Multimodal mapping of the brain’s functional connectivity and the adult outcome of attention deficit hyperactivity disorder

Gustavo Sudre, Eszter Szekely, Wendy Sharp, Steven Kasperek, and Philip Shaw

We have a limited understanding of why many children with attention deficit hyperactivity disorder do not outgrow the disorder by adulthood. Around 20–30% retain the full syndrome as young adults, and about 50% show partial, rather than complete, remission. Here, to delineate the neurobiology of this variable outcome, we ask if the persistence of childhood symptoms into adulthood impacts on the brain’s functional connectivity. We studied 205 participants followed clinically since childhood. In early adulthood, participants underwent magnetoencephalography (MEG) to measure neuronal activity directly and functional MRI (fMRI) to measure hemodynamic activity during a task-free period (the “resting state”). We found that symptoms of inattention persisting into adulthood were associated with disrupted patterns of typical functional connectivity in both MEG and fMRI. Specifically, those with persistent inattention lost the typical balance of connections within the default mode network (DMN; prominent during introspective thought) and connections between this network and those supporting attention and cognitive control. By contrast, adults whose childhood inattentive symptoms had resolved did not show significantly different connectivity from their never-affected peers, both hemodynamically and electrophysiologically. The anomalies in functional connectivity tied to clinically significant inattention centered on midline regions of the DMN in both MEG and fMRI, boosting confidence in a possible pathophysiological role. The findings suggest that the clinical course of this common childhood onset disorder impacts the functional connectivity of the adult brain.

Significance

Many children do not simply “outgrow” attention deficit hyperactivity disorder (ADHD). The disorder often persists and affects around one in 40 adults, presenting a major public health challenge. Defining the mechanisms that underpin this variable clinical outcome could stimulate novel approaches to boost recovery in ADHD. We map the brain’s functional architecture in 205 young adults followed clinically since childhood. We find clinically significant inattention persisting from childhood has a disruptive effect on the functional connections within and between the brain’s major networks. These disruptions are similar whether defined through direct observation of neuronal activity or measures of hemodynamic change. By contrast, adults who remit from childhood ADHD showed typical brain connectivity, suggesting convergence toward typical brain function may underpin recovery.

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anomalies across modalities, this would bolster the case for a possible pathophysiological role of these networks.

Based on the prior literature, we expect that anomalies in functional connectivity pertinent to the adult outcome of childhood ADHD would center on the default mode network (DMN) (9–11). This network is prominent during introspective processing and is held to be pivotal in the pathophysiology of ADHD (10). Specifically, it has been hypothesized that a loss of the counterbalance between the DMN and networks supporting cognitive processes (e.g., attention and cognitive control) leads to intrusion of the DMN into task-oriented processing. Such dysregulated interactions, in turn, have been tied to core symptoms of ADHD, particularly increased distractibility, behavioral impulsivity, and deficient sustained attention (12–14).

In summary, we determine functional connectivity both electrophysiologically and hemodynamically. We hypothesize that symptoms of ADHD persisting from childhood would be associated with disruptions to functional connectivity, centered on the DMN. By contrast, adults whose symptoms have resolved are predicted to show functional connectivity that resembles that seen in those never affected by the disorder.

Results
In total, 205 individuals participated in this study (mean age = 23.4 y; SD = 3.9 y, 115 males). Of these, 101 had DSM-5 (Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition; ref. 15)–defined childhood ADHD; 50 showed persistence of the full syndrome into adulthood (Table S1). Of the 205 participants, 67 had both good-quality fMRI and MEG resting-state data, 80 had fMRI alone, and 58 had MEG alone. Connectivity matrices were defined for the MEG data (considering the consistency of phase coupling between all possible combination of 2,146 regions of a cortical grid) and fMRI data (measuring BOLD signal correlations across the same cortical grid). Next, using a bootstrapped-based independent component analysis (ICA), we reduced these matrices to independent connectivity patterns or “stable components” (Fig. S1). We identified six such stable components in fMRI resting-state data and 56 stable components in MEG resting-state data (12 in delta bands, 13 in theta bands, 10 in alpha bands, 10 in beta bands, and 11 in gamma bands). Cross-modal similarities were found (Fig. S2). For example, one fMRI component showed strong positive connections within and between the default mode, cognitive control, and attention networks. One of the MEG components similarly showed strong connectivity within and between the default mode, cognitive control, and ventral attention networks. Hence, these components revealed both intranetwork patterns and a complex scaffolding of internetwork connections, similar to some prior reports (16, 17).

