Functional connectivity of EEG is subject-specific, associated with phenotype, and different from fMRI

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A variety of psychiatric, behavioral, and cognitive phenotypes have been linked to brain “functional connectivity” — the pattern of correlation observed between different brain regions. Most commonly assessed using functional magnetic resonance imaging (fMRI), here, we investigate the connectivity-phenotype associations with functional connectivity measured with electroencephalography (EEG), using phase-coupling. We analyzed data from the publicly available Healthy Brain Network Biobank. This database compiles a growing sample of children and adolescents, currently encompassing 1657 individuals. Among a variety of assessment instruments we focus on ten phenotypic and additional demographic measures that capture most of the variance in this sample. The largest effect sizes are found for age and sex for both fMRI and EEG. We replicate previous findings of an association of Intelligence Quotient (IQ) and Attention Deficit Hyperactivity Disorder (ADHD) with the pattern of fMRI functional connectivity. We also find an association with socioeconomic status, anxiety, and the Child Behavior Checklist Score. For EEG we find a significant connectivity-phenotype relationship with IQ. The actual spatial patterns of functional connectivity are quite different between fMRI and source-space EEG. However, within EEG we observe clusters of functional connectivity that are consistent across frequency bands. Additionally we analyzed reproducibility of functional connectivity. We compare connectivity obtained with different tasks, including resting state, a video and a visual flicker task. For both EEG and fMRI the variation between tasks was smaller than the variability observed between subjects. We also found an increase of reliability with increasing frequency of the EEG, and increased sampling duration. We conclude that, while the patterns of functional connectivity are distinct between fMRI and phase-coupling of EEG, they are nonetheless similar in their robustness to the task, and similar in that idiosyncratic patterns of connectivity predict individual phenotypes.

1. Introduction

The term “functional connectivity” (FC) in neuroscience refers to various measures of how neural activity in one brain area relates to activity in another. Although conceptually simple, FC has emerged as a mainstream approach in the fMRI community for delineating large-scale brain “networks” (i.e. groups of spatially segregated brain areas which fluctuate in unison), which exhibit a high degree of reproducibility across laboratories and methods. Importantly, studies have found that with sufficient data, functional networks can be reliably and reproducibly identified in the FC during rest (Elliott et al., 2019; Noble et al., 2019; O’Connor et al., 2017); and that variations appear to be associated with neuropsychiatric developmental variables and disorders (Finn et al., 2015; Gao et al., 2019; Rosenberg et al., 2016; Shehzad et al., 2014; Smith et al., 2015; Takagi et al., 2019). Specifically, patterns of FC have been associated with IQ and ADHD (Shehzad et al., 2014), fluid intelligence (Finn et al., 2015), attention (Rosenberg et al., 2016), and lifestyle, demographic and psychometric variables (Smith et al., 2015). Recognizing the successes of FC studies in fMRI, an obvious question that arises is whether FC methods have the same potential to become mainstream tools for other modalities, such as EEG.

For fMRI, FC is commonly measured as the Pearson’s correlation of...
the time courses between different brain areas (Biswal et al., 1995; Fox and Raichle, 2007). Recently, more sophisticated methods for the estimation of FC in fMRI have been developed to extend the traditional approach on FC (Bullmore and Sporns, 2009; Bullmore and Bassett, 2011; Smith et al., 2011). These attempts to capture different time scales (Bullmore et al., 2004), reduce common sources of variance (Salvador et al., 2005), capture delayed correlations (Kitzbichler et al., 2009), or capture causation (Reid et al., 2019). Some of them have also been linked to phenotypic variables such as age (Meunier et al., 2009; Mowinckel et al., 2012), fluid intelligence (Ezaki et al., 2019), and schizophrenia (Fornito et al., 2012), and different methods for correlating with phenotype have been benchmarked (Oadi et al., 2019). However, the vast majority of work in this regard is based on Pearson’s correlation, which we will use in the current analysis.

For EEG and MEG, several FC measures have been devised focusing either on the amplitude or the phase of oscillatory activity in different frequency bands (Bastos and Schoffelen, 2016; Colclough et al., 2016; Demuru et al., 2020; Marzetti et al., 2019; Nolte et al., 2004; Palva et al., 2018; Siems and Siegel, 2020; Wang et al., 2017). Correlation in amplitude, referred to as amplitude-coupling, results in FC patterns that can be similar to resting state FC in fMRI (Brookes et al., 2011a, 2011b; Hiltunen et al., 2014; Liu et al., 2018, 2017; Pasquale et al., 2010). A common concern with amplitude-coupling is that volume conduction results in spurious instantaneous correlations. Efforts to remove these artifacts yield amplitude-coupling patterns in MEG (Hipp and Siegel, 2015) and ECoG (Hacker et al., 2017) which are also similar to FC in fMRI. Indeed, one can find associations of amplitude-coupling patterns with age (Bathelt et al., 2013; Coquelet et al., 2017; Schäfer et al., 2014), or phenotypic variables such as autism (Kitzbichler et al., 2015) and schizophrenia (Brookes et al., 2016). Correlation of the voltage fluctuations with some time delay, referred to as phase-coupling, reduces the effects of volume conduction (Nolte et al., 2004). They have been used to characterize neuronal interactions (Fries, 2005), although more recent work shows that spurious interactions remain a concern (Palva et al., 2018b). There is some evidence that patterns of phase-coupling are similar to conventional FC in fMRI (Wirsich et al., 2017), but some components of these networks also appear to differ from fMRI (Wirsich et al., 2020). Phase-coupling has also been associated with some phenotypes such as age (He et al., 2019; Lavagna et al., 2018), sex (Fujimoto et al., 2016), and ADHD (Sudre et al., 2017). Amplitude and phase coupling measures capture fundamentally different aspects of FC (Nolte et al., 2019; Siems and Siegel, 2020), although amplitude coupling measures retain a dependence on phase (Palva et al., 2018). Specifically, phase and amplitude-coupling measures are most similar in short range connectivity and differ in long range connectivity which suggests different underlying neuronal mechanisms (Siems and Siegel, 2020). Here we focus on a phase-coupling measure that is insensitive to volume conduction (Nolte et al., 2004), namely, the imaginary part of coherency (iCOH), which has been extensively validated (Marzetti et al., 2019; Nolte et al., 2017; Wang et al., 2014).

