DEVELOPMENT OF A REASONABLE LATERALIZATION INDEX FOR FUNCTIONAL MAGNETIC RESONANCE IMAGING

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Introduction:

A challenge in lateralization index (LI) of functional magnetic resonance imaging (fMRI) lies in ensuring how to compute LI reasonably. Conventional LI sets a t-value threshold to calculate "Left–Right/Left+Right" where Left and Right are suprathreshold voxel numbers or summations of t-values of a pair of regions of interest (ROIs) in left and right hemispheres. In reality, the LI substantially varies across the thresholds (Fig. 1). We propose an improved method in calculating LI called AveLI, which indicates the laterality of a subject's activation at each and every t-value level for the task, providing an intuitive comprehension of the asymmetry in fMRI activation.

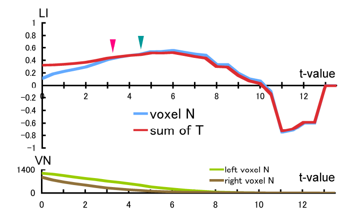

Fig. 1 Reality of the laterality index. The pink arrowhead indicates t-value from SPM p<0.001 (t=3.11 for this dataset), whereas the turquoise arrowhead indicates the "half of the mean of the top 5% voxels" within the ROIs [3]. The laterality index (often called weighted laterality index, wLI) varies according to where the t-value threshold is set. The wLI is computed by the general formula [Left-Right]/[Left+Right], where Left/Right is either the voxel number (VN) or sum of T values in the suprathreshold voxels at a given t-value threshold within ROIs of left/right hemisphere. This subject had a few voxels with extremely high t-values in the right hemisphere ROI so that the LI is shifting from left (LI>0) to right (LI<0) along with the t-value thresholds.

Rationale:

There are mainly two terms for the LI computation; voxel number (VN) and summation of t-values (sum T). The sum T within ROIs is a more reasonable measure than VN when considering datasets with equal VN activation but higher t-values in one hemisphere. Not setting a threshold for t-values [1-2] is preferable because of the difficulty in determining where to set the threshold (Fig. 1). Here, suppose a forced ranking of laterality as illustrated in Fig. 2. We can rank order the data under the curve. This area under the curve can be used as the new general LI. However, a problem arises when very few voxels happen to have extremely high t-values, and the areas become unjustly wide. Thus we can redefine the horizontal axis as the ranking of the t-values (Fig. 2, S03(2)). The area can be simply computed by integrating the t-values within the ROIs to calculate the subordinate LIs for suprathreshold voxels at each t-value, and then averaging the subordinate LIs to obtain the AveLI.

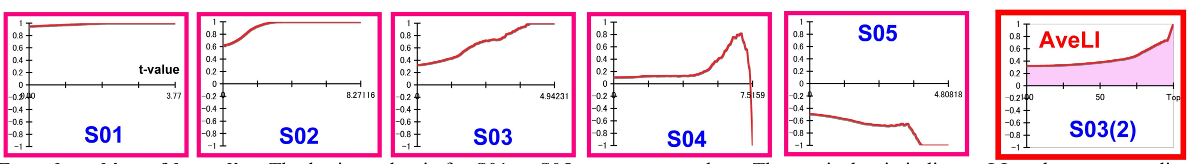

Fig. 2 Forced ranking of laterality. The horizontal axis for S01 to S05 represents t-values. The vertical axis indicates LI at the corresponding t-value threshold, where upper half indicates left lateralized (0<LI<1) whereas lower half indicates right lateralized (-1<LI<0). S01 obviously has the strongest left asymmetry among the 5 people because the LI is constantly near to 1 at all t-value range. On the other hand, S05 obviously has the rightward asymmetry because the graph line never comes up to the upper LI>0 area. S02 has a leftward asymmetry but weaker than S01 because of the decreased LI at the lower t-values. In this way, the 5 people can be ranked using the area width between the graph lines and the horizontal axis. Here, if the voxels with top t-values have too extreme values, the area becomes unjustly wide. For example, suppose the situation with only 1 voxel that happens to have t=10 whereas all other voxels have t<0.5. To address this bias, we rank order the t-values from low to high on the horizontal axis seen in S03(2). AveLI is represented by the pink area under the curve, which is computationally equivalent to the average of LIs at each t-value threshold within the ROIs. Here, we only use voxels with positive t-values, excluding voxels with 0 and negative values.

