Supplementary Material for:

The pulse: transient fMRI signal increases in subcortical arousal systems during transitions in attention

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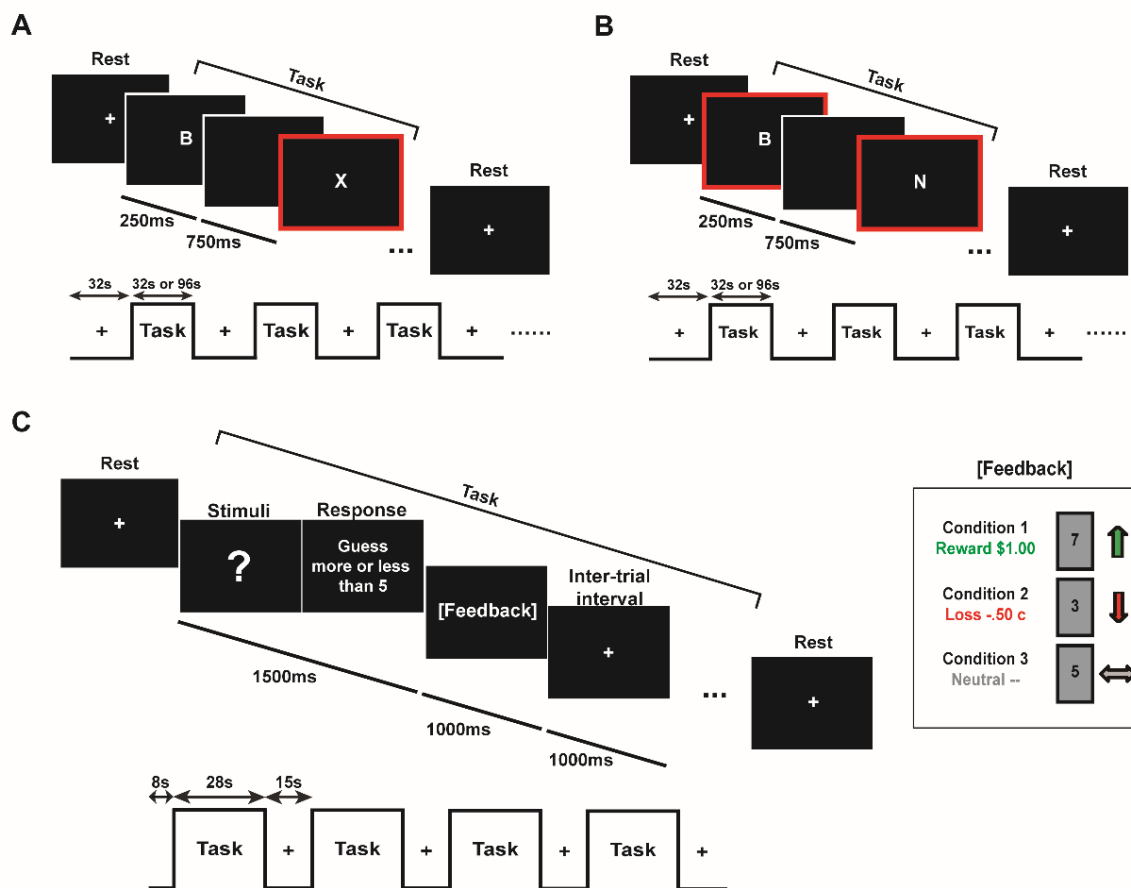
**S**upplementary **Figure 1: Behavioral paradigms for CPT/RTT (A-B) and HCP gambling task (C).** Each CPT/RTT run consisted of alternating blocks of 32s of fixation and 32s or 96s periods of task. The task block duration (32s or 96s) was constant within any given run. (A) During the CPT task, participants were instructed to respond to the target letter X by using their right thumb to push a button. 16 letters were displayed for 250ms each in a randomized sequence (e.g. A B C D E F H I L M N O T X Y Z) and twenty-five percent of all letters shown were the target X. (B) The RTT block required the subjects to push the button with their right thumb for every displayed letter and no letter X appeared in the sequence. During the rest block, participants were instructed to passively view a white fixation cross shown at the center of the screen on top of a black background. (C) Each HCP gambling task run consisted of an 8s count