There is also a growing interest in FC evaluated not just during rest but during task performance, and in particular during viewing of natural stimuli such as video (Elliott et al., 2019; O’Connor et al., 2017; Schmälzle et al., 2017; Vanderwal et al., 2017). Therefore we here combine data from resting state as well as viewing of videos. For fMRI, FC patterns are highly correlated between tasks (Cole et al., 2014; Geerligs et al., 2015b; Vanderwal et al., 2017) and more similar within the same subject than between different subjects doing the same task (Finn et al., 2016; Schmälzle et al., 2017). This suggests that FC is a property of the individual, more so than a property of the task. Together with its correlation to phenotypic information, this suggests that FC can be used as a diagnostic metric to assess individuals. Here we explore these issues of robustness, individuality, and correlation to phenotype for the phase-coupling of EEG, and compare this to fMRI in a large cohort of children and adolescents.

We find that phase-coupling of EEG clusters into distinct FC networks that are consistent across frequency bands, hemispheres, and tasks but differ across subjects, making them predictive of individual demographic and phenotypic variables. While this parallels findings with FC in fMRI, the actual networks are genuinely different from fMRI networks, providing a potential new direction for future FC research.

2. Results

We analyzed data from children and adolescents (5–21 years old) collected by the Healthy Brain Network (HBN) (Alexander et al., 2017). From the total of 1657 participants (up to data release 6), clean EEG data was available from 1330 participants and fMRI data from 766 participants (Fig. 1B and Section 5.1). fMRI and EEG recordings were available during rest and during passive viewing of naturalistic narrative videos (see Section 5.1). Additional EEG data was available during visual presentation of flashing gratings designed to measure steady state visual evoked potentials (Vanegas et al., 2015) (see Section 5.1).

fMRI data was preprocessed as reported previously (Craddock et al., 2015) (see Section 5.7). Cortical fMRI activity was averaged across voxels belonging to each area of the Schaefer atlas (N = 200 areas) (Schaefer et al., 2018) and FC was calculated as the Pearson’s correlation coefficients between these areas. After automated preprocessing (see Sections 5.3 to 5.5), EEG activity was source-localized to the Freesurfer fsaverage surface template with 2003 voxels using the eLORETA algorithm in cartesian x,y,z directions (Pascual-Marqui, 2007). The source-space time series from each area of the Schaefer parcellation (Schaefer et al., 2018) were aggregated using principal component analysis (PCA). FC between each area of the Schaefer atlas was then calculated using the imaginary part of coherency (iCOH) (Nolte et al., 2004) on the strongest PCA components (see Section 5.6). The iCOH method reduces the contribution of volume conduction to FC compared to standard coherence (absolute value of complex coherency). iCOH is computed for frequency bins of 0.5 Hz resolution up to the Nyquist frequency (62.5 Hz). Delta, theta, alpha and beta band FC was obtained by averaging across respective frequency bins (see Section 5.8). Broadband FC averages the entire range from 0.5 to 30 Hz.

2.1. FC of EEG clusters into distinct brain networks, consistently across frequency bands, but differently from FC of fMRI

The iCOH connectivity matrices in EEG source space can be organized by clusters of voxels with similar connectivity patterns (Fig. 2A, top). Here we used the connectivity matrix averaged over all subjects and cluster this following the same procedure as in previous work for fMRI (Yeo et al., 2011) (see Section 5.9). The clustering of the FC obtained using the HBN fMRI data is very similar to that of Yeo et al. (Fig. A1). When the same clustering method is applied to the FC of EEG we obtain consistent clusters across frequency bands, but they differ substantially from the clusters in the FC of the fMRI (Fig. 2B). We note that the spatial arrangement of the clusters in EEG are extended in space and not necessarily contiguous (Fig. 2A, bottom). They are also fairly consistent between hemispheres, despite clustering hemispheres separately from one another (Fig. 2A, bottom). This rules out spatial proximity as the primary cause for this consistent clustering. In fact, note that the connectivity within clusters is lower than between clusters (Fig. 2A, top). This is the result of the iCOH method, which is designed to remove instantaneous correlations, so that all correlations imply a time delay.

2.2. FC of fMRI is different from the FC of EEG

Given the distinct clustering it seems that the FC of EEG and fMRI are genuinely different. To quantify this we measure the similarity of FC between EEG and fMRI on individual subjects. For each subject we computed the Pearson’s correlation coefficient between the EEG and fMRI FC matrix (vectorized), and then averaged these correlations over subjects. The mean correlation is low and not significant in any of the frequency bands. Significance was determined by shuffling the subject labels and computing the
same average correlation coefficient. (Delta, r = 0.052, p = 0.19; Theta, r = 0.078, p = 0.58; Beta, r = 0.102, p = 0.89; Broadband, r = 0.12, p = 0.75). We confirm these findings using three other measures of similarity, image intraclass correlation coefficient (I2C2) (Shou et al., 2013), Multiscale Graph Correlation (MGC) algorithm (Shen et al., 2018; Vogelstein et al., 2019) and geodesic distance (Venkatesh et al., 2020) (see Supplement). Given these results and the distinct clusters of connectivity shown in Fig. 2 we conclude that the patterns of FC in EEG and fMRI are different in all frequency bands measured.

2.3. FC is similar across tasks, for both fMRI and EEG

We wanted to establish how similar FC patterns are across the different tasks (resting state, video viewing, flashing gratings). To this end, we measured the similarity of FC between different tasks (similarity is measured as Pearson’s correlation across edges of the FC matrix). We contrast this with the similarity of FC between different subjects (Fig. 3A). Evidently FC are significantly better reproduced across tasks than across subjects. This is true for fMRI, replicating known results (O’Connor et al., 2017), but also for EEG in all frequency bands tested. (Wilcoxon signed rank test: Delta: Δr = 0.061, p = 3.9*10^-7, n = 50; Theta: Δr = 0.13, p = 9.5*10^-6, n = 50; Alpha: Δr = 0.22, p = 7.6*10^-10, n = 50; Beta: Δr = 0.22, p = 7.6*10^-10, n = 50; Broadband: Δr = 0.24, p = 8*10^-10, n = 50; fMRI: Δr = 0.16, p = 1.6*10^-39, n = 355; Δr: median difference of Pearson’s correlation coefficient. Given the strength of these effects this analysis was limited to 50 subjects that completed all EEG recordings and whose data is of good quality.)

