SUPPLEMENT 1

Analysis

In a supplementary analysis, we specifically targeted auditory cortical regions along Heschl's gyrus and asked whether the classically observed suppression of auditory cortical activity was attenuated in our attention-deficit/hyperactivity disorder (ADHD) cohort. Two spherical regions of interest (ROI) located in bilateral Heschl's gyri (Origins [−52, −4, 12] for left and [54, −4, 4] for right, with radius R = 5 mm) were identified in the Montreal Neurological Institute (MNI) space, then mapped back to the individual structural magnetic resonance imaging (MRI) and, in turn, to the functional magnetic resonance imaging (fMRI) scans. For each participant, we quantitatively calculated the two-tailed Pearson temporal correlation between the average time series of each ROI and the time series of the task design. Group differences were compared using the General Linear Model, with normal controls and patients with ADHD as groups, and hemisphere (left and right ROIs) as repeated measures, the two-tailed correlation coefficient as dependent variables, and age and gender as random-effect and fixed-effect covariates, respectively. Significant group differences were revealed (p = .041). A post hoc t test also showed significant group differences in the correlation coefficients within both hemispheres (left side Heschl's gyrus: controls [−0.101 ± 0.108], ADHD [−0.055 ± 0.116], p = .030; right side Heschl's gyurs: controls [−0.199 ± 0.178], ADHD [−0.103 ± 0.210], p = .046). Also from Figure 4, the ADHD cohort showed significantly reduced suppressive activity relative to controls in both Heschl's gyri.

SUPPLEMENT 2

Analysis

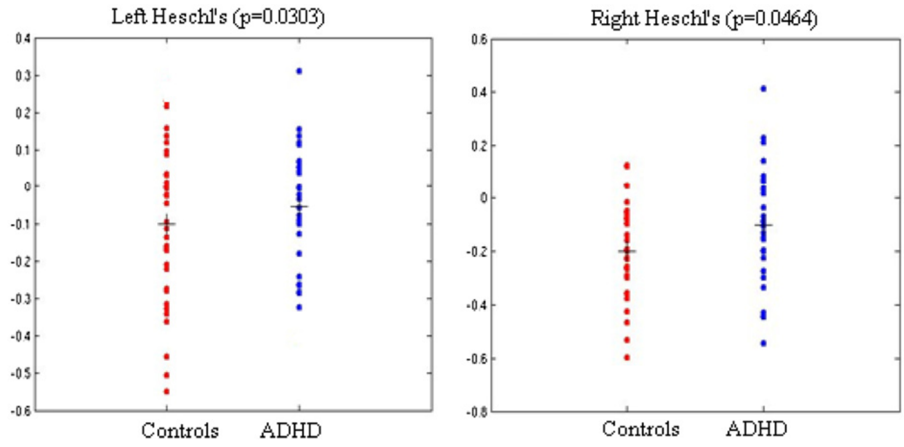
Psychophysiological Interactions (PPI) analysis was also carried out in each individual, using the fMRI Expert Analysis Tool (FEAT) PPI analysis tool as implemented in functional magnetic resonance imaging (fMRI) Expert Analysis Tool (FEAT) (http://www.fmrib.ox.ac.uk/Members/joreilly/how-to-run-a-ppi-analysis-in-feat). The two regions of interest (ROIs) from bilateral pulvinar nuclei defined in the main text were used in this PPI analysis. The psychological regressor was set up by defining the task condition as 1 and the rest as −1. The physiological regressor was the time-course extracted from each ROI after preprocessing. Interaction between these two regressors was then assessed. The Z statistic images were thresholded using clusters determined by Z>2.3 and a corrected cluster significance threshold of $p < .05$. Group comparisons were analyzed using the GML by adding sex as a fixed-effect covariate, and accuracy and omission error rates as random-effect covariates. The Z statistic images were thresholded using clusters determined by Z>2.3 and a cluster corrected significance threshold of $p < .05$. Figure S2 (available online) shows the results of the between-group comparisons. Significantly decreased effective connectivities between bilateral pulvinar nuclei and right prefrontal cortex were found in subjects with attention-deficit/hyperactivity disorder (ADHD) compared to normal controls. Also, significantly increased effective connectivity between the right pulvinar nucleus and bilateral occipital regions were found in subjects with ADHD compared to controls. These results further support the findings from the main study, and suggest disruption of cortical–pulvinar–cortical circuits for attention processing in individuals with ADHD.