Altered Functional Connectivity Patterns and the Adult Outcome of Childhood ADHD. We then asked if symptoms of adult ADHD persisting from childhood impacted an individual’s expression of each component. Individual expression of each stable component was represented as a beta weight calculated using linear regression. We then correlated these components (the beta weights) with symptoms. In MEG, four of the 56 stable components were significantly associated with adult symptoms of inattention persisting from childhood (Table 1). These correlations ranged from $\rho = 0.45$, $P = 1.1 \times 10^{-5}$ (for a MEG component in the theta band); to $\rho = 0.47$, $P = 5.1 \times 10^{-4}$ (beta-frequency component); to $\rho = 0.48$, $P = 3.8 \times 10^{-4}$ (beta band); to $\rho = 0.54$, $P = 1.9 \times 10^{-6}$ (gamma band). No component showed a significant association with hyperactivity-impulsivity.

We next conducted categorical analyses of these inattention-related components by classifying the adults into those with persistent ADHD and those with remitted ADHD, thus facilitating the clinical interpretation of the findings. We also drew contrasts against the never-affected control group to determine the degree to which the remitted group showed the predicted typical functional connectivity patterns. Group differences were found in all four of the MEG components significantly associated with inattention. These differences were consistently driven by the persistent group (as can be seen from Fig. 1, which shows heat maps of the associations between each network for each outcome group). Specifically, post hoc pairwise contrasts showed that the persistent group showed significantly higher expression of all four components compared with the never-affected group (all $P < 0.001$; Table 1) and higher expression compared with the remitted group for two of the stable components ($P = 0.01$ for the theta component and $P = 0.001$ for one of the beta components). By contrast, the remitted and never-affected groups showed mostly similar patterns of connectivity within and between the brain’s intrinsic networks (i.e., the two groups did not generally differ significantly in their expression levels of the inattention-related stable components).

We used the same approach to consider the correlation between symptoms and the expression of each component in fMRI. Only one of the six components showed significant association with inattentive ($\rho = 0.31$, $P = 0.0062$) but not hyperactive-impulsive ($\rho = 0.15$, $P = 0.19$) symptoms. In categorical contrasts, a group difference [Kruskal–Wallis, $\chi^2(2) = 7.8$, $P = 0.022$] was driven by higher levels of expression of the stable component in the persistent ADHD group compared with both the remitted ($P = 0.03$) and never-affected ($P = 0.008$) groups, which did not differ significantly from one another ($P = 0.85$).

In summary, adult inattention persisting from childhood was tied to disruption in patterns of connectivity within and across brain networks, mapped both hemodynamically (fMRI) and electrophysiologically (MEG). Individuals with persistent inattention showed atypical (higher) expression of connectivity patterns between the brain’s networks in both modalities, whereas those who remitted did not differ from those who were never affected.

The Functional Architecture of ADHD-Related Stable Components. We further characterized the four inattention-associated components detected by MEG against the 52 MEG components that were unrelated to symptoms. Informed by current models of

Table 1. Components that had a significant association with symptoms of inattention

<table>
<thead>
<tr>
<th>Component (connectivity pattern)</th>
<th>Spearman correlation rho (P value)</th>
<th>Kruskal–Wallis $\chi^2$ (P value)</th>
<th>Post hoc Mann–Whitney U tests</th>
</tr>
</thead>
<tbody>
<tr>
<td>MEG, theta</td>
<td>0.45 (1.1 × 10^{-4})</td>
<td>19 (7.5 × 10^{-5})</td>
<td>Never affected vs. persistent (P value) 3.9 × 10^{-5} 3.9 × 10^{-5} 1.1 × 10^{-2}</td>
</tr>
<tr>
<td>MEG, beta</td>
<td>0.47 (5.1 × 10^{-4})</td>
<td>11.1 (3.9 × 10^{-4})</td>
<td>Never affected vs. remitted (P value) 1.8 × 10^{-7} 2.0 × 10^{-1} 2.0 × 10^{-2}</td>
</tr>
<tr>
<td>MEG, beta</td>
<td>0.48 (3.8 × 10^{-4})</td>
<td>29.7 (1.0 × 10^{-4})</td>
<td>Persistent vs. remitted (P value) 1.6 × 10^{-7} 1.6 × 10^{-4} 1.2 × 10^{-3}</td>
</tr>
<tr>
<td>MEG high gamma</td>
<td>0.54 (1.9 × 10^{-4})</td>
<td>16.5 (2.0 × 10^{-4})</td>
<td>7.3 × 10^{-4} 3.2 × 10^{-1} 1.1 × 10^{-4}</td>
</tr>
<tr>
<td>fMRI</td>
<td>0.31 (6.2 × 10^{-4})</td>
<td>7.8 (2.0 × 10^{-4})</td>
<td>8.0 × 10^{-3} 8.4 × 10^{-1} 2.5 × 10^{-2}</td>
</tr>
</tbody>
</table>