This consistency of the FC across tasks (relative to variability observed across subjects) can be quantified in a single metric, namely the inter-class correlation (ICC) (McGraw and Wong, 1996; Shrout and Fleiss, 1979). An ICC value of 1 would indicate perfect consistency of FC between tasks, whereas an ICC of 0 would indicate perfect consistency of FC between subjects and not tasks (see Section 5.13). For EEG we measured reliability of FC across tasks, and did this separately for different frequency bands. Reliability increases from low to high frequency bands (Fig. 3B). In the beta band tasks are most consistent within the visual network, while in all other bands tasks are least consistent within the visual network (Fig. A2). For fMRI we measured reliability across sessions to determine if longer segments of data lead to more stable FC matrices. We do this separately for resting state (2C) and video viewing (2D). As expected we see that longer data segments increase reliability of the FC matrix (O’Connor et al., 2017). Therefore, in all further analysis we compute FC using combined data from rest and task conditions, as they appear to be stable within subjects and provide more robust estimates with longer data segments.

2.4. FC is associated with phenotypic and demographic information, for both fMRI and EEG

Of the available phenotypic data we selected a subset of 10 assessment instruments, which were available for most subjects and which contributed most strongly to shared variance in the population (Fig. 4A). Specifically, these 10 had the strongest component weights in a principal component analysis and the assessments questionnaires had been...
completed by at least 50% of participants (see Section 5.2). We also included age and sex as two important demographic variables that are well known to affect neuroimaging results (Biswal et al., 2010; Geerligs et al., 2015a; Ingalhalikar et al., 2014; Kilpatrick et al., 2006; Tomasi and Volkow, 2012). When referring to “phenotype” in the following we implicitly also refer to these two demographic variables. To establish a link between connectivity patterns and phenotype we used multivariate distance matrix regression (MDMR) (Mcardle and Anderson, 2001; Shehzad et al., 2014) (see Section 5.11). In essence, MDMR measures whether individuals with similar patterns of connectivity also have similar scores on a given phenotypic assessment instrument. Similarity of connectivity is measured by Pearson’s correlation across edges of the FC matrix. Pearson’s correlation is not affected by differences in means and measures the similarity of patterns of connectivity. Thus, overall strength of FC is not used as a predictive factor. Analysis is performed separately for each of the 10 phenotypic assessment instrument, in addition to the two demographic variables age and sex.

2.5. fMRI FC - phenotype associations

The MDMR analysis reveals a significant association between fMRI FC for a number of the measures tested (Fig. 4A). This includes age (F = 8.71, p < 0.004, N indicated in Fig. 4A), sex (F = 1.87, p < 0.004), the WISC IQ score (F = 1.72, p < 0.004), the CBCL score for multiple disorders (F = 1.42, p = 0.0072), the Barratt SES score (F = 1.36, p = 0.006) and SWAN ADHD score (F = 1.32, p = 0.01). An additional weak correlation is found between FC and the SCARED Anxiety score (F = 1.28, p = 0.031). P-values are FDR corrected. To avoid confounds with age and...
sex we regressed out a possible linear effects of age and categorical effect of sex from the other phenotypic and demographic variables prior to MDMR (see Fig. A4). The MDMR analysis reported above was done on FC combining resting state and video viewing. Notably, connectivity-phenotype relationships are found for similar phenotypes even when MDMR is performed separately on FC of resting state and the video task (Fig. 4B), albeit with somewhat weaker effect sizes. See Table A1 for full statistics. This further validates our choice for combining data from multiple tasks to reduce noise and improve power for this analysis.

### 2.6. EEG source space FC - phenotype associations

FC of EEG computed in the source space (see Sections 5.6 and 5.8) shows a strong association with age and sex in all frequency bands tested (Fig. 5A). Associations with the same 10 phenotypic variables only show a significant effect for IQ in the delta and beta bands (see Table A.2 for full statistics). In addition to regressing out the effects of sex and age, we have regressed out head size as it is correlated with age and sex (Fig. A4). The highest connectivity-phenotype relationship is seen in the broadband FC, followed by the higher frequency bands, beta and alpha (Fig. 5A). This could be explained by the higher reliability of FC in the broadband signal and the beta band (Fig. 3A), consistent with prior literature (Hipp and Siegel, 2015; Siems and Siegel, 2020).

The associations found with EEG coincide with those of fMRI connectivity. The analysis has also been conducted for different age groups (Fig. A6). While the specific statistics are somewhat different, the results are largely the same in the two age groups tested (5–9 years and 21–25 years). As with fMRI, the analysis here was done by combining EEG recordings from resting state and task performance. When we split the data by task (rest, video, flicker) the results do not differ much (Fig. 5B), again, consistent with the robustness of FC across tasks (Fig. 3). We find similar results when we perform the FC-phenotype analysis using alternative methods (see Fig. A7).

### 2.7. EEG sensor space FC - phenotype associations

Functional connectivity computed directly on sensor-space EEG data shows relationships to similar phenotypes as source-space FC (Fig. 5C). However, the effect size is larger in source space. Additionally, it has been shown that spatial patterns of FC in sensor space depend on the selection of the reference channel (Mahjoory et al., 2017). Therefore, we here focus on analyzing the spatial patterns of connectivity-phenotype relationships in source space.

### 2.8. Spatial patterns of FC-phenotype associations

Thus far we have associated phenotypes with a global pattern of FC. To determine which brain areas are specifically involved, we repeat the MDMR analysis separately for each brain region (based on the Schaefer atlas) (see Section 5.11). This indicates which nodes of the total brain network vary with phenotype (e.g. Fig. 6A). Additionally, we conducted the MDMR analysis for various resting-state networks (Yeo et al., 2011). This analysis reveals whether connectivity within or between networks drives the relationship to phenotypes (e.g. Fig. 5B). Both analyses were performed for the variables sex, age and IQ, which were linked to whole-brain FC for both fMRI and EEG. We can additionally establish the direction of the change by directly correlating connection strength with the phenotype (Figure A.9 and Figure A.10). However, the correlation of fMRI to age is weak and therefore very few nodes are significantly correlated to age after correction for multiple comparisons.

