NeuroImage 156 (2017) 43–64

Contents lists available at ScienceDirect

NeuroImage

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

Freesurfer cortical normative data for adults using Desikan-Killiany-Tourville and ex vivo protocols

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ARTICLE INFO

Keywords:
Magnetic resonance imaging
Atrophy
Morphometry
Normality
Aging
Sex
Segmentation

ABSTRACT

We recently built normative data for *FreeSurfer* morphometric estimates of cortical regions using its default atlas parcellation (Desikan-Killiany or DK) according to individual and scanner characteristics. We aimed to produced similar normative values for Desikan-Killianny-Tourville (DKT) and ex vivo-based labeling protocols, as well as examine the differences between these three atlases. Surfaces, thicknesses, and volumes of cortical regions were produced using cross-sectional magnetic resonance scans from the same 2713 healthy individuals aged 18–94 years as used in the reported DK norms. Models predicting regional cortical estimates of each hemisphere were produced using age, sex, estimated intracranial volume (eTIV), scanner manufacturer and magnetic field strength (MFS) as predictors. The DKT and DK models generally included the same predictors and produced similar R^2. Comparison between DK, DKT, ex vivo atlases normative cortical measures showed that the three protocols generally produced similar normative values.

Introduction

We recently developed normative data for *FreeSurfer* morphometric estimates of cortical (Potvin et al., 2017) and subcortical (Potvin et al. 2016a; Potvin et al., 2016b) measures according to age, sex, estimated intracranial volume (eTIV), scanner manufacturer and magnetic field strength (MFS) using a large number of individuals with a wide age range. Such norms allow one to measure the extent of deviation from normality in individuals, while taking into account factors influencing these estimates. In our previous study (Potvin et al. 2017), we produced regional cortical normative values using *FreeSurfer*'s default atlas parcellation, the Desikan-Killiany (DK) labeling protocol (Desikan et al., 2006). While the DK atlas is probably the most popular human cortical labeling protocol, Klein and Tourville (2012) proposed another cortical labeling parcellation, the Desikan-Killianny-Tourville (DKT) protocol, inspired from the DK but based upon one of the largest set of publicly-available manually-labeled human brains (n=101). In order to facilitate the labeling algorithm and increase the reliability of manual editing, three regions with highly variable boundaries (i.e. frontal and temporal poles and the banks of the superior temporal sulcus), which are distinctly labeled in the DK atlas, were aggregated in the DKT atlas (31 regions per hemisphere).

Furthermore, *FreeSurfer* also includes an ex vivo segmentation protocol for the entorhinal and perirhinal cortices, using an approach based on cytoarchitectonic features from ultra-high resolution ex vivo MRI (Augustinack et al., 2013; Fischl et al., 2009). This technique has the advantage of producing more accurate entorhinal segmentations when compared to other atlases, in addition to providing perirhinal cortical measures which are otherwise not available using either DK or DKT.

Our first objective was to develop normative values for the DKT and ex vivo labeling protocols using the same procedure used for the DK normative values (Potvin et al., 2017), that is within a very large sample of individuals with a wide age range. Our second objective was to describe the differences in predicting models between labeling protocols. We expected the models to display similar R^2 and include the same predictors across the same regions. Finally, our third objective was to determine whether the choice of atlas resulted in substantial differences when using normative Z scores in pathological populations; to this end we elected to study individuals with Alzheimer's disease (AD) and schizophrenia (SZ).

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[1] Part of the data used in this article were obtained from the Alzheimer's Disease Neuroimaging Initiative (ADNI) database (adni.loni.usc.edu). As such, the investigators within the ADNI contributed to the design and implementation of ADNI and/or provided data but did not participate in analysis or writing of this report. A complete listing of ADNI investigators can be found at: http://adni.loni.usc.edu/wp-content/uploads/how_to_apply/ADNI_Acknowledgement_List.pdf.

http://dx.doi.org/10.1016/j.neuroimage.2017.04.035
Received 28 November 2016; Accepted 14 April 2017
Available online 04 May 2017
1053-8119/

Table 1
Participants' characteristics according to the dataset.

Dataset	n	%	Age (mean ± SD range)	Female %
1. Autism Brain Imaging Data Exchange (ABIDE)	184	6.8	26.1 ± 7.0 18–56	12.5
2. Alzheimer's Disease Neuroimaging Initiative (ADNI1)	199	7.3	75.7 ± 5.0 60–90	47.2
3. Alzheimer's Disease Neuroimaging Initiative (ADNI2)	179	6.6	73.6 ± 6.3 56–89	52.5
4. Australian Imaging Biomarkers and Lifestyle flagship study of ageing (AIBL)	158	5.8	72.1 ± 7.2 60–88	52.5
5. BMB - Berlin Mind and Brain (Margulies, Villringer) CoRR sample (BMB)	50	1.8	30.3 ± 7.1 19–59	52.0
6. Cleveland Clinic (Cleveland CCF)	30	1.1	43.1 ± 11.1 24–60	63.3
7. Center of Biomedical Research Excellence (COBRE)	71	2.6	35.5 ± 11.3 18–62	29.6
8. DS-108 from the OpenfMRI database	32	1.2	22.2 ± 4.6 18–41	50.0
9. DS-170 from the OpenfMRI database	15	0.6	25.4 ± 4.6 19–35	20.0
10. Functional Biomedical Informatics Research Network (FBIRN)	34	1.3	38.9 ± 13.1 19–65	41.2
11. FIND lab sample (FIND)	13	0.5	24.1 ± 3.7 18–29	61.5
12. International Consortium for Brain Mapping (ICBM)	148	5.5	25.0 ± 4.9 18–44	43.2
13. Information eXtraction from Images (IXI)	558	20.5	48.5 ± 16.4 20–86	55.7
14. F.M. Kirby Research Center neuroimaging reproducibility data (KIRBY-21)	20	0.7	31.9 ± 9.7 22–61	45.0
15. Minimal Interval Resonance Imaging in Alzheimer's Disease (MIRIAD)	21	0.8	69.8 ± 7.5 58–86	47.8
16. NIH MRI Study of Normal Brain Development (NIHPD)	59	2.2	18.9 ± 1.0 18–22	52.4
17. Nathan Kline Institute Rockland phase 1 (NKI-R1)	138	5.1	42.4 ± 18.3 18–85	43.5
18. Nathan Kline Institute Rockland phase 2 (NKI-R2)	253	9.3	46.1 ± 18.8 18–85	64.8
19. Open Access Series of Imaging Studies (OASIS)	301	11.1	43.9 ± 23.6 18–94	61.8
20. POWER Neuroimage sample (POWER)	26	1.0	23.0 ± 1.4 20–25	84.6
21. Parkinson's Progression Markers Initiative (PPMI)	164	6.0	60.1 ± 11.5 31–83	34.2
22. TRAIN-39 sample (TRAIN)	35	1.3	22.5 ± 2.6 18–28	71.4
23. University of Wisconsin (Birn, Prabhakaran, Meyerand) CoRR sample (UWM)	25	0.9	25.0 ± 3.2 21–32	44.0
Total	**2713**	**100.0**	**47.6 ± 21.7 18–94**	**49.8**

Materials and methods

Participants

The present study comprises the sample used in Potvin et al. (2017), that is T1-weighted MRI scans of Siemens Healthcare (57%), Philips Medical Systems (29%), or GE Healthcare (14%) manufacturer at MFS of either 1.5 (45%) or 3 (55%) Tesla from 2713 cognitively healthy men (50%) and women (50%) aged 18 to 94 years (see Table 1 and Acknowledgments for details). Of note, this includes the Alzheimer's Disease Neuroimaging Initiative (ADNI) and the Australian Imaging, Biomarkers and Lifestyle study of aging (AIBL) databases. The ADNI (adni.loni.usc.edu) was launched in 2003 as a public-private partnership, led by Principal Investigator Michael W. Weiner, MD. (www.adni-info.org). The AIBL data was collected by the AIBL study group and AIBL study methodology has been reported previously by Ellis et al. (2009). For each dataset, approval from the local ethics board and informed consent of the participants were obtained.

All samples specifically recruited healthy control participants, except NKI1 and NKI2. Databases with older adults excluded neurological diseases and neuropsychiatric disorders with extensive assessments for age-related disorders. For databases recruiting in the general population (NKI1 and NKI2), we excluded participants with schizophrenia or other psychotic disorders, bipolar disorders, major depressive disorders and substance abuse/dependence disorders. Additional exclusions were made for NKI2: neurodegenerative and neurological disorders, head injury with loss of consciousness/amnesia, and lead poisoning. Moreover, for PPMI, additional exclusions were made for participants with a Geriatric Depression Scale (Sheikh and Yesavage, 1986) score of more than 5 (inclusion criterion used in the ADNI and AIBL databases). In order to prevent that the same individual appears more than once throughout the multiple datasets, participants with similar eTIV (difference $< 1000\ mm^3$) were compared according to available information: age, scan date, sex, handedness, height, and study location (city and country). Nineteen pairs of participants were deemed to be potential duplicates. For each pair, MRIs were compared and none of them had similar head shapes.

All original images were visually inspected and four participants were discarded because of evident abnormalities. Five participants with extreme eTIV values were also excluded (Z scores higher than 3.29, $p < .001$).

The models predicting normative values were also validated using the same groups used in Potvin et al. (2017): a random subset of the healthy individuals from the normative sample stratified by manufacturer and MFS (5%; n=137) and clinical samples of individuals with SZ (n=72; age: 38.2 ± 13.9, range 18–65; 19% female) from the COBRE dataset and mild AD (n=50 age: 72.7 ± 7.7, range 56–87; 44% female) randomly selected from the ADNI-2 dataset. SZ was diagnosed using the Structured Clinical Interview for DSM-IV disorders (First et al., 1996). AD was diagnosed according to National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer's Disease and Related Disorders Association (NINCDS/ADRDA) criteria for probable AD (McKhann et al., 1984) and had a Clinical Dementia Rating of 0.5 or 1.

