Online supplementary materials for "Functional and structural brain asymmetries in language processing" published in *Handbook of Clinical Neurology*: Lateralization in meta-analyses of language processing and speech production

Patrick C. Trettenbrein[1,2,*] and Angela D. Friederici[1,§]

[1]Department of Neuropsychology, Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany

[2]International Max Planck Research School on Neuroscience of Communication: Structure, Function, & Plasticity (IMPRS NeuroCom), Leipzig, Germany

[*]Main contact for supplementary materials: trettenbrein@cbs.mpg.de

[§]Principal contact: friederici@cbs.mpg.de

Background

This document contains supplementary information for analyses performed and described as part of the chapter on "Functional and structural brain asymmetries in language processing" published in the *Handbook of Clinical Neurology* (Corballis, P. & Papagno, C., eds.) in the volume on "Cerebral asymmetries" in 2023. The analyses referenced and discussed only briefly in this chapter and illustrated in Figure 2 are described below in full.

The goal of the different analyses described in this document was to assess the meta-analytic evidence for the lateralization of different language(-related) processes using a publicly available large-scale dataset of functional magnetic resonance imaging (fMRI) and positron emission tomography (PET) studies. To achieve this, we retrieved foci data from several hundred fMRI and PET studies from BrainMap (Fox & Lancaster, 2002; Laird et al., 2011), performed activation likelihood estimation (ALE; Eickhoff et al., 2009, 2012, 2017; Turkeltaub et al., 2012) on these datasets, and then computed a weighted lateralization index (AveLI; Matsuo et al., 2012) using hemispheric masks and the different meta-analytic convergence masses containing ALE scores.

All the analyses reported here followed approaches and procedures which we have already used for and described in the context of previous meta-analyses of functional neuroimaging data (Papitto et al., 2020; Trettenbrein et al., 2021).

Materials and methods

Foci data of relevant contrasts from fMRI and PET studies was extracted from the BrainMap database entirely on the basis of the taxonomy and tagging used in the database. In total, we performed 5 database searches, using Sleuth version 3.0.4, available from http://brainmap.org/sleuth, which always used the following restrictions: (1) healthy subjects by setting the parameter "Experiments: Context" IS "Normal Mapping"; (2) only activations and no deactivations by requiring that "Experiments: Activations" IS "Activations Only", and (3) the relevant behavioral domain as specified by the BrainMap taxonomy, available from https://brainmap.org/taxonomy/behaviors/. This setting therefore was either "Cognition.Language" for language processing in general, "Cognition.Language.Phonology" for phonological processing, "Cognition.Language.Semantics" for semantic processing, "Cognition.Language.Syntax" for syntactic processing, or "Action.Execution.Speech" for language production.

These searches in the BrainMap database resulted in a total of five different foci datasets which were used as input to the ALE algorithm. The "language processing" dataset contained 16,435 foci from contrasts of 658 studies with a total of 8,568 participants. The "phonology" dataset contained 2,293 foci from 118 different studies with 1,697 participants. The "semantics" dataset contained 8,889 foci from 391 experiments with 5,215 participants. The "syntax" dataset contained 1,436 foci from 71 studies with 1,400 participants. Lastly, the "speech production" dataset contained 2,624 foci from 117 different studies with a total of 1,200 participants.

All ALE analyses of the five different datasets were carried out using GingerALE version 3.0.2, available from https://brainmap.org/ale. As in previous work, we used GingerALE's more conservative gray matter mask. The recommended thresholds of $p < .001$ as a cluster-forming threshold and $p < .05$ for cluster-level family-wise error with 10,000 thresholding permutations were applied to the output images of GingerALE (Müller et al., 2018). Anatomical labels (Brodmann areas; BA) for peaks in clusters were obtained using the MNI-BA map included in the Yale BioImaging Suite Web version 1.0.0 (Lacadie et al., 2008), accessible at https://bioimagesuiteweb.github.io.

The lateralization of the convergence mass from the different ALE analyses was determined using a weighted laterality index, the so-called AveLI, which represents the degree of lateralization across all voxels with positive ALE scores within our two volumes of interest, the left and right hemisphere respectively. (For the advantages of AveLI over classical lateralization indexes see Matsuo et al., 2012.). Computations were performed using the AveLI script (version April 3, 2017), available from http://aveli.web.fc2.com. With regard to its interpretation, AveLI, ranges from 1 (completely left-lateralized) to –1 (completely right-lateralized). The significance of AveLI scores was determined using a custom-made permutation test exactly as described in Trettenbrein et al. (2021).

Results

All output files of the above-mentioned software are available as part of these supplementary materials. Consequently, the main results of the different ALE analyses will only be summarized briefly in table form here. An additional table summarizing the lateralization analysis is also provided. For details please refer to the files/data provided.