**Sex effects:** EEG connectivity differs with sex mostly for nodes in the occipital and parietal cortex (Fig. 6A). This is not a local property of the

![Fig. 3. FC for subjects engaged in different tasks is more similar than for different subjects engaged in the same task. A) Violin plots depict the distribution of the Pearson’s correlation between FC (iCOH) matrices across subjects. Dashed lines indicate the median of the distributions. Pearson’s R for ‘Same Subject/Different Task’ measures the similarity between different tasks (resting state, videos viewing, flashing gradings) computed for each subject separately. Pearson’s R for ‘Different Subject/Same Task’ measures the similarity between different subjects completing the same task. The correlation values between different subjects in the same task have been averaged per subject across all possible subject pairs. Then, the correlation coefficients from different tasks have been averaged. B) ICC measures reliability across tasks relative to variability across subjects. Distribution of ICC of FC (iCOH) between each pair of brain regions in the Schaefer atlas. We compare connectivity matrices between three tasks (videos, resting state and inhibition/excitation paradigm). The distribution of ICC is displayed for connectivity in each frequency band. Corresponding matrices are shown in Fig. A2. C) Distribution of ICC of FC between brain areas in resting state increases with length of recording time. ICC is computed between connectivity matrices of different sessions. Dashed lines show the median of the distributions. Median difference of ICC between 2.5 and 5 min sessions: \( \Delta \) ICC = 0.094, \( p \approx 0 \). Matrices of ICC for all pairs of regions are shown in Fig. A3A. D) ICC of FC during a video task (10 min of “Despicable Me”) increases with recording time. ICC is computed between sessions of the same movie task. Median difference of ICC between 2.5 and 5 min sessions: \( \Delta \) ICC = 0.16, \( p \approx 0 \). Corresponding matrices of reliability are shown in Fig. A3B.
occipital visual network, but rather, it is the link of the visual network with the frontoparietal, default mode and attention networks that differ between the sexes (Fig. 6B). The strong effects of connectivity originating in the visual cortex can partly be explained by the relatively high reliability of connectivity in the visual cortex (Colclough et al., 2016). In the beta band median connectivity in most brain regions is larger in girls than in boys (Fig. A.9). This effect is a strong contrast to other frequency bands where the median connectivity is larger in boys. Interestingly, the absolute median difference of connectivity between boys and girls is largest in the visual cortex (Fig. A.9), while the patterns of connectivity are dissimilar within the visual cortex (Fig. 6B). fMRI connectivity also differs with sex but the network nodes that are most affected appear to be quite different from the EEG connectivity. The strongest effects of the fMRI connectivity are seen in parietal and frontal lobes as well as the cingulate gyrus and are more focal than in EEG (Fig. 6A). In contrast to EEG connectivity, differences in fMRI connectivity within the ventral attention and default mode network are most strongly related to sex (Fig. 6B).

Age effects: EEG connectivity changes with age in all bands over broad cortical regions (Fig. 7A). Connectivity in the frontal lobe is related to age in all bands but the delta band. Age is related to connectivity between the visual and default mode, frontoparietal and ventral attention networks effects in delta and theta band (Fig. 7B). In the alpha and beta bands age differences correspond to differences in connectivity between the frontoparietal and default mode networks (Fig. 7B). In the beta band there is also a strong relationship of connectivity of the ventral attention network to other networks (Fig. 7B). Correlating age to connectivity in individual pairs of regions there is a drastic difference between bands. Delta, theta and beta band connectivity decrease with age and alpha connectivity increasing with age in most regions (Fig. A.10). fMRI connectivity is most strongly related to age in the parietal cortex, precuneus and posterior cingulate (Fig. 7A). This relationship is stronger and more focal than in EEG. The most distinct relationship between resting state networks and age is found within the ventral attention network and between the ventral attention and dorsal attention, frontoparietal and default mode networks (Fig. 7B). There is also a strong relationship of age to the connectivity within the visual, limbic, frontoparietal and default mode networks. Further, the relationship between age and the visual and dorsal attention network is strong. In terms of the correlation of age to connectivity in the ventral attention network, fMRI and EEG results are similar.

The effects of IQ - and SES - connectivity relationships are much weaker and thus harder to localize (Fig. 8). Given the general limitations localizing EEG sources these results should be regarded with care (Anzolin et al., 2019; Liu et al., 2018; Mahjoory et al., 2017). The relationship of fMRI connectivity to IQ is strongest in temporal and parietal lobes and is dominated by connectivity within the default mode network (Fig. 8).

3. Discussion

We have shown that phase-coupling measures of EEG cluster consistently across hemispheres and frequency bands. Notably, these clusters are different from clusters in fMRI (Yeo et al., 2011). Further, phase-coupling FC patterns can be seen as neural fingerprints that can distinguish subjects between each other and are consistent across tasks. Lastly, while FC patterns between EEG and fMRI are distinct, both are predictive of phenotypes such as age, sex and IQ.

3.1. Clustering of EEG FC

Clusters of EEG FC are extended in space and not always contiguous. This is important because clustering of FC could be confounded by “ghost interactions” (see Section 3.6). The spatially extended and distributed clusters suggest that “ghost interactions” are not the main effect driving clusters. Instead, clusters more probably represent functional units of EEG FC.

Phase-coupling FC is known to represent short range connectivity with less interhemispheric connections than amplitude coupling (Siems and Siegel, 2020). Thus the difference of clusters in EEG FC to fMRI could be partly driven by the measures of FC. Given the potential differences of phase-coupling and correlation, as well as physiological differences between EEG and fMRI, it is perhaps not surprising that clusters differ. This may warrant to use atlases specific to EEG FC in future studies.

3.2. Differences and similarities of FC in EEG and fMRI

The differences in FC between several EEG and fMRI measures have been investigated extensively (Colclough et al., 2016; Demuru et al., 2020; Siems and Siegel, 2020; Wirsich et al., 2020). Here we find that the structure of the FC of EEG differs from that of fMRI (Fig. 2), at least for EEG “connectivity” measured using the method of imaginary coherence (iCOH). Nevertheless, the FC of fMRI and EEG behave similarly in several regards. In both modalities, FC are well preserved across tasks relative to the variability observed across subjects (Fig. 3). This has previously been established for fMRI (Finn et al., 2015; Laumann et al., 2015; O'Connor et al., 2017), and is found to be true also here for source-localized EEG at all frequency bands tested. For both modalities, FC is predictive of similar phenotypes and demographic variables (Figs. 4 and 5). Specifically, age, sex and IQ are all associated with whole-brain FC measured of either EEG or fMRI. In
Fig. 5. EEG FC in various frequency bands are associated to sex, age and IQ. A) FC (iCOH) was computed after source localization. FDR correction was performed here across 12 measures (the same as in Fig. 4A), but not across bands. The 9 phenotypes not shown here, but shown in Fig. 4A, had no significant association with EEG FC in any frequency band. B) FC of EEG (source space, beta band) is associated with phenotype when FC is computed separately for each task. C) The FC-phenotype association is stronger when FC is computed in source space as opposed to sensor space. Sex and age effect are shown for one frequency band as an example. Effects of IQ are shown for all other frequency bands (Fig. A8). FDR control, at a level of \( \alpha = 0.05 \), was performed over the 12 variables tested here.

