Neuroscience Letters 633 (2016) 210–214

Contents lists available at ScienceDirect

Neuroscience Letters

journal homepage: www.elsevier.com/locate/neulet

Research article

Voxel-wise grey matter asymmetry analysis in left- and right-handers

Sebastian Ocklenburg*, Patrick Friedrich, Onur Güntürkün, Erhan Genç

Institute of Cognitive Neuroscience, Biopsychology, Department of Psychology, Ruhr-University of Bochum, Germany

HIGHLIGHTS

- We investigated grey matter asymmetries in left- and right-handers.
- We used a new voxel based morphometry toolbox optimized for asymmetry detection.
- We detected typical grey matter asymmetries in the overall sample.
- No significant differences between left- and right-handers were observed.
- Grey matter asymmetries are not a major structural correlate of handedness.

ARTICLE INFO

Article history:
Received 22 August 2016
Received in revised form
23 September 2016
Accepted 25 September 2016
Available online 26 September 2016

Keywords:
Handedness
Voxel based morphometry
Neuroimaging
MRT
Lateralization
Hemispheric asymmetries

ABSTRACT

Handedness is thought to originate in the brain, but identifying its structural correlates in the cortex has yielded surprisingly incoherent results. One idea proclaimed by several authors is that structural grey matter asymmetries might underlie handedness. While some authors have found significant associations with handedness in different brain areas (e.g. in the central sulcus and precentral sulcus), others have failed to identify such associations. One method used by many researchers to determine structural grey matter asymmetries is voxel based morphometry (VBM). However, it has recently been suggested that the standard VBM protocol might not be ideal to assess structural grey matter asymmetries, as it establishes accurate voxel-wise correspondence across individuals but not across both hemispheres. This could potentially lead to biased and incoherent results. Recently, a new toolbox specifically geared at assessing structural asymmetries and involving accurate voxel-wise correspondence across hemispheres has been published [F. Kurth, C. Gaser, E. Luders. A 12-step user guide for analyzing voxel-wise gray matter asymmetries in statistical parametric mapping (SPM), Nat Protoc 10 (2015), 293–304]. Here, we used this new toolbox to re-assess grey matter asymmetry differences in left- vs. right-handers and linked them to quantitative measures of hand preference and hand skill. While we identified several significant left-right asymmetries in the overall sample, no difference between left- and right-handers reached significance after correction for multiple comparisons. These findings indicate that the structural brain correlates of handedness are unlikely to be rooted in macroscopic grey matter area differences that can be assessed with VBM. Future studies should focus on other potential structural correlates of handedness, e.g. structural white matter asymmetries.

1. Introduction

When conducting fine motor activities such as writing, a large majority of humans consistently prefer one hand over the other [1]. On average, roughly 10% of the population prefers to use the left hand, while the remaining 90% prefers to use the right hand [2]. Since there are no obvious muscular, osseous or peripheral nervous system differences between the left and right hands of left- and right-handers, it has been suggested that handedness originates in the central nervous system [3,4]. One idea put forward by several authors is that structural asymmetries in grey matter areas might underlie handedness, but empirical results have been surprisingly incoherent. Areas for which associations with handedness have been reported include the left precentral sulcus [5], left central sulcus [6], planum temporale [7] and Boca's area [8]. However, other studies have failed to find any associations between structural asymmetries in these areas and handedness [9]. The largest study so far has been conducted by Guadalupe et al. [10].

* Corresponding author at: Abteilung Biopsychologie, Institut für Kognitive Neurowissenschaft, Fakultät für Psychologie, Ruhr Universität Bochum, Universitätsstraße 150, 44780 Bochum, Germany.
E-mail address: sebastian.ocklenburg@rub.de (S. Ocklenburg).

http://dx.doi.org/10.1016/j.neulet.2016.09.046

They analyzed cortical surface area differences between 106 left-handed and 1960 right-handed subjects, reporting that no cortical region showed any association with left-handedness that survived statistical correction for multiple testing.

A common technique to assess grey matter asymmetries is voxel based morphometry (VBM). VBM allows for a voxel-wise comparison of local grey matter concentration between two groups of subjects, e.g. left- and right-handers or patients and controls. It involves spatial normalization of structural MRI scans from all participants into the same stereotactic space, followed by segmentation into grey and white matter, and smoothing of grey matter segments. Using these smoothed grey-matter images, voxel-wise statistical tests are then used to compare the two groups [11,12].

