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Left handers are less lateralized than right handers for both left and right hemispheric functions

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ABSTRACT

Many neuroscientific techniques have revealed that more left- than right-handers will have unusual cerebral asymmetries for language. After the original emphasis on frequency in the aphasia and epilepsy literatures, most neuropsychology and neuroimaging efforts rely on measures of central tendency to compare these two handedness groups on any given measure of asymmetry. The inevitable reduction in mean asymmetry in the left-handed group is often postulated as being due to reversed asymmetry in a small subset of them, but it could also be due to a reduced asymmetry in many of the left-handers. These two possibilities have hugely different theoretical interpretations. In this study, we demonstrate that left handers with typical cerebral asymmetries are less lateralized for language, faces and bodies than their right-handed counterparts. These results are difficult to reconcile with current models of language asymmetry or of handedness.

Keywords: brain asymmetry; handedness; fMRI; left hemisphere; right hemisphere

Humans have asymmetrical brains. Since pioneering investigations by Broca, Wernicke, Dax, Lichteim and others in the late 19th century, the association between left hemisphere lesions and language abnormalities in right handers became thoroughly documented (Bogen and Bogen, 1976; Critchley, 1970; Tesak and Code, 2008). Given this early prominence of language in early behavioural neurology, a large proportion of the research on brain asymmetry has concentrated on the left hemisphere's dominance for speech perception.

There are well-established links between handedness and cerebral asymmetry for language. Early accounts suggested that the left-handed people would be right-hemisphere dominant for speech and language. This sensible hypothesis has turned out to be untrue; in fact, almost 70% of left handers are left-hemisphere dominant for speech and language (Carey and Johnstone, 2014). This unusual characteristic of the majority of left handers was largely forgotten, in part perhaps because of suggestions of subtle pathology in left handers - an idea now largely discredited.

Specialisations that are thought to favour the right hemisphere have not been given the same attention as language asymmetry. This gap is in part due to a small number of early behavioural studies which suggested reduced right-hemispheric bias in left handers for face and spatial processing (e.g. Levy et al., 1983; Bryden, Hécaen and DeAgostini, 1983). Indeed, much of the literature centred on handedness from behaviour (e.g. Bless et al., 2015; Kertesz et al., 1992), electrophysiology (e.g. Dundas, Plaut and Behrmann, 2015; Reid and Serrien, 2012), and *a limited number of* imaging experiments (Powell, Kemp and Garcia-Finana, 2012; Willems, Peelen and Hagoort, 2009) support reduced average asymmetry in left-handed groups relative to right-handed “controls”. This reduced asymmetry in left handers is found so routinely that most people no longer bother to look. In fact, the face validity of such findings is so convincing that it is likely to have resulted in publication biases that favour findings with such reductions (see for example Karlsson, Johnstone and Carey, 2019). The, often implicit, assumption is that these right hemisphere functions, such as processing faces or emotional prosody in speech, are allocated by some causal mechanism to the non-speech/language half of the brain (Bryden 1982; Behrmann and Plaut, 2015; Dehaene et al., 2015).

One result of the expectation of asymmetry reduction, *or more variability in asymmetry*, in left handers, is their general exclusion from much electrophysiology and neuroimaging work related to language and speech processing (Bailey, McMillan and Newman, 2019; Willems et al., 2014). Reduced asymmetries “on average”, however, may disguise a more nuanced picture in the actual data itself. It could result from most left handers having identical cerebral dominance to right handers, but with some individuals having reversed dominance. Of course, a weaker mean bias is just as plausibly accounted for by reduced asymmetries in left handers *en masse*, independent of the hemisphere which is dominant. These two distinct causes of reduced average asymmetry have *dramatically distinct theoretical implications* (Karlsson, Johnstone, and Carey 2019). The often-implicit assumption in laterality studies follows the first argument: a reduced mean asymmetry in the left handers is the result of the small proportion showing a reversed lateralization, with the majority being lateralized in both direction and degree as the right handers. There is no obvious reason why the second argument is not just as credible: that many of the left handers are typically lateralized, but to a lesser extent than their right-handed counterparts.