Segmentation

The procedure was identical to that of Potvin et al., except that DKT (Klein and Tourville, 2012) and ex vivo (Augustinack et al., 2013; Fischl et al., 2009) labeling protocols were used instead of the DK atlas. Briefly, cortical segmentation was conducted using *FreeSurfer* Version 5.3 (http://freesurfer.net) using the "recon –all" pipeline with the default set of parameters (no flag options). Estimated total intracranial volumes (eTIV) (Buckner et al., 2004) was taken from the aseg.stats *Freesurfer* output file. Surfaces (white surface areas), thicknesses, and volumes originated from the aparc.DKTatlas40 stats files. Visual inspection of each brain segmentation was conducted using *FreeView* (http://freesurfer.net) by scrolling the entire brain at least through the coronal and axial planes. No manual editing was conducted. For each cortical region, the criterion for failed segmentation was inadequate inclusion (e.g. dura mater, ventricle) or omission of approximately 100 voxels or more. The mean percentage of exclusion across regions was 1.7% (SD: 2.4%).

Statistical analyses

To produce normative values, we built linear regression models predicting each cortical measure using age, sex, eTIV, MFS, and scanner manufacturer as predictors with quadratic and cubic terms

Table 2
Coefficients of models predicting cortical surface for the Desikan-Killiany-Tourville and ex vivo protocols.

		Sociodemographics					Estimated total intracranial volume (eTIV)			Scanner			Interactions					
Region	**RMSE**	**Int**	**Age**	**Age^2**	**Age^3**	**Sex**	**eTIV**	**eTIV^2**	**eTIV^3**	**Strength**	**Manufacturer**		**GE X MFS**	**Philips X MFS**	**eTIV X MFS**	**Age X Sex**	**eTIV X GE**	**eTIV X Philips**
						M/F				**1.5T/3T**	**GE/ Siemens**	**Philips/ Siemens**						
Superior temporal L	401.87	5001.8	**−5.36E+00**	−4.64E-02	–	**1.27E+02**	**2.29E-03**	**6.89E-10**	–	**7.02E+01**	1.02E+01	−4.79E+01	−1.02E+02	**−1.60E+02**	–	−1.50E+00	–	–
Superior temporal R	353.88	4723.5	**−5.72E+00**	–	–	–	**2.18E-03**	7.65E-10	–	−1.62E+00	**−7.97E+01**	**−1.21E+02**	–	–	1.55E-04	–	−8.49E-05	**−3.01E-04**
Middle temporal L	413.12	4060.6	**−6.41E+00**	**−1.21E-01**	–	**5.52E+01**	**2.09E-03**	*4.42E-10*	–	**−8.11E+01**	−1.49E+01	**−1.49E+02**	−1.90E+00	**1.24E+02**	–	–	3.37E-05	**−3.72E-04**
Middle temporal R	382.24	4062.9	**−6.13E+00**	**−8.12E-02**	–	*4.72E+01*	**2.23E-03**	*3.89E-10*	**−1.71E-15**	**−7.45E+01**	−2.84E+01	**−7.03E+01**	–	–	–	−1.23E+00	2.14E-04	−1.67E-04
Inferior temporal L	362.78	3301.5	**−5.14E+00**	**−7.51E-02**	–	**5.87E+01**	**1.78E-03**	**6.34E-10**	*−1.36E-15*	1.18E+01	**1.43E+02**	−1.42E+01	**−1.70E+02**	−1.89E+01	1.23E-04	−8.71E-01	1.30E-04	**−2.56E-04**
Inferior temporal R	364.87	3504.6	**−3.94E+00**	**−7.60E-02**	−1.73E-03	**5.19E+01**	**1.90E-03**	**5.64E-10**	–	**−9.89E+01**	2.45E+01	**−9.46E+01**	−4.59E+01	**1.06E+02**	–	–	−4.46E-05	**−2.86E-04**
Transverse temporal L	67.14	445.7	**−4.11E-01**	*−9.18E-03*	–	*7.55E+00*	**1.90E-04**	5.08E-11	–	3.20E+00	−2.73E+00	5.36E+00	−1.33E+01	−3.18E+01	–	–	–	–
Transverse temporal R	49.63	334.1	**−2.99E-01**	**−1.18E-02**	–	4.58E+00	**1.58E-04**	*5.75E-11*	*−1.80E-16*	2.46E+00	2.26E+00	5.89E+00	−6.87E+00	−2.26E+01	–	–	–	–
Entorhinal L	62.42	372.8	*3.65E-01*	**−1.52E-02**	**−6.54E-04**	**1.71E+01**	**1.76E-04**	**8.57E-11**	–	–	*8.20E+00*	**1.09E+01**	–	–	–	−1.29E-01	–	–
Entorhinal R	74.71	367.7	*4.08E-01*	*−1.36E-02*	−4.46E-04	**1.48E+01**	**1.96E-04**	**1.09E-10**	–	**−2.48E+01**	**−1.78E+01**	**−2.30E+01**	**4.12E+01**	**3.28E+01**	–	–	−2.59E-05	**−5.45E-05**
Fusiform L	326.44	2943.4	**−5.28E+00**	*−4.91E-02*	–	*3.94E+01*	**1.60E-03**	*2.98E-10*	**−1.61E-15**	*−3.23E+01*	−3.24E+01	**−6.63E+01**	–	–	–	–	−9.76E-05	**−2.37E-04**
Fusiform R	296.69	2753.7	**−2.90E+00**	−4.14E-02	−1.39E-03	**9.55E+01**	**1.35E-03**	**4.22E-10**	*−9.48E-16*	**−8.74E+01**	−2.95E+01	**−6.73E+01**	–	–	–	−8.41E-01	–	–
Parahippocampal L	84.75	706.5	**−1.21E+00**	**−2.61E-02**	–	–	**3.01E-04**	**1.85E-10**	–	**−1.23E+01**	−1.93E+00	**−1.76E+01**	–	–	–	–	–	–
Parahippocampal R	79.75	667.1	**−1.03E+00**	**−2.01E-02**	–	**1.22E+01**	**2.97E-04**	**1.31E-10**	–	**−2.14E+01**	3.71E+00	**−1.51E+01**	–	–	−2.60E-05	–	**7.94E-05**	−1.95E-05
Superior frontal L	633.20	7956.7	**−1.37E+01**	−6.73E-02	–	**1.22E+02**	**3.98E-03**	**1.19E-09**	–	*7.19E+01*	−1.55E+01	**−2.23E+02**	**−2.66E+02**	−1.15E+02	–	–	3.66E-04	−2.46E-04
Superior frontal R	722.76	9055.0	**−1.47E+01**	*−9.39E-02*	–	**1.50E+02**	**4.85E-03**	**1.24E-09**	−2.21E-15	6.27E+01	*−1.45E+02*	**−1.99E+02**	*−2.25E+02*	*−1.72E+02*	–	−1.40E+00	2.61E-04	−3.21E-04
Rostral	427.89	3898.4	**−8.12E**	−2.64E-	–	**7.66E**	**2.46E-**	**7.84E-**	**−2.20E-**	*−4.27E*	*−5.15E*	**−1.23E+02**	–	–	*−2.47E-04*	–	–	–

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Table 2 *(continued)*

		Sociodemographics					Estimated total intracranial volume (eTIV)			Scanner			Interactions					
Region	**RMSE**	**Int**	**Age**	**Age^2**	**Age^3**	**Sex**	**eTIV**	**eTIV^2**	**eTIV^3**	**Strength**	**Manufacturer**		**GE X MFS**	**Philips X MFS**	**eTIV X MFS**	**Age X Sex**	**eTIV X GE**	**eTIV X Philips**
						M/F				**1.5T/3T**	**GE/ Siemens**	**Philips/ Siemens**						
middle frontal L			**+00**	02		**+01**	**03**	**10**	**15**	*+01*	*+01*							
Rostral middle frontal R	450.06	3742.9	**−7.45E +00**	−4.95E-02	–	**7.58E +01**	**2.15E-03**	**9.38E-10**	–	−3.27E +01	*−5.61E +01*	**−8.36E+01**	–	–	–	–	2.21E-04	−2.03E-04
Caudal middle frontal L	324.30	2351.3	**−3.68E +00**	1.33E-04	−1.27E-03	1.72E +01	**1.45E-03**	**4.17E-10**	*−1.14E-15*	−6.66E +00	−1.05E +01	**−7.25E+01**	−7.48E+01	4.28E+00	–	5.83E-01	1.67E-04	−1.17E-04
Caudal middle frontal R	316.96	2175.3	**−4.27E +00**	–	–	–	**1.54E-03**	*3.31E-10*	**−1.48E-15**	3.02E+01	2.07E +01	−3.88E+01	*−9.60E+01*	−5.63E+01	–	–	1.70E-04	*−1.95E-04*
Pars opercularis L	203.09	1453.0	**−2.20E +00**	–	–	1.90E +01	**6.61E-04**	1.57E-10	–	−9.21E +00	−4.10E +00	**−3.93E+01**	**−7.11E +01**	−1.32E+01	–	−6.89E-01	–	–
Pars opercularis R	201.87	1433.9	**−2.31E +00**	−2.18E-02	–	1.65E +01	**7.45E-04**	1.71E-10	**−7.71E-16**	1.99E+01	−1.56E +01	**−4.16E+01**	**−7.56E +01**	−2.20E+01	–	–	–	–
Pars triangularis L	218.54	1559.8	**−3.12E +00**	–	–	**5.99E +01**	**6.56E-04**	**3.71E-10**	–	**−2.63E +01**	**−4.64E +01**	**−6.23E+01**	–	–	–	−5.97E-01	–	–
Pars triangularis R	241.26	1529.3	**−4.18E +00**	−1.78E-02	*1.55E-03*	**7.07E +01**	**5.44E-04**	*2.64E-10*	–	−5.64E +00	**−5.12E +01**	**−5.69E+01**	–	–	*1.27E-04*	*−9.60E-01*	–	–
Pars orbitalis L	73.32	694.4	**−5.31E-01**	−4.33E-03	−4.14E-04	**1.13E +01**	**2.77E-04**	5.96E-11	–	−2.61E +00	−1.02E +01	*−1.17E+01*	−1.25E+01	**−1.88E+01**	–	–	–	–
Pars orbitalis R	93.25	823.3	**−1.14E +00**	−9.31E-03	–	**2.76E +01**	**3.09E-04**	–	–	*−8.35E +00*	**−1.45E +01**	**−2.23E+01**	–	–	–	–	–	–
Lateral orbitofrontal L	269.33	2840.6	*−1.53E +00*	−3.56E-02	−1.42E-03	–	**1.61E-03**	**3.30E-10**	**−1.57E-15**	**−1.38E +02**	**−1.10E +02**	**−1.04E+02**	5.99E+01	**1.39E+02**	–	–	*2.39E-04*	*−1.35E-04*
Lateral orbitofrontal R	277.79	2844.1	**−3.15E +00**	**−5.95E-02**	–	–	**1.54E-03**	*2.89E-10*	**−1.31E-15**	2.57E+01	7.03E +00	1.40E-01	**−9.09E +01**	−2.44E+01	–	–	**2.80E-04**	−1.16E-04
Medial orbitofrontal	147.75	1554.6	**−1.60E +00**	**−2.63E-02**	–	–	**7.57E-04**	–	–	9.68E+00	**6.88E +01**	−1.61E+01	**−9.19E +01**	**−4.19E+01**	–	–	–	–