VBM is a workhorse tool in neuroimaging that has been used in hundreds of published studies. However, it has recently been pointed out that the standard VBM protocol might not be ideally suited to specifically assess group differences in structural grey matter asymmetries, as it involves accurate voxel-wise correspondence across individuals but not necessarily across both hemispheres [13]. This methodological issue might have lead to biased results in previous asymmetry studies, potentially omitting existing asymmetries or causing false positive results. Recently, Kurth et al. [13] published a novel 12-step protocol for specifically analyzing voxel-wise grey matter asymmetries. This protocol solves the problems standard VBM encounters in asymmetry analyses by ensuring accurate voxel-wise correspondence across individuals and hemispheres by means of spatial normalization into a symmetric space using DARTEL (Diffeomorphic Anatomical Registration using Exponentiated Lie algebra) [14]. Additionally, the protocol avoids blurring of information across hemispheres and controls the possible impact of noise in the data by applying an explicit brain mask and a spatial smoothing procedure. The protocol has recently been successfully used in a study investigating differences in gray matter asymmetry between long-term meditators and non-meditating controls [15], but has not yet been used in the context of handedness.

Here, we used the protocol by Kurth et al. [13,15] to re-investigate structural grey matter asymmetries in left-and right-handers. Using the advanced statistical analysis features of the toolbox, we not only compared left- and right-handers on the group level, but also linked grey matter asymmetries to inter-individual quantitative measures of hand preference and hand skill, an aspect not investigated in previous studies.

2. Material and methods

2.1. Participants and handedness assessment

Overall, 60 volunteers participated in the present study (30 males; 30 females). Mean age was 23.33 years, with a range of 18 to 33 years. None of the participants had any history of psychiatric or neurological disorders.

Participants' hand preference was assessed with the Edinburgh Handedness Inventory [16]. This ten-item questionnaire yields a so-called lateralization quotient (LQ) ranging from −100 (consistent left-handedness) to +100 (consistent right-handedness). There were two groups of participants: right-handers (n = 30) with positive LQs (LQ range: 50–100), and left-handers (n = 30) with negative LQs (LQ range: −100 to −15.79). To also gain a quantitative measure of hand skill, the classic pegboard task was used [17]. In this simple motor task, participants have to move ten pegs from holes on the upper side of a so-called pegboard to its lower side. This is done three times with the left and three times with right hand, and the time needed to perform this task with each hand is recorded. In order to gain a quantitative measure of hand skill asymmetries, we calculated the so-called PegQ measure using the formula $PegQ = (2 \times (L-R)/(L+R))$, with L being the average time in seconds needed to perform the task with the left hand and R being the average time in seconds needed to perform the task with the right hand.

The study was approved by the local ethics committee of the Faculty of Psychology at Ruhr-University Bochum. Participants were treated in accordance with the declaration of Helsinki. Written informed consent was obtained from each subject. Participation was either paid or compensated with course credit.

2.2. MRI acquisition and processing

MRI data were acquired using a Philips Achiva 3-Tesla MRI scanner equipped with a 32-channel head coil located at the University Clinic Bergmannsheil in Bochum, Germany. The maximum gradient strength of the scanner was 40 mT/m. A T1-weighted high-resolution anatomical scan (MP-RAGE, TR = 8179 ms, TE = 3.7 ms, flip angle = 8°, 220 slices, matrix size = 240 × 240, resolution = 1 × 1 × 1 mm, acquisition time = 6 min) was obtained from each subject.