The underlying cause of reduced average asymmetry in left-handed groups is easily tested, but rarely ever carried out. Two obvious approaches are worthy of consideration. The first is to focus on estimates of the *frequency* of left typical and atypical cerebral asymmetries (particularly non-language ones) in right- and left-handed groups (Carey and Johnstone, 2014; Karlsson et al., 2019).

The second approach which is pursued here, is to ensure that the handedness groups or subgroups are directly comparable with one another and then compare the characteristics of the measured asymmetry. The over-representation of people with right hemisphere or bilateral language dominance in the left-handed group means that any comparison of typical dominance averages as a function of handedness is confounded. Instead, the most telling contrast is handedness, but within right or left dominance groups. For example, an important *unasked* question for language asymmetry is whether the 70 percent of left handers with left-hemispheric dominance are as lateralized as right handers with left-hemispheric dominance (about 95% of them). This important contrast has yet to be made for language, let alone with any other asymmetries, such as those that favour the right hemisphere.

Here, we used fMRI to measure four different cerebral asymmetries (language, face perception, body perception, and scene perception) in the same 58 left handers and 33 right handers. We quantified asymmetries in individual people using a robust and reliable (Johnstone et al., 2020) technique that does not depend on an arbitrary statistical threshold decided on for an entire group (Wilke and Lidzba, 2007). Because individuals are classified as left- or right-dominant, we can control for the confounding effects of more individuals with the rare atypical asymmetry (which is potentially more common in left handers) on any overall estimate of hemispheric specialization. Therefore, we investigated averages for the "typical" pattern of hemispheric lateralization (left-hemisphere dominant for verbal fluency, right-hemisphere dominant for faces, bodies and scenes). Removing the confound of heterogeneous left-handed groups in terms of cerebral dominance should result in either no difference between the right handed and left handed participants, or a remaining (albeit more difficult to account for) reduced mean asymmetry in the left handers. Only then can an unbiased estimate of magnitude of asymmetry for individuals who show the typical bias be generated.

MATERIALS AND METHODS

Participants

Ninety-three participants took part in this experiment – 33 right handed (21 female) and 58 left handed (22 female). Two participants (both left handed, one male and one female) were excluded from the analysis due to excessive head movements (>4mm). Right handed subjects had a mean age of 26.09 (SD = 5.92) and a mean Waterloo handedness questionnaire (WHQ; Steenhuis and Bryden, 1989) scores of +28.00 (SD = 2.06). Left handed subjects had a mean age of 24.83 (SD = 7.55) and a mean WHQ of -20.38 (SD = 13.31). This study received ethical approval from Bangor University Ethics Committee and informed consent was obtained from all subjects. Participants were debriefed in detail and offered individual feedback and brain images.

Language Localizer

A verbal fluency style paradigm was employed. Both an active and a control condition were used in a blocked design. Fourteen active and 14 control blocks were alternated with 30 rest blocks, each with a duration of 15 seconds. In the active blocks, participants were presented with a single letter in the middle of the screen for the duration of the block. During this time, participants were instructed to silently think of as many words as they could which begin with that letter. A practice phase was run outside the scanner using the letter “D”. In the control blocks, participants were shown either the letter string “RARA” or “LALA”, and were instructed to mentally repeat these non-words for as long as they were presented on the screen. In the 30 rest blocks a fixation cross was presented and participants were instructed to relax. The 14 letter chosen were the letters that begin the most words in English: T, A, S, H, W, I, O, B, M, F, C, L, D, P (as reported in the Natural Language Toolkit 3.0 - http://www.nltk.org/). This task was presented across two runs, comprising seven active/control blocks per run. The letters were randomly presented in any order across these two runs.

Face/Body/Scene Localizer

A four-condition localizer was used to identify any asymmetry in face-, body-, and scene-selective brain activation. The task involved viewing blocks of images from the categories: faces, bodies, chairs, and scenes. Whilst viewing the stimuli, participants completed a simple one-back task, pressing a button if they saw a consecutive, repeated image. Which hand participants held the button box in was counterbalanced within the right handed and left handed groups. Each localizer run consisted of 16 active blocks (4 for each stimulus category) and 5 rest blocks (taking place in block 1, 6, 11, 16 and 21). Each block lasted 16 s during which 16 images were displayed for 300 ms followed by a blank screen for 700 ms. Participants completed two runs of this task, with two different fixed stimulus orders, which were counterbalanced across participants, separately for the right handed and left handed groups.