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Table 2 *(continued)*

		Sociodemographics					Estimated total intracranial volume (eTIV)			Scanner			Interactions					
Region	**RMSE**	**Int**	**Age**	**Age^2**	**Age^3**	**Sex**	**eTIV**	**eTIV^2**	**eTIV^3**	**Strength**	**Manufacturer**		**GE X MFS**	**Philips X MFS**	**eTIV X MFS**	**Age X Sex**	**eTIV X GE**	**eTIV X Philips**
						M/F				**1.5T/3T**	**GE/ Siemens**	**Philips/ Siemens**						
L																		
Medial orbito-frontal R	142.94	1499.7	**−1.09E +00**	*−2.20E-02*	–	**2.35E +01**	**6.69E-04**	–	–	**−2.58E +01**	2.54E +00	**−4.60E+01**	−3.57E+01	1.12E+01	–	–	4.93E-05	*−8.38E-05*
Precentral L	400.75	4718.6	**−4.07E +00**	–	–	**1.40E +02**	**1.91E-03**	**6.94E-10**	–	**6.21E +01**	**−9.83E +01**	**−1.88E+02**	–	–	1.88E-04	−1.05E+00	2.58E-04	−1.06E-04
Precentral R	390.83	4593.1	**−3.28E +00**	–	–	**1.41E +02**	**1.86E-03**	**6.45E-10**	1.21E-15	**9.09E +01**	**−9.30E +01**	**−1.39E+02**	*−1.02E+02*	−5.42E+01	1.63E-04	−8.53E-01	–	–
Paracentral L	181.46	1543.7	**−1.25E +00**	–	–	−1.88E +00	**7.84E-04**	**3.97E-10**	*−6.99E-16*	*1.74E+01*	**−7.35E +01**	**−5.98E+01**	–	–	–	−4.53E-01	–	–
Paracentral R	197.36	1585.1	**−1.56E +00**	–	–	–	**7.92E-04**	**3.61E-10**	−4.32E-16	**4.46E +01**	**−4.70E +01**	−1.39E+01	−3.64E+01	**−6.64E+01**	–	–	–	–
Postcentral L	396.77	4603.2	**−4.43E +00**	–	–	**7.42E +01**	**2.20E-03**	*4.00E-10*	−1.28E-15	1.73E+01	**−1.16E +02**	**−7.73E+01**	6.50E+00	**−1.07E+02**	–	–	–	–
Postcentral R	390.38	4280.0	**−4.19E +00**	*5.45E-02*	–	**5.93E +01**	**2.00E-03**	**4.74E-10**	−1.21E-15	–	**−9.13E +01**	**−1.29E+02**	–	–	–	–	–	–
Supramarginal L	418.66	3683.1	**−4.15E +00**	–	–	**9.93E +01**	**2.13E-03**	**5.06E-10**	**−2.41E-15**	**−4.86E +01**	−4.64E +01	**−6.83E+01**	–	–	–	–	–	–
Supramarginal R	386.44	3451.6	**−3.79E +00**	–	–	3.52E +01	**1.79E-03**	**7.45E-10**	*−1.38E-15*	–	**−9.36E +01**	**−1.07E+02**	–	–	–	*−1.42E+00*	–	–
Superior parietal L	457.30	4315.8	**−6.44E +00**	−3.33E-02	–	−2.00E +01	**2.04E-03**	**5.79E-10**	*−1.69E-15*	−2.72E +00	**−7.85E +01**	**−9.00E+01**	–	–	1.24E-04	–	–	–
Superior parietal R	464.60	4619.3	**−5.64E +00**	−4.73E-02	–	3.19E +01	**1.96E-03**	4.34E-10	–	9.37E-01	**−1.18E +02**	**−1.36E+02**	–	–	1.51E-04	−1.36E+00	–	–
Inferior parietal L	476.53	4259.7	**−3.18E +00**	*6.70E-02*	**−4.04E-03**	**7.96E +01**	**2.13E-03**	*4.42E-10*	−8.82E-16	−1.02E +01	*−5.77E +01*	**−1.08E+02**	–	–	*2.53E-04*	**−2.44E +00**	2.46E-04	−1.77E-04
Inferior parietal R	535.88	4992.9	**−5.59E +00**	3.37E-02	*−3.60E-03*	**2.08E +02**	**2.28E-03**	*5.24E-10*	–	**−8.51E +01**	**−1.55E +02**	**−1.73E+02**	–	–	*2.70E-04*	–	2.02E-04	−2.40E-04
Precuneus L	345.41	3621.3	**−5.37E +00**	–	–	**5.83E +01**	**1.84E-03**	3.18E-10	*−1.33E-15*	−4.92E +00	**−1.32E +02**	−2.87E+01	−5.11E+01	**−9.90E+01**	–	–	1.66E-04	−7.91E-05
Precuneus R	383.67	3922.8	**−5.50E +00**	–	–	**9.33E +01**	**1.98E-03**	**5.62E-10**	*−1.18E-15*	*−3.20E +01*	**−1.51E +02**	**−9.65E+01**	–	–	–	−8.11E-01	–	–
Lingual L	362.55	3065.9	−5.87E-01	*−5.12E-02*	*−2.78E-03*	**6.95E +01**	**1.24E-03**	2.08E-10	−8.47E-16	**−1.40E +02**	**−1.30E +02**	**−8.56E+01**	**1.57E+02**	3.80E+01	–	−1.16E+00	−8.47E-06	*−2.28E-04*
Lingual R	347.23	3115.0	**−3.03E +00**	**−8.05E-02**	–	**5.32E +01**	**1.10E-03**	2.62E-10	–	**−1.20E +02**	**−1.10E +02**	**−9.65E+01**	*1.01E+02*	*7.72E+01*	–	–	3.15E-05	*−2.07E-04*
Pericalcarine L	213.57	1372.3	**−1.54E +00**	–	–	*2.10E +01*	**5.61E-04**	**2.89E-10**	–	**−8.72E +01**	**−1.01E +02**	**−5.04E+01**	**1.15E+02**	**6.70E+01**	–	–	1.04E-05	**−1.38E-04**
Pericalcarine R	223.88	1507.2	**−1.52E +00**	–	–	1.89E +01	**7.00E-04**	**2.79E-10**	−5.27E-16	**−8.37E +01**	**−8.83E +01**	**−6.03E+01**	**7.69E+01**	**8.50E+01**	**−1.39E-04**	–	–	–
Cuneus L	241.68	2005.5	**−1.99E**	**−4.34E-**	–	**6.33E**	**7.19E-**	2.18E-	–	*−3.04E*	**−1.06E**	−1.57E+01	**1.10E+02**	−5.20E+00	–	*−1.07E+00*	–	–

