Handedness measures for the Human Connectome Project: Implications for data analysis

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HUMAN BRAIN EVOLUTION LAB

Background and Motivation

› Handedness is of interest in psychological and brain sciences due to its presumed association with other lateralized functions, including language.

› The Edinburgh Handedness Inventory (EHI) [1] is a near-universal tool for evaluating subject handedness in neuroimaging contexts, and EHI values are often used as independent variables in statistical analyses of lateralization.

› Using the EHI as a sole handedness metric, many have found poor association between handedness and other forms of laterality [2, 3, 4, 5, 6].

› Despite the widespread use of the EHI, there is no consensus on how well EHI values correspond to actual hand preferences or performance. Thus, it is unclear how the use of the EHI has impacted previous analyses.

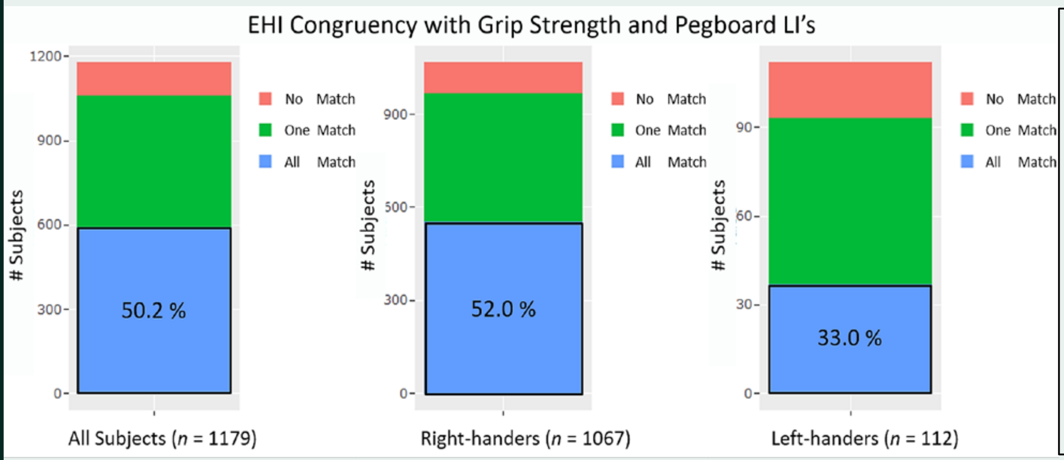
Is the EHI a reliable proxy for handedness?

› Using open data from the Human Connectome Project (HCP) [7, 8, 9], we evaluated the congruence between EHI values and laterality indices (LI's) for 1,179 subjects, which were calculated* from two NIH Toolbox behavioral tasks:

› **PBLI** – Annett 9-hole Pegboard Dexterity task

› **GSLI** – Dynamometer Grip Strength task

› **Only 50% of the HCP subjects have all three handedness measures (EHI, PBLI, and GSLI) indicating the same directional bias, with even worse congruency for presumed left-handers (EHI– subjects).**



* LI's were calculated so that positive values indicate right hand bias and negative values indicate left hand bias.

$$\text{Grip Strength (GS) LI} = \frac{Right\ hand\ GS - Left\ hand\ GS}{Right\ hand\ GS + Left\ hand\ GS} * 100$$

$$\text{9-hole Pegboard (PB) LI} = \frac{Left\ hand\ PB - Right\ hand\ PB}{Right\ hand\ PB + Left\ hand\ PB} * 100$$

Figure 1. Congruency measures indicate directional sign-matching between the three handedness values within each subject.

An "all match right-handed" subject would have three positive values (EHI+, GSLI+, PBLI+).

A "one match left-handed" subject may have rightward bias for either behavioral value (EHI–, GSLI+, PBLI–; EHI–, GSLI–, PBLI+).

A "no match" subject has both behavioral LI's opposing their EHI direction (EHI+, GSLI–, PBLI–; EHI–, GSLI+, PBLI+) .