MRI Acquisition

All scans were acquired in a Philips 3 T Achieva magnetic resonance scanner, using a 32-channel head coil, located at the Bangor Imaging Unit at Bangor University. T1-weighted structural images were obtained with the following parameters: TR = 12 ms, TE = 3.5 ms, FA = 8°, FOV (mm) = 240 × 240, acquisition matrix = 80 × 79; 175 contiguous slices were acquired, voxel size (mm) = 1 × 1 x 2 (reconstructed voxel size = 1 mm^3). Functional images were acquired with the following parameters: a T2-weighted gradient-echo EPI sequence; field of view (FOV) = 220 × 220, acquisition matrix = 96 × 96, 36 slices were acquired; acquired voxel size (mm) = 2.3 × 2.3 x 2.5 (reconstructed voxel size [mm] = 2.3 × 2.3 x 2.5). Verbal fluency (repetition time (TR) = 2500 ms, echo time (TE) = 30 ms, flip angle (FA) = 90°) consisted of two runs of 174 volumes, and the four-condition localizer (TR = 2000 ms, TE = 30 ms, FA = 90°) consisted of two runs of 166 volumes. The first 5 scans of each functional run were discarded before image acquisition to establish steady-state magnetization.

MRI Processing

All MRI data were pre-processed and analyzed using SPM12 (Wellcome Department of Cognitive Neurology, University College London, http://www.fil.ion.ucl.ac.uk/spm/) implemented in MATLAB R2015b 8.6 (Mathworks Inc., Sherborn, MA, USA). Anatomical images were first manually aligned to the anterior and posterior commissure (AC-PC). Pre-processing of functional scans consisted of corrections for head motion (spatial realignment; trilinear interpolation), and images were realigned to the first functional volume of the first session (the volume closest to the anatomical scan). Functional scans were coregistered to their corresponding individual anatomical scans and normalized to standard MNI space (3 mm isotropic voxels). Normalized data were then spatially smoothed using a Gaussian kernel of 6 mm full-width at half-maximum. The general linear model was used to map the hemodynamic response curve onto each experimental condition using boxcar regressors. This boxcar function was then fitted to the time series at each voxel resulting in a weighted beta-image. The fitted model was converted to a t-statistic image, comprising the statistical parametric map.

Statistical Analysis

To assess hemispheric contribution for processing a particular stimulus type, the LI-toolbox plugin for SPM was used (Wilke and Lidzba, 2007; Wilke and Schmithorst, 2006). This toolbox provides an estimate of how lateralized a participant is for a given contrast by calculating a laterality index (LI) value for each individual contrast. LI values range from -1 (exclusively right hemispheric) to +1 (exclusively left hemispheric). Whole brain LIs were calculated for each person and task using the following contrasts: faces > scenes, bodies > chairs, and scenes > chairs. A whole brain analysis with the cerebellum excluded was carried out for fluency > letter string, as cerebellar involvement in language processing is contralateral to the activation of the cerebral cortex.

Participants were first classified as right hemispheric (LI < 0) or left hemispheric (LI > 0) for each of the four tasks. Only participants with typical (i.e. left hemisphere dominance for verbal fluency and right hemisphere dominance for faces, bodies, and scenes) dominance for each of the task, independent of their dominance for the other tasks were included for the average analysis. IBM SPSS Statistics for Macintosh (Version 25.0. Armonk, NY: IBM Corp.) was used to calculate the mean and standard error for each task by handedness group. One-tailed t-tests were used to compare the mean LIs for the two handedness groups for fluency, faces, bodies, and scenes respectively, using an alpha level of .05.

A second analysis comparing average asymmetries for faces, bodies and scenes respectively, was also carried out. This analysis was to ensure that the reduced asymmetries for these three right hemisphere functions were not driven by individuals who were right hemisphere dominant for language. In this analysis, individuals who were right hemisphere dominant for verbal fluency were excluded, and t-tests were carried out to compare the two handedness groups.