SUPPLEMENT 3

Analysis

Head motion in functioning magnetic resonance imaging (fMRI) data often causes position shifts of the brain structures, and can induce artifacts in the blood-oxygen level–dependent (BOLD) signals at each voxel that cannot be fully corrected. Severity of head motion is a key issue to be considered for inclusion criteria in any fMRI study. Traditional measurement of head motion uses six parameters generated from the rigid body transformation for head realignment. Recent studies using resting-state fMRI data collected from large cohorts have demonstrated that patterns of head movement can have a significant impact on the dynamic patterns of resting-state BOLD signals,[1] and are significantly associated with decreased functional connectivity between long-distance seed regions. In contrast, these motion effects serve to increase measures of short-distance local functional coupling,[2] even after head motion spatial correction. These studies suggest that head motion-induced artifact may be a critical component of resting-state BOLD signals, and may confound spontaneous brain dynamics.

FIGURE S1 Group comparisons of the task-responding correlation coefficients in bilateral Heschl's gyri. Note: ADHD = attention-deficit/hyperactivity disorder.



Head motion effects in the BOLD signals and their putative effects on functional connectivity patterns in our block-designed, visual attention task–based fMRI data were assessed in this supplementary document. The framewise measurements of the six realignment parameters, the absolute values of the differentials of the time-courses (Diff), the sum of the absolute values of the differentials of the six realignment parameters (FD) (calculation details provided in Power *et al.*[1]), and the Mean Motion (mean of the absolute values of the displacements along x-, y-, and z-axes compared to the previous volume) were calculated from the 44 fMRI data sets. Three spherical (R = 4 mm) regions of interest (ROIs) were located in the right pulvinar nucleus [14, −26, 8], the right prefrontal lobe [45, 30, 4], and the left occipital lobe [−12, −94, 7], given that the main hypothesis and resultant significant findings were associated with these brain regions. Functional connectivities in the pulvinar-prefrontal pairing and in the pulvinar–occipital pairing were calculated from the time series of the three ROIs (after all preprocessing steps introduced in main text). We did not see any pattern of significant relationship between head motion and changes in the BOLD signals in any of the 44 data sets. Figure S3, panels A–F (available online), demonstrate the framewise head motion measures and comparisons with the BOLD signals and derivatives in a randomly selected subject. In addition, we did not find significant between-group differences in Mean Motion, and there were no significant correlations between Mean Motion and the functional connectivities in the pulvinar–prefrontal and pulvinar–occipital pairings across the whole sample (shown in Figures S3G and S3H, available online). These results suggest that BOLD signals collected during active visual attention tasks, such as the one used here, are much less sensitive to head motion–induced noise signals compared to the spontaneous brain dynamics recorded during resting-state scans.

REFERENCES

1. Power JD, Barnes KA, Snyder AZ, *et al*. Spurious but systematic correlations in functional connectivity MRI networks arise from subject motion. Neuroimage. 2012;59:2142-2154.
2. Van Dijk KR, Sabuncu MR, Buckner RL. The influence of head motion on intrinsic functional connectivity MRI. Neuroimage. 2012;2;59:431-438.

FIGURE S2 (A) Brain regions with significantly decreased effective connectivity with the left pulvinar nuclei in participants with attention-deficit/hyperactivity disorder (ADHD); (B and C) brain regions with significantly decreased/increased effective connectivity with the right pulvinar nucleus in participants with ADHD compared to neurotypical controls. Note: R = right hemisphere.