down period followed by 4 alternating blocks of 28s of task and 15s of fixation. At the onset of each trial, participants were asked to guess whether the number on a mystery card (represented by a "?") was higher or lower than 5 by pressing one of the two buttons on the response box using their right hands. After a choice was made, the value of the card was revealed and followed by the appropriate feedback. See Methods text and references describing the tasks in greater detail.
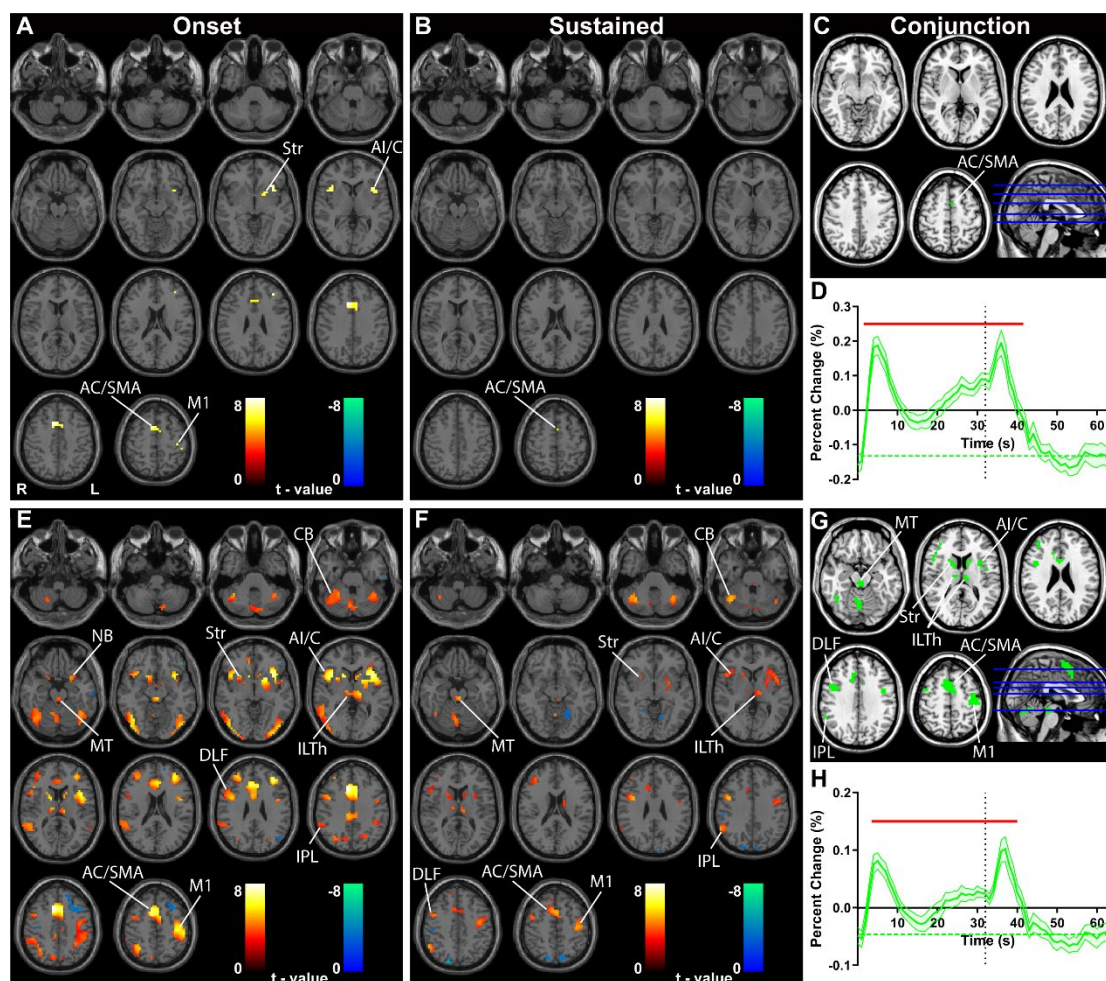
Supplementary Figure 2 (Related to Figure 1): Transient and sustained fMRI changes in subcortical and cortical networks during CPT/RTT task in 22 healthy adolescents. (A-B) GLM-based t-maps are shown for the transient onset HRF (A) and sustained boxcar function convolved with the HRF (B) at FWE-corrected height threshold p < 0.05 and extent threshold k = 3 voxels. (C) Conjunction analysis of fMRI increases in the onset and sustained t-maps from A and B. (D) Mean time course and standard error (across participants) of fMRI percent change in all voxels from conjunction analysis in C. Time 0 s is onset of CPT/RTT task block, and time 32 s is onset of fixation (indicated by vertical dotted line). Significant changes from baseline (horizontal green dashed line) are indicated by the horizontal red bar (two-tailed t-test, Bonferroni-corrected p < 0.05). (E-F) t-maps for the transient onset HRF (E) and sustained