› A Principal Components Analysis (PCA) of EHI, PBLI, and GSLI measures for 1,179 HCP subjects resulted in three components:

› **PC1** – overall handedness bias (positive loadings on all handedness measures)

› **PC2** – dexterity vs. strength (positive GSLI loading, negative PBLI loading)

› **PC3** – EHI vs. actual behavioral measures

PCA with EHI, GSLI, PBLI	% Variance explained
PC1	45
PC2	31
PC3	24

Loadings	PC1	PC2	PC3
EHI	0.659	−0.088	0.747
GSLI	0.577	0.812	−0.330
PBLI	0.482	−0.578	−0.577

› In addition to the original handedness measures, PCA scores were used to sample HCP subjects, and as variables for the analyses described below.

Methods

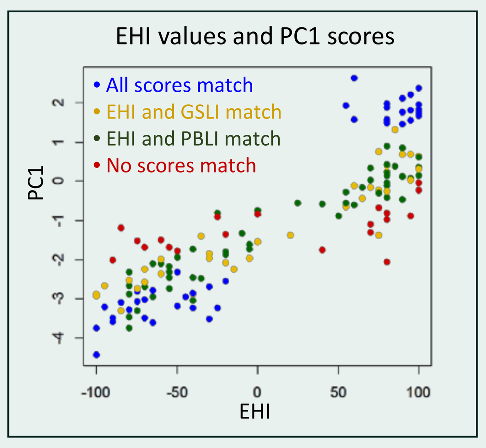
Sample selection: All HCP subjects with negative EHI values and complete MRI data (n = 76) were matched for age, sex, and handedness-measure congruency as closely as possible to an EHI+ subject (n = 152 total; mean age = 28.7, mean EHI = 12.46).

› PC1 scores correlate significantly with EHI scores (Pearson's r = 0.87)

› Still, many of the sampled EHI+ subjects with left-biased behavioral LI's (GSLI– and/or PBLI–) are PC1–

EHI–	N	EHI	PC1
All Match	22	−63.2	−3.2
One Match	44	−50.3	−2.3
No Match	10	−53.0	−1.4

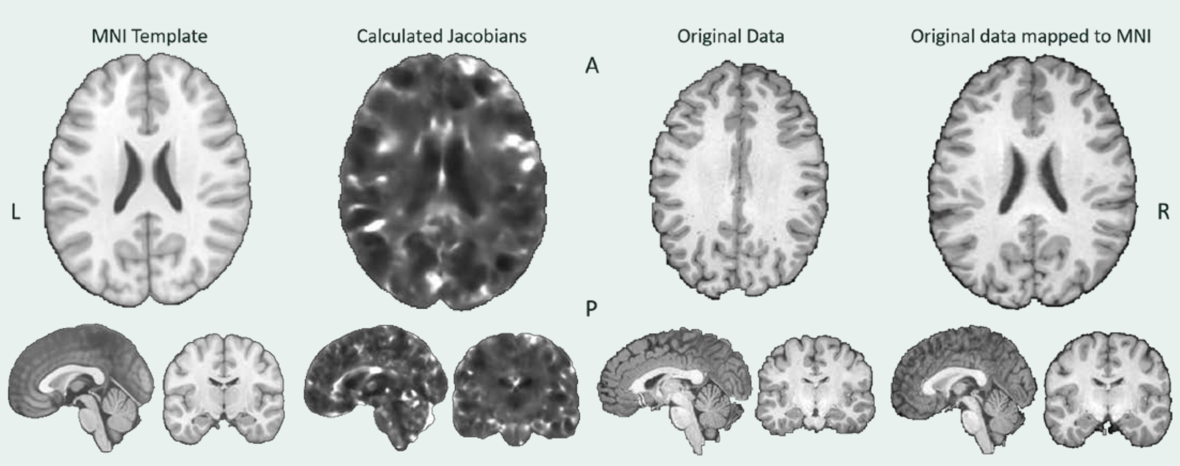
EHI+	N	EHI	PC1
All Match	22	+86.9	+1.8
One Match	44	+75.7	0.0
No Match	10	+79.0	−1.0



Anatomical Data – Voxel-Based Morphometry (VBM):

› T1w MRI images for 152 subjects were morphed into the MNI template brain using the Advanced Normalization Tools package [10, stnava.github.io/ANTs/].