RESULTS

Figure 1 (verbal fluency) and Figure 2 (bodies, faces and scenes) show threshold-dependent group activation maps for the right-handed and left-handed participants. Figure 3 shows the average threshold-independent laterality indices (LIs; calculated on a scale from -1 [exclusive right hemisphere activation] to +1 [exclusive left hemisphere activation]), with standard errors, as a function of handedness group. As mentioned above, inclusion criterion for the four elements of this analysis was typical dominance (i.e. left hemisphere dominance for verbal fluency and right hemisphere dominance for faces, bodies, and scenes). As Figure 3 shows, the left-handed participants have significantly lower LIs than the right handers for all four asymmetries tested.

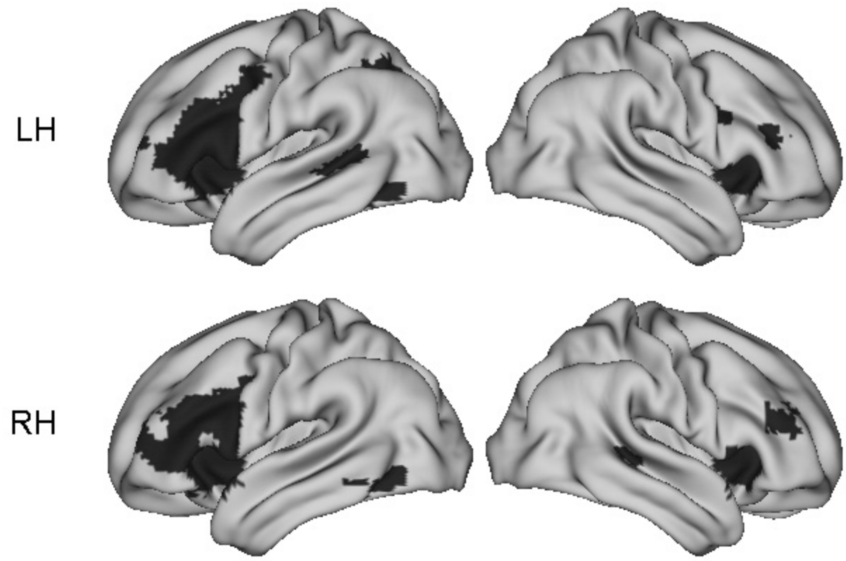

Figure 1. Threshold-dependent group activation maps for individuals left lateralized for verbal fluency, as a function of handedness. (LH = 43; RH = 31). The data is visualised at a threshold of $p < .001$ with FWE-correction at the cluster level.

