SUPPLEMENTARY MATERIAL

Supplement to: Spatiotemporal patterns of high-frequency activity (80-170 Hz) in long-term intracranial EEG.

Contents

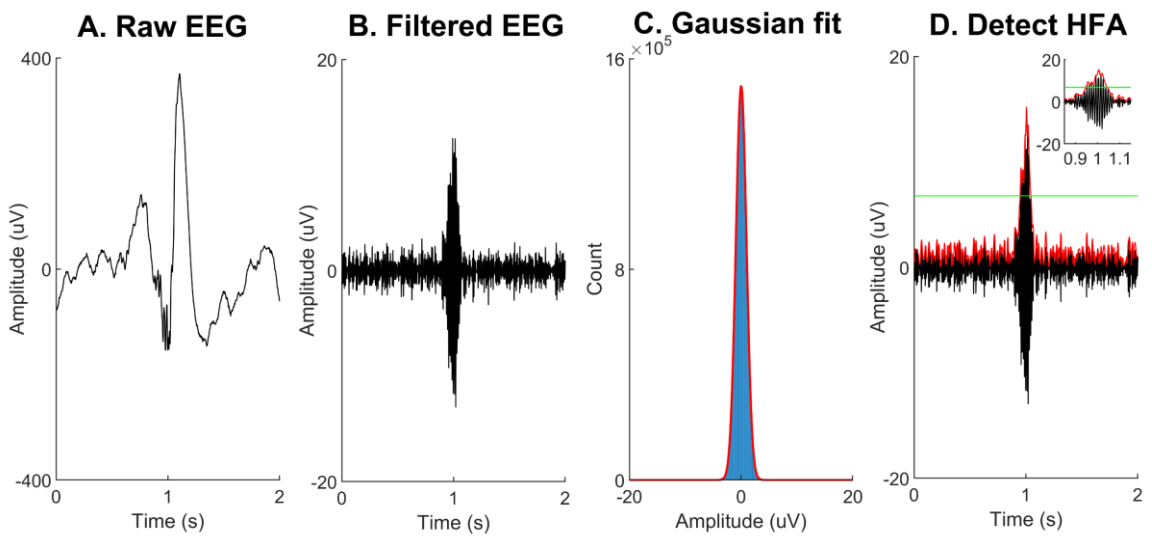

Figure e-1. High-frequency activity (HFA) detection procedure. (**A**) Raw iEEG was (**B**) filtered using an order-12 infinite impulse response (IIR) bandpass filter with frequency range 80-170 Hz. (**C**) A Gaussian curve was fitted to the histogram of the amplitudes from 300 randomly selected filtered iEEG samples each of 10 minutes duration. The Gaussian curve was fitted separately for each electrode. (**D**) A threshold of 5 standard deviations (SD) of the fitted Gaussian curve was selected as a threshold (green line) to detect HFA. An HFA was detected if the envelope (red curve) exceeded the amplitude threshold.