Materials and Methods:

We examined how the AveLI behaves in comparison with other thresholding methods of LI: (1) spmLI_v: LI at p<0.001 by statistical parametric mapping (SPM) using the suprathreshold VN as the measure (this is a conventional method many papers use), (2) spmLI: the same as (1) but using sum T as the measure, and (3) hmt5LI: LI at the t-value threshold of "half of the mean of the top 5% voxels" using sum T of the suprathreshold voxels as the measure [3]. Twenty-two normal native Chinese-speaking college students (M/F=13/9, mean age 22.9 years, right/left-handed=11/11, with a written informed consent approved by the IRB) participated in 2 runs of language fMRI tasks: word generation (WG) and homophone judgment of characters (HJ). Each run consisted of 5 cycles of contrast and task blocks. A GE-EPI was employed using the following parameters; TR/TE = 2000 ms/45 ms, flip angle = 90 deg, field of view = 240 x 240 mm, matrix size = 64 x 64 and slice thickness = 3.8 mm. A total of 150 volumes were acquired in the 5-min run. Images were analyzed using SPM8 (University College London, UK). First level GLM analysis was conducted on each subject to obtain the task vs. contrast block contrast for each run separately. We took the resulted files (spmT_0001.img) that contained t-values, applied a pair of masks of the posterior part of the inferior frontal gyrus (IFG) by MARINA software [4]. We extracted voxels with positive t-values within the mask. Conventional LIs (i.e. spmLI_v, spmLI and hmt5LI) were computed by wLI = (Lt–Rt)/(Lt+Rt), where wLI is weighted LI, Lt is VN or sum T above the threshold within the left mask, and Rt is that within the right mask. AveLI was computed by AveLI = Σ(wLI)/VN, where VN is voxel number within the masks, and wLI was computed at every t-value within the masks using sum T as the term. These 4 kinds of LIs were analyzed using a one-factor within-subject repeated measures analysis of variance (ANOVA) for each task separately. Changes of the subjects' ranks of the LIs between tasks (WG vs. HJ) were analyzed using Spearman's rank correlation coefficient.

Results and Discussion:

Two subjects did not show significant activations at the threshold of p<0.001 (t=3.15) for the homophone judgment task. Three subjects showed right asymmetry for both tasks. The ANOVA for WG (n=22) indicated significant differences (F(3,63)= 5.2529, p<.005), as well as that for HG (n=20, F(3,57)= 16.2514, p<.001). The order of the means (WG, HJ) was spmLI (0.6107, 0.7736), spmLI_v (0.5975, 0.7685), hmt5LI (0.5442, 0.7075) and AveLI (0.4572, 0.5807) for both tasks, respectively. A post hoc test of Holm's Sequentially Rejective Bonferroni Procedure indicated AveLI<htm5LI for WG, whereas all combinations were significantly different except spmLI_v=spmLI for HJ. When only right-handed people were analyzed, AveLI was significantly smaller than all other LIs for both tasks. Thus the AveLI provided more conservative values than the other methods. Spearman's rank correlation coefficient indicated that AveLI and hmt5LI showed strong correlations between WG and HJ (p<.01), and spmLI and spmLI_v also showed significant correlations but at p<.05. The results suggested an acceptable reproducibility of the AveLI between different tasks.

Conclusions:

The new laterality index AveLI, which aims to provide a comprehensive grasp of the asymmetry of the activation, makes it feasible to examine lower activation that otherwise did not reach conventional SPM threshold, and evidenced an acceptable reproducibility between different tasks.

References

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