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Table 2 *(continued)*

		Sociodemographics					Estimated total intracranial volume (eTIV)			Scanner			Interactions					
Region	**RMSE**	**Int**	**Age**	**Age^2**	**Age^3**	**Sex**	**eTIV**	**eTIV^2**	**eTIV^3**	**Strength**	**Manufacturer**		**GE X MFS**	**Philips X MFS**	**eTIV X MFS**	**Age X Sex**	**eTIV X GE**	**eTIV X Philips**
						M/F				**1.5T/3T**	**GE/ Siemens**	**Philips/ Siemens**						
			+00	**02**		**+01**	**04**	10		*+01*	**+02**							
Cuneus R	200.25	1852.2	**−2.22E +00**	*−2.70E-02*	–	**4.17E +01**	**8.73E-04**	1.35E-10	*−7.45E-16*	–	**−5.07E +01**	−7.01E+00	–	–	–	–	–	–
Lateral occipital L	479.40	4837.7	**−6.67E +00**	−7.44E-02	–	**1.76E +02**	**2.03E-03**	**8.37E-10**	–	–	−5.40E +01	**−7.32E+01**	–	–	–	–	9.07E-05	−2.32E-04
Lateral occipital R	490.68	4750.0	**−6.31E +00**	–	–	**1.93E +02**	**2.23E-03**	**6.30E-10**	−1.45E-15	–	**−1.10E +02**	*−5.51E+01*	–	–	–	−1.59E+00	−1.41E-04	*−2.82E-04*
Rostral anterior cingulate L	155.26	1120.1	**−6.26E-01**	**−2.83E-02**	–	−1.68E +00	**8.15E-04**	**3.08E-10**	**−8.00E-16**	**−5.15E +01**	**−5.07E +01**	**−3.18E+01**	−5.03E+00	2.53E+01	–	*6.17E-01*	*1.21E-04*	−6.64E-05
Rostral anterior cingulate R	128.59	791.3	**−3.76E-01**	**−2.02E-02**	–	–	**5.65E-04**	**2.64E-10**	*−4.63E-16*	**−3.36E +01**	**−2.86E +01**	**−2.60E+01**	–	–	–	–	5.95E-05	−3.77E-05
Caudal anterior cingulate L	144.11	1090.1	*−8.13E-01*	−5.38E-03	−6.81E-04	–	**6.34E-04**	**2.12E-10**	*−4.65E-16*	*−1.34E +01*	**−3.20E +01**	**−2.72E+01**	–	–	−5.71E-05	–	*1.24E-04*	−1.07E-05
Caudal anterior cingulate R	142.26	809.4	**−8.89E-01**	−1.06E-02	–	2.05E +00	**4.27E-04**	6.39E-11	*−5.05E-16*	**−1.68E +01**	**−3.81E +01**	**−2.78E+01**	–	–	–	4.56E-01	8.29E-05	−2.07E-05
Posterior cingulate L	152.74	1257.5	**−1.21E +00**	9.88E-03	−7.41E-04	**2.93E +01**	**6.20E-04**	6.56E-11	**−7.98E-16**	*−1.62E +01*	**−7.09E +01**	**−5.32E+01**	–	–	–	−5.35E-01	*1.23E-04*	−9.19E-06
Posterior cingulate R	152.58	1268.0	**−1.82E +00**	*−1.92E-02*	–	–	**7.06E-04**	*1.74E-10*	**−6.61E-16**	**−2.01E +01**	**−8.56E +01**	**−3.75E+01**	–	–	–	–	–	–
Isthmus cingulate L	142.93	998.5	**−5.80E-01**	–	–	**3.00E +01**	**6.39E-04**	*1.28E-10*	**−8.89E-16**	–	**−5.95E +01**	**−5.85E+01**	–	–	–	–	–	–
Isthmus cingulate R	131.64	946.5	**−6.35E-01**	–	–	**2.27E +01**	**5.49E-04**	**2.47E-10**	–	**1.52E +01**	**−5.15E +01**	**−5.69E+01**	–	–	–	–	–	–
Insula L	143.86	1910.3	4.29E-02	**−3.37E-02**	–	**2.07E +01**	**8.91E-04**	**2.96E-10**	−3.10E-16	−3.62E +00	**−5.28E +01**	**−3.79E+01**	−1.31E+00	*−2.83E+01*	*8.33E-05*	–	−3.22E-05	*−9.71E-05*
Insula R	156.23	2013.8	−2.60E-01	**−4.00E-02**	–	**3.80E +01**	**8.75E-04**	**3.35E-10**	−3.90E-16	–	**−4.66E +01**	**−5.07E+01**	–	–	–	–	–	–
Ex vivo entorhin-	28.62	219.9	−1.33E-01	**−1.06E-02**	−1.33E-04	**8.83E +00**	**7.76E-05**	–	–	**−8.78E +00**	−2.09E-01	−2.76E+00	6.24E+00	4.49E+00	–	−6.97E-02	–	–

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Table 2 *(continued)*

Region	RMSE	Sociodemographics				Estimated total intracranial volume (eTIV)			Scanner			Interactions						
		Int	Age	Age^2	Age^3	Sex	eTIV	eTIV^2	eTIV^3	Strength	Manufacturer		GE X MFS	Philips X MFS	eTIV X MFS	Age X Sex	eTIV X GE	eTIV X Philips
						M/F				1.5T/3T	GE/ Siemens	Philips/ Siemens						
al L																		
Ex vivo entorhinal R	30.14	182.0	**−1.25E-01**	**−8.27E-03**	–	**6.07E+00**	**7.74E-05**	**4.75E-11**	–	**−9.21E+00**	−2.03E+00	**−9.46E+00**	*8.32E+00*	*6.78E+00*	–	–	−4.26E-06	**−2.55E-05**
Ex vivo perirhinal L	78.27	647.9	*−4.64E-01*	**−2.03E-02**	*−5.62E-04*	**2.38E+01**	**2.48E-04**	–	–	**−1.06E+01**	–	–	–	–	–	–	–	–
Ex vivo perirhinal R	61.84	428.0	−4.21E-02	**−1.41E-02**	−3.58E-04	**1.54E+01**	**1.70E-04**	*6.99E-11*	–	**−2.47E+01**	−7.04E+00	**−1.40E+01**	**2.16E+01**	*1.42E+01*	–	–	2.87E-06	**−4.30E-05**

Note. Categories are coded 0 and 1 with reference categories (Female, Siemens, and 3T) coded 0. Age and eTIV are centered by the mean (Age = 47.58; eTIV = 1528926.15). DC: diencephalon, Int: Intercept. RMSE: Root mean square error. *Italic p* <.05; **Bold** *p* <.01.

for age and eTIV and age X sex, eTIV X MFS, MFS X manufacturer, and eTIV X manufacturer interactions. To avoid over fitting and maximize generalizability of the predictions, 10-fold cross-validation (Hastie et al., 2008) with a backward elimination procedure was used to retain the model with the subset of predictors that produced the lowest predicted residual sum of squares using SAS 9.4 PROC GLMSELECT (SAS Institute Inc., Cary, NC, USA). For each brain subdivision, outliers with surface/thickness/volume Z scores higher than 3.29 ($p < .001$) were excluded. Depending on the region, between 0 and 33 outliers out of 2713 were excluded.

A validation R^2 (squared correlation between observed and predicted measures) was calculated using the independent validation sample of healthy controls. The patterns of normality deviations in the validation samples of healthy controls, individuals with AD, and individuals with SZ, was examined through the Z_{OP} effect sizes (Crawford et al., 2012).

Results

DKT atlas

Prediction of normative values

Coefficients predicting surfaces, thicknesses, and volumes for each region are presented in Tables 2–4. The mean explained variance for all regions was 44% (range: 20–65) for surfaces, 29% (range 11–43) for thicknesses, and 48% (range 20–73) for volumes (Fig. 1). The total R^2 were similar to those of the DK protocol for nearly all regional measures, the mean R^2 difference (DKT–DK) of all regions being 0.6% for surfaces, 0.6% for thicknesses, and 0.5% for volumes (Fig. 2). The largest discrepancies were for the left caudal anterior cingulate (R^2 higher in the DKT protocol: 16% surface, 9% thickness, and 24% volume) and rostral middle frontal/rostral anterior cingulate regions (R^2 slightly higher in the DK and DKT protocols, respectively: ≤7%). We observed few discrepancies between DK and DKT protocols in terms of retained predictors (e.g. sex) and predictors' R^2 across regions (Fig. 3), but it resulted in relatively minor discrepancies in overall R^2 (mean 1%, range 1–7% for models with sex discrepancies). Fig. 4 illustrates an example of regions labeling with the largest R^2 discrepancies between protocols.

Validation

Healthy controls. The mean difference between validation and original R^2 for the DKT protocol was 1.4% (range −14 to 13%) for surfaces, 5.3% (range −5 to 19%) for thicknesses, and 1.2% (range −10 to 11%) for volumes, which shows adequate generalization of the models (Fig. 5). The largest negative discrepancies were for bilateral caudal middle frontal surfaces (−13% and −14%), right caudal middle frontal volume (−10%) and right medial orbitofrontal surface (−12%).

The mean Z_{OP} effect size in the healthy control validation group showed very little deviation from the normative values across regions (mean surfaces: −0.04, range −0.26 to 0.18, thicknesses: 0.03, range −0.10 to 0.20, volumes: −0.03, range −0.24 to 0.19). Supplementary Table 1 indicates that for all measures, the mean actual surface, thickness, and volume did not significantly differ from the mean predicted normative value.

AD and SZ individuals. In the AD and SZ groups, normative Z scores showed little difference between DK and DKT protocols, with the left caudal anterior cingulate showing the largest discrepancies (Fig. 6). In individuals with SZ, the mean absolute difference of all regions were 0.04 for surfaces (range: −0.2 to 0.3), 0.05 for thicknesses (range: −0.2 to 0.4), and 0.04 for volumes (range: −0.1 to 0.5). In individuals with AD, the mean absolute difference of all regions were 0.05 for surfaces

Table 3
Coefficients of models predicting cortical thickness for the Desikan-Killiany-Tourville and ex vivo protocols.