Using the T1-scans, we then performed voxel-wise grey matter asymmetry analysis following the recently published protocol for analyzing voxel-wise gray matter asymmetries in statistical parametric mapping (SPM) by Kurth et al. [13]. This protocol represents an adapted workflow for classic voxel based morphometry [11,12] that includes modifications to the standard VBM workflow to optimize the accurate detection of grey matter asymmetries. Data were analyzed using the VBM8 toolbox (http://dbm.neuro.uni-jena.de/vbm8/) for SPM8 (http://www.fil.ion.ucl.ac.uk/spm/) running in Matlab. First, images were segmented into separate grey and white matter images and were then flipped using, ImCalc'. From the flipped and unflipped versions we then created a symmetric DARTEL template. Subsequently, the unflipped and flipped grey and white segment images were warped to the DARTEL template. After that, we created a right-hemispheric mask in symmetric template space in MRIcron (http://people.cas.sc.edu/rorden/mricron/index.html). This was done in order to limit the following analysis to the right hemisphere. We then calculated an asymmetry index (AI) for grey matter asymmetries using the formula $AI = ((i1 - i2)/((i1 + i2)*0.5))*i3$, with i1 being the warped non-flipped images, i2 being the warped flipped images, and i3 being the right-hemispheric mask. Negative AIs indicated larger left-hemispheric grey matter volume in a cluster, while positive AIs indicated larger right-hemispheric grey matter volume in a cluster. The resulting AI images were then smoothed using an 8 mm smoothing kernel. For statistical comparisons, we used voxel-wise FWE (family-wise error) correction and an alpha level of 0.05. In order to avoid spurious findings driven by noise, we applied a cluster extent threshold of 20 [13,18–20]. Anatomical locations of significant clusters were determined using their MNI coordinates in MRIcron (http://people.cas.sc.edu/rorden/mricron/index.html) using the AAL template.

3. Results

3.1. Structural grey matter asymmetries in the overall sample

First we set up two statistical models to check for clusters with AIs significantly different from zero using a one-sample *t*-test (cluster extent threshold = 20, FWE-corrected, $p < 0.05$). One was for positive AIs and the other for negative AIs. Overall, 11 clusters reached significance for positive AIs, indicating larger right-hemispheric volume (see Table 1 and Fig. 1). The three largest clusters were located in middle temporal gyrus, precuneus, and

Table 1
Clusters showing positive AIs significantly different from zero in the overall sample. For each cluster, location, MNI coordinates in mm, the T-values, as well as the p-values corrected for multiple comparisons and the cluster size in voxel are provided.

Cluster	Location	mm	mm	mm	T	p_{FWE}	size
1	Middle temporal gyrus	53	−12	−15	12.93	p < 0.001	3297
2	Precuneus	21	−58	13	9.30	p < 0.001	1565
3	Superior frontal gyrus	30	63	3	9.20	p < 0.001	2206
4	Thalamus	12	−9	12	9.14	p < 0.001	466
5	Cerebellum	14	−61	−48	8.75	p < 0.001	299
6	Anterior cingulum	8	21	24	8.46	p < 0.001	580
7	Caudate nucleus	12	23	6	7.89	p < 0.01	192
8	Putamen	34	−4	4	6.82	p < 0.001	34
9	Superior and medial frontal gyrus	9	62	21	6.71	p < 0.001	309
10	Superior temporal gyrus	57	−46	18	5.97	p < 0.01	25
11	Medial frontal gyrus	43	48	4	5.90	p < 0.001	61

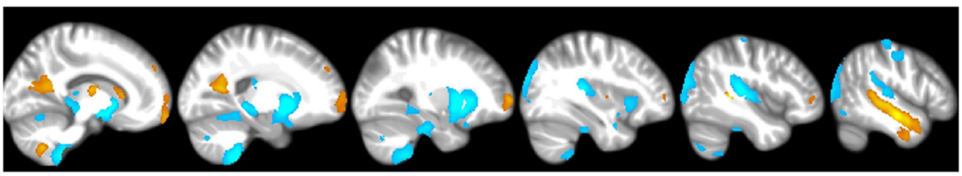

Fig. 1. Significant rightward (orange and yellow) and leftward (blue and turquoise) structually asymmetric clusters with a cluster size of at least 20 voxel shown on the right hemisphere of a mean template generated by averaging the brain images of all 60 subjects. Within each brain picture, posterior is left and anterior is right, superior is up and inferior is down. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

superior frontal gyrus. Additional clusters were observed in thalamus, cerebellum, anterior cingulum, caudate nucleus, putamen and medial frontal gyrus.

Compared to right-hemispheric asymmetries, leftward asymmetric clusters were larger and more numerous. Overall, 14 clusters reached significance for negative AIs, indicating larger left-hemispheric volume (see Table 2 and Fig. 1). The three largest leftward asymmetric clusters were located in superior temporal gyrus, putamen and cerebellum. Additional smaller clusters were observed in parahippocampal gyrus, medial occipital gyrus, postcentral gyrus, and angular gyrus.