ALE for "language processing"

			MNI coordinates (mm)				
Cluster	Hemisphere	BA	x	y	z	Z score	Cluster size (mm^3)
1	Left	44	-46	16	24	19.15	136,848
2	Right	13	36	22	-4	13.68	27,112
3	Left	8	-2	18	46	18.88	23,536
4	Right	18	28	-90	-6	6.91	17,400
5	Left	7	-28	-62	46	11.48	16,672
6	Right	22	58	-26	2	10.97	15,760
7	Left	Thalamus	-8	-16	4	8.96	7,680
8	Right	39	32	-60	46	7.67	5,816

ALE for "phonology"

			MNI coordinates (mm)				
Cluster	Hemisphere	BA	x	y	z	Z score	Cluster size (mm^3)
1	Left	44	-48	20	20	10.88	36,024
2	Left	37	-44	-58	-16	8.23	18,856
3	Left	6	-2	14	50	9.92	13,536
4	Left	40	-38	-46	44	7.43	9,776
5	Right	13	36	22	-2	8.87	8,208
6	Right	41	60	-12	0	9.34	6,512
7	Right	Cerebel-lum	28	-64	-26	5.3	1,608
8	Right	39	42	-50	44	4.79	1,520
9	Right	6	44	4	28	4.36	1,272
10	Right	7	34	-62	52	4.43	1,256

ALE for "semantics"

			MNI coordinates (mm)				
Cluster	Hemisphere	BA	x	y	z	Z score	Cluster size (mm^3)
1	Left	44	-46	20	24	15.08	108,536
2	Left	8	-4	18	46	14.61	18,568
3	Right	13	36	24	-6	9.19	15,640
4	Right	18	28	-90	6	6.44	9,256
5	Left	7	-30	-62	48	7.58	8,416
6	Right	22	52	-32	2	7.3	6,896
7	Left	Thala-mus	-6	-16	6	6.31	3,128
8	Right	37	34	-44	-22	5.51	1,840

ALE for "syntax"

			MNI coordinates (mm)				
Cluster	Hemisphere	BA	x	y	z	Z score	Cluster size (mm^3)
1	Left	44	-50	16	26	7.75	22,976
2	Left	21	-56	-34	2	7.51	9,024
3	Right	22	54	-28	2	5.37	1,792
4	Left	8	-6	16	48	5.29	1,768
5	Left	18	-10	-94	0	4.86	1,416
6	Right	45	42	24	0	4.69	1,216
7	Left	38	-54	8	-18	4.70	928

ALE for "language production"

			MNI coordinates (mm)				
Cluster	Hemisphere	BA	x	y	z	Z score	Cluster size (mm^3)
1	Left	6	-56	-4	22	11.36	69,192
2	Right	6	54	-6	36	10.5	24,920

3	Left	Cerebel-lum	-14	-62	-18	7.83	18,424
4	Right	6	0	8	56	10.39	15,016
5	Right	Thala-mus	14	-18	6	6.88	9,112
6	Right	44	50	8	2	4.4	1,792

Lateralization analysis

The following AveLI values were observed for the five different meta-analyses (significance is indicated using common levels: * for p < .05, ** for p < .01, and *** for p < .001):

Dataset	**AveLI**	**LI (non-weighted)**
Language processing	0.66 ***	0.48
Phonology	0.64 ***	0.52
Semantics	0.80 ***	0.62
Syntax	0.93 ***	0.86
Speech production	0.32 ***	0.28

Discussion

Due to the supplementary nature of these analyses, we do not provide any additional in-depth discussions of these materials at this point. In short, these analyses have confirmed that language processing is, in many respects, a left-lateralized process. Different sub-components of the language system (i.e. phonology, semantics, and syntax), as identified by the BrainMap taxonomy, exhibit different degrees of lateralization. Language processing is generally more left-lateralized than speech production.

The main findings are summarized and illustrated in Figure 2 from the target book chapter which is reproduced in full below (without the complete figure caption).