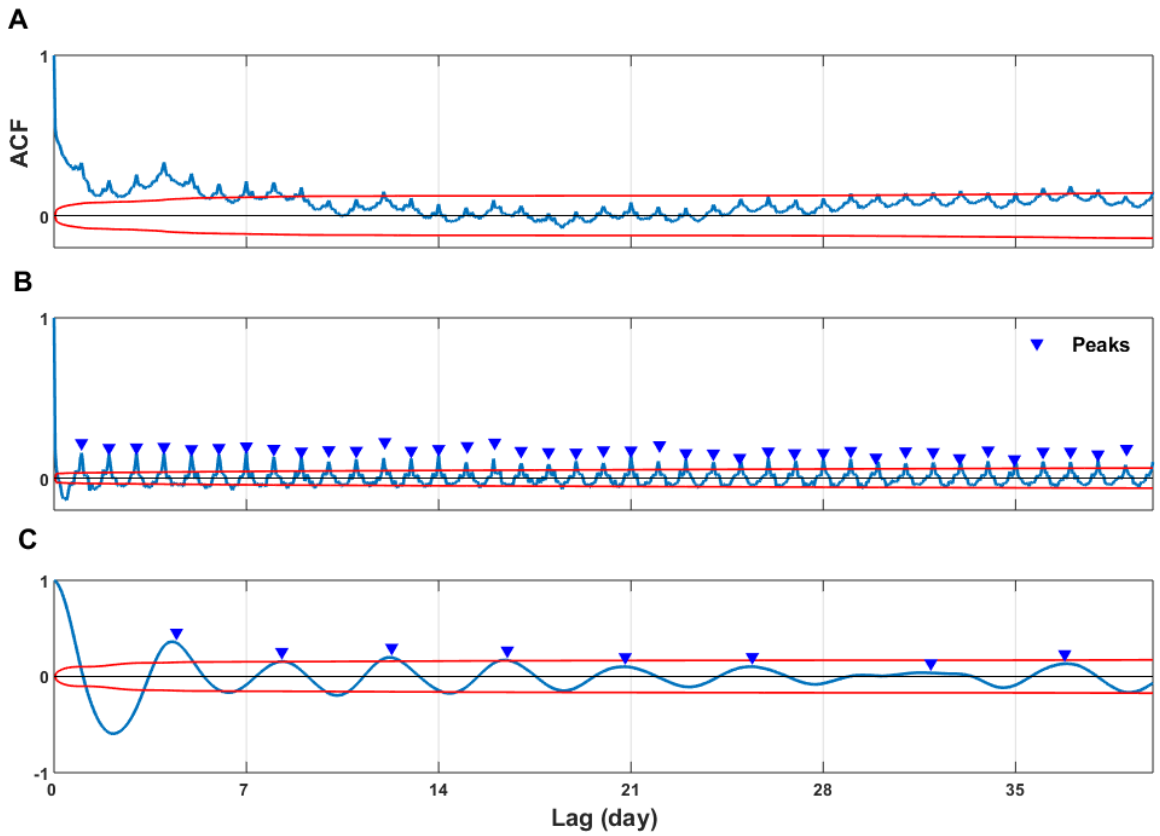

Figure e-2. Illustration of the periodicity detection method based on the regularity of peaks in the autocorrelation function (ACF) of the signal. (**A**) The ACF of the raw signal (HFA rate from one example patient). (**B**) The ACF of the signal with short cycles, which was obtained by subtracting the signal smoothed with a moving average filter of length 1 day from the unfiltered signal. (**C**) The ACF of the signal with long cycles, which was obtained by subtracting the signal smoothed with a moving average filter of length 7 days from the signal smoothed with a moving average filter of length 1 day. The red curves show the 99% confidence bounds; an ACF value outside the bounds indicates that the ACF value is significant and is statistically unlikely to be caused by chance.

Table e-1. HFA detection validation. One experienced neurologist (US) marked HFOs in 2688 minutes (i.e., 384 1-min epochs per patient × 7 patients) of iEEG data that were randomly sampled from seven patients. Manually marked HFOs were compared to automatically detected HFA.

Patient	HFA	HFOs	Proportion of HFOs detected as HFA	Proportion of HFA not marked as HFOs	Similarity
3	7,692	6,767	0.84	0.15	0.84
7	866	762	0.66	0.39	0.64
8	2,608	2,119	0.72	0.28	0.72
10	1,585	550	0.87	0.66	0.47
12	2,137	1,010	0.93	0.55	0.61
13	5,528	2,311	0.93	0.51	0.62
15	1,501	1,147	0.60	0.49	0.55
Total	21,917	14,666	0.82	0.37	0.71

Table e-2. The inter-rater agreement on HFO marking. Three neurologists (US, WD, and CF) independently marked HFOs in the same randomly selected 112 minutes of iEEG data. Manually marked HFOs were compared to the automatically detected HFA and HFOs marked by different reviewers were also compared.