boxcar function convolved with the HRF (F) at uncorrected height threshold p < 0.005, extent threshold k = 3 voxels. This less stringent height threshold was used to allow visualization of changes that may occur below the corrected threshold for statistical significance. (G) Conjunction analysis of fMRI increases in the onset and sustained t-maps from E and F. (H) Mean and standard error time course of all voxels from conjunction analysis in G (same format as D). Note that time courses in D and H show only the 32s task block data to simplify temporal alignment of task onset and offset, however very similar results were obtained when analyzing the 96s task blocks separately (data not shown). Warm colors in A, B, E, F show fMRI changes in parallel to the model and cool colors show negative changes. Midbrain tegmentum (MT), thalamus (Th), striatum (Str), nucleus basalis (NB), cerebellum (CB), anterior insula/claustrum (AI/C), inferior parietal lobule (IPL), anterior cingulate cortex (AC), supplementary motor area (SMA), dorsolateral frontal cortex (DLF), left hemisphere hand primary motor cortex (M1). n = 22 subjects.
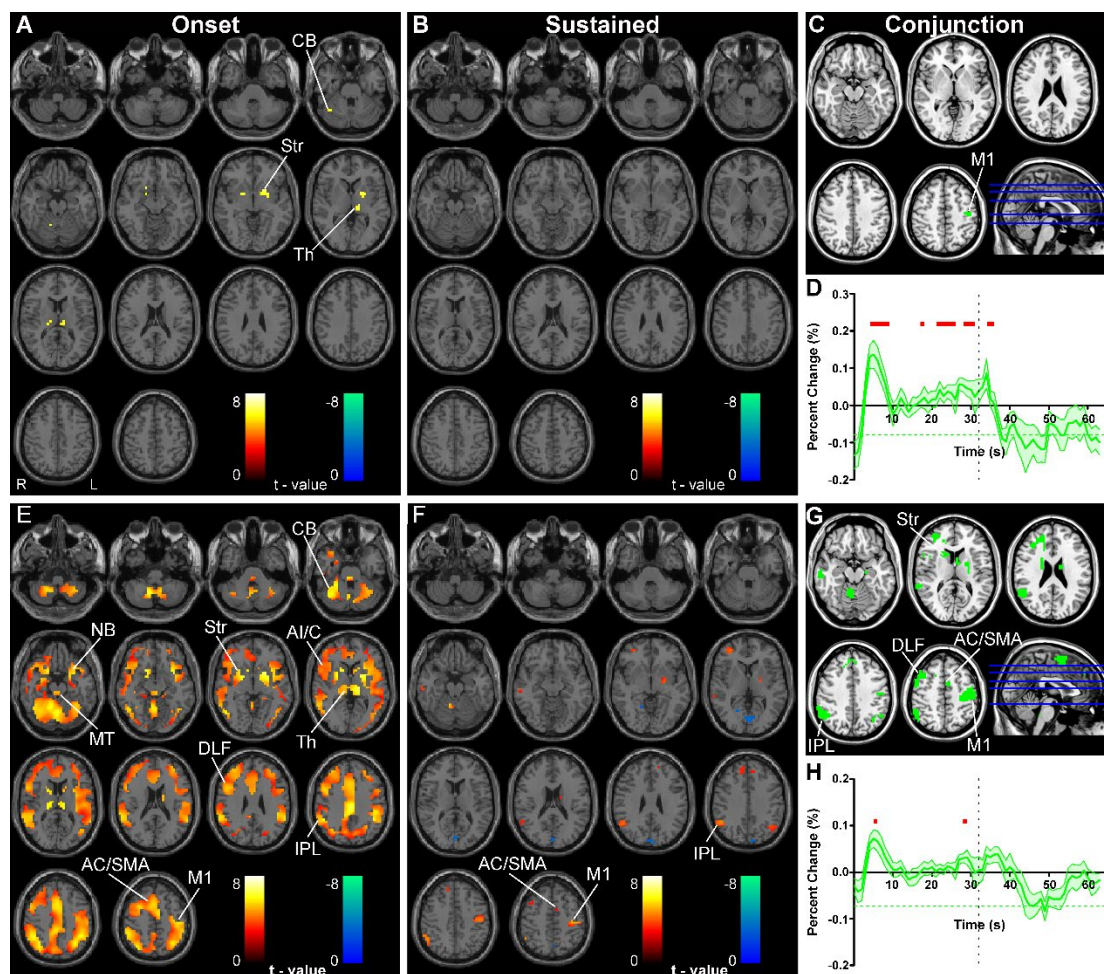
Supplementary Figure 3 (Related to Figure 1): Transient and sustained fMRI changes in subcortical and cortical networks during CPT/RTT task in 24 absence epilepsy patients.