Fig. 6. Functional connections with significant sex effect. A) Spatial pattern of connectivity - sex relationship in EEG source space and fMRI. The subject-by-subject distance matrix is computed for each brain region. The distance is the Pearson’s correlation between the vectors of connectivity for each region. Pseudo F-Statistic for EEG and fMRI connectivity - sex association is computed by MDMR (Shehzad et al., 2014). Significant pseudo F-statistic values are plotted on the surface of the Freesurfer fsaverage template after correcting for multiple comparisons (FDR correction at \( \alpha = 0.05 \)). A high pseudo F-statistic in a brain region indicates that between-subject differences in connectivity patterns to all other regions correspond to differences in sex. B) Pseudo F-Statistic for the relationship between sex and the connectivity patterns in resting state networks of the Yeo parcellation (Schaefer et al., 2018; Yeo et al., 2011). Each square depicts the strength of the relationship of sex and the connectivity within (diagonal) or between (off-diagonal) networks. FDR correction at \( \alpha = 0.05 \) was performed. Visual, SomMot: Somatomotor, DorsAttn: Dorsal Attention, VentAttn: Ventral Attention, FrontPar: Frontoparietal.
addition, we have found a relationship of fMRI FC to attention deficit disorder, anxiety, socio-economic status and an aggregate measure of behavioral and emotional problems. These connectivity-phenotype relationships are largely independent of the task subjects were performing. Thus, as with fMRI (Elliott et al., 2019; Noble et al., 2019; O’Connor et al., 2017) we recommend concatenating EEG data across different tasks to achieve more reliable measurements of FC and a stronger relationship to phenotypes. When we look at the details of the connectivity-phenotype association we do see some differences between the two modalities. EEG connectivity is more strongly related to sex than age (Fig. 4A) and vice versa for fMRI (Fig. 4A). Additionally, the spatial patterns of the connectivity-phenotype relationship are different in the two modalities (Figs. 6–8). This is perhaps not surprising given that the connectivity matrices themselves are quite different between modalities (Fig. 2).

Our results show that FC differs between EEG and fMRI, yet FC of both modalities correlate with phenotypes. This suggests that FC of EEG and fMRI contain complementary information consistent with previous literature (Wirsich et al., 2017). Both fMRI (Finn et al., 2015; Gao et al., 2019; Rosenberg et al., 2016; Shehzad et al., 2014; Smith et al., 2015; Takagi et al., 2019) and EEG FC (Bathelt et al., 2013; Brookes et al., 2016; Coquelet et al., 2017; Kitzbichler et al., 2009; Schafer et al., 2014) have been related to phenotypes in separate studies. Therefore, both measures likely represent distinct aspects of neuronal activity that are behaviorally relevant.

3.3. Factors that may contribute to differences between EEG and fMRI

Factors that could explain these differences are the physiological origin of the two signals and the methods used to compute “connectivity”. Both factors vary drastically between modalities.

Both EEG and fMRI are thought to be related to post-synaptic potentials (Hall et al., 2014). Specifically, it has been shown that the fMRI BOLD signal is related to local field potentials in the gamma and high-frequency power (50–150 Hz and above 250 Hz respectively).
3.5. Reliability of FC in fMRI and EEG

Reliability of fMRI FC increases from 2.5 to 5 min of recording time for both resting state and video data (Fig. 3C and D) consistent with O’Connor et al. (O’Connor et al., 2017). Spatial patterns of reliability of FC (Fig. A3) are roughly similar to those previously reported (O’Connor et al., 2017). Specifically, high reliability in the visual network has been reported (Schmälze et al., 2017). An exception is that reliability in the visual network does not differ much in our data between the resting state and video task (Fig. A3). Such a difference between resting state and video conditions has been observed in O’Connor et al. (O’Connor et al., 2017). This might stem from differences in subjects keeping their eyes open or closed (Patriat et al., 2013).

Lacking suitable data to measure the reliability of EEG FC with recording time (Fig. 1C) we investigate the difference in reliability across tasks for different frequency bands. We have found that the reliability of FC increases with frequency (Fig. 3B). This may be the result of more focal activity as frequency increases (Freeman et al., 2003, 2000) and thus inverse modeling is more reliable. We conclude that EEG connectivity phenotype relationships are most reliably measured in the high frequency bands, especially the beta band.

3.6. Caveats and alternative approaches

The imaginary part of coherency is robust to artifacts of volume conduction (Nolte et al., 2004; Palva et al., 2018). Some issues with this measure remain: True interactions with a close to zero-phase time lag are excluded, the strength of connectivity depends on the phase, and spurious correlations are still present (Palva et al., 2018). New methods have been proposed to alleviate these spurious “ghost interactions” for amplitude coupling (Wang et al., 2018). Future studies have to develop similar methods for phase coupling measures.

The total length of recordings included in this study is about 23 min (Fig. 1C) and at the lower end of the recommended 25 min to measure reliable connectivity in fMRI (Elliott et al., 2019; Laumann et al., 2015). Using additional task paradigms, which are available for EEG in this dataset (Alexander et al., 2017), could improve reliability of EEG connectivity. However, we intentionally constrained ourselves to “passive” tasks so as to be comparable to previous FC work on fMRI.

We have used Pearson’s correlation to quantify the similarity of connectivity patterns. Other measures, such as Euclidean distance, can also capture differences of means and have been discussed in Shehzad et al. (2014). In fact, the absolute median difference between male and female subjects in each channel pair is most distinct within the visual cortex (Fig. A.9). On the contrary, we find the strongest connectivity-sex relationship with MDMR for connections between the visual and the attention, frontoparietal and default mode networks (Fig. 6). The absolute median difference is driven by absolute differences in strength of connectivity at each link, while MDMR compares the similarity of patterns of connectivity within and between networks. Alternative analysis methods such as Joint and Individual Variation Explained (JIVE) (Lock et al., 2013; Yu et al., 2017) or Multiscale Graph Correlation (Shen et al., 2018; Vogelstein et al., 2019) give us similar results for MDMR (Fig. A7).

We have chosen a functional cortical parcellation for practical purposes. The Schaefer atlas is available in volume and surface space. Different cortical parcellations could change the subject-by-subject similarity and in consequence the connectivity-phenotype relationship. However, using an anatomical parcellation (Destekan et al., 2006) we find very similar connectivity-phenotype relationships (Fig. A11). Similarly, we expect that using a clustering of connectivity as proposed by Wang et al. would not influence the connectivity-phenotype relationships (Wang et al., 2018). Conversely, it has been suggested to use parcellations defined on EEG or MEG to improve signal-to-noise ratio (Colclough et al., 2016). Indeed, we have shown that clustering of EEG and fMRI connectivity is distinct (Fig. 2). A note of caution on the clustering of EEG functional connectivity is that the spatially contiguous parcels of connectivity might be enhanced by “ghost interactions” (Palva et al., 2018; Wang et al., 2018). These spurious correlations in the vicinity of true interactions can result from local field spread or genuine short-range connectivity.

