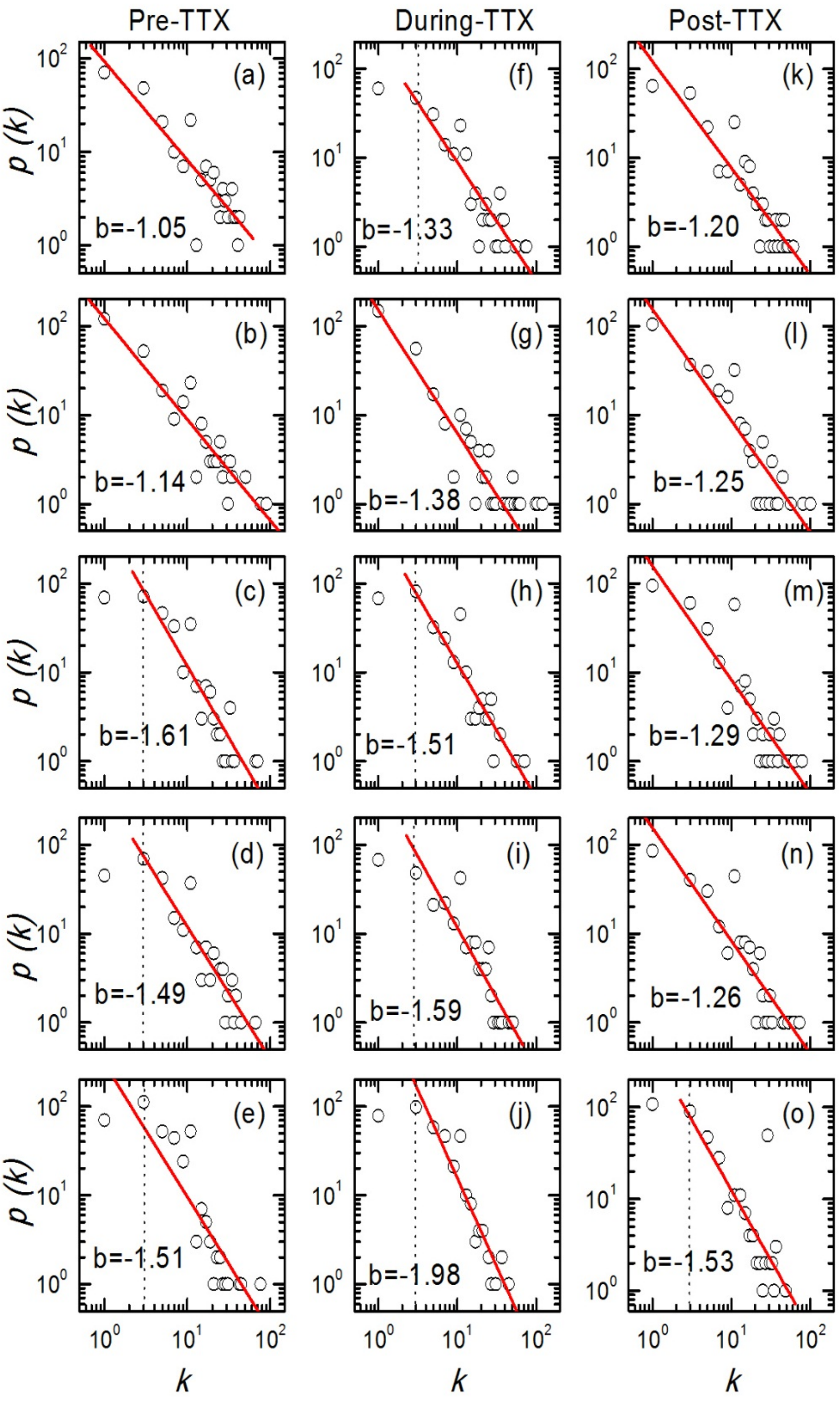

Fig. S2 The distribution of out-degree for each slice, (a-e) in the stage of pre-TTX, (f-j) in the stage of during-TTX , (k-o) in the stage of post-TTX. X-axis and Y-axis represents the node degree K_{out} and the number of nodes with K_{out}, respectively. The parameter b represents the slope of the fitted straight line, i.e., the scaling exponent. The dotted line indicates the start point for the fitted straight line