(A-B) GLM-based t-maps are shown for the transient onset HRF (A) and sustained boxcar function convolved with the HRF (B) at FWE-corrected height threshold $p < 0.05$ and extent threshold $k = 3$ voxels. (C) Conjunction analysis of fMRI increases in the onset and sustained t-maps from A and B. (D) Mean time course and standard error (across participants) of fMRI percent change in all voxels from conjunction analysis in C. Time 0 s is onset of CPT/RTT task block, and time 32 s is onset of fixation (indicated by vertical dotted line). Significant changes from baseline (horizontal green dashed line) are indicated by the horizontal red bar (two-tailed t-test, Bonferroni-corrected $p < 0.05$). (E-F) t-maps for the transient onset HRF (E) and

sustained boxcar function convolved with the HRF (F) at uncorrected height threshold p < 0.005, extent threshold k = 3 voxels. This less stringent height threshold was used to allow visualization of changes that may occur below the corrected threshold for statistical significance. (G) Conjunction analysis of fMRI increases in the onset and sustained t-maps from E and F. (H) Mean and standard error time course of all voxels from conjunction analysis in G (same format as D). Note that time courses in D and H show only the 32s task block data to simplify temporal alignment of task onset and offset, however very similar results were obtained when analyzing the 96s task blocks separately (data not shown). Warm colors in A, B, E, F show fMRI changes in parallel to the model and cool colors show negative changes. Midbrain tegmentum (MT), thalamus (Th), striatum (Str), nucleus basalis (NB), cerebellum (CB), anterior insula/claustrum (AI/C), inferior parietal lobule (IPL), anterior cingulate cortex (AC), supplementary motor area (SMA), dorsolateral frontal cortex (DLF), left hemisphere hand primary motor cortex (M1). n = 24 subjects.
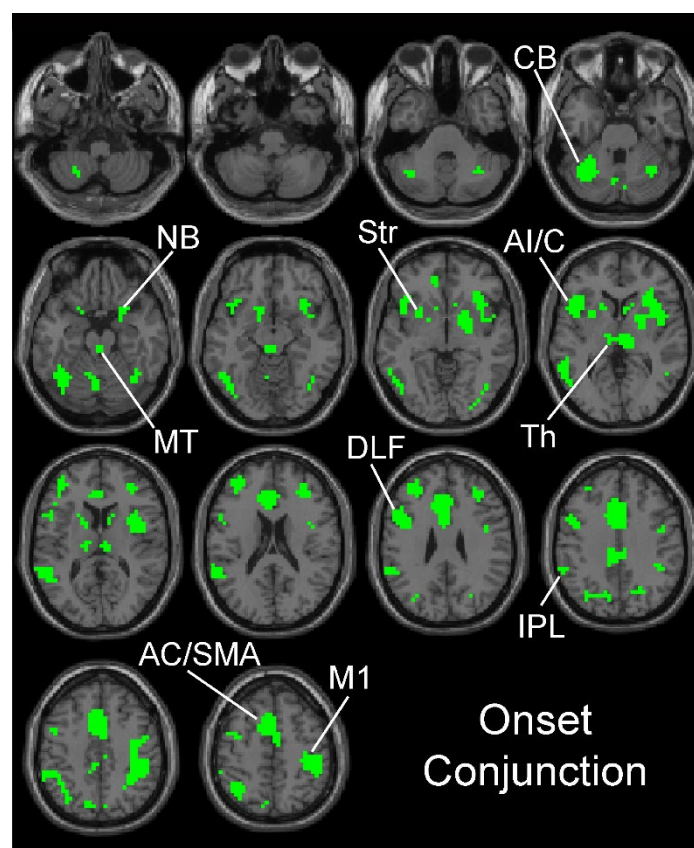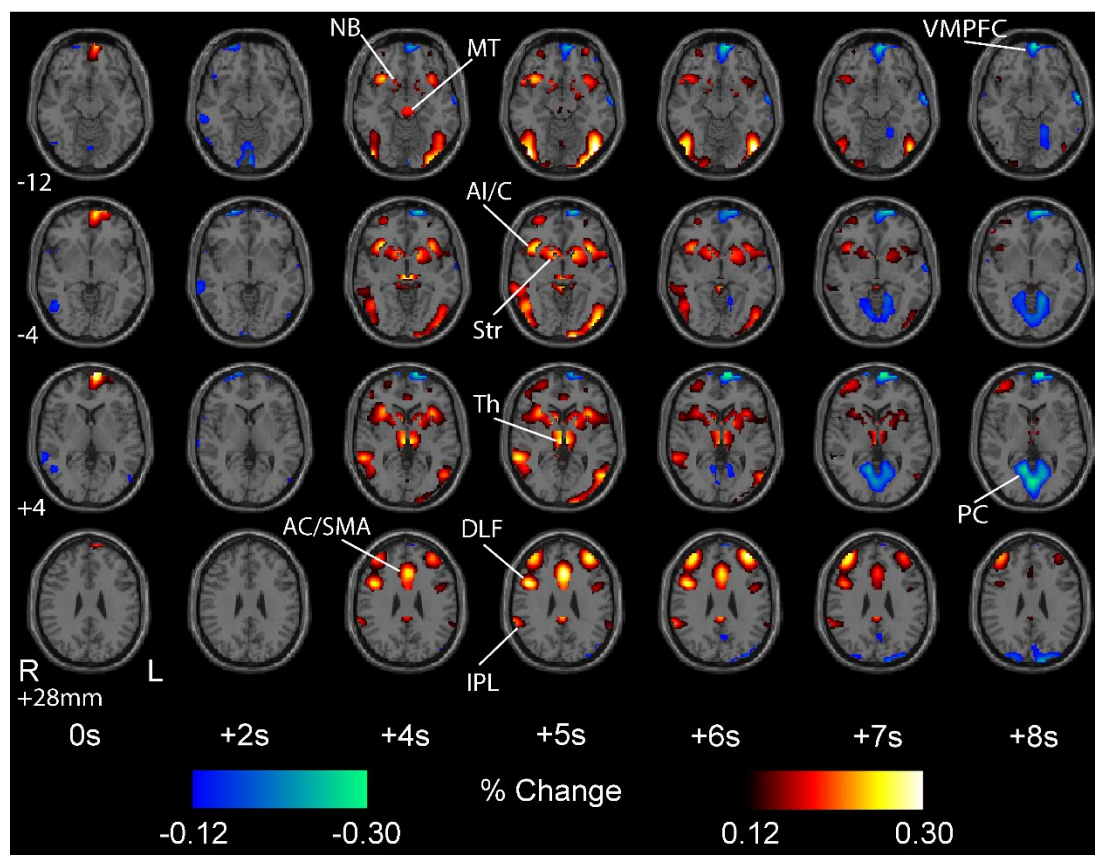
Supplementary Figure 4: Conjunction analysis of transient onset maps between healthy adolescents and absence epilepsy patients. Intersection of uncorrected (p < 0.005) fMRI increases from the CPT/RTT onset analysis of normal cohort (**Supplementary Figure 2E**) and patient cohort (**Supplementary Figure 3E**). Consistent activations in the midbrain tegmentum (MT), thalamus (Th), striatum (Str), nucleus basalis (NB), cerebellum (CB), anterior insula/claustrum (AI/C), anterior