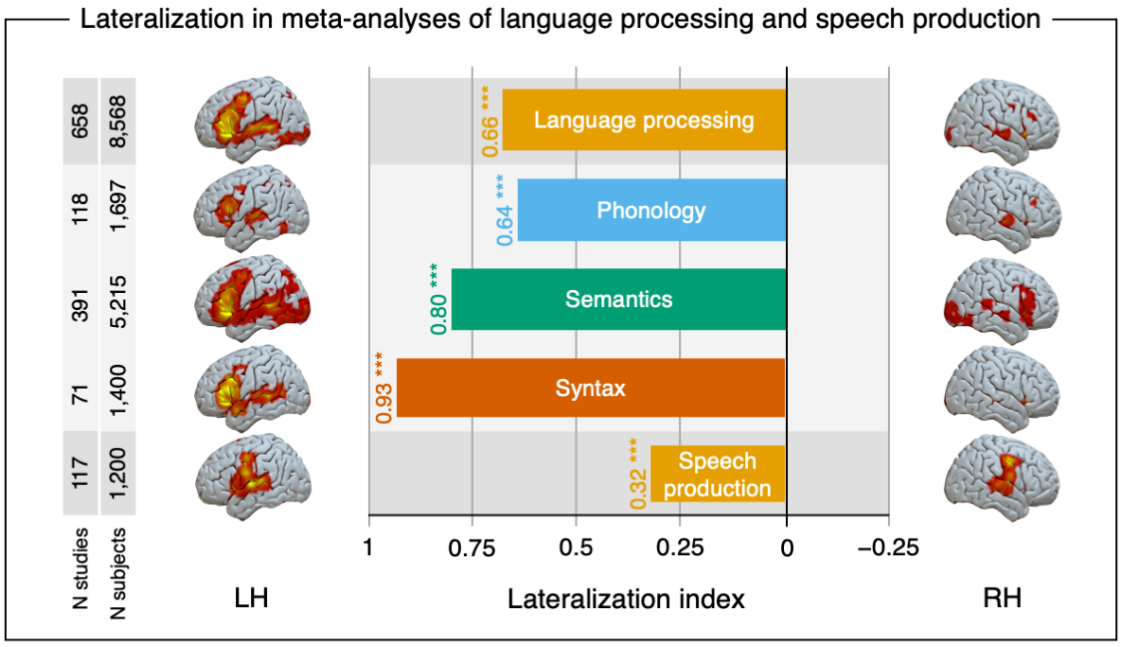

Figure: Lateralization in meta-analyses of language processing and speech production.

Data availability

The data retrieved using Sleuth (including a copy of workspaces), the output of GingerALE, as well as the output of the AveLI script are all available as part of this online supplement: https://doi.org/10.6084/m9.figshare.21836079

Bibliography

Eickhoff, S. B., Bzdok, D., Laird, A. R., Kurth, F., & Fox, P. T. (2012). Activation likelihood estimation meta-analysis revisited. *NeuroImage*, *59*(3), 2349–2361. https://doi.org/10.1016/j.neuroimage.2011.09.017

Eickhoff, S. B., Laird, A. R., Fox, P. M., Lancaster, J. L., & Fox, P. T. (2017). Implementation errors in the GingerALE Software: Description and recommendations: Errors in the GingerALE Software. *Human Brain Mapping*, *38*(1), 7–11. https://doi.org/10.1002/hbm.23342

Eickhoff, S. B., Laird, A. R., Grefkes, C., Wang, L. E., Zilles, K., & Fox, P. T. (2009). Coordinate-based activation likelihood estimation meta-analysis of neuroimaging data: A random-effects approach based on empirical estimates of spatial uncertainty. *Human Brain Mapping*, *30*(9), 2907–2926. https://doi.org/10.1002/hbm.20718

Fox, P. T., & Lancaster, J. L. (2002). Mapping context and content: The BrainMap model. *Nature Reviews Neuroscience*, *3*(4), 319–321. https://doi.org/10.1038/nrn789

Lacadie, C. M., Fulbright, R. K., Arora, J., Constable, R. T., & Papademetris, X. (2008). *Brodmann Areas defined in MNI space using a new Tracing Tool in BioImage Suite*. Organization for Human Brain Mapping.

Laird, A. R., Eickhoff, S. B., Fox, P. M., Uecker, A. M., Ray, K. L., Saenz, J. J., McKay, D. R., Bzdok, D., Laird, R. W., Robinson, J. L., Turner, J. A., Turkeltaub, P. E., Lancaster, J. L., & Fox, P. T. (2011). The BrainMap strategy for standardization, sharing, and meta-analysis of neuroimaging data. *BMC Research Notes*, *4*(1). https://doi.org/10.1186/1756-0500-4-349

Matsuo, K., Chen, S.-H. A., & Tseng, W.-Y. I. (2012). AveLI: A robust lateralization index in functional magnetic resonance imaging using unbiased threshold-free computation. *Journal of Neuroscience Methods*, *205*(1), 119–129. https://doi.org/10.1016/j.jneumeth.2011.12.020

Müller, V. I., Cieslik, E. C., Laird, A. R., Fox, P. T., Radua, J., Mataix-Cols, D., Tench, C. R., Yarkoni, T., Nichols, T. E., Turkeltaub, P. E., Wager, T. D., & Eickhoff, S. B. (2018). Ten simple rules for neuroimaging meta-analysis. *Neuroscience & Biobehavioral Reviews*, *84*, 151–161. https://doi.org/10.1016/j.neubiorev.2017.11.012

Papitto, G., Friederici, A. D., & Zaccarella, E. (2020). The topographical organization of motor processing: An ALE meta-analysis on six action domains and the relevance of Broca's region. *NeuroImage*, *206*, 116321. https://doi.org/10.1016/j.neuroimage.2019.116321

Trettenbrein, P. C., Papitto, G., Friederici, A. D., & Zaccarella, E. (2021). Functional neuroanatomy of language without speech: An ALE meta-analysis of sign language. *Human Brain Mapping*, *42*(3), 699–712. https://doi.org/10.1002/hbm.25254

Turkeltaub, P. E., Eickhoff, S. B., Laird, A. R., Fox, M., Wiener, M., & Fox, P. (2012). Minimizing within-experiment and within-group effects in activation likelihood estimation meta-analyses. *Human Brain Mapping*, *33*(1), 1–13. https://doi.org/10.1002/hbm.21186