3.2. Comparison between right- and left-handers

Right-handers had a mean LQ of 88.44 and left-handers a mean LQ of −73.77. The LQ difference between the two groups was significant ($t_{(58)} = -30.51$, $p < 0.001$). Similar results were found for the pegboard task. Here, right-handers had a mean PegQ of 0.09 and left-handers had a mean LQ of −0.11. The PegQ difference between the two groups was significant ($t_{(58)} = -9.64$, $p < 0.001$).

In a first step we set up two statistical models to check for clusters with AIs significantly different between the two groups using independent-samples *t*-tests (cluster extent threshold = 20, FWE-corrected, $p < 0.05$). One was for clusters more asymmetric in left-handers than in right-handers, and the other one was for clusters more asymmetric in right-handers than in left-handers. For both comparisons, there were no suprathreshold clusters after correction for multiple comparisons. Since smoothing kernel size can affect cluster size and thus potentially structural hemispheric asymmetries [21], we re-ran these analyses with the following alternative smoothing kernels: 4 mm, 6 mm, 10 mm, 12 mm. Comparable to the 8 mm smoothing kernel, no clusters survived correction for multiple comparisons. This proves that the null result for the 8 mm smoothing kernel is not an artefact of smoothing kernel size. Moreover, we also recalculated our analysis with a cluster extent threshold of 0. Again, no clusters survived correction for multiple comparisons.

To explore whether there were any clusters close to significance, we recalculated the analyses with a cluster extent threshold of 20 and an uncorrected significance threshold of $p < 0.001$. Analyzing clusters more asymmetric in left-handers than in right-handers, one cluster in the supplementary motor area (MNI coordinates: 7 mm/2 mm/76 mm) reached significance ($t = 3.97$; $p < 0.001$). Here, left-handers showed a more negative AI (−0.16) than right-handers (0.02). Moreover, the comparision for clusters more asymmetric in right-handers than in left-handers revealed three significant clusters: one in the middle occipital gyrus (MNI coordinates: 27 mm/–78 mm/28 mm) and two in undefined regions in the temporal lobe (MNI coordinates: 38 mm/–13 mm/–8 mm and: 5 mm/–12 mm/–20 mm).

In a second step we then extracted the individual AIs for all participants for all clusters that showed significant asymmetries in the overall sample and compared them between left- and right-hander using independent-samples *t*-tests. Here, one comparison reached nominal significance (rightward Cluster 4 in the thalamus) ($t_{(58)} = 2.05$; $p = 0.045$), but did not survive correction for multiple comparisons. All other comparisons failed to reach nominal significance (all p's > 0.14).

In a third step, we investigated associations between the quantitative measures of hand preference and hand skill and the AIs extracted in the second step. For both LQ and PegQ, we calculated Neyman-Pearson correlation coefficients (see Table 3 for right-handers and Table 4 for left-handers). In right-handers, two correlations reached nominal significance (Cluster 5 in medial occipital gyrus with LQ: $r = -0.41$, $p = 0.02$; Cluster 2 in the cerebellum with PegQ: $r = -0.42$, $p = 0.02$), but did not survive corrections for multiple comparisons (the required p-value was 0.0045). The corrected p-value was also very narrowly missed by the only correlation that reached significance in left-handers (Cluster 11 in medial frontal gyrus with PegQ: $r = 0.50$; $p = 0.0047$).

4. Discussion

Preferences to use one forelimb over the other when performing fine motor tasks have been observed in dozens of animal species and represent an important functional principle in mammalian motor system organization [22]. Despite continuous research efforts, the structural correlates of human handedness in the brain are still not well understood. One idea is that structural grey matter asymmetries influence handedness, but the literature is very inco-

Table 2
Clusters showing negative AIs significantly different from zero in the overall sample. For each cluster, location, MNI coordinates in mm, the T-values, as well as the p-values corrected for multiple comparisons and the cluster size in voxel are provided.