Results of pairwise post hoc comparisons shown in bold were significant at an unadjusted $P < 0.05$. The remitted and never-affected groups either did not differ significantly (three components) or differed at nominal levels of significance ($P < 0.05$).
ADHD, we focused on patterns of connectivity within the DMN and between the DMN and other networks [as defined by Yeo et al. (18)]. We found that the four MEG inattention-related components showed a significant alteration in the ratio of such intra- to internetwork connectivity. Specifically, the components related to inattention showed relatively less intra-DMN connectivity and more internetwork connectivity, a difference which reached significance in a group rank test ($P = 0.02$; Fig. 2).

Finally, we tested for similarities in the spatial structure of the MEG and fMRI inattention-related components. For every cortical region and each component, we calculated a metric summarizing the connectivity between that cortical region and all others. High values of this metric indicated greater deviation away from mean connectivity. Ranking regions by this metric, we found that the left precuneus and bilateral posterior cingulate showed the most atypical connectivity in MEG and fMRI modalities; overlap was less prominent in lateral cortical regions (Fig. 3). Both the precuneus and posterior cingulate are regarded as key components of the DMN (9).

**Discussion**

We show that clinically significant symptoms of adult ADHD were tied to similar disruptions to the brain’s functional connectivity, mapped using both resting-state fMRI and MEG data. Specifically, adult inattention persisting from childhood was associated with an atypical balance of connectivity within the DMN and between the DMN and task-positive networks. These patterns

![Fig. 1. Group differences in the expression of stable components associated with inattention, detected by MEG (Top) and fMRI (Bottom). The box plots show the expression of each component in the persistent ADHD, remitted, and never-affected groups. Throughout, the persistent ADHD group showed atypically high levels of expression of these components. The adjacent connectivity matrices (“heat maps”) show the strength of intra- and internetwork connectivity for each group. Hotter colors indicate stronger connectivity. The persistent ADHD group differs significantly from the never-affected and remitted ADHD groups. The latter two groups did not differ from one another. DAN, dorsal attention network; VAN, ventral attention network.](image)

![Fig. 2. Patterns of network connectivity in components related to inattention (A) against those that are not (B). The thickness of the arrows corresponds to the strength of the connection. Inattention-related components showed more internetwork connectivity than unrelated components, particularly between the default mode and ventral attention network (VAN) and cognitive control network. DAN, dorsal attention network. (C) Scatterplot shows that the four inattention-related MEG components had a significantly lower ratio of intranetwork/internetwork default mode connections than those not associated with inattention.](image)
of connectivity, tied to symptom severity, had a similar spatial structure, whether defined hemodynamically or electrophysiologically. We also find that adult remission from childhood ADHD was associated with essentially typical functional connectivity. As the adults in our study had been followed clinically since childhood, the findings inform our understanding of recovery from the disorder.

The Impact of Adult Inattention on Neural Oscillations. While fMRI data acquired during the resting state have been widely used to parse the brain’s functional architecture in ADHD, only a handful of studies have used MEG. Prior MEG studies have exclusively focused on adults with persistent ADHD, and, consistent with our findings, they report atypical neural oscillations in beta-, delta-, and theta-frequency bands (19, 20). Neural oscillations scaffold cognitive domains, and some of these cognitive domains are impaired in ADHD, such as working memory and the processing of temporal information. For example, working memory capacity is predicted by peak theta-band activity, working memory load correlates with gamma-band power, and interventions that boost working memory also augment beta-band activity (6, 21–23). Coupling across the frequency bands is also implicated in working memory, specifically modulation of the gamma band amplitude by the theta band phase (24–26). ADHD is also linked with the aberrant processing of temporal information, with errors in time perception, reproduction, and estimation (27). Neural oscillations convey temporal information, and the encoding of time intervals and temporal prediction has been linked to theta-, beta-, and delta-range activity (28–31). Imaging brain activity during working memory and temporal processing tasks would delineate more clearly the links between symptoms, cognitive deficits, and anomalous neural oscillations.