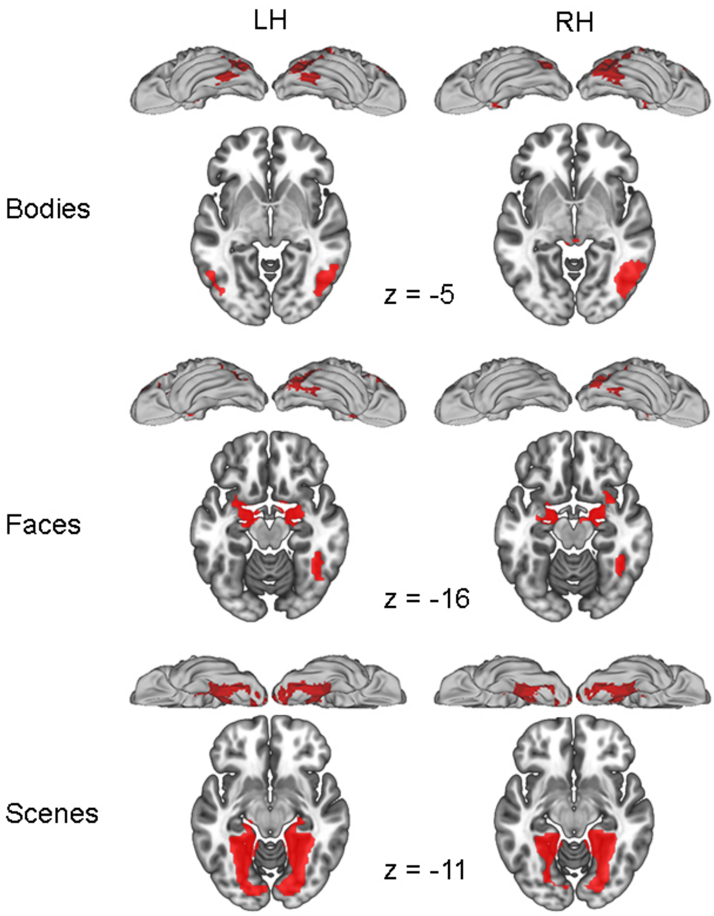

Figure 2. **Threshold-dependent group activation maps for individuals right lateralized for bodies (LH = 38, RH = 31; top row), faces (LH = 34, RH = 25; middle row) and scenes (LH = 33, RH = 25; bottom row) as a function of handedness**. The data is visualised at a threshold of $p < .001$ with FWE-correction at the cluster level.

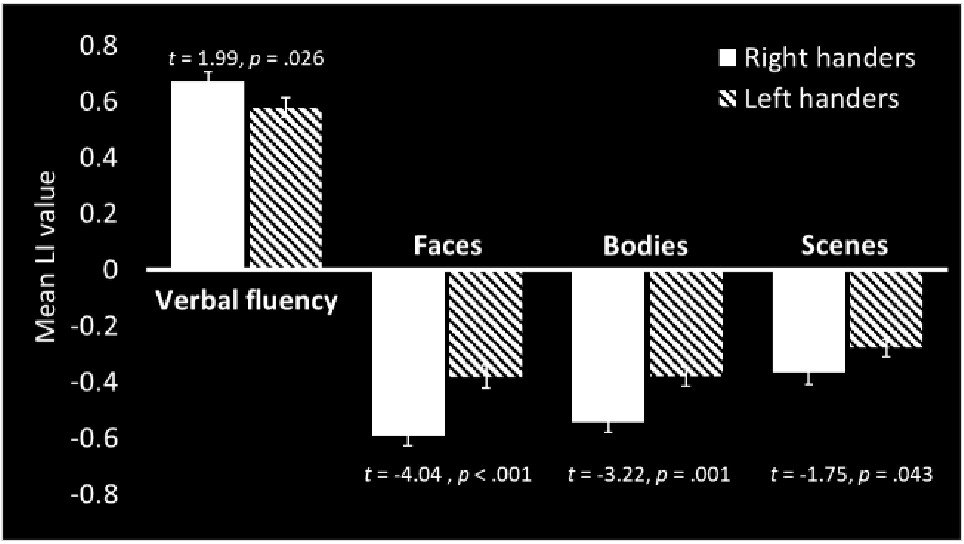

Figure 3. **Mean laterality index (LI) scores for the four functions, only in individuals who show typical dominance for each**. LI values > 0 represent threshold-independent left hemispheric dominance. The mean LI asymmetry is reduced in all four left-handed samples Note that the bars for the four different asymmetries were derived from slightly different individuals, as the only inclusion criteria for each was typical dominance for that function. All *p*-values are one-tailed.

Controlling for all the other asymmetries within each function (e.g., face dominance within the estimates for body dominance) would be admirable, but would require an even larger sample. Nevertheless, to assess whether the group differences for the three right hemispheric functions could be in part driven by reduced bias in the left-handed individuals with atypical, right, language asymmetry, these participants were removed. Despite the decreases in sample size (n = 7, 9 and 3 for faces, bodies and scenes, respectively), removing them does not change the pattern, although the difference between groups is no longer statistically significant for right-hemispheric scene perception (see Figure 4).