Cluster	Location	mm	mm	mm	T	p_{FWE}	size
1	Putamen	24	6	−6	18.5	p < 0.001	5080
2	Cerebellum	20	−45	−59	14.55	p < 0.001	2453
3	Superior temporal gyrus	39	−30	13	13.34	p < 0.001	2217
4	Parahippocampal gyrus	23	−33	−6	11.19	p < 0.001	1865
5	Medial occipital gyrus	46	−82	18	10.16	p < 0.001	2349
6	Parahippocampal gyrus	29	−22	−27	9.82	p < 0.001	547
7	Postcentral gyrus	49	−25	64	7.98	p < 0.001	672
8	Cerebellum	5	−61	−42	7.71	p < 0.001	73
9	Cerebellum	24	−70	−39	7.14	p < 0.001	104
10	Cuneal Cortex	2	−90	30	7.10	p < 0.001	134
11	Undefined	20	−21	18	6.76	p < 0.001	120
12	Superior temporal gyrus	65	−27	24	6.72	p < 0.001	114
13	Brain stem	2	−33	−20	6.24	p < 0.01	72
14	Angular gyrus	48	−67	46	5.67	p < 0.01	22

Table 3
Correlations between behavioral variables and leftward asymmetric clusters in right-handers. Nominally significant effects are indicated in bold.

	EHI LQ		**PegQ**	
	r	**p**	**r**	**p**
Cluster 1	0.12	0.52	−0.19	0.32
Cluster 2	−0.08	0.67	−**0.42**	**0.02**
Cluster 3	0.16	0.41	0.02	0.94
Cluster 4	−0.06	0.75	0.18	0.33
Cluster 5	−**0.41**	**0.02**	−0.09	0.63
Cluster 6	−0.04	0.84	−0.12	0.54
Cluster 7	−0.10	0.60	0.12	0.52
Cluster 8	0.10	0.60	−0.03	0.86
Cluster 9	0.00	0.98	−0.14	0.47
Cluster 10	−0.14	0.46	0.13	0.49
Cluster 11	0.29	0.13	−0.12	0.52
Cluster 12	−0.07	0.71	0.10	0.59
Cluster 13	−0.23	0.21	−0.03	0.86
Cluster 14	−0.07	0.72	−0.04	0.83

Table 4
Correlations between behavioral variables and rightward asymmetric clusters in left-handers. Nominally significant effects are indicated in bold.

	EHI LQ		PegQ	
	r	p	r	p
Cluster 1	0.02	0.93	−0.10	0.58
Cluster 2	0.25	0.19	0.08	0.69
Cluster 3	0.24	0.21	0.09	0.64
Cluster 4	0.04	0.84	−0.12	0.54
Cluster 5	0.10	0.59	−0.14	0.47
Cluster 6	−0.22	0.23	−0.34	0.07
Cluster 7	−0.03	0.87	−0.18	0.34
Cluster 8	0.18	0.34	0.14	0.46
Cluster 9	−0.02	0.92	0.21	0.26
Cluster 10	0.14	0.47	−0.11	0.55
Cluster 11	0.36	0.05	**0.50**	**0.0047**

herent with regard to the question, which areas are involved and whether there are any grey matter asymmetry correlates of handedness at all [5–10]. Since some of the discrepant findings might have been caused by the use of suboptimal protocols to investigate grey matter asymmetries in previous studies, the present study aimed to re-investigate structural grey matter asymmetries in left-and right-handers using the newly developed VBM asymmetry toolbox by Kurth et al. [13].

The analysis of grey matter asymmetries in our overall sample indicated that this new toolbox is a reliable tool to detect grey matter asymmetries, as our data largely replicate previous studies on structural grey matter asymmetries. For example, when looking at the top three leftward asymmetric areas, previous studies have reported leftward asymmetries for all these regions (putamen [23], posterior lobe of the cerebellum [24], superior temporal gyrus [25]). The leftward asymmetry we found in the superior temporal gyrus was located at the posterior part of this gyrus, at the border to the parietal lobe. It likely represents the well-known leftward asymmetry of the planum temporale containing Wernicke's area that has been reported by numerous studies (for a review, see [26]). Rightward asymmetries were also in line with the literature for the top three clusters (middle temporal gyrus: [27], precuneus [15], superior frontal gyrus [28]). Of particular interest is the here replicated rightward structural asymmetry in the precuneus, previously reported by Kurth et al. [15] in the control group by using the same toolbox. Taken together, these findings implicate that the VBM asymmetry toolbox [13] is a powerful, reliable and easy to use research tool for the laterality community that will certainly prove advantageous for future studies.