We found that adults with persistent inattention show an atypical balance of intra- to internetwork connectivity pertaining to the DMN. As discussed earlier, such disruptions within the DMN and its interactions with task-positive networks are associated with core cognitive deficits in ADHD, such as increased distractibility, motor disinhibition, and deficient sustained attention (12–14). These connectivity patterns change with age, with most studies finding developmental increases in functional connectivity within the DMN along with maturational change in its interconnections with task-positive networks (17, 32). Indeed, the extent of deviation from the patterns of normative network maturation has been found to predict both deficient sustained attention and the diagnosis of childhood ADHD (16, 17). Here, we extend this finding into adulthood by showing that the degree of deviation from adult norms in the balance of connectivity within and beyond the DMN is tied to the degree of persistence of childhood inattention.

Cross-Modal Similarities in the Patterns of Functional Connectivity Tied to Inattention. We find similarities in the spatial structure of the fMRI- and MEG-defined connectivity patterns related to inattention. This is consistent with our prior studies of typically developing adults that find resting-state neural oscillations as measured by MEG in theta, alpha, and beta bands coalesce into networks that have a similar spatial structure to networks defined using fMRI (7, 8). We extend these findings by showing that cross-modal similarities can also be detected in a neuropsychiatric disorder. We found that in both MEG and fMRI, the patterns of abnormal connectivity related to inattention were centered on the midline regions of the DMN. Differences in the functional networks uncovered by MEG and fMRI were also apparent and to be expected, given factors such as the different spatial and temporal resolutions of each modality.

Models of the Adult Outcome of Childhood ADHD. Functional connectivity in adults whose childhood ADHD symptoms had remitted did not differ significantly from their never-affected peers, both hemodynamically and electrophysiologically. This finding of “typical” function in remitted ADHD is consonant with our prior demonstration that remission is also associated with more typical neuroanatomy and white matter microstructural properties (2, 4). Our current findings are less consistent with the concept of remission arising through the recruitment of new brain systems that help the individual overcome the core symptoms (33). Such compensation would entail some atypical, albeit functionally beneficial, changes in functional networks on those who remit, which we did not find.

Inattention, rather than hyperactivity-impulsivity, tracked with anomalies in the DMN and its interconnectivity with other networks, consistent with pathophysiological models that link default mode disruption with inattention. Associations between brain function and hyperactivity-impulsivity may be better detected through cognitive probes which directly investigate pertinent cognitive domains. Indeed, using a subsample of this group, we have found links between hyperactive-impulsive symptoms persisting from childhood and anomalous activation of frontostriatal-cerebellar circuitry during motor inhibition (34).

The study has its limitations. First, some adults with persistent ADHD were taking psychostimulant medication. To mitigate acute effects, all participants stopped psychostimulant medication the day before scanning. In addition, we repeated all analyses excluding those on psychostimulant treatment, and the overall pattern of results remained the same (Table S2). We also did not collect childhood functional data as the study started before the widespread use of resting-state fMRI and MEG as tools for parsing intrinsic functional connectivity. Meta-analyses report intrinsic connectivity differences between children with and without ADHD (11). However, such group-level analyses do not exclude the possibility that some of the children within the ADHD group do not differ from typicals. Only longitudinal data can rule out the possibility that children with ADHD who are destined for remission as adults have a typical childhood functional architecture that is carried into adulthood.

While it is often argued that anomalies in connectivity cause symptoms, the reverse relationships may also be in play. For example, children growing up with ADHD are likely, by virtue of their symptoms, to have a partly distinct set of environmental exposures and experiences compared with those who are unaffected that could impact the development of the functional connectome. A relevant population-based, longitudinal imaging study found that ADHD symptoms in early childhood were more predictive of some white matter microstructural properties 2 y later than the inverse relationship (35). However, evidence against the concept that symptoms cause connectivity anomalies comes from the finding that unaffected siblings show similar, if attenuated,
anomalies in white matter tract microstructure to their siblings who have ADHD (36). Neither study examined the functional connectome. In short, longitudinal studies using cross-lagged panel and similar designs are needed to delineate fully the temporal links between symptoms and the functional connectome.