cingulate/supplementary motor area (AC/SMA), inferior parietal lobule (IPL), dorsolateral frontal cortex (DLF) and left hemisphere hand primary motor cortex (M1) were observed in the overlapped map of the two cohorts.
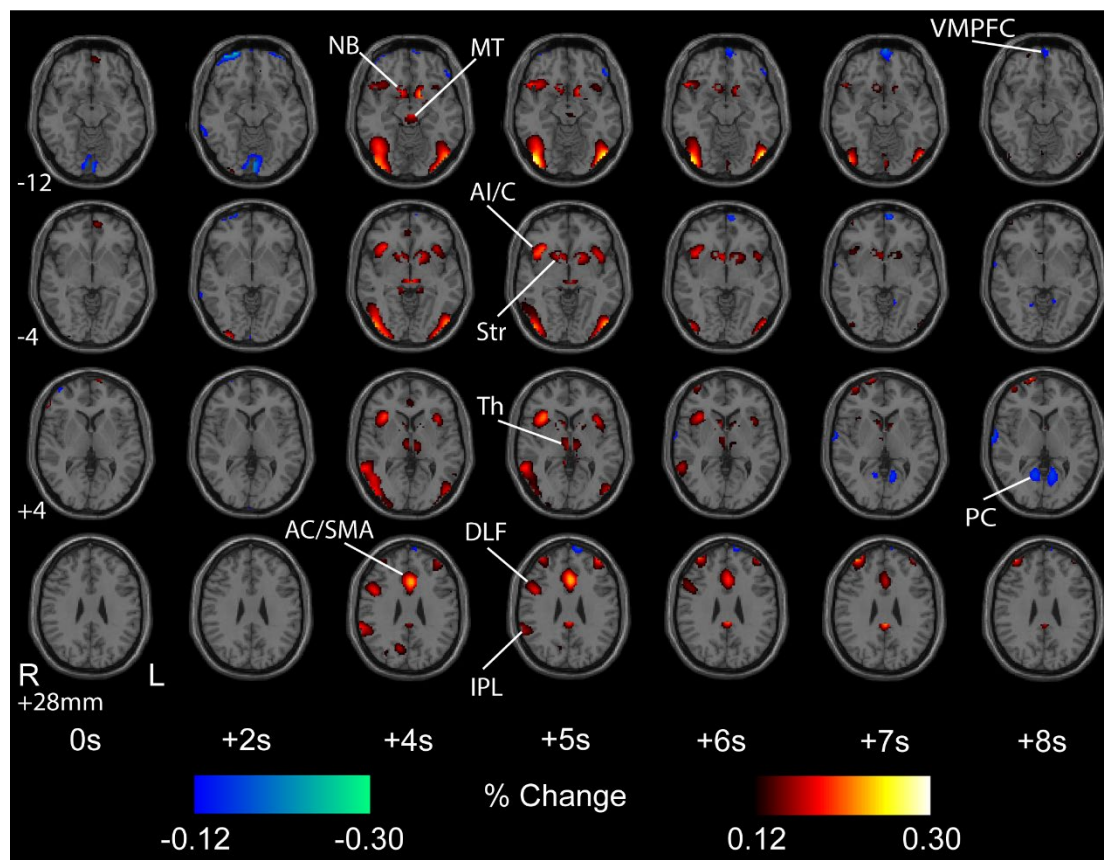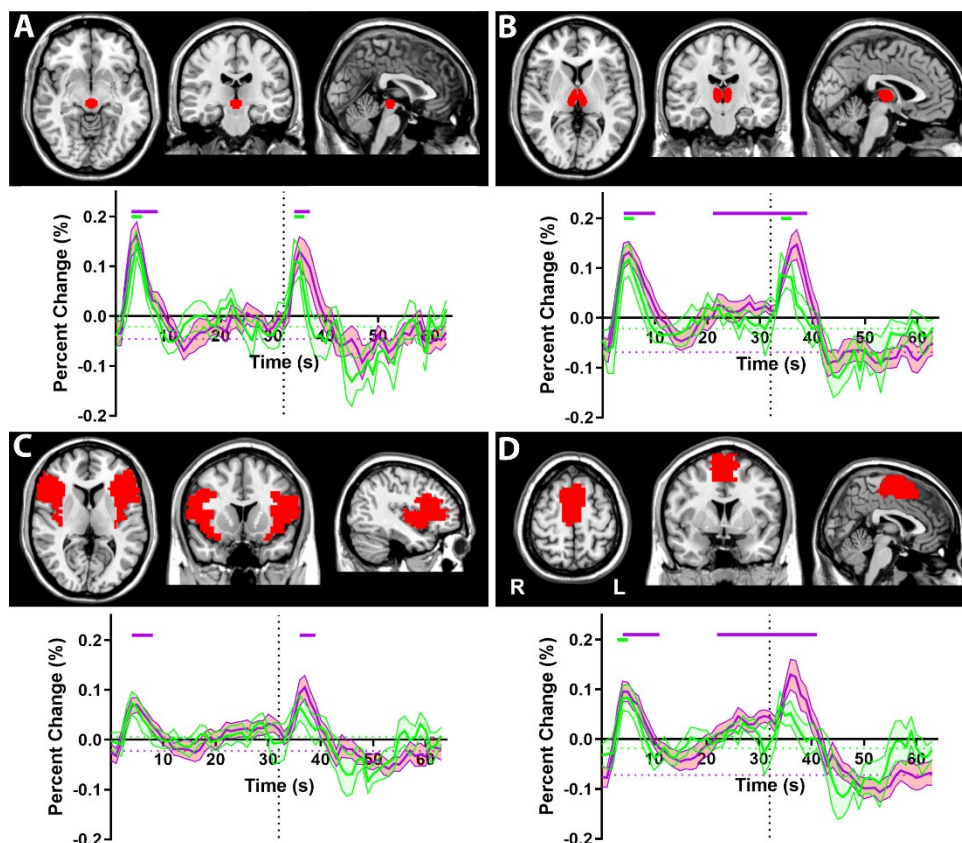
Supplementary Figure 5 (Related to Figure 3A): Mean percent fMRI signal changes in 22 healthy adolescents during the CPT/RTT task. fMRI percent change increases (warm colors) and decreases (cool colors) with respect to voxel baselines (whole run average) are shown, with a display threshold of 0.12%. Initial changes are shown for both tasks after block onset at 0 s. Similar to Figure 3 in the main text, fMRI increases were observed in subcortical structures, including the midbrain tegmentum (MT), thalamus (Th), nucleus basalis (NB), and the striatum (Str), as well as in cortical regions, such as the anterior insula/claustrum (AI/C), inferior parietal lobule (IPL), anterior cingulate cortex (AC), supplementary motor area (SMA) and dorsolateral frontal cortex (DLF). Later fMRI decreases occurred in ventral medial frontal cortex (VMPFC) and precuneus (PC). Only 32s task blocks were used to facilitate temporal