The re-investigation of structural grey matter asymmetries in left-and right-handers using this toolbox revealed no supra-threshold asymmetrical clusters that differed significantly between left- and right-handers. Moreover, there were no direct AI differences or correlations between quantitative measures of hand preference and hand skill that survived correction for multiple comparisons. While in contrast to some earlier studies on the role of grey matter asymmetries for handedness [5–8], these findings are in line with two recent large scale studies [9,10], one of which used VBM [9]. Importantly, our study confirms these findings with an analysis protocol fine-tuned for asymmetry detection, indicating that previous null findings were not the result of methodological issues with the standard VBM protocol when analyzing asymmetries. Our results do, however, not completely exclude the possibility that grey matter asymmetries play a role for handedness. VBM is limited to the resolution of MRI, and therefore enables the detection of macroscopic, but not microscopic grey matter asymmetries, whose relation to handedness should be investigated in future studies.

5. Conclusion

The present findings imply that macroscopic structural grey matter asymmetries as assessed with VBM are not a major determinant of handedness. Recently, it has been suggested that functional lateralization can only be understood by taking into account callosal interactions, gray matter asymmetries and asymmetrical interhemispheric pathways (the triadic model [29]). The present results suggest that researchers looking for the structural determinants of handedness may want to focus more on the corpus callosum [30] and white matter [31] than on structural grey matter asymmetries.