		Sociodemographics					Estimated total intracranial volume (eTIV)			Scanner			Interactions					
Region	**RMSE**	**Int**	**Age**	**Age^2**	**Age^3**	**Sex**	**eTIV**	**eTIV^2**	**eTIV^3**	**Strength**	**Manufacturer**		**GEXMFS**	**PhilipsXMFS**	**eTIVXMFS**	**AgeXSex**	**eTIVXGE**	**eTIVXPhilips**
						M/F				**1.5T/3T**	**GE/ Siemens**	**Philips/ Siemens**						
Superior temporal L	0.1474	2.8096	**−2.84E-03**	**−3.28E-05**	*−1.12E-06*	**−2.05E-02**	**8.24E-08**	–	–	**−1.31E-01**	**−5.41E-02**	−1.01E-02	**1.02E-01**	**1.21E-01**	–	*−6.33E-04*	–	–
Superior temporal R	0.1563	2.8579	**−2.69E-03**	**−3.04E-05**	−9.12E-07	−1.22E-02	**6.42E-08**	–	–	**−1.67E-01**	**−8.13E-02**	1.17E-02	**1.68E-01**	**1.51E-01**	–	−5.63E-04	–	–
Middle temporal L	0.1585	2.7494	**−2.04E-03**	5.32E-06	**−1.72E-06**	–	**1.14E-07**	–	–	**−1.61E-01**	**−4.89E-02**	−2.45E-03	**1.37E-01**	**1.41E-01**	–	–	−4.23E-08	*−8.87E-08*
Middle temporal R	0.1605	2.8214	**−2.30E-03**	−7.79E-06	−8.29E-07	−1.24E-02	**1.07E-07**	−1.07E-13	–	**−1.70E-01**	**−6.68E-02**	3.88E-03	**1.58E-01**	**1.60E-01**	–	*−6.04E-04*	−3.01E-09	*−9.38E-08*
Inferior temporal L	0.1828	2.7958	**−8.03E-04**	**−4.24E-05**	–	*−2.09E-02*	**9.49E-08**	–	–	**−1.36E-01**	−2.51E-02	−3.93E-05	**1.40E-01**	**1.62E-01**	4.67E-08	–	−1.23E-07	*−1.09E-07*
Inferior temporal R	0.1881	2.8153	**1.31E-03**	−2.08E-05	**−1.67E-06**	−9.38E-03	**1.38E-07**	−7.50E-14	–	**−2.38E-01**	**−4.91E-02**	−1.47E-02	**2.13E-01**	**2.59E-01**	–	**−1.00E-03**	*−1.57E-07*	**−1.62E-07**
Transverse temporal L	0.2257	2.3237	**−3.57E-03**	**5.42E-05**	**−1.91E-06**	**−6.87E-02**	**1.06E-07**	–	–	−1.86E-02	−2.03E-02	**−1.27E-01**	−2.37E-02	1.01E-01	–	–	–	–
Transverse temporal R	0.2353	2.3636	**−3.27E-03**	*4.17E-05*	*−1.76E-06*	**−6.84E-02**	**1.92E-07**	–	–	**−4.40E-02**	5.33E-03	**−1.10E-01**	−3.26E-02	**1.26E-01**	8.68E-08	–	−1.41E-07	*−1.36E-07*
Entorhinal L	0.3637	3.2858	**3.72E-03**	**−1.09E-04**	−1.94E-06	**7.00E-02**	4.24E-08	–	–	**−3.19E-01**	5.67E-02	2.02E-02	**1.64E-01**	**2.76E-01**	–	–	−3.94E-08	**−2.40E-07**
Entorhinal R	0.4049	3.5046	**3.70E-03**	**−1.39E-04**	–	3.26E-02	1.03E-07	*−4.30E-13*	–	**−4.29E-01**	−5.07E-02	−2.63E-03	2.92E-01	3.80E-01	–	–	−9.54E-08	**−3.67E-07**
Fusiform L	0.1605	2.6293	**−1.17E-03**	**−3.25E-05**	−9.60E-07	*−1.75E-02*	**7.37E-08**	*−1.80E-13*	–	**−2.18E-01**	**4.32E-02**	−1.08E-02	**8.51E-02**	**1.52E-01**	–	–	−7.64E-08	*−8.64E-08*
Fusiform R	0.1707	2.6814	−4.62E-04	*−3.18E-05*	−8.55E-07	−1.23E-02	**8.10E-08**	–	–	**−2.82E-01**	**4.59E-02**	**−6.32E-02**	**1.15E-01**	**2.31E-01**	–	*−7.15E-04*	−1.02E-07	*−1.07E-07*
Parahippocampal L	0.3220	2.7108	**−1.69E-03**	–	–	–	**−1.66E-07**	−2.00E-13	8.81E-19	**−2.96E-01**	4.13E-02	**6.31E-02**	**1.48E-01**	**1.37E-01**	–	–	−1.80E-07	*−1.82E-07*
Parahippocampal R	0.2802	2.7216	−5.27E-04	−2.68E-05	–	**−4.69E-02**	−6.08E-09	–	–	**−3.06E-01**	5.87E-03	2.20E-02	**1.62E-01**	**1.91E-01**	–	−5.35E-04	−1.75E-07	*−1.64E-07*
Superior frontal L	0.1460	2.6235	**−3.73E-03**	**5.84E-05**	**−2.01E-06**	**−4.85E-02**	−4.79E-08	−2.12E-14	*5.01E-19*	**−4.06E-02**	**−3.68E-02**	**−3.83E-02**	**5.87E-02**	**1.22E-01**	–	**−7.42E-04**	*1.33E-07*	2.06E-08
Superior frontal R	0.1455	2.5435	**−3.42E-03**	**6.91E-05**	**−2.08E-06**	**−4.97E-02**	–	–	–	−8.94E-03	7.36E-03	**3.66E-02**	*3.48E-02*	**6.28E-02**	–	**−8.42E-04**	–	–
Rostral middle	0.1432	2.3643	**−3.29E-03**	**6.34E-05**	**−1.80E-06**	**−4.12E-02**	−1.79E-08	−1.65E-14	**5.45E-19**	**−3.79E-02**	−2.02E-02	**−4.57E-02**	**4.55E-02**	**1.12E-01**	–	*−5.88E-04*	**1.50E-07**	−1.21E-08

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Table 3 *(continued)*

		Sociodemographics					Estimated total intracranial volume (eTIV)			Scanner			Interactions					
Region	**RMSE**	**Int**	**Age**	**Age^2**	**Age^3**	**Sex**	**eTIV**	**eTIV^2**	**eTIV^3**	**Strength**	**Manufacturer**		**GEXMFS**	**PhilipsXMFS**	**eTIVXMFS**	**AgeXSex**	**eTIVXGE**	**eTIVXPhilips**
						M/F				**1.5T/3T**	**GE/ Siemens**	**Philips/ Siemens**						
frontal L																		
Rostral middle frontal R	0.1438	2.2627	**−2.99E-03**	**7.22E-05**	**−1.71E-06**	**−3.61E-02**	−1.34E-08	3.37E-14	*4.39E-19*	**2.60E-02**	4.70E-04	**3.15E-02**	1.87E-02	*3.39E-02*	–	*−5.43E-04*	–	–
Caudal middle frontal L	0.1479	2.5169	**−2.97E-03**	**5.52E-05**	**−1.65E-06**	**−4.93E-02**	5.52E-08	−1.56E-14	3.57E-19	**−5.35E-02**	**−3.60E-02**	**−8.09E-02**	*3.67E-02*	**1.32E-01**	–	*−6.24E-04*	–	–
Caudal middle frontal R	0.1494	2.4870	**−2.31E-03**	**6.20E-05**	**−2.25E-06**	**−6.17E-02**	5.76E-08	−6.95E-14	2.94E-19	**−4.80E-02**	**−3.91E-02**	**−3.96E-02**	**5.95E-02**	**8.26E-02**	–	**−9.91E-04**	–	–
Pars opercularis L	0.1518	2.5548	**−4.17E-03**	**6.40E-05**	*−9.96E-07*	**−2.70E-02**	**1.02E-07**	–	–	**−7.50E-02**	*−2.98E-02*	4.10E-03	**5.82E-02**	**4.03E-02**	–	**−7.38E-04**	9.49E-08	−2.86E-08
Pars opercularis R	0.1578	2.5106	**−3.62E-03**	**8.50E-05**	**−1.77E-06**	*−1.58E-02*	**6.88E-08**	–	–	**−6.76E-02**	**−6.19E-02**	1.86E-02	**9.82E-02**	2.89E-02	–	**−8.41E-04**	–	–
Pars triangularis L	0.1516	2.3629	**−4.45E-03**	**6.09E-05**	**−1.32E-06**	**−2.53E-02**	3.51E-08	–	–	**−3.62E-02**	**−4.32E-02**	1.03E-02	**5.75E-02**	*3.10E-02*	–	**−7.50E-04**	**1.67E-07**	3.43E-09
Pars triangularis R	0.1579	2.3455	**−4.93E-03**	**6.91E-05**	−9.57E-07	**−2.51E-02**	−8.06E-09	–	–	8.96E-03	*−3.28E-02*	**7.04E-02**	2.98E-02	*−3.78E-02*	–	−3.99E-04	**1.53E-07**	2.17E-08
Pars orbitalis L	0.1932	2.5641	**−3.81E-03**	**6.48E-05**	**−1.61E-06**	−1.30E-02	−4.39E-08	−1.19E-13	*6.32E-19*	**−8.05E-02**	−3.15E-02	**6.95E-02**	**1.08E-01**	*4.29E-02*	4.37E-08	**−1.03E-03**	–	–
Pars orbitalis R	0.2005	2.5709	**−2.90E-03**	**5.95E-05**	**−2.04E-06**	**−3.50E-02**	−6.26E-09	−1.30E-13	4.15E-19	**−5.28E-02**	−2.63E-03	**7.11E-02**	**7.92E-02**	*4.70E-02*	–	**−1.27E-03**	–	–
Lateral orbitofrontal L	0.1716	2.5795	**−1.93E-03**	**3.27E-05**	−1.06E-06	−1.17E-03	*−9.77E-08*	−6.04E-14	*5.85E-19*	**−9.28E-02**	**7.51E-02**	**7.43E-02**	2.69E-02	**1.02E-01**	*9.63E-08*	**−1.42E-03**	−1.54E-08	*−8.99E-08*
Lateral orbitofrontal R	0.1789	2.5168	**−2.10E-03**	**5.45E-05**	*−1.28E-06*	−1.44E-02	**−1.24E-07**	−1.07E-13	**9.03E-19**	−3.46E-03	**1.03E-01**	**9.35E-02**	−4.17E-02	1.09E-02	–	**−1.16E-03**	–	–
Medial orbitofrontal L	0.1669	2.3386	**−2.60E-03**	**4.65E-05**	−1.06E-06	1.08E-02	−4.63E-08	4.56E-15	**8.41E-19**	*−2.16E-02*	**1.06E-01**	1.16E-02	**−6.33E-02**	*3.99E-02*	–	**−9.91E-04**	–	–
Medial	0.1744	2.3062	**−2.68E-**	**7.66E-**	**−1.49E-**	1.67E-03	−6.02E-	3.42E-14	**7.42E-**	1.59E-02	**1.39E-01**	**1.01E-01**	*−5.95E-*	*−4.09E-02*	–	−6.11E-	–	–