Reviewer	HFA	HFOs	Proportion of HFOs detected as HFA	Proportion of HFA not marked as HFOs	Similarity / Inter-rater Agreement
US	1,334	886	0.81	0.38	0.70
WD	1,334	738	0.82	0.51	0.61
CF	1,334	1,440	0.64	0.26	0.69
US vs. WD	-	-	-	-	0.75
US vs. CF	-	-	-	-	0.72
WD vs. CF	-	-	-	-	0.61

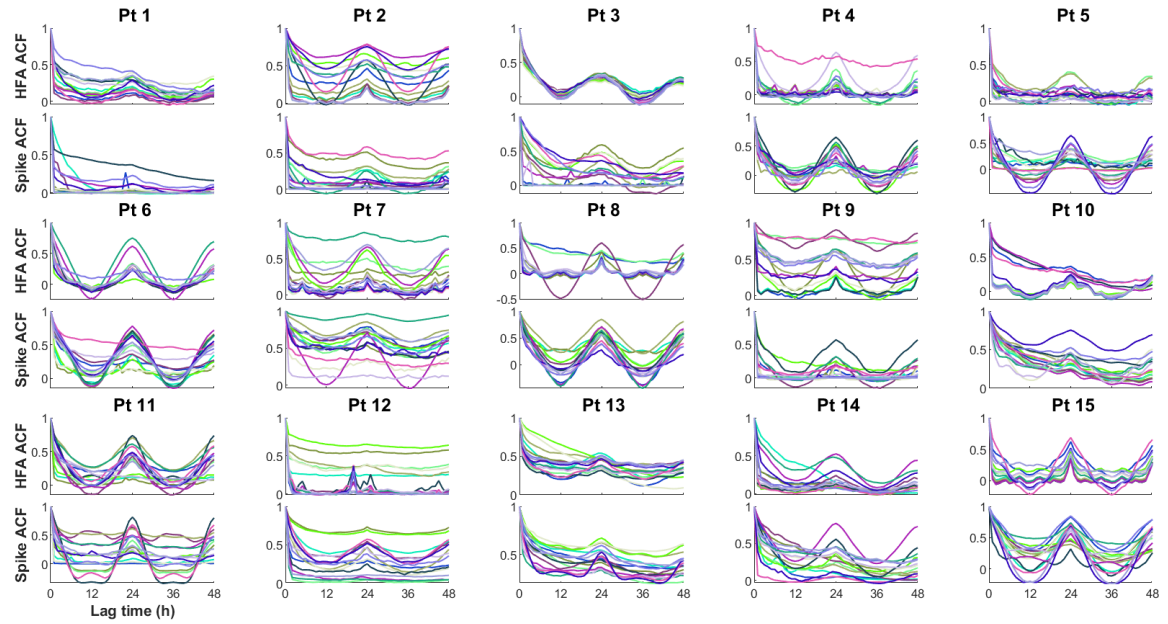

Figure e-3. The ACFs of HFA and spike rates showing lag times up to 48 h. The different colors indicate the 16 different electrodes; colors are consistent between HFA and spike plots.