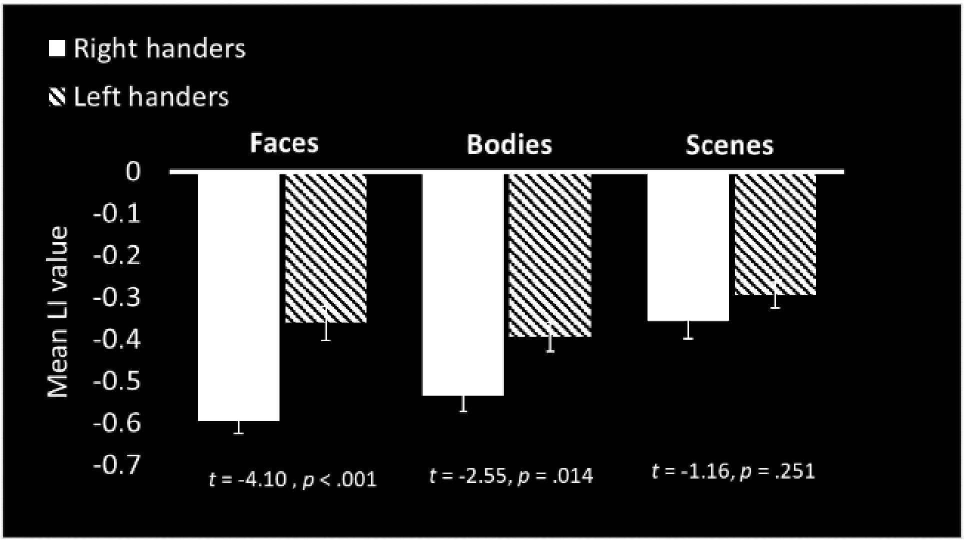

Figure 4. **Mean laterality index (LI) scores for the three non-language functions, only in individuals who show typical dominance for each, without the left handed language atypicals (who happened to be typical on these functions)**. The mean LIs remain significantly reduced in the left handers for face and body processing.

DISCUSSION

Decreased asymmetries in left handers within typical dominance groups for at least three of our four asymmetries is indeed curious. For verbal fluency, the decrease cannot be driven by atypical language dominance because such individuals, by definition, were not included in the calculation. The decrease in the mean right hemispheric bias in left handers, for faces and bodies, cannot be explained by inclusion of atypical language dominance either, given our exclusion of these individuals in the secondary analysis.

Stronger asymmetries in right handers are invariably found in experiments of any sort. None of them, to the best of our knowledge, control for the (potentially) increased proportions of atypical dominance in the left-handed group in the way done here. In fact, with this confound removed, the reductions in typical dominance magnitude are puzzling, indeed. If they are not driven by increased numbers of individuals with atypical language asymmetry in left handers, there are remarkably few models that could account for them. For example, explanations based on experiential consequences of left handedness, such as living in a right-handed world (Westmoreland, 2017), seem fanciful as a decent model of reduced right-hemispheric bias for face and body perception.

The only other likely possibility would follow from genetic models of handedness that suggest more varied patterns of asymmetry in some left-handed people. These models postulate a subset of such people, whose genotype results in random localization of different functions to one hemisphere or the other. Excessive co-localization of certain asymmetries could lead to crowding, which might lessen their magnitudes favouring the dominant hemisphere. For example, visual functions that share similar circuitry within a hemisphere, such as reading and face/body perception (Behrmann and Plaut, 2015; Centanni et al., 2018; Dehaene et al., 2015) might be the exception to completely random development of asymmetry, particularly if functions have different developmental time courses.

If these models are correct, individuals who do lateralize randomly might be more easily identifiable, phenotypically, at least, if multiple cerebral asymmetries are measured and quantified on an individual basis in large numbers of left handers. This kind of large sample size initiative is more likely now, given better sharing by neuroimaging groups interested in asymmetry as part of the general trend to more open, transparent science. The historical focus on speech/language asymmetry and the left hemisphere in neurology and neuropsychology, is understandable, given the centrality of language, handedness and motor skill in many models of hominid evolution. It may be time to have a second look at the so-called minor hemisphere, in left-handed people in particular.

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Data Availability

The dataset generated during this study is available on OSF, https://osf.io/u9f75/.

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Captions

Figure 1. Threshold-dependent group activation maps for individuals left lateralized for verbal fluency, as a function of handedness. (LH = 43; RH = 31). The data is visualised at a threshold of $p < .001$ with FWE-correction at the cluster level.

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Figure 4. Mean laterality index (LI) scores for the three non-language functions, only in individuals who show typical dominance for each, without the left handed language atypicals (who happened to be typical on these functions). The mean LIs remain significantly reduced in the left handers for face and body processing.