References

[1] M. Somers, L.S. Shields, M.P. Boks, R.S. Kahn, I.E. Sommer, Cognitive benefits of right-handedness: a meta-analysis, Neurosci. Biobehav. Rev. 51 (2015) 48–63.
[2] R.M. Willems, L. Van der Haegen, S.E. Fisher, C. Francks, On the other hand: including left-handers in cognitive neuroscience and neurogenetics, Nat. Rev. Neurosci. 15 (2014) 193–201.
[3] S. Ocklenburg, C. Beste, O. Güntürkün, Handedness: a neurogenetic shift of perspective, Neurosci. Biobehav. Rev. 37 (2013) 2788–2793.
[4] S. Ocklenburg, A. Garland, F. Ströckens, A. Uber Reinert, Investigating the neural architecture of handedness, Front. Psychol. 6 (2015) 148.
[5] K. Amunts, G. Schlaug, A. Schleicher, H. Steinmetz, A. Dabringhaus, P.E. Roland, K. Zilles, Asymmetry in the human motor cortex and handedness, Neuroimage 4 (1996) 216–222.
[6] K. Amunts, L. Jäncke, H. Mohlberg, H. Steinmetz, K. Zilles, Interhemispheric asymmetry of the human motor cortex related to handedness and gender, Neuropsychologia 38 (2000) 304–312.
[7] H. Steinmetz, J. Volkmann, L. Jäncke, H.J. Freund, Anatomical left-right asymmetry of language-related temporal cortex is different in left- and right-handers, Ann. Neurol. 29 (1991) 315–319.
[8] J.L. Powell, G.J. Kemp, N. Roberts, M. García-Finaña, Sulcal morphology and volume of Broca's area linked to handedness and sex, Brain Lang. 121 (2012) 206–218.
[9] C.D. Good, I. Johnsrude, J. Ashburner, R.N. Henson, K.J. Friston, R.S. Frackowiak, Cerebral asymmetry and the effects of sex and handedness on brain structure: a voxel-based morphometric analysis of 465 normal adult human brains, Neuroimage 14 (2001) 685–700.
[10] T. Guadalupe, R.M. Willems, M.P. Zwiers, A. Arias Vasquez, M. Hoogman, P. Hagoort, G. Fernandez, J. Buitelaar, B. Franke, S.E. Fisher, C. Francks, Differences in cerebral cortical anatomy of left- and right-handers, Front. Psychol. 5 (2014) 261.
[11] J. Ashburner, K.J. Friston, Voxel-based morphometry: the methods, Neuroimage 11 (2000) 805–821.
[12] J. Ashburner, K.J. Friston, Why voxel-based morphometry should be used, Neuroimage 14 (2001) 1238–1243.
[13] F. Kurth, C. Gaser, E. Luders, A 12-step user guide for analyzing voxel-wise gray matter asymmetries in statistical parametric mapping (SPM), Nat. Protoc. 10 (2015) 293–304.
[14] J. Ashburner, A fast diffeomorphic image registration algorithm, Neuroimage 38 (2007) 95–113.
[15] F. Kurth, A. MacKenzie-Graham, A.W. Toga, E. Luders, Shifting brain asymmetry: the link between meditation and structural lateralization, Soc. Cogn. Affect. Neurosci. 10 (2015) 55–61.
[16] R.C. Oldfield, The assessment and analysis of handedness: the Edinburgh inventory, Neuropsychologia 9 (1971) 97–113.
[17] T.S. Scerri, W.M. Brandler, S. Paracchini, A.P. Morris, S.M. Ring, A.J. Richardson, J.B. Talcott, J. Stein, A.P. Monaco, PCSK6 is associated with handedness in individuals with dyslexia, Hum. Mol. Genet. 20 (2011) 608–614.
[18] U.S. Torres, F.L. Duran, M.S. Schaufelberger, J.A. Crippa, M.R. Louzã, P.C. Sallet, C.Y. Kanegusuku, H. Elkis, W.F. Gattaz, D.P. Bassitt, A.W. Zuardi, J.E. Hallak, C.C. Leite, C.C. Castro, A.C. Santos, R.M. Murray, G.F. Busatto, Patterns of regional gray matter loss at different stages of schizophrenia: a multisite: cross-sectional VBM study in first-episode and chronic illness, Neuroimage Clin. 12 (2016) 1–15.
[19] P. Fusar-Poli, J. Radua, P. McGuire, S. Borgwardt, Neuroanatomical maps of psychosis onset: voxel-wise meta-analysis of antipsychotic-naive VBM studies, Schizophr. Bull. 38 (2012) 1297–1307.
[20] T. Uwatoko, M. Yoshizumi, J. Miyata, S. Ubukata, H. Fujiwara, R. Kawada, M. Kubota, A. Sasamoto, G. Sugihara, T. Aso, S. Urayama, H. Fukuyama, T. Murai, H. Takahashi, Insular gray matter volume and objective quality of life in schizophrenia, PLoS One 10 (2015) e0142018.
[21] S.M. Henley, G.R. Ridgway, R.I. Scahill, S. Klöppel, S.J. Tabrizi, N.C. Fox, J. Kassubek, EHDN Imaging Working Group, Pitfalls in the use of voxel-based morphometry as a biomarker: examples from huntington disease, AJNR Am. J. Neuroradiol. 31 (2010) 711–719.
[22] F. Ströckens, O. Güntürkün, S. Ocklenburg, Limb preferences in non-human vertebrates, Laterality 18 (2013) 536–575.
[23] I. Savic, Asymmetry of cerebral gray and white matter and structural volumes in relation to sex hormones and chromosomes, Front. Neurosci. 8 (2014) 329.
[24] L. Fan, Y. Tang, B. Sun, G. Gong, Z.J. Chen, X. Lin, T. Yu, Z. Li, A.C. Evans, S. Liu, Sexual dimorphism and asymmetry in human cerebellum: an MRI-based morphometric study, Brain Res. 1353 (2010) 60–73.
[25] M. Meyer, F. Liem, S. Hirsiger, L. Jäncke, J. Hänggi, Cortical surface area and cortical thickness demonstrate differential structural asymmetry in auditory-related areas of the human cortex, Cereb. Cortex 24 (2014) 2541–2552.
[26] H. Steinmetz, Structure: functional and cerebral asymmetry: in vivo morphometry of the planum temporale, Neurosci. Biobehav. Rev. 20 (1996) 587–591.
[27] V.M. Saenger, F.A. Barrios, M.L. Martínez-Gudiño, S. Alcauter, Hemispheric asymmetries of functional connectivity and grey matter volume in the default mode network, Neuropsychologia 50 (2012) 1308–1315.
[28] E. Goldberg, D. Roediger, N.E. Kucukboyaci, C. Carlson, O. Devinsky, R. Kuzniecky, E. Halgren, T. Thesen, Hemispheric asymmetries of cortical volume in the human brain, Cortex 49 (2013) 200–210.
[29] S. Ocklenburg, P. Friedrich, O. Güntürkün, E. Genç, Intrahemispheric white matter asymmetries: the missing link between brain structure and functional lateralization? Rev. Neurosci. 27 (2016) 465–480.
[30] N. Cherbuin, E. Luders, Y.Y. Chou, P.M. Thompson, A.W. Toga, K.J. Anstey, Right left, and center: how does cerebral asymmetry mix with callosal connectivity? Hum. Brain Mapp. 34 (2013) 1728–1736.
[31] N.S. McKay, S.J. Iwabuchi, I.S. Häberling, M.C. Corballis, I.J. Kirk, Atypical white matter microstructure in left-handed individuals, Laterality (2016) 1–11 (Epub ahead of print).