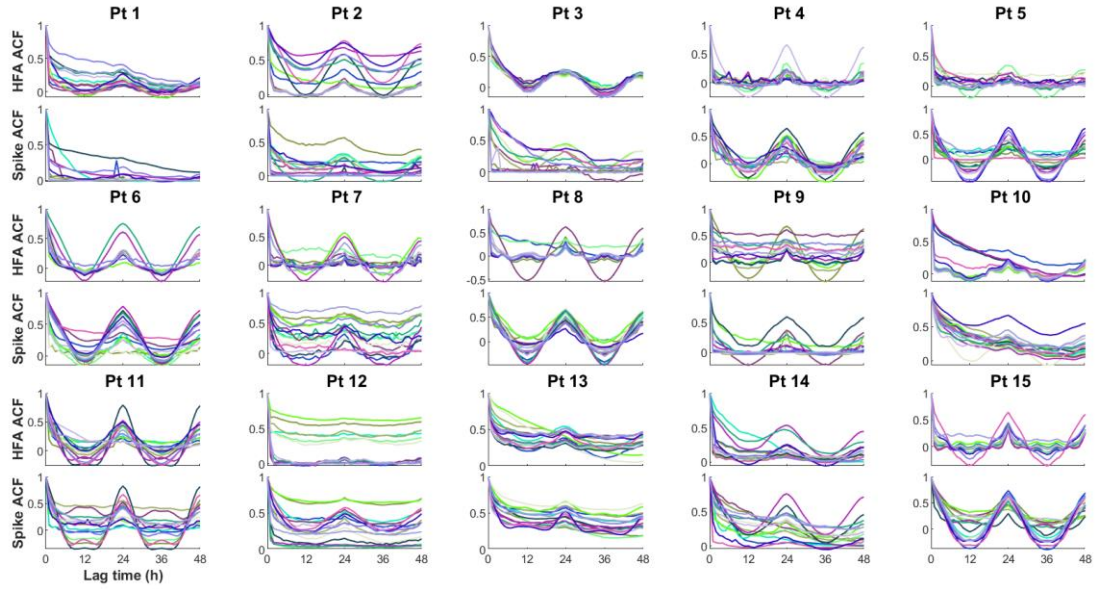

Figure e-4. The ACFs of HFA and spike rates (excluding data from the first 100 days). The different colors indicate different electrodes; colors are consistent between HFA and spike plots.

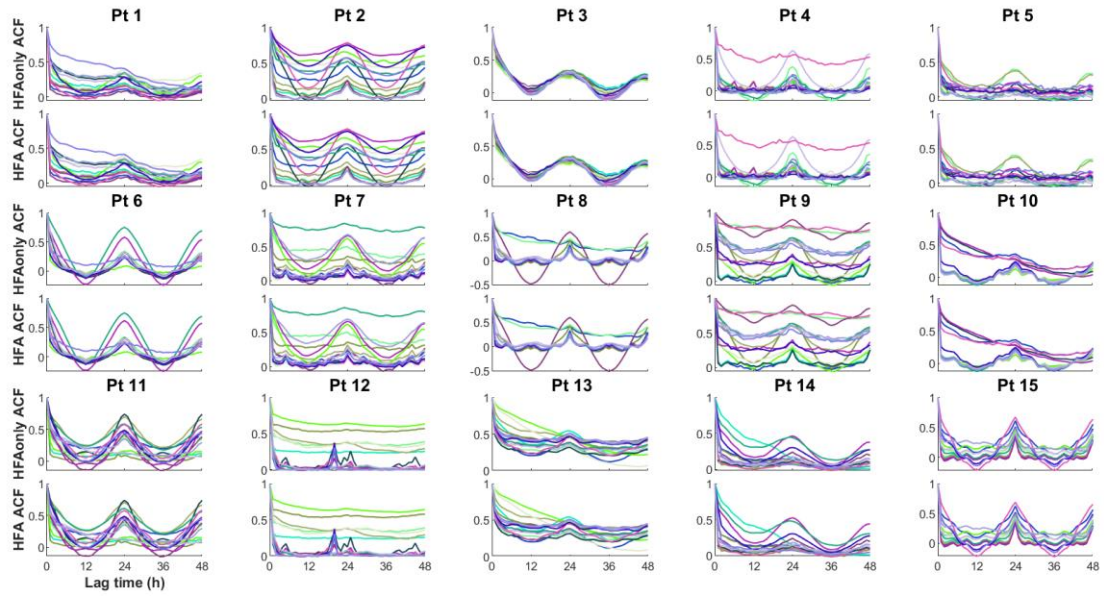

Figure e-5. The ACFs of rates of HFA without spikes (indicated as HFA only) and HFA. HFA without spikes were obtained by deleting any HFA indices that were up to 2 indices before the peak of spike and up to 8 indices after the peak of spike. The different colors indicate different electrodes; colors are consistent between HFA only and HFA plots.