› Jacobian values* were calculated on each voxel for each subject's distortion map, relative to the MNI brain, and then logged.



* Jacobians are scaling coefficients which show how the local volume of the original T1w image compares to the matching area of the MNI brain. Values greater than 1 indicate areas where the subject brain is larger than the template; values less than 1 indicate where the subject brain is smaller than the template. Jacobians were log transformed for statistical tests.

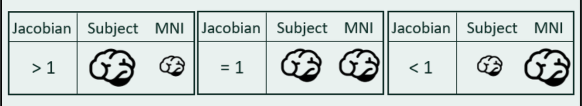


Figure 2. *Far left:* MNI template. *Left:* Jacobian values for localized size changes; white represents shrinking voxels and grey-black represents expanding voxels. *Right:* original T1w image for one subject. *Far right:* the same subject morphed into the MNI brain.

Statistical Analyses and Results

› Jacobian images were log-transformed (using ANTsR) [10] for analysis. Statistical models run on the whole sample (n = 152) include:

› **Model 1** – a linear model between logged Jacobians and EHI scores, at each voxel, controlling for overall brain size.

› **Model 2** – a linear model between logged Jacobians and PC1 scores, at each voxel, controlling for overall brain size*.

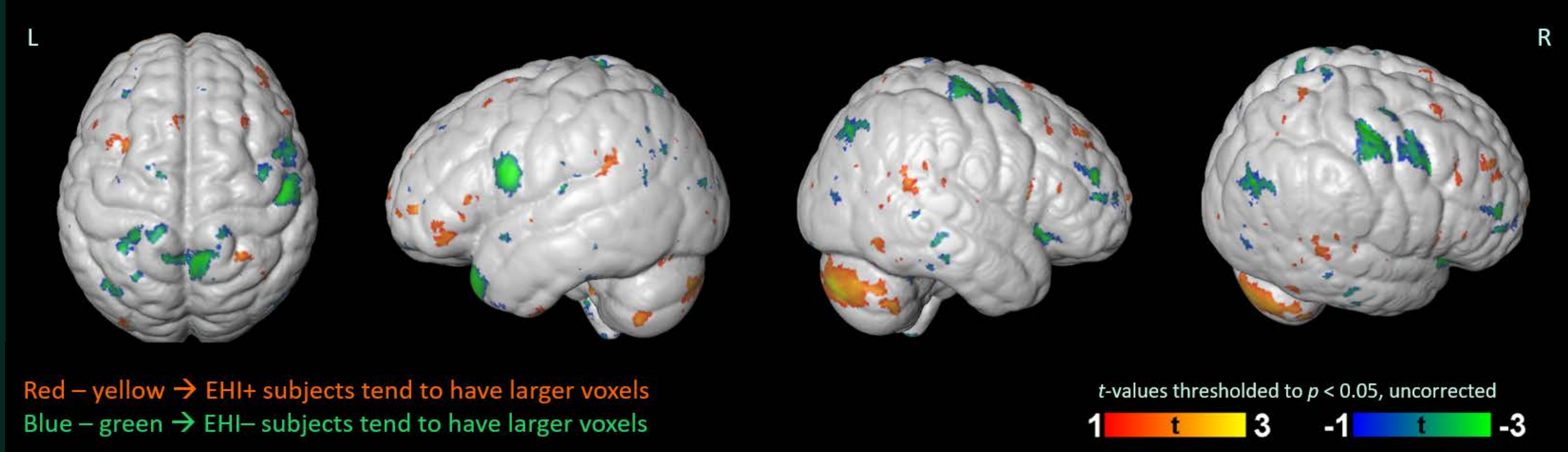
*The resulting t-value images show which voxels are significantly correlated with the EHI scores (Model 1) or with the PC1 scores (Model 2).

For both models, positive t-values indicate voxels where right-handers (EHI+ or PC1+ subjects) tend to have larger voxels, and negative t-values indicate voxels where left-handers (EHI– or PC1– subjects) tend to have larger voxels.