Our subjects population consists of both healthy subjects and those...
exhibiting developmental psychopathology (Alexander et al., 2017). It is known that several of the phenotypes investigated in this study are correlated to each other. Socioeconomic status, for example, has a strong influence on IQ (Hanscombe et al., 2012; Turkheimer et al., 2003). Similarly, it has been shown that subjects with autism rely more on connectivity in visual areas when solving tasks in IQ tests than healthy subjects (Simard et al., 2015). Only ~12% of subjects in our sample have been diagnosed with autism; therefore interactions with IQ are unlikely in our data. However, the interactions between different psychiatric phenotypes should be the subject of future studies.

We have identified a number of possible anatomical confounds, that differ with age and sex such as head size (Fig. A4) or cardiac artifacts (Fig. A5A). The effect of this would be expected to be broadly distributed (in contrast to findings in Figs. 6 and 7) and should have the same sign in different frequency bands (in contrast to findings in Fig. A9). Age and sex effects could also influence the analysis of within- and between-subject correlation of FC (Fig. 3). Specifically, the lower between-subject correlation could result from anatomical differences in age and sex. However, this has been explicitly controlled for in the fMRI data and we do not expect that age and sex differences account for all the differences of connectivity between different subjects. Thus, while we do not rule out such confounds, we suggest that purely neurological factors may play a role in the age and sex effects. Future studies will be necessary to clearly dissociate anatomical and neurological effects of age, sex, head size and cardiac artifacts on FC in EEG.

3.7. Future directions

Given the different physiological origin of EEG and fMRI as well as differences in connectivity measures (Haufe et al., 2018; Siems and Siegel, 2020; Wirsich et al., 2020), it is not surprising that we do not find any similarities between the connectivity matrices. However, it has been shown that the two measures capture complementary information of connectivity (Wirsich et al., 2017). In light of this, making use of simultaneous EEG and fMRI recordings opens new possibilities in investigating the properties and behavioral relevance of FC. Investigating the differences of FC patterns in different modalities can improve the understanding of the physiological origin of FC. Further, by combining data from EEG and fMRI, subject identification by FC and the connectivity-phenotype relationship could be improved. In contrast to fMRI, EEG allows the analysis of FC on a faster timescale and a more detailed analysis of directed FC. This can be useful in the context of the recent effort to extend FC analysis by a causality framework (Reid et al., 2019).

4. Conclusion

We have systematically investigated the FC measured with phase-coupling of EEG and compare this to phenotypic and demographic variables as well as to FC in fMRI. Using a large database we were able to show that EEG FC networks are similar in robustness to fMRI networks. Specifically, EEG FC networks are most robust in the higher frequency bands, such as the beta band. As reported in the fMRI literature, functional networks are more similar between tasks measured in the same subject than between different subjects during the same task. The relationship between whole-brain EEG FC and various phenotypes is similar to that observed for fMRI. Therefore, EEG has the potential to predict behavior comparable to fMRI. We have shown that the functional organization of the cortex look different when measured with phase-coupling of EEG than fMRI. We hope that this work provides the basis for a new research direction in FC based on EEG, that is distinct from the functional network established with fMRI.

5. Methods

5.1. Participants and tasks

Participants recruited through the HBN initiative are children and adolescents aged 5–21. A diverse sample has been collected from the New York City area including a large proportion of subjects with psychiatric disorders (Alexander et al., 2017). We analyzed both fMRI scans and EEG recordings available on the HBN Biobank. For fMRI we used FC data of participants during resting state (two sessions of 300 s each) and watching naturalistic stimuli (‘The Present’; duration 201 s, and ‘Despicable Me’, duration 600 s). This dataset consists of fMRI scans from 766 participants. We included EEG data from the first six releases, with a total of 1657 subjects. Depending on availability and data quality we combined several paradigms; resting state (duration 300 s), two blocks of the inhibition/excitation paradigm (duration 210 s each), and four naturalistic stimuli (‘Despicable Me’, duration 170 s, ‘The Present’, duration 230 s, ‘Diary of a Wimpy Kid’, duration 117 s, and ‘Fun with Fractals’, duration 163 s) (Fig. 1C).

Data collection for the Healthy Brain Networks Biobank is described in detail elsewhere (Alexander et al., 2017). Briefly, EEG is recorded using a 128-channel EEG godesic hydrocel system by Electrical Geodesics Inc. (EGI) with a reference at the vertex of the head (Cz). fMRI data is recorded at different sites with varying scanner parameters.

5.2. Phenotypic data

The HBN dataset includes several psychiatric, behavioral, cognitive, and lifestyle phenotypes collected with standard assessment instruments (Alexander et al., 2017). All analysis has been conducted in MATLAB R2019b (Natick, MA, The MathWorks Inc.) A data driven approach was applied to select a subset of these phenotypes for further analysis. First, the total scores of all available assessments were retrieved from the database, subcores were not included. Phenotypes that capture exclusively physical features were excluded (e.g. fitness level, bio-electric impedance analysis, pregnancy). Of the remaining 47 phenotypes, ten were selected in two steps. First, 22 phenotypes with more than 50% missing data were excluded. Data of the remaining 47 phenotypes was normalized by z-scoring. Missing values in the remaining data were estimated using the alternating least squares (ALS) algorithm (Ilin and Raiko, 2010; Roweis, 1998). Principal component analysis (PCA) was applied on the data including the estimate of missing values. The PCA coefficients of the components explaining at least 40% of the variance (3 top components) were averaged and the phenotypes with the largest average coefficients were selected for further analysis.