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Table 3 *(continued)*

		Sociodemographics					Estimated total intracranial volume (eTIV)			Scanner			Interactions					
Region	**RMSE**	**Int**	**Age**	**Age^2**	**Age^3**	**Sex**	**eTIV**	**eTIV^2**	**eTIV^3**	**Strength**	**Manufacturer**		**GEXMFS**	**PhilipsXMFS**	**eTIVXMFS**	**AgeXSex**	**eTIVXGE**	**eTIVXPhilips**
						M/F				**1.5T/3T**	**GE/ Siemens**	**Philips/ Siemens**						
orbito-frontal R			**03**	**05**	**06**		08		**19**				*02*			04		
Precentral L	0.1462	2.5149	**−2.71E-03**	**2.86E-05**	**−1.58E-06**	**−3.88E-02**	*6.95E-08*	*−1.40E-13*	–	**−9.90E-02**	−2.44E-02	**−6.64E-02**	−2.55E-02	**7.78E-02**	*−7.27E-08*	*−6.58E-04*	**1.82E-07**	1.46E-08
Precentral R	0.1466	2.4877	**−2.72E-03**	1.17E-05	*−1.09E-06*	**−4.31E-02**	2.76E-08	**−1.83E-13**	–	**−8.04E-02**	−2.23E-02	**−4.87E-02**	−8.04E-03	**3.94E-02**	–	*−6.83E-04*	**1.55E-07**	4.94E-09
Paracentral L	0.1571	2.3549	**−2.85E-03**	**4.96E-05**	**−1.86E-06**	**−3.60E-02**	2.20E-08	–	–	**−5.69E-02**	−1.94E-02	**−1.11E-01**	−1.07E-02	**8.60E-02**	–	–	**1.83E-07**	7.42E-08
Paracentral R	0.1527	2.3734	**−2.55E-03**	**5.00E-05**	**−1.60E-06**	**−3.03E-02**	*5.85E-08*	–	–	**−1.13E-01**	**−4.86E-02**	**−1.53E-01**	1.40E-02	**1.28E-01**	–	*−6.54E-04*	**1.95E-07**	−6.23E-09
Postcentral L	0.1238	2.1015	**−2.45E-03**	3.44E-06	**−1.06E-06**	**−4.91E-02**	**1.05E-07**	–	–	**−4.09E-02**	**−4.03E-02**	**−1.05E-01**	−2.67E-02	**7.47E-02**	–	–	7.76E-08	3.67E-09
Postcentral R	0.1285	2.0765	**−2.43E-03**	−3.00E-06	*−8.97E-07*	**−4.89E-02**	**1.16E-07**	–	–	**−4.78E-02**	**−4.60E-02**	**−1.02E-01**	1.90E-03	**6.99E-02**	–	–	–	–
Supramarginal L	0.1417	2.5217	**−3.28E-03**	5.53E-06	**−1.56E-06**	**−4.85E-02**	**9.30E-08**	–	–	**−6.63E-02**	**−6.67E-02**	**−3.12E-02**	**6.77E-02**	**7.23E-02**	−4.37E-08	−4.61E-04	3.25E-08	−6.83E-08
Supramarginal R	0.1474	2.5348	**−3.57E-03**	3.21E-06	**−1.23E-06**	**−4.33E-02**	**1.05E-07**	–	–	**−8.23E-02**	**−7.83E-02**	**−6.98E-02**	**8.84E-02**	**9.70E-02**	*−7.09E-08*	–	–	–
Superior parietal L	0.1310	2.2055	**−1.68E-03**	3.79E-06	**−1.90E-06**	**−4.89E-02**	**9.42E-08**	–	–	**−6.07E-02**	**−4.78E-02**	**−1.32E-01**	3.91E-03	**1.22E-01**	–	–	–	–
Superior parietal R	0.1317	2.1963	**−1.72E-03**	−5.94E-06	**−1.79E-06**	**−5.51E-02**	**1.23E-07**	–	–	**−4.23E-02**	−1.88E-02	**−1.36E-01**	*−3.33E-02*	**1.02E-01**	*−5.93E-08*	−3.92E-04	–	–
Inferior parietal L	0.1374	2.4172	**−2.91E-03**	−1.01E-05	**−1.63E-06**	**−4.50E-02**	2.89E-08	1.66E-14	*4.15E-19*	**−5.99E-02**	**−5.43E-02**	**−5.60E-02**	**5.62E-02**	**9.39E-02**	–	–	6.53E-08	−3.98E-08
Inferior parietal R	0.1379	2.4623	**−3.13E-03**	−1.62E-05	**−1.47E-06**	**−4.22E-02**	3.28E-08	2.86E-14	3.40E-19	**−9.01E-02**	**−6.82E-02**	**−1.09E-01**	**6.35E-02**	**1.43E-01**	−6.08E-08	–	–	–
Precuneus L	0.1386	2.3536	**−2.72E-03**	1.09E-05	**−1.77E-06**	**−2.88E-02**	**7.99E-08**	–	–	**−7.63E-02**	−1.92E-02	**−7.31E-02**	1.04E-03	**9.17E-02**	–	**−7.01E-04**	–	–
Precuneus R	0.1319	2.3593	**−2.72E-03**	1.20E-05	**−1.68E-06**	**−3.58E-02**	**8.54E-08**	–	–	**−6.58E-02**	2.12E-02	**−7.56E-02**	**−7.14E-02**	**7.31E-02**	–	**−7.08E-04**	*1.09E-07*	−4.06E-08
Lingual L	0.1364	1.9498	**−2.98E-03**	1.30E-05	*−1.02E-06*	*−1.53E-02*	**5.43E-08**	–	–	1.41E-02	**6.86E-02**	**−1.11E-01**	**−1.06E-01**	2.37E-02	–	*−5.32E-04*	–	–
Lingual R	0.1400	1.9990	**−3.38E-03**	9.37E-06	−7.34E-07	−1.23E-02	2.40E-08	*1.35E-13*	3.09E-19	**2.63E-02**	**5.73E-02**	**−1.33E-01**	**−1.40E-01**	−1.44E-02	5.48E-08	–	−8.09E-09	*−7.50E-08*
Pericalcarine L	0.1662	1.5634	**−3.52E-03**	**3.32E-05**	–	−1.46E-02	2.70E-08	*1.81E-13*	3.93E-19	**9.04E-02**	**5.85E-02**	**−1.51E-01**	**−2.17E-01**	−3.10E-02	–	–	–	–
Pericalcarine R	0.1638	1.5636	**−2.51E-03**	**5.81E-05**	**−1.35E-06**	–	−3.00E-09	*1.64E-13*	**6.10E-19**	**7.36E-02**	8.46E-03	**−1.59E-01**	**−1.68E-01**	*−3.90E-02*	–	–	–	–
Cuneus L	0.1425	1.8611	**−2.44E-03**	**3.27E-05**	**−1.48E-06**	**−3.50E-02**	**8.56E-08**	9.32E-14	–	*1.93E-02*	**3.23E-02**	**−1.16E-01**	**−1.09E-01**	*2.92E-02*	–	–	–	–
Cuneus R	0.1429	1.8618	**−2.52E-03**	**3.24E-05**	**−1.30E-06**	**−3.15E-02**	**8.86E-08**	–	–	**3.86E-02**	2.02E-04	**−1.37E-01**	**−1.31E-01**	−3.55E-03	–	–	–	–