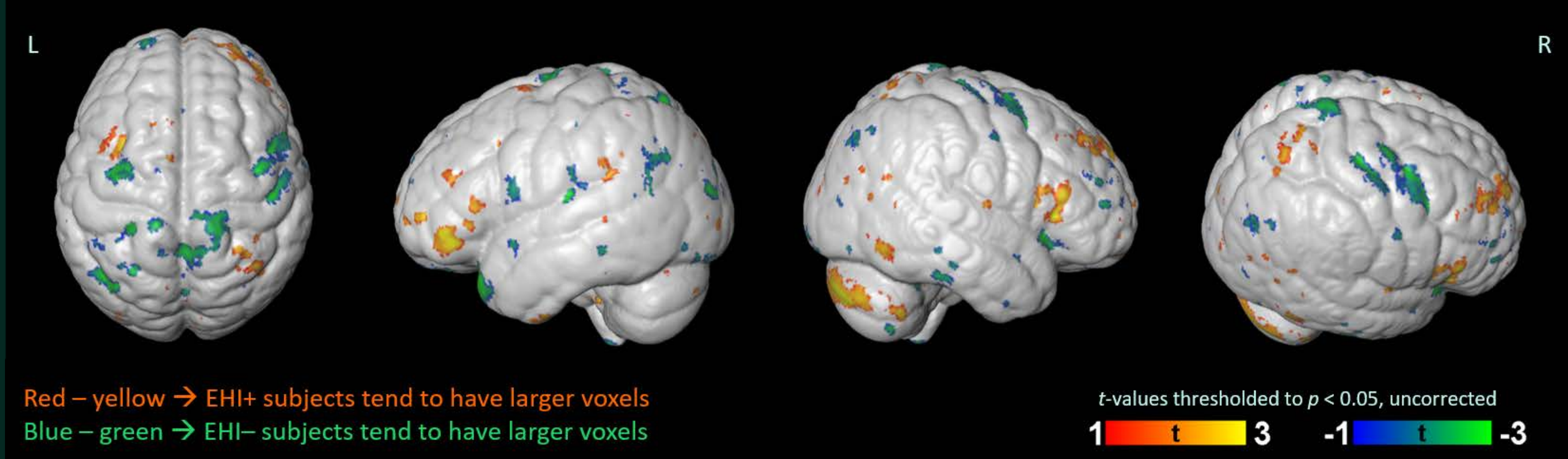
› **Both models show that the more left-biased a subject is, the larger their sensory and motor control areas tend to be for their left hand.**

› **The reverse is *not* true for sensory and motor control for the right hand.**

Linear Model 1 – EHI scores and Logged Jacobians



Linear Model 2 – PC1 scores and Logged Jacobians



Mapping Congruency Effects

› In order to assess the differences between subjects whose scores all indicate the same hand bias to those with at least one mismatched score, additional analyses were run, at each voxel, for subsets of the larger sample:

› **Model 3** – t-test comparing consistent right-biased subjects (EHI+, GSLI+, PBLI+) and inconsistent right-biased subjects (n = 76).