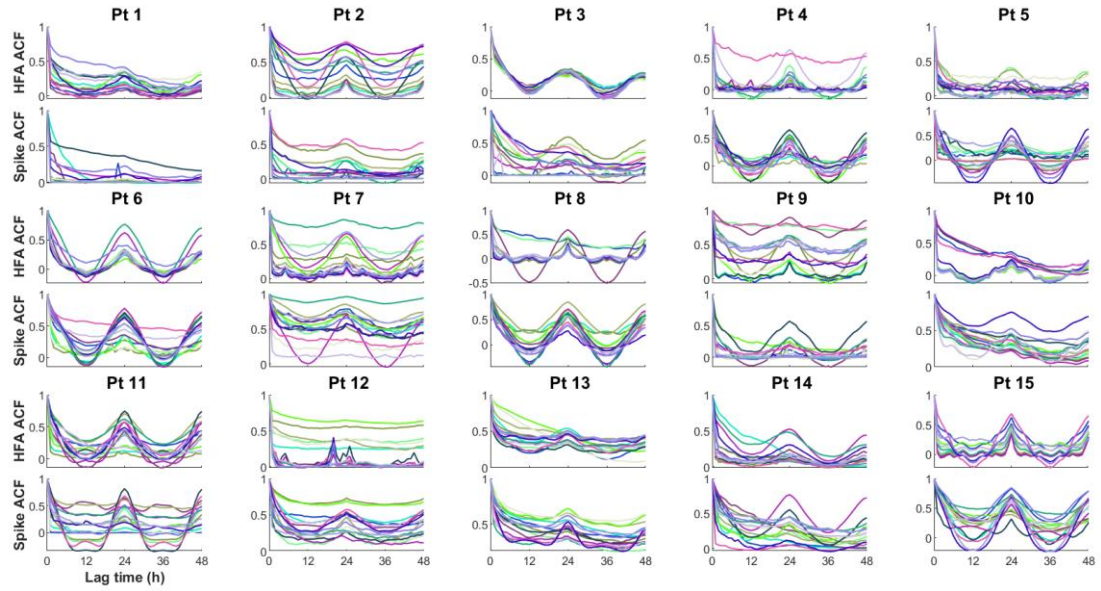

Figure e-6. The ACFs of rates of HFA and spike (excluding events in seizure periods). The different colors indicate different electrodes; colors are consistent between HFA and spike plots.

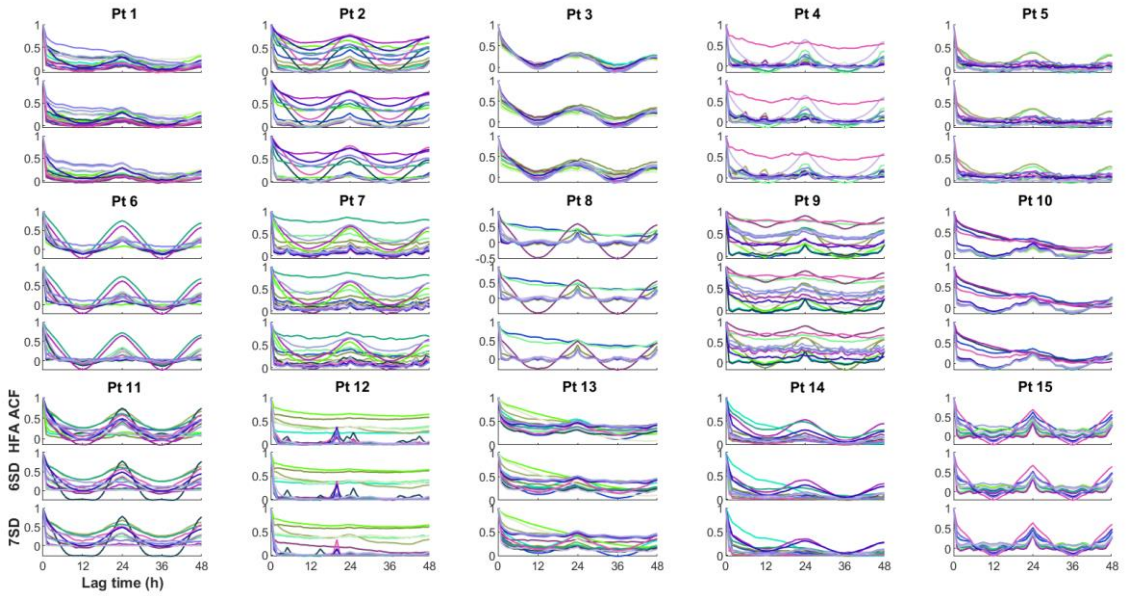

Figure e-7. The ACFs of HFA rates detected after increasing the amplitude thresholds to 6 SD and 7 SD. The different colors indicate different electrodes; colors are consistent in plots of HFA detected by different thresholds.