By studying the adult outcome of childhood ADHD, we show how persisting inattention is tied to anomalous connectivity centered on the DMN, both electrophysiologically and hemodynamically. Such steps toward understanding the neurobiological mechanisms that underpin remission in some individuals might guide the development of interventions to promote recovery in all.

Methods

Participants were drawn from studies at the intramural programs of the NIH. Of the 101 participants with childhood ADHD, 90 had their initial diagnosis made at the NIH using the Parent Diagnostic Interview for Children and Adolescents (37). The other 11 had a community diagnosis, which we confirmed through both collateral informants and reference to records. The assessment of adult symptoms of ADHD was through the clinician-administered ADHD Rating Scale, version 5, which provides prompts appropriate for late adolescent and young adult groups (38). Two clinicians (P.S. and W.S.) rated each of the nine possible symptoms of ADHD, which were free of current Axis I DSM-IV mental disorders. For all participants, the Diagnostic Interview Schedule for Children, version 5 (39), was used to assess for other psychiatric disorders. Diagnosis histories obtained from prison records were matched against 104 subjects who never had ADHD, who were drawn from a study of typical brain development. These subjects, referred to as “never affected,” were free of current Axis I DSM-IV mental disorders. For all participants, intellectual quotient (IQ) was estimated using age-appropriate versions of the Wechsler intelligence scales. Exclusion criteria were a full-scale IQ of <80, evidence of neurological disorders known to affect brain structure, current substance dependence, or psychotic disorders. The Institutional Review Boards of the National Human Genome Research Institute and National Institute of Mental Health approved the research protocol, and written informed consent was obtained from participants.

MEG Acquisition and Preprocessing.

Resting-state data were acquired in the MEG scanner, with participants instructed to relax for 240 s with their eyes closed. MEG data were acquired using a 275-gradiometer, whole-helmet MEG system (CTF Systems) at 64 Hz. The locations of three fiducial points (nasion and left/right auricular) were determined for signal source localization. A combination of CTF SAMTools (https://www.ctf.com/products/meg/ctf/software.htm), MNE-Python (39), and custom scripts were used in analyses.

To control data quality, head position with respect to the MEG helmet was recorded at the beginning and end of the session, and data were retained only if there was less than 0.5 cm of total movement. Next, data were visually inspected for the presence of artifacts (e.g., movement, muscle, noise), and bad channels were excluded before and after each occurrence of an artifact were marked. The data outside artifact boundaries were then split into 13.65-s contiguous epochs to achieve a good balance between frequency resolution and connectivity estimation (40). Only subjects with at least five clean epochs (68.25 s) were used in the analysis. As a result of these measures, 56 of the initial 181 datasets were excluded, leaving 125 datasets for analysis. There was no group difference (remitted vs. persistent ADHD vs. never affected) in the amount of data analyzed (Kruskal-Wallis, χ²(2) = 0.90, P = 0.64) or correlation between the amount of data analyzed and symptom counts (n = 67; inattention: r = 0.07, P = 0.58; hyperactivity/impulsivity: r = 0.16, P = 0.20). Furthermore, there was no group difference in a latency measure (tscore) that was estimated over the data analyzed (Kruskal-Wallis, χ²(2) = 3.32, P = 0.19) or correlation between the amount of movement and symptom counts (n = 76; inattention: r = 0.13, P = 0.28; hyperactivity/impulsivity: r = 0.07, P = 0.55). The functional image was nonlinearly registered to a Montreal Neurological Institute (MNI) template (42), and ANATICOR (43) was used to remove the first three principal components of the lateral ventricles mask and the mean of a white matter mask, both extracted using FreeSurfer (surfer.nmr.mgh.harvard.edu). The result of this fMRI preprocessing was a functional image with a time series of residuals in each of 67,821 voxels.

Mapping Functional Connectivity.

The goal of the analysis was to detect connectivity patterns in the brain associated with symptoms of ADHD using data-driven methods. In brief, first, connectivity matrices were defined for the MEG and fMRI data. Second, ICA reduced these matrices to independent connectivity patterns (called stable components here). Finally, we determined the degree to which each individual expressed each of these stable components (a methods overview is provided in Fig. S1).

Stage 1: Defining Resting-State fMRI and MEG Connectivity Matrices.