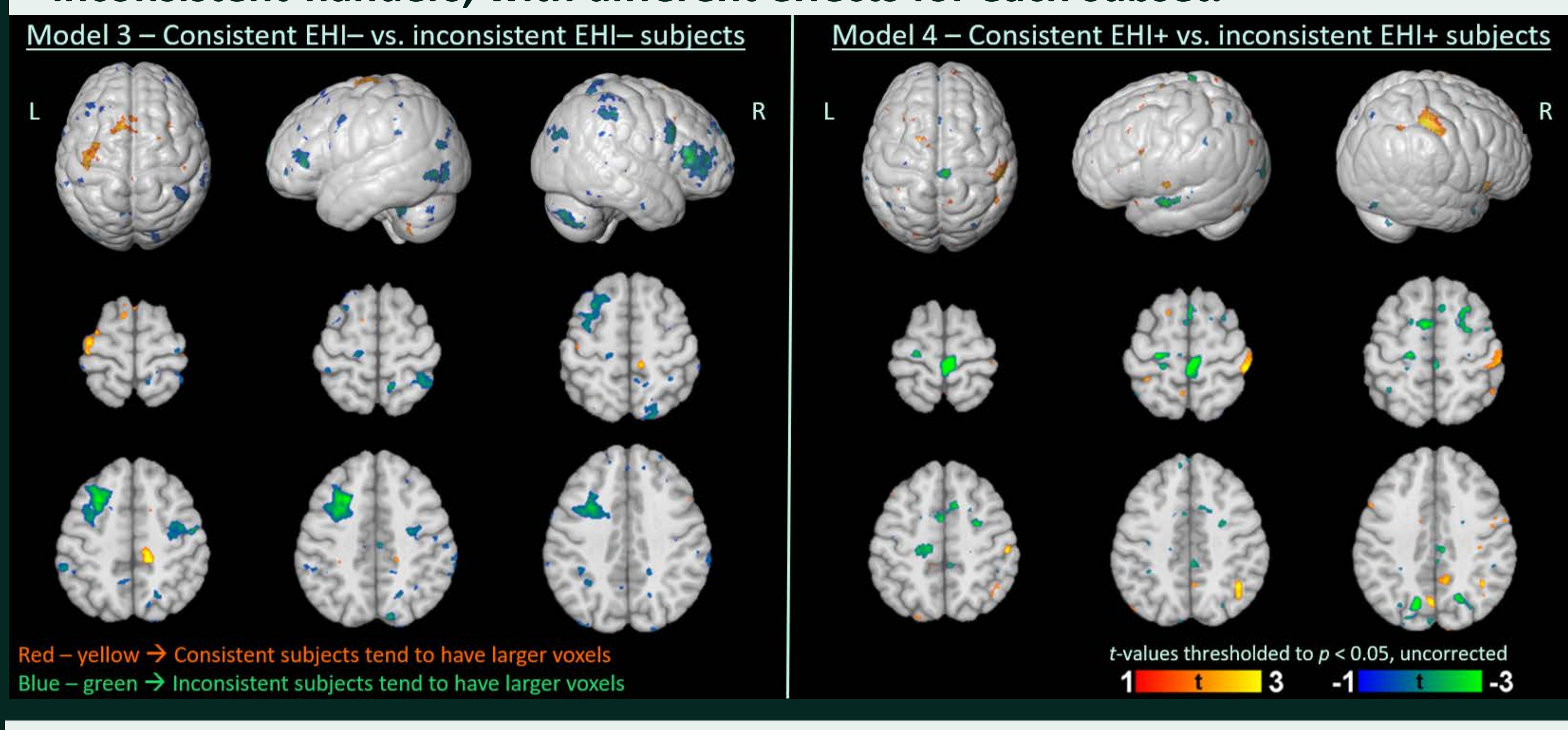
› **Model 4** – t-test comparing consistent left-biased subjects (EHI –, GSLI –, PBLI –) and inconsistent left-biased subjects (n = 76)*.

* The resulting t-value images show comparisons between "all-match" subjects to "partial-or-no match" subjects.

For both models, positive t-values indicate voxels where "all-match" subjects tend to have larger voxels, and negative t-values indicate voxels where "partial-or-no match" subjects tend to have larger voxels.

› **Both models suggest that consistent-handers have larger sensory or motor voxels for their *non-dominant* hand, compared to inconsistent-handers.**

› **Overall, there are complex differences between consistent-handers and inconsistent-handers, with different effects for each subset.**



Summary of Results

› **Many Human Connectome Project subjects have mixed handedness scores.**

› **There are complex effects of hand preference direction *and* congruency on localized brain areas, including for sensory and motor control of the hands.**

› **Although EHI scores communicate handedness information, they should not be considered a direct proxy for actual manual preference or performance.**

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[10] This research was supported in part by Lilly Endowment, Inc., through its support for the Indiana University Pervasive Technology Institute, and in part by the Indiana METACyt Initiative. The Indiana METACyt Initiative at IU was also supported in part by Lilly Endowment, Inc.

This research is supported by funding from:
The Stone Age Institute
John Templeton Foundation