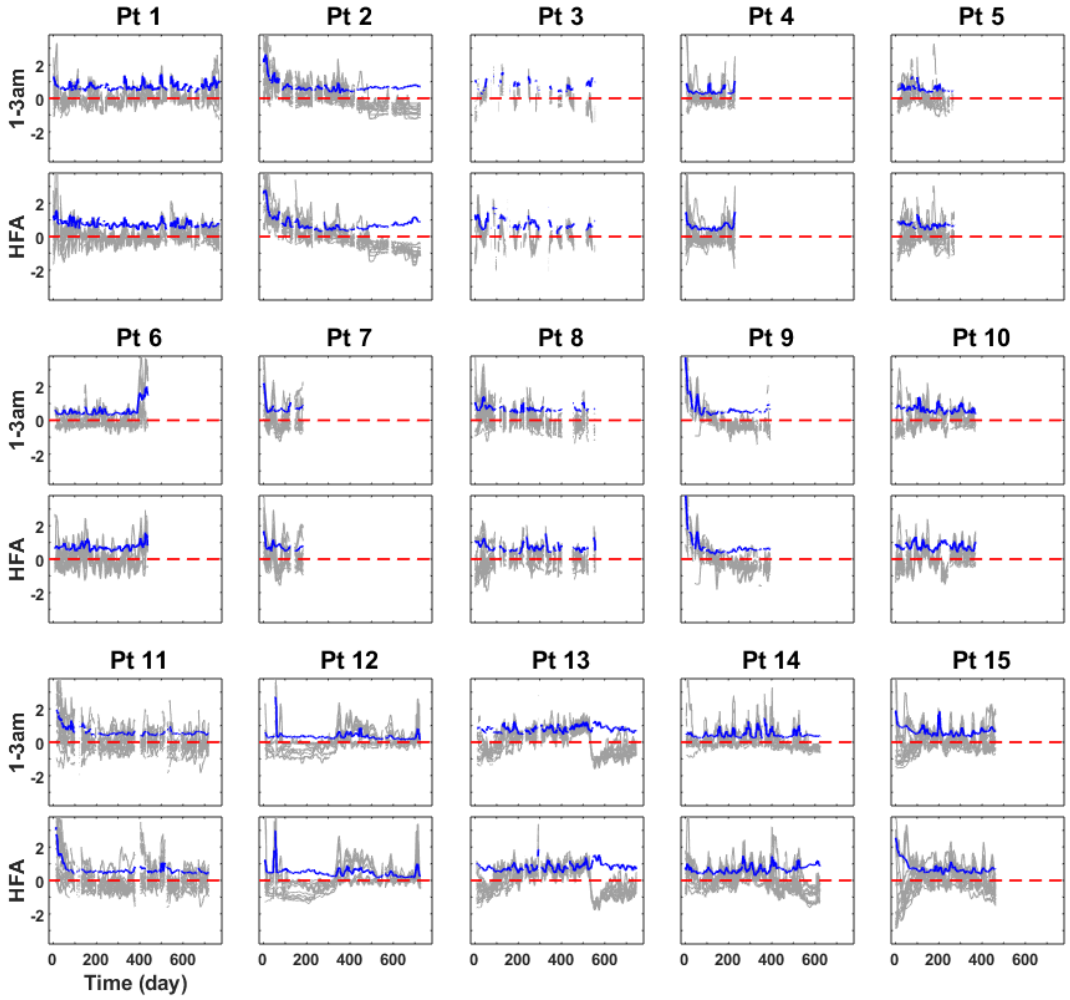

Figure e-8. Changes in HFA rates during the whole day (indicated as HFA) and HFA rates during 1-3 am. Rates were normalized using the z-score. The grey line indicates the z-scored rates of each electrode. The blue line indicates the average of the magnitude of the z-scores across the 16 electrodes. For visualization purposes, the z-scores were smoothed using a moving average filter with a window length of 10 days.