alignment, but very similar results were obtained analyzing 96s task blocks separately (not

shown). No statistical threshold was used in this analysis.

Supplementary Figure 6 (Related to Figure 3A): Mean percent fMRI signal changes in 24 absence epilepsy patients during the CPT/RTT task. fMRI percent change increases (warm colors) and decreases (cool colors) with respect to voxel baselines (whole run average) are shown, with a display threshold of 0.12%. Initial changes are shown for both tasks after block onset at 0 s. Similar to Figure 3 in the main text, fMRI increases were observed in subcortical structures, including the midbrain tegmentum (MT), thalamus (Th), nucleus basalis (NB), and the striatum (Str), as well as in cortical regions, such as the anterior insula/claustrum (AI/C), inferior parietal lobule (IPL), anterior cingulate cortex (AC), supplementary motor area (SMA) and dorsolateral frontal cortex (DLF). Later fMRI decreases occurred in ventral medial frontal cortex (VMPFC) and precuneus (PC). Only 32s task blocks were used to facilitate

temporal alignment, but very similar results were obtained analyzing 96s task blocks separately

(not shown). No statistical threshold was used in this analysis.

Supplementary Figure 7 (Related to Figure 4): Mean time courses of selected regions of interest showing transient and sustained responses for CPT/RTT in 22 healthy normal adolescents and 24 adolescent people with epilepsy. (A) midbrain tegmentum (B) thalamus (C) anterior insula/ frontal operculum (D) supplementary motor area. Analyses are the same as in Figure 4 except that we are displaying CPT/RTT only with normal controls (purple) and patients (green) traces separated out and overlaid. The CPT/RTT time courses are shown from 0 s to 63 s relative to the task onset, with task offset at 32 s (dotted line). Time courses for controls and patients appear very similar to each other and to the combined CPT/RTT group shown in Figure 4. All time courses are mean and standard error across subjects, with

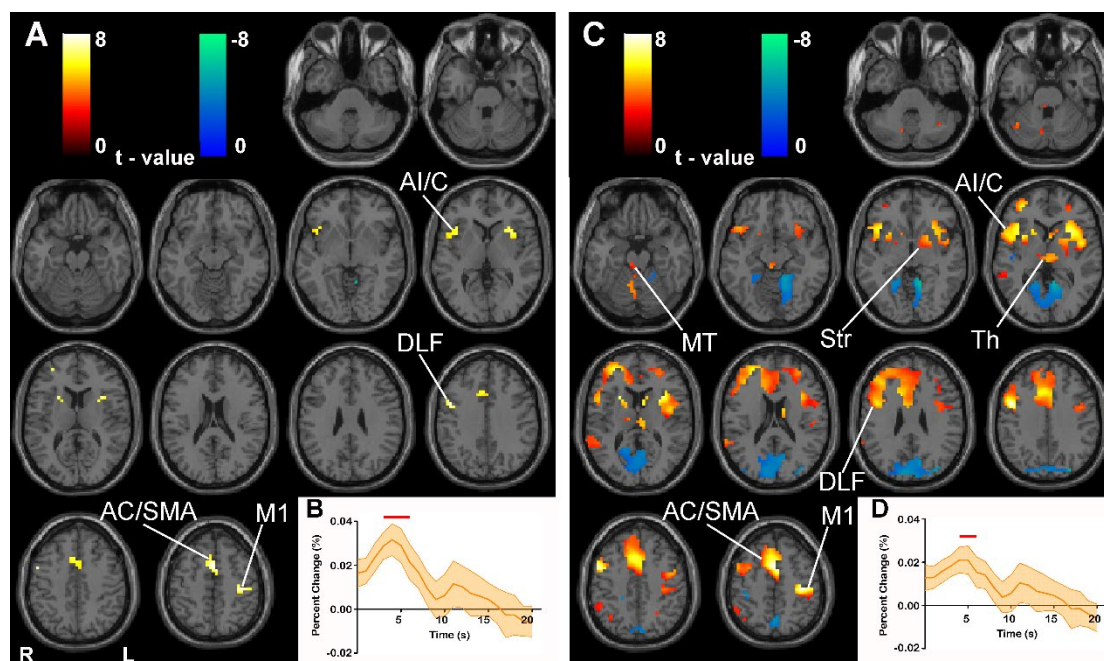significant changes from baseline (horizontal dashed line) indicated by horizontal purple and