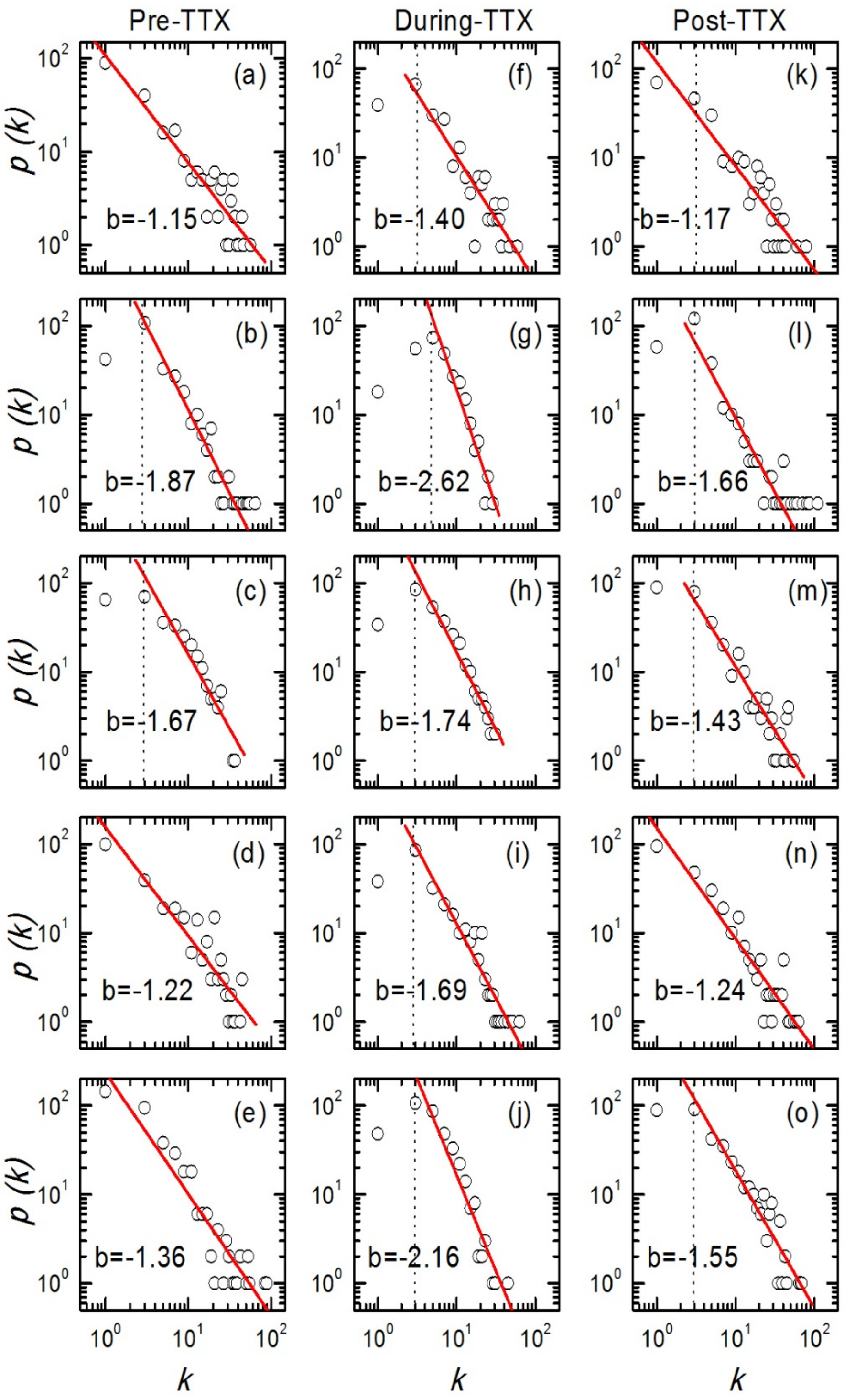

Fig. S3 The distribution of in-degree for each slice, (a-e) in the stage of pre-TTX, (f-j) in the stage of during-TTX, (k-o) in the stage of post-TTX. X-axis and Y-axis represents the node degree K_{in} and the number of nodes with K_{in}, respectively. The parameter b represents the slope of the fitted straight line, i.e., the scaling exponent. The dotted line indicates the start point for the fitted straight line

IV Correlation between out-degree and in-degree

We examine whether there is a correlation between out-degrees and in-degrees (Fig. S4). A negative correlation is observed in the stage of pre-TTX (R=-0.30$\pm$0.03, mean ± se) and post-TTX (R=-0.29$\pm$0.03, mean ± se), and weak or no correlation is observed in the stage of during-TTX (R=-0.08$\pm$0.1, mean ± se). The correlation coefficient *R* is significantly larger in the stage of pre-TTX (paired t-test, *P*=0.01) or post-TTX (paired t-test, *P* =0.01) than in the stage of during-TTX. A negative correlation in the stage of pre-TTX and post-TTX represents that a node of a larger out-degree is likely to have a smaller in-degree, and vice versa, e.g., the neurons in the VL which have more out-links to the DM neurons, but have less in-links.

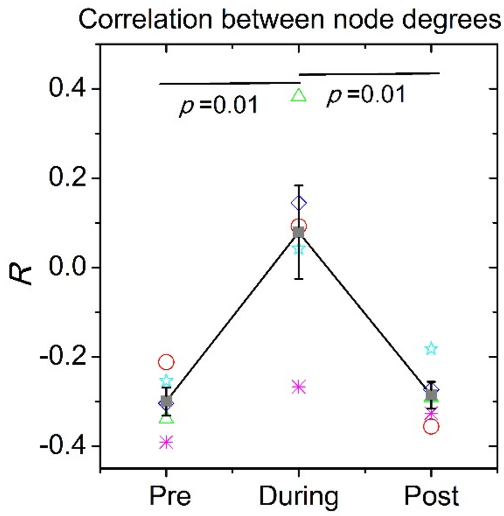

Fig. S4 The correlation coefficient R between out-degree and in-degree within each stage.

V Relationship between the synchronization and the average node-degree

We use the method of univariate/multiple linear regression to check the relationship of the synchronization degree $\boldsymbol{\rho}$ to the average node degree *K*. We find that the relationship is not significant. In particular, for univariate linear regression, the Pearson coefficient is *R*=0.5 *(P* =0.06). The results for multiple linear regression are as follows. The contribution of three variables, which are the average node degree, the disassortativity coefficient for the out-degrees and the disassortativity coefficient for the in-degrees, to the synchronization degree is examined by the method of multiple linear regression (sample size is 3*5=15). There is a significant linear relationship of the synchronization degree to these three variables together (Multiple *R* =0.88, *F* of 12.2 > Significance *F* of 0.0008). The relationship of the synchronization degree to the average node degree alone is not significant (*P* = 0.99), the relationship of the synchronization degree to the disassortativity coefficient for the out-degrees alone is also not significant (*P* = 0.49), but the relationship of the synchronization degree to the disassortativity coefficient for the in-degrees is significant (p = 0.001). Therefore, we conclude that the effect of the average node degree is not significant.

Reference

1. Alstott J, Bullmore E, Plenz D (2014) Powerlaw: a Python package for analysis of heavy-tailed distributions. *PLoS One* 9: e85777.