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Table 3 *(continued)*

		Sociodemographics					Estimated total intracranial volume (eTIV)			Scanner			Interactions					
Region	**RMSE**	**Int**	**Age**	**Age^2**	**Age^3**	**Sex**	**eTIV**	**eTIV^2**	**eTIV^3**	**Strength**	**Manufacturer**		**GEXMFS**	**PhilipsXMFS**	**eTIVXMFS**	**AgeXSex**	**eTIVXGE**	**eTIVXPhilips**
						M/F				**1.5T/3T**	**GE/ Siemens**	**Philips/ Siemens**						
Lateral occipital L	0.1276	2.1616	**−1.04E-03**	**−4.84E-05**	**−1.66E-06**	**−3.37E-02**	**5.19E-08**	–	–	**−3.61E-02**	−7.28E-03	**−9.12E-02**	−2.16E-02	**6.19E-02**	–	–	–	–
Lateral occipital R	0.1335	2.2233	**−1.23E-03**	**−5.45E-05**	**−1.32E-06**	**−3.27E-02**	**1.02E-07**	–	–	**−4.57E-02**	2.16E-02	**−1.12E-01**	**−6.55E-02**	**8.30E-02**	–	–	−6.20E-08	−5.97E-08
Rostral anterior cingulate L	0.2330	2.7176	**−1.79E-03**	**9.39E-05**	–	−1.24E-04	**−2.22E-07**	5.65E-14	**1.04E-18**	**−2.13E-01**	**8.68E-02**	**8.04E-02**	**9.67E-02**	**1.81E-01**	–	**−1.62E-03**	2.21E-08	−1.08E-07
Rostral anterior cingulate R	0.2487	2.6317	*−1.44E-03*	**1.02E-04**	−1.27E-06	*2.52E-02*	**−2.58E-07**	1.09E-13	*7.09E-19*	**−8.66E-02**	**1.72E-01**	**2.33E-01**	–	–	–	–	–	–
Caudal anterior cingulate L	0.2020	2.6200	**−2.80E-03**	**8.69E-05**	–	**−3.16E-02**	*−7.03E-08*	–	–	**−1.59E-01**	*3.54E-02*	1.07E-02	**1.05E-01**	**1.85E-01**	–	−6.48E-04	–	–
Caudal anterior cingulate R	0.2432	2.4383	−7.32E-04	**1.27E-04**	**−2.25E-06**	–	**−2.90E-07**	−1.48E-14	*8.78E-19*	**−9.44E-02**	**1.38E-01**	**7.23E-02**	3.51E-02	**6.41E-02**	*1.24E-07*	–	–	–
Posterior cingulate L	0.1586	2.4466	**−2.55E-03**	**6.22E-05**	**−1.68E-06**	*−1.34E-02*	–	–	–	**−1.18E-01**	**8.42E-02**	−4.84E-03	1.92E-03	**9.69E-02**	–	**−8.57E-04**	–	–
Posterior cingulate R	0.1557	2.4111	**−3.14E-03**	**6.97E-05**	−7.60E-07	**−2.33E-02**	–	–	–	**−8.85E-02**	**1.38E-01**	**3.04E-02**	*−3.78E-02*	**4.91E-02**	–	**−1.06E-03**	–	–
Isthmus cingulate L	0.2078	2.4190	**−3.57E-03**	1.65E-05	−1.02E-06	3.11E-03	**−1.19E-07**	–	–	**−9.68E-02**	**8.93E-02**	1.16E-02	−3.73E-02	*5.06E-02*	–	*−7.84E-04*	–	–
Isthmus cingulate R	0.1938	2.3492	**−2.69E-03**	**3.86E-05**	**−1.96E-06**	−1.03E-02	**−1.75E-07**	5.54E-14	5.41E-19	**−5.83E-02**	**1.26E-01**	3.88E-03	*−5.83E-02*	1.26E-02	–	**−1.37E-03**	–	–
Insula L	0.1822	3.0081	**−2.39E-03**	**5.99E-05**	−9.38E-07	4.80E-03	−8.24E-09	−1.02E-13	*6.09E-19*	**−1.60E-01**	1.76E-02	2.30E-02	**1.14E-01**	**1.54E-01**	*1.04E-07*	**−9.15E-04**	*1.40E-07*	**−1.42E-07**
Insula R	0.1895	2.9820	**−3.15E-03**	**4.56E-05**	–	−1.93E-03	7.78E-08	3.27E-14	4.94E-19	**−1.67E-01**	7.85E-04	1.75E-02	**1.25E-01**	**1.37E-01**	–	*−9.08E-04*	7.46E-08	−8.59E-08
Ex vivo entorhinal L	0.3521	3.2827	**6.01E-03**	**−8.65E-05**	−2.86E-06	**1.07E-01**	*1.22E-07*	**−4.63E-13**	–	**−2.53E-01**	**−1.81E-01**	**−1.21E-01**	**2.31E-01**	**2.22E-01**	–	–	1.79E-07	**−2.45E-07**
Ex vivo entorhin-	0.3875	3.4615	**6.70E-03**	**−9.72E-05**	*−2.45E-06*	**8.27E-02**	**2.24E-07**	**−4.51E-13**	−5.60E-19	**−3.57E-01**	**−2.04E-01**	**−1.71E-01**	**2.57E-01**	**3.20E-01**	–	–	8.16E-08	**−3.97E-07**

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Table 3 *(continued)*

Region	RMSE	Sociodemographics					Estimated total intracranial volume (eTIV)			Scanner			Interactions					
		Int	Age	Age^2	Age^3	Sex	eTIV	eTIV^2	eTIV^3	Strength	Manufacturer		GEXMFS	PhilipsXMFS	eTIVXMFS	AgeXSex	eTIVXGE	eTIVXPhilips
						M/F				1.5T/3T	GE/ Siemens	Philips/ Siemens						
al R																		
Ex vivo perirhinal L	0.3495	3.1784	**1.89E-03**	**−7.34E-05**	–	*3.77E-02*	**−2.17E-07**	–	–	**−3.40E-01**	2.56E-02	4.50E-02	**1.95E-01**	**2.50E-01**	–	−5.63E-04	–	–
Ex vivo perirhinal R	0.3692	3.3676	**3.07E-03**	**−1.01E-04**	–	–	1.79E-08	*−3.46E-13*	–	**−3.97E-01**	−2.64E-02	−1.48E-02	**2.32E-01**	**3.39E-01**	–	–	−9.84E-08	**−3.13E-07**

Note. Categories are coded 0 and 1 with reference categories (Female, Siemens, and 3T) coded 0. Age and eTIV are centered by the mean (Age = 47.58; eTIV = 1528926.15). DC: diencephalon, Int: Intercept. RMSE: Root mean square error. *Italic p* <.05; **Bold** *p* <.01.

(range: −0.2 to 0.2), 0.04 for thicknesses (range: −0.1 to 0.3), and 0.04 volumes (range: −0.2 to 0.3).

Pearson correlations revealed that the mean correlations between DK and DKT normative Z scores of all regions were very strong in both groups (SZ: .96 for surfaces, .98 for thicknesses, and .96 for volumes, AD: .95 for surfaces, .98 for thicknesses, and .96 for volumes). In the AD group, the weakest correlations were the left caudal anterior cingulate surface (.67) and volume (.49), and bilateral pars orbitalis surface (Left: .78, Right: .71), thickness (Left: .73, Right: .86), and volume (Left: .80, Right: .74). In the SZ group, the weakest correlations were the left pars orbitalis surface (.67), thickness (.71), and volume (.72), the left caudal anterior cingulate surface (.79) and volume (.73), and right insula surface (.75).

Ex vivo atlas

Prediction of normative values

Coefficients to predict entorhinal and perirhinal normative values are shown in Tables 2–4. R^2 values for the entorhinal cortex were similar to those of the DK and DKT protocols (Surface L: 32% R: 22%, Thickness L: 15% R: 19%, Volume L: 25% R: 24%) with a mean absolute difference of 1.5% for ex vivo and DK and 1.6% for ex vivo and DKT atlases (highest difference: 3%). R^2 values for the perirhinal cortex were similar to those of the entorhinal (Surface L: 36% R: 26%, Thickness L: 16% R: 18%, Volume L: 22% R: 25%).

Validation

The mean difference between validation and original R^2 was 1.6% (range −7 to 7%), the largest negative discrepancies being the right perirhinal volume (Fig. 5) and the mean actual surface, thickness, and volume did not significantly differ from the mean predicted normative value (Supplementary Table 1). Similar to the DKT results, the mean Z_{OP} effect size for the ex vivo entorhinal and perirhinal measures in the healthy control validation group showed minor deviation from the normative values (range −0.17 to 0.21).

Comparison of the entorhinal cortex between DK, DKT, and ex vivo atlases

The distribution of entorhinal cortical normative Z scores of the three protocols (DK, DKT, and *ex vivo*) in the AD group are displayed in Fig. 7. Except for the left surface, the entorhinal Z scores deviations from the normality were highly similar between atlases and the differences between true and normative expected values yielded equivalent *p*-values (Fig. 7). Pearson correlations revealed very strong associations between DKT and DK entorhinal normative Z scores (Surface L: .96, R: .93; Thickness L: .99, R: .99; Volume L: .95, R: .93) and moderate to strong associations between ex vivo and DK atlases (Surface L: .61, R: .67; Thickness L: .86, R: .83; Volume L: .79, R: .68).

Discussion

The first objective of this study was to produce *FreeSurfer* morphometric cortical normative data using the DKT and ex vivo protocol using the same procedure to produce normative values for the DK protocol (Potvin et al., 2017). We provide formulas to compute expected surfaces, thicknesses, and volumes based on the characteristics of the individual and the scanner. The regression formula is the addition of the intercept and each predictors' coefficient multiplied by its value (e.g. left superior temporal: 5001.8+−5.36*(age-centered)+−0.0464*(age-centered squared)+ …). Deviations from the normative sample in terms of Z scores effect size can also be computed by dividing the difference between real and expected values by the root

Table 4
Coefficients of models predicting cortical volume for the Desikan-Killiany-Tourville and ex vivo protocols.