green bars (two-tailed t-test, Bonferroni-corrected p < 0.05).
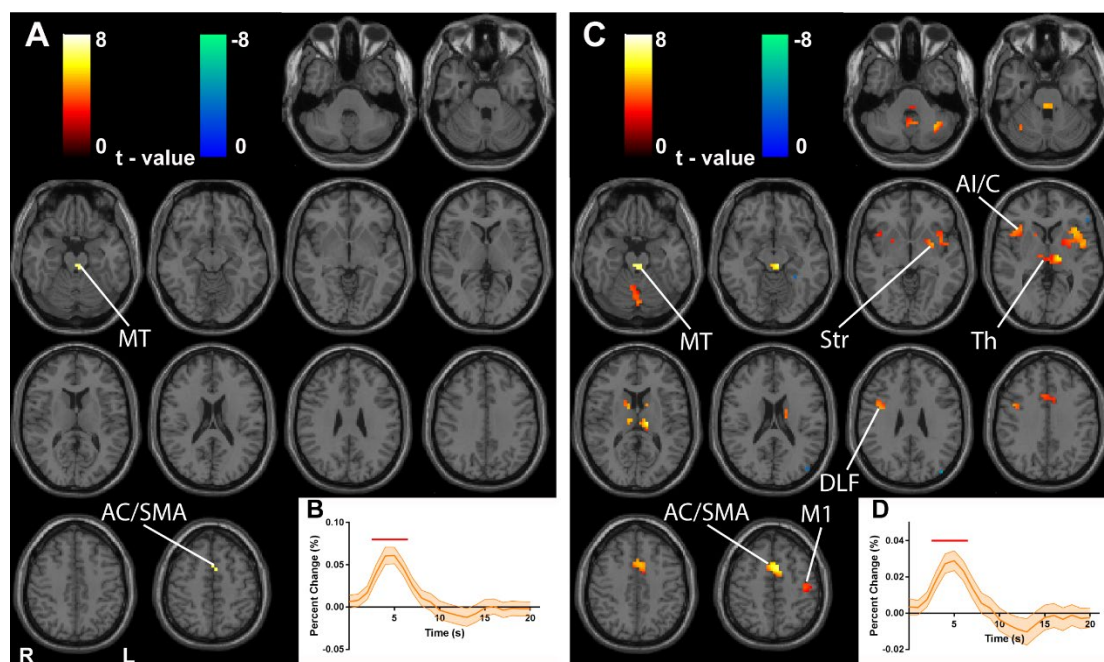
Supplementary Figure 8 (Related to Figure 5): Event-related analysis of individual CPT target stimuli from 21 healthy adolescents. GLM-based t-maps illustrate event-related activity with extent threshold of k = 3 voxels and height thresholds of FWE-corrected p < 0.05 (A) and uncorrected p < 0.005 (C). Subthreshold analysis in part C was included to demonstrate similarity of changes here with small sample size to those observed in the larger group analyzed with conventional thresholds in Figure 5. (B, D) fMRI mean time courses and standard error (across subjects) averaged across all voxels showing significant positive changes in (A, C) respectively. Time points showing significant changes from baseline (two-tailed t-test, Bonferroni-corrected p < 0.05) are indicated by the horizontal red bar. Time 0s is event onset for target stimuli. Midbrain tegmentum (MT), thalamus (Th), striatum (Str), anterior insula/claustrum (AI/C), anterior cingulate/supplementary motor area (AC/SMA), dorsolateral

frontal cortex (DLF), left hemisphere hand primary motor cortex (M1). Warm colors indicate

fMRI changes in parallel to the model and cool colors show negative changes.

Supplementary Figure 9 (Related to Figure 5): Event-related analysis of individual CPT target stimuli from 24 absence epilepsy patients. GLM-based t-maps illustrate event-related activity with extent threshold of k = 3 voxels and height thresholds of FWE-corrected p < 0.05 (A) and uncorrected p < 0.005 (C). Subthreshold analysis in part C was included to demonstrate similarity of changes here with small sample size to those observed in the larger group analyzed with conventional thresholds in Figure 5. (B, D) fMRI mean time courses and standard error (across subjects) averaged across all voxels showing significant positive changes in (A, C) respectively. Time points showing significant changes from baseline (two-tailed t-test, Bonferroni-corrected p < 0.05) are indicated by the horizontal red bar. Time 0s is event onset for target stimuli. Midbrain tegmentum (MT), thalamus (Th), striatum (Str), anterior insula/claustrum (AI/C), anterior cingulate/supplementary motor area (AC/SMA), dorsolateral frontal cortex (DLF), left hemisphere hand primary motor cortex (M1). Warm colors indicate fMRI changes in parallel to the model and cool colors show negative changes.

Supplementary PowerPoint 1:

Axial maps of mean percent fMRI signal changes during CPT/RTT task displayed at 1 s intervals from task onset to fixation. A total of 64 maps were obtained from the same data and subjects as in Figure 3A. fMRI increases (warm colors) and decreases (cool colors) are shown with color scales representing percent change relative to voxel baselines, using a display threshold of 0.12%. No statistical threshold was used in this analysis. The times denote seconds after task onset; task offset occurred at time 32 s.

Supplementary PowerPoint 2:

Axial maps of mean percent fMRI signal changes during gambling task displayed at 1 s intervals from task onset to fixation. A total of 43 maps were obtained from the same data and subjects as in Figure 3B. fMRI increases (warm colors) and decreases (cool colors) are shown with color scales representing percent change relative to voxel baselines, using a display threshold of 0.12%. No statistical threshold was used in this analysis. The times denote seconds after task onset; task offset occurred at time 28 s.