5.3. EEG preprocessing

We developed an algorithm for automated preprocessing of EEG data to handle the large amount of data in the HBN database. Since FC measures the consistency of phase between channels, special care was taken to use filters that do not distort phase. Subspace projection methods such as PCA and ICA might introduce dependencies between channels and were not applied to the data. The preprocessing algorithm consists of a number of steps removing artificial samples and channels based on statistical thresholds. 1) Zero phase 5th order Butterworth filters are applied to remove drift (0.5 Hz high-pass) and line noise (60 Hz and harmonics). 2) Channels without signal or with large portions of flat signal (>5 s) are removed. 3) Channels whose standard deviation is larger than 2 times the interquartile range of the standard deviations across all channels are rejected. 4) The effect of eyeblinks and eye movements are removed from the EEG data by subtracting the signal estimated by a least squares regression model using EOG channels (Reposv, Grega, 2010). 5) Channels of high frequency power are removed by computing the ratio of the standard deviation of the high-passed signal (35 Hz cutoff) over the standard deviation of the
signal with full frequency spectrum. Similar to step 3) a channel is excluded when the ratio of the standard deviation of high frequency versus the full spectrum is above 2 times the interquartile range across channels. 6) Samples with an absolute voltage above 4 times the interquartile range of voltage per channel are removed. 7) To remove high-frequency samples the data is high-pass filtered (5th order zero-phase Butterworth filter with a cutoff at 35 Hz) and split into segments of 200 ms. Epochs are z-scored across channels and time points and epochs with a z-score above 4 are rejected (Mahjoory et al., 2017). For steps 8–10) steps 3, 8 and 9 are repeated. With overall cleaner data more artifacts can be removed through a second pass. 11) Channels that have more than 25% of data removed though the previous steps are removed completely. 12) Removed samples are interpolated from other channels if at least two thirds of the samples at the same time point are available in other channels (Madsen et al., 2019). Other samples are set to zero and the edges are smoothed by a mask. 13) The cardiac artifact occurs in similar channels in different subjects. Peaks of the cardiac artifact do not occur at a precise frequency and their amplitude is often similar to the neural signal. We use a subspace subtraction method to remove the artifact, similar to what is used for electro-ballistogrm removal in fMRI. Specifically, we visually inspect the EEG to identify channels with obvious cardiac signals (Fig. A5A). A peak-finding routine is applied and the signal in a window of 264 ms (33 samples at 125 Hz) surrounding each peak is selected. Principal components analysis of this data identifies the subspace that dominates the artifact and this subspace is subtracted from the EEG (Parra et al., 2005). This procedure is only applied if an electrode is found with an obvious cardiac signal.

5.4. Movement artifacts

FC in channels on the neck are most strongly affected by differences in sex (data not shown). This effect is most likely due to movement artifacts. Channels close to neck and face have been excluded from the analysis to reduce the effects of movement artifacts that have not been removed by the preprocessing algorithm. 38 channels with the following labels in the 128 channel EGI Geodesics Sensor Net were excluded: E1, E8, E14, E17, E21, E25, E32, E38, E43, E44, E48, E49, E56, E57, E63, E64, E69, E73, E74, E81, E82, E88, E89, E94, E95, E99, E100, E107, E113, E114, E119, E120, E121, E125, E126, E127, E128.

5.5. Automated rating of data quality

Data quality is rated by four criteria: 1) The number of bad channels removed by the preprocessing algorithm. 2) The number of samples rejected as artifacts divided by the total number of samples. 3) The ratio of samples with an absolute voltage above 15 mV. 4) Time points with a standard deviation across channels above 14 mV. Only time points that include at least 30% of samples across channels are included in measuring standard deviation.

For each measure a rating from 1 (worst) to 5 (best) is assigned based on the distribution of quality measures over all subjects. The percentile thresholds are given in Table 1. The total rating per subject is the mean of the ratings assigned to all four measures. If the rating of high voltage or high variance is only 1 or 2 the overall rating is set to 1. This ensures that subjects with very bad quality in one measure are excluded from the analysis. Recordings with low sum of power across channels (<3 × 10^5 mV^2) are also set to a rating of 1. Ratings 4 and 5 describe data of reasonably good quality which was included in the analysis. In total 1330 subjects have at least one recording with a rating of 4 or 5 (Fig. 1).

5.6. Source reconstruction

Source reconstruction was conducted for every subject based on the (Fischl et al., 1999). The leadfield was created with Brainstorm (Tadel et al., 2011) and OpenMEEG (Gramfort et al., 2010; Kybic et al., 2005) using a 3-shell BEM model and the EGI Hydrocel 129 cap. We imported the 200 parcel parccellation matched to the Yeo 7 network parcellation defined by Schaefer et al. (2018). The pial surface of the fsaverage standard head was resampled to 2003 voxels using Matlab’s resubpatch method. The BEM model consists of a scalp layer with 1082 voxels and a relative conductivity of 0.0125 and a brain layer with 1922 voxels and a relative conductivity of 1. The OpenMEEG head model was computed using adaptive registration. Before source reconstruction, both the EEG data and the head model were converted to a common average reference. This has been done, because it is important that forward model and electrode reference match one another (Nunez and Srinivasan, 2016; Pascual-Marqui et al., 2011). EEG data is projected into source space by the eLORETA inverse projection kernel with 5% regularization (Pascual-Marqui, 2007). Signals in source space are then z-scored. For each region of interest of the Schaefer atlas the strongest 3 PCA components of the source space signal are selected. iCOH is calculated in source space for each PCA component separately. To account for the random polarity of the source signals introduced by the source reconstruction and PCA steps, the absolute value was taken. The final FC matrix consists of the mean connectivity across the three PCA components per region of interest. Computing connectivity on PCA components mitigates the effect of signals leaking from a parcellation to others.

5.7. fMRI preprocessing

The fMRI data were preprocessed using the Configurable Pipeline for the Analysis of Connectomes (C-PAC) (Craddock et al., 2013). The structural preprocessing includes: 1) Brain extraction using AFNI, 2) tissue segmentation using FAST, 3) registration to the MNI152 template using ANTs. The functional preprocessing includes: 1) Motion correction, 2) motion spiking regression with mean framewise displacement threshold at 0.5 mm, 3) nuisance regression with aCompCor, cerebrospinal fluid, and Friston-24 motion parameters, 4) linear and quadratic detrending, 5) band-pass filtering (0.01–0.1 Hz), 6) boundary-based co-registration from functional space to native anatomical space and subsequent registration to MNI152 template space, 7) projection from MNI152 vol space to the Freesurfer subject surface space and down-sampling to a 10k resolution surface (10,242 voxels per hemisphere).

5.8. Functional connectivity

A common measure for FC is coherency, a measure of phase synchronicity between two signals (Bastos and Schoffelen, 2016; Mahjoory et al., 2017). Coherency is a complex-valued quantity reflecting the average phase difference between two time series as well as the stability of that difference across repeated measurements. In many application domains, the absolute value of coherency (referred to as coherence) is used to obtain a metric of phase coupling that is independent of the actual delay between the time series. In EEG, however, it is necessary to distinguish zero from non-zero phase delays as zero-lag interactions are likely to have trivial origin. Since EEG electrodes measure a mixture of signals from several neural sources through instantaneous volume conduction from the brain to the scalp, electrodes appear to be coherent with zero delay as the signal from one neural source arrives at several electrodes at the same time. The same holds true for reconstructed source
activity, for which the instantaneous mixing introduced by volume conduction can in general not be undone completely. To prevent spurious connectivity due to source mixing the imaginary part of coherency (iCOH) can be employed (Nolte et al., 2004). iCOH is robust to volume conduction artifacts in function connectivity by excluding coherency at zero phase delay.