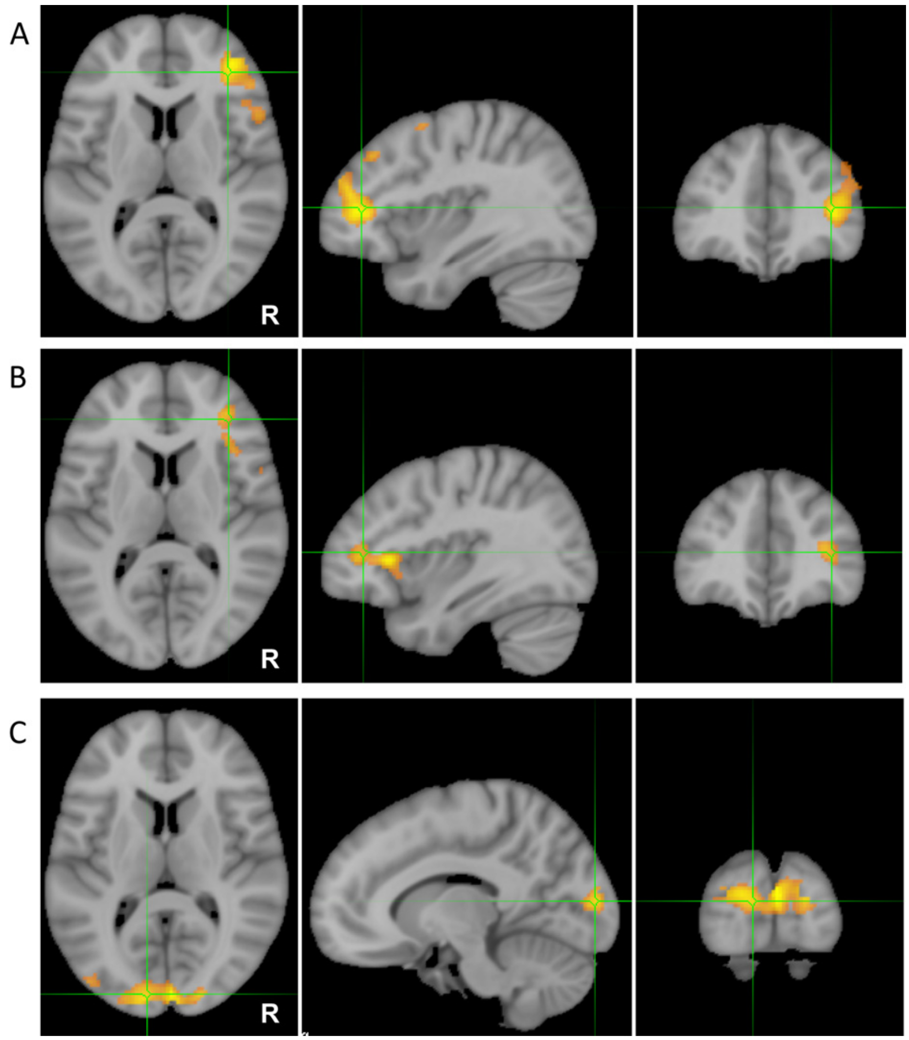


FIGURE S3 Framewise changes in the functional magnetic resonance imaging (fMRI) signals during the block-design visual attention task are not related to the framewise changes of head position after head motion correction. Note: (A to C) fMRI timecourses from 3 regions of interest (ROIs) in a randomly selected participant. The ROIs are 8-mm-diameter spheres centered on the coordinates of [14, −26, 8] (right pulvinar nucleus), [45, 30, 4] (right prefrontal lobe), and [−12, −94, 7] (left occipital lobe). (D) Six frame-by-frame realignment parameters. (E) Absolute values of the differential of each timecourse in the three ROIs. (F) Sum of the absolute values of the differentials of the six realignment parameters (FD). (G and H) These show that there are no significant correlations between Mean Motion and functional connectivity in either the pulvinar–prefrontal pairing (linear: r = 0.20, p = .22; nonlinear: r = 0.22, p = .17), or in the pulvinar–occipital pairing (linear: r = 0.17, p = .28; nonlinear: r = 0.16, p = .34). BOLD = blood-oxygen–level dependence.