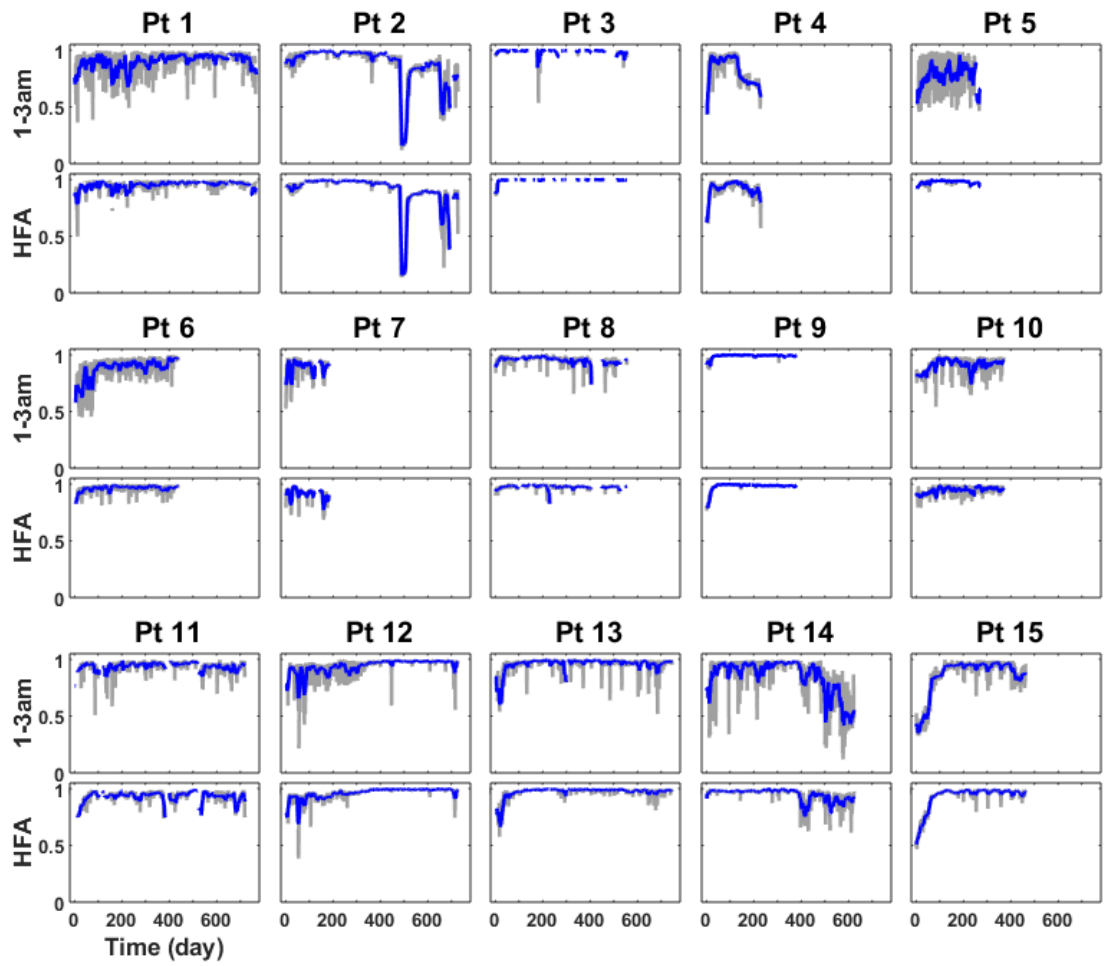

Figure e-9. Changes in the spatial distributions of HFA rates during the whole day and the spatial distributions of HFA rates during 1-3 am. The changes in the spatial distributions were calculated as cosine similarities of the spatial distributions of HFA rate on each recording day to the spatial distribution of HFA rate averaged across all recording days. The grey lines represent the similarity values on each recording day. The blue line indicates the smoothed similarity values, which were smoothed using a moving average filter with a window length of 10 days.