The FC matrices are computed in MATLAB using the FieldTrip Toolbox (Oostenveld et al., 2011) based on an implementation described previously (Bastos and Schoffelen, 2016; Nolte et al., 2004). First, the Fourier spectrum of the preprocessed EEG signal is computed using multi taper frequency transformation with discrete prolate spheroidal sequences. The cross-spectral density is then computed from the Fourier spectrum by multiplying the Fourier spectrum of the signal of one EEG channel with the complex conjugate of the Fourier spectrum of all other channels and averaging over epochs of 2 s. Epochs are averaged over trials of all EEG source space data of all tasks with good data quality, as defined above. iCOH is the absolute value of the imaginary part of the cross-spectral density scaled by the square root of the product of the power of the signal of each channel. By creating epochs of 2 s an iCOH matrix can be calculated for frequencies of 0.5 Hz and above. iCOH matrices were computed for 126 frequency between 0.5 Hz and 62.5 Hz with a resolution of 0.5 Hz. To obtain an iCOH matrix for each frequency band, iCOH values for each pair of parcellations were averaged across all bins within a band. The delta band is defined between 0.5 and 4 Hz, the theta band between 4 and 7.5 Hz, the alpha band between 7.5 and 15 Hz and the beta band between 15 and 30 Hz.

FC in fMRI is measured by Pearson’s correlation between the time series of activations between each pair of parcellations in the Schaefer atlas.

5.11. Multivariate distance matrix regression (MDMR)

To compare whole-brain FC to phenotypes first a subject-by-subject distance matrix of whole brain FC is calculated. To this end, the iCOH connectivity matrix between areas of the Schaefer atlas was arranged as a vector by stacking its columns. Subjects with short recordings below 20s were excluded. The vectorized connectivity matrices were then concatenated into a m-by-n matrix, where m is the number of subjects and n is the square of the number of areas in the Schaefer parcellation. The m-by-n subject-by-subject distance matrix is obtained by calculating Pearson’s correlation coefficient for each pair of rows of this matrix.

We repeat this analysis resolved in space, namely, instead of the whole-brain FC we now analyze the connectivity emanating from a single parcellation area. Thus the m-by-n matrix now refers to m subjects and n parcellation areas. Lastly, distance matrices relating to networks defined by Yeo et al. are computed by selecting the submatrices containing parcellations corresponding to each network.

MDMR tests whether subjects with similar connectivity also have similar phenotypes (Shehzad et al., 2014). The pseudo F-statistic is a measure of the ratio of hypothesis-sums-of-squares to residual-sums-of-squares following a linear model relating the subject-by-subject distance matrix to the phenotypic data (McCullough and Anderson, 2001). Since the distribution of the pseudo F-statistic is unknown, significance is assessed by establishing an empirical null distribution. This is achieved by recomputing the pseudo F-Statistic after shuffling the subject labels of the distance matrix (Shehzad et al., 2014).

Not every subject includes a full set of phenotypic measures. MDMR is computed on the subset of FC matrices with matching phenotypes data separately for each phenotype.

Several of the selected phenotypes are strongly correlated to sex, age or head size. ADHD, for example, is diagnosed more often in boys than girls. MDMR can be formulated to test the association of a subject-by-subject distance matrix to phenotypes taking into account nuisance covariates (Reiss et al., 2010; Shehzad et al., 2014). The effects of age, sex and head size can be arranged in a design matrix that is subtracted from the design matrix including the phenotype of interest. The Pseudo F-statistic then measures the connectivity-phenotype relationship controlled for nuisance covariates.

To account for multiple comparisons the Benjamini-Hochberg procedure to correct for false discoveries is applied (Benjamini and Hochberg, 1995). The procedure limits the false discovery rate (FDR; rate of type-I errors) to $\alpha = 0.05$. MATLAB’s implementation of the Benjamini-Hochberg procedure is used.

5.12. Visualization

The value of the pseudo F-statistic describing the strength of the connectivity-phenotype association in a cortical parcellation is plotted on a smoothed fsaverage surface (Haufe and Ewald, 2019). Sources on the medial surface are not meaningful in the EEG analysis and are not shown but included in the analysis.

5.13. Reliability of measurements

Reliability of connectivity measurements was tested for each possible pair of connectivity between parcellations. The measure used was intraclass-correlation (ICC). ICC was measured between actual or virtual sessions in the case of fMRI and between tasks (resting state, excitation/inhibition paradigm and videos) in EEG. For this purpose the ICC(3,1) model was chosen to measure consistency between sessions or tasks (McGraw and Wong, 1996). ICC(3,1) is based on a mixed effect model. The measure of FC is modeled by a fixed effect of sessions or task, and a random effect of subjects. ICC(3,1) is defined as the variance between subjects divided by the total variance. The total variance is the sum of the variance between subjects and the variance between tasks. An ICC(3,1) value of 1 would indicate perfect consistency between sessions or tasks.
An ICC(3,1) value of 0 would indicate that subjects have the same values.

fMRI data for each 5 min resting state session was split into two virtual sessions of 2.5 min each. FC matrices were computed for each virtual session. ICC(3,1) between all possible combinations of 2.5 min virtual sessions was computed and averaged. Further, ICC(3,1) was computed between the actual 5 min resting state sessions. For the video task we compare connectivity matrices computed for virtual sessions of 2.5 and 5 min generated from the same recording session. Statistical significance of the difference between ICC(3,1) for 2.5 min and 5 min was tested with a Wilcoxon signed rank test across all pairs of connectivity. The analysis was conducted using data from 359 subjects for which data were available for each condition.

For the EEG analysis iCOH matrices were computed for each component (resting state, excitation/inhibition paradigm and videos) after concatenating all available sessions within each task. ICC(3,1) was computed for all pairs of parcellations separately for each frequency band. Amongst all subjects with data available for all sessions in all tasks, 50 subjects were included in the analysis (data from 59 subjects were excluded as insufficient numbers of subjects were included in each task to pass the ICC(3,1) threshold). The analysis was conducted using data from 359 subjects for which data were available for each condition.

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The authors declare no conflict of interest.