We laid an 8 × 8 × 8-mm grid with 2,146 locations constrained to the cerebral cortex for the MEG data and calculated all pairwise connections [2,301,585 possible connections (nconn)]. For the fMRI data, we placed the same grid across the cerebral cortex (again with 2,146 locations) to facilitate the comparison of MEG and fMRI connectivity matrices. As both MEG and fMRI were registered to the same MNI template, the same 2,146 locations were defined for all subjects. Each location was mapped to one of the seven canonical resting-state networks provided by Yeo et al. (18): visual, somatomotor, dorsal attention, ventral attention, default mode, executive, and social networks. Each network was then defined as a connectivity matrix that contained all correlations between the 2,146 locations for each network from which each connection originated and ended. For MEG, we quantified connectivity using a measure of the consistency of phase coupling between two signals over time: the imaginary part of the coherency (44). Specifically, for each frequency band, we computed the imaginary coherency between each possible combination of localized sources. Imaginary coherency ranges from 1 to −1, where 0 represents no synchronizing and 1 represents perfect phase coupling between two signals depending on which one is lagging/leading the interaction. As this approach projects the coherency onto the imaginary axis, it estimates phase synchrony without zero-lag contributions, thus removing potential contributions due to field spread and source localization leakage (45). These analyses produced matrices for each subject (one for each frequency band) that characterize the connectivity between every possible pairwise of the 2,146 locations of the cortical grid. For fMRI, we similarly generated connectivity matrices between the locations of the same grid. Specifically, we averaged the residualized time series in each location of the grid and calculated Pearson correlations between these time series.

Stage 2: Extracting Stable Components (Connectivity Patterns).

We applied ICA to the connectivity matrices to extract independent components of spatial connectivity. Before defining these components, we first regressed out age, sex, group, and movement signal on the basis of the previous analyses, we then added the mean effect due to inattention and hyperactivity symptoms to augment the variance associated with these effects of interest (17). We reduced the data to 15 components for fMRI and for each MEG band.
in line with previous analyses (to give a total 105 components) (17). We then identified which of these components were stable using an ICA-based approach [ICA DEC (46)], which estimates a stability metric between 0 and 1 (with 1 indicating perfect stability) (SI Methods). We ran 1,000 iterations using different initializations and bootstrappings of the data, and kept all components that had a stability metric of 0.85 or greater. This returned six stable components in fMRI and 56 stable components in MEG.

Stage 3: Individual Expression of Each Stable Component and Association with Symptoms. Individual expression of each stable component was represented as a beta weight calculated using linear regression (Fig. S1). Our main question was whether an individual's expression of these stable components (the beta weights) was associated with the severity of symptoms of inattention and hyperactivity/impulsivity. In these analyses, we controlled for multiple testing by applying a Bonferroni correction for the number of components in each modality (six for fMRI and 56 for MEG). We also conducted categorical analyses, contrasting adults with persistent ADHD against adults with remitted ADHD and the never-affected control group.

Stage 4: Interrogation of Components Associated with Inattentive Symptoms. We next examined the components that were shown in stage 3 to be associated with adult outcome, and we contrasted these components against those unrelated to outcome. As discussed earlier, ADHD has been linked to a loss in the typical balance between connectivity within the DMN and connectivity between the DMN and other networks. We thus asked if the stable components we found to be linked to outcome showed such atypical patterns of intra- and internetwork connectivity. Specifically, we averaged all network connections where both locations mapped to the DMN (intra), and then all connections where one location mapped to the DMN but the other (inter) did not. Each component was assigned this ratio of intra- to internetwork connectivity, and a Mann-Whitney U test was used to test whether this ratio varied according to component association with outcome.

Finally, we asked whether there were spatial similarities between MEG and fMRI disorder-relevant stable components. Using the stereotaxic atlas of Talairach and Tournoux (47) to define 60 cortical subregions, we estimated the average connectivity weight for every stable component for those regions. Thus, for each cortical region, we calculated the average strength of the connection between that region and all others. We ranked the regions based on their absolute connectivity strength and compared the spatial structure of the fMRI- and MEG-derived stable components.

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17. Kessler D, Angstadt M, Sripada C (2016) Growth charting of brain connectivity networks with adult outcome, and we contrasted these components against those unrelated to outcome. As discussed earlier, ADHD has been linked to a loss in the