			Sociodemographics				**Estimated total intracranial volume (eTIV)**			**Scanner**			**Interactions**					
Region	**RMSE**	**Int**	**Age**	**Age^2**	**Age^3**	**Sex**	**eTIV**	**eTIV^2**	**eTIV^3**	**Strength**	**Manufacturer**		**GEXMFS**	**PhilipsXMFS**	**eTIVXMFS**	**AgeXSex**	**eTIVXGE**	**eTIVXPhilips**
						M/F				**1.5T/3T**	**GE/ Siemens**	**Philips/ Siemens**						
Superior temporal L	1462.36	16144.2	**−3.30E+01**	9.30E-02	*−1.22E-02*	**3.36E+02**	**6.95E-03**	**1.93E-09**	–	**−3.43E+02**	**−2.68E+02**	**−2.93E+02**	–	–	–	**−1.21E+01**	–	–
Superior temporal R	1320.86	15420.4	**−3.63E+01**	1.51E-01	−7.33E-03	5.10E+01	**6.69E-03**	**2.65E-09**	–	**−5.09E+02**	**−4.17E+02**	**−2.67E+02**	*3.70E+02*	*2.91E+02*	–	−5.00E+00	−2.59E-04	*−7.99E-04*
Middle temporal L	1414.22	13099.5	**−2.95E+01**	5.33E-02	*−1.16E-02*	*1.68E+02*	**7.48E-03**	7.09E-10	−4.23E-15	**−7.55E+02**	−2.26E+02	**−6.47E+02**	2.17E+02	**8.02E+02**	–	**−8.85E+00**	−4.17E-04	−1.53E-03
Middle temporal R	1366.08	13306.0	**−3.24E+01**	*1.99E-01*	*−1.08E-02*	1.26E+02	**7.66E-03**	1.24E-09	**−6.18E-15**	**−6.58E+02**	3.57E+01	**−3.59E+02**	−1.52E+02	**5.20E+02**	−4.20E-04	**−8.16E+00**	7.62E-04	*−8.03E-04*
Inferior temporal L	1344.27	11104.2	**−1.73E+01**	−4.89E-02	−6.42E-03	**1.77E+02**	**5.58E-03**	**1.76E-09**	–	**−2.75E+02**	**4.06E+02**	*−2.27E+02*	*−3.60E+02*	**4.54E+02**	5.57E-04	−4.42E+00	−3.22E-04	*−8.79E-04*
Inferior temporal R	1415.87	11776.5	**−1.04E+01**	−6.61E-02	**−1.25E-02**	1.17E+02	**6.63E-03**	*1.67E-09*	–	**−9.57E+02**	−6.38E+01	**−4.61E+02**	*4.24E+02*	1.13E+03	–	*−5.49E+00*	−7.02E-04	**−1.17E-03**
Transverse temporal L	197.35	1130.5	**−2.40E+00**	*3.24E-02*	**−1.73E-03**	−1.71E+01	**5.74E-04**	1.40E-10	−4.22E-16	*2.21E+01*	−2.89E+01	**−6.21E+01**	**−6.34E+01**	−3.44E+01	–	–	–	–
Transverse temporal R	150.44	875.3	**−1.72E+00**	−4.64E-03	*−1.10E-03*	–	**4.39E-04**	1.30E-10	−3.58E-16	–	−1.46E+01	**−4.85E+01**	–	–	–	–	–	–
Entorhinal L	294.25	1691.3	**3.70E+00**	**−9.74E-02**	**−3.06E-03**	**1.05E+02**	**7.51E-04**	–	–	**−1.09E+02**	−4.77E+00	−8.83E+00	**1.45E+02**	**1.65E+02**	*1.43E-04*	–	4.59E-05	**−2.31E-04**
Entorhinal R	344.61	1796.3	**3.34E+00**	**−1.14E-01**	–	**7.47E+01**	**9.80E-04**	–	–	**−2.60E+02**	**−8.14E+01**	**−1.52E+02**	**2.58E+02**	**3.25E+02**	–	–	−6.72E-05	−4.16E-04
Fusiform L	1094.87	8499.2	**−1.60E+01**	3.43E-03	*−9.00E-03*	**1.59E+02**	**4.57E-03**	3.66E-10	*−3.92E-15*	**−5.80E+02**	−9.49E+01	**−4.77E+02**	6.22E+01	**3.72E+02**	–	–	−6.07E-04	**−8.57E-04**
Fusiform R	1015.28	8173.1	**−1.11E+01**	−7.88E-02	−5.57E-03	**3.27E+02**	**3.81E-03**	*1.02E-09*	–	**−9.55E+02**	−5.37E+01	**−6.83E+02**	1.67E+02	**7.34E+02**	–	**−5.47E+00**	1.67E-04	**−6.79E-04**
Parahippocampal L	307.83	2236.8	**−2.59E+00**	−2.66E-02	**−2.65E-03**	–	**8.12E-04**	–	–	**−2.21E+02**	−1.63E+01	−4.21E+01	*8.74E+01*	5.60E+01	−1.32E-04	–	–	–
Parahippocampal R	274.43	2066.5	**−2.73E+00**	*−4.54E-02*	−1.15E-03	–	**7.72E-04**	2.06E-10	–	**−2.30E+02**	−3.81E+01	*−4.05E+01*	**1.30E+02**	**7.63E+01**	–	–	9.71E-05	−1.32E-04
Superior frontal L	1965.74	23790.9	**−7.94E+01**	**1.11E+00**	**−2.09E-02**	2.36E+01	**1.09E-02**	**4.39E-09**	–	3.10E+01	**−4.56E+02**	**−1.07E+03**	**−6.49E+02**	1.41E+02	–	**−1.18E+01**	–	–
Superior frontal R	2205.37	26159.9	**−8.51E+01**	**1.26E+00**	**−2.40E-02**	4.88E+01	**1.33E-02**	**4.74E-09**	**−8.99E-15**	−3.17E+01	*−4.54E+02*	**−7.46E+02**	*−6.10E+02*	−1.59E+01	–	**−1.42E+01**	9.80E-04	−5.18E-04
Rostral middle frontal L	1229.03	10538.8	**−4.83E+01**	**4.90E-01**	–	3.48E+01	**6.34E-03**	**2.29E-09**	**−5.93E-15**	*−1.45E+02*	1.19E+02	**−6.28E+02**	*−3.85E+02*	*2.77E+02*	−5.76E-04	*−5.23E+00*	**1.31E-03**	−3.55E-04
Rostral middle frontal R	1244.55	9747.1	**−3.93E+01**	**5.30E-01**	*−8.63E-03*	–	**5.68E-03**	**3.28E-09**	−3.23E-15	3.65E+01	1.68E+02	*−1.85E+02*	**−4.23E+02**	−7.34E+01	–	–	–	–
Caudal middle frontal L	953.99	6445.6	**−2.00E+01**	**2.83E-01**	**−8.36E-03**	−8.36E+01	**4.06E-03**	**1.47E-09**	*−3.40E-15*	**−1.45E+02**	−1.52E+02	**−3.66E+02**	−1.92E+02	1.83E+02	–	–	4.14E-04	*−4.78E-04*
Caudal middle frontal R	929.85	5945.9	**−1.76E+01**	**2.42E-01**	*−6.51E-03*	**−1.87E+02**	**4.39E-03**	8.12E-10	**−5.06E-15**	−3.63E+01	2.81E+01	**−2.09E+02**	−2.18E+02	−5.51E+01	–	*−4.32E+00*	5.66E-04	**−6.09E-04**
Pars opercularis L	617.49	4179.1	**−1.63E+01**	**1.61E-01**	–	−9.17E+00	**2.06E-03**	5.12E-10	–	*−8.61E+01*	−3.13E+01	**−1.52E+02**	**−1.96E+02**	−2.88E+01	–	**−3.91E+00**	2.44E-04	−2.20E-04
Pars opercularis R	586.63	3988.8	**−1.54E+01**	**1.04E-01**	–	1.78E+01	**2.10E-03**	2.59E-10	**−2.47E-15**	–	**−1.80E+02**	**−1.97E+02**	–	–	–	**−3.06E+00**	–	–
Pars triangularis L	651.46	4094.8	**−1.78E+01**	**1.85E-01**	−2.40E-03	**1.09E+02**	**1.71E-03**	**1.30E-09**	–	**−7.44E+01**	**−1.22E+02**	**−1.91E+02**	–	–	–	**−3.86E+00**	–	–
Pars triangularis	720.25	4063.4	**−2.04E**	**2.25E-**	–	**1.53E**	**1.34E-**	*8.33E-*	–	−8.58E	**−1.66E**	**−1.66E**	–	–	*3.39E-04*	**−4.07E**	–	–

(continued on next page)

Table 4 *(continued)*

Region	RMSE	Int	Sociodemographics				Estimated total intracranial volume (eTIV)			Scanner			Interactions					
			Age	Age^2	Age^3	Sex	eTIV	$eTIV^2$	$eTIV^3$	Strength	Manufacturer		GEXMFS	PhilipsXMFS	eTIVXMFS	AgeXSex	eTIVXGE	eTIVXPhilips
						M/F				1.5T/3T	GE/ Siemens	Philips/ Siemens						
R			**+01**	**01**		**+02**	**03**	*10*		+00	**+02**	**+02**				**+00**		
Pars orbitalis L	279.70	2083.1	**−5.15E +00**	**9.45E-02**	**−2.84E-03**	*3.27E +01*	**7.90E-04**	–	–	**−6.87E +01**	–	–	–	–	–	**−1.65E +00**	–	–
Pars orbitalis R	345.16	2504.9	**−6.42E +00**	**1.18E-01**	**−2.98E-03**	**6.40E +01**	**8.56E-04**	1.36E-11	5.22E-16	**−6.82E +01**	−1.77E +01	−2.23E+01	–	–	–	**−2.41E +00**	1.69E-04	−6.97E-05
Lateral orbitofrontal L	755.30	8087.7	**−1.64E +01**	**2.18E-01**	*−5.89E-03*	5.43E +01	**3.85E-03**	6.81E-10	–	**−4.56E +02**	9.08E +01	**−2.60E +02**	−9.19E +01	**5.81E+02**	*4.04E-04*	**−5.54E +00**	*5.41E-04*	*−4.55E-04*
Lateral orbitofrontal R	743.23	8053.4	**−1.85E +01**	**2.68E-01**	**−6.50E-03**	5.16E +01	**3.61E-03**	6.43E-10	–	*8.71E+01*	**3.56E +02**	*−1.08E+02*	**−6.25E +02**	3.31E+01	–	**−4.90E +00**	**7.88E-04**	−1.87E-04
Medial orbitofrontal L	460.96	4195.4	**−1.20E +01**	**1.07E-01**	−1.77E-03	2.58E +01	**2.02E-03**	**7.45E-10**	–	**8.04E +01**	**4.02E +02**	**−1.23E +02**	**−4.82E +02**	−8.55E+01	–	*−2.22E +00*	–	–
Medial orbitofrontal R	442.73	4096.9	**−1.05E +01**	**1.49E-01**	−2.64E-03	**6.57E +01**	**1.71E-03**	*4.53E-10*	–	−2.32E +01	**2.40E +02**	**−9.01E +01**	**−2.97E +02**	−5.52E+01	2.06E-04	*−2.02E +00*	–	–
Precentral L	1269.81	12807.4	**−2.72E +01**	**3.47E-01**	**−1.06E-02**	**2.14E +02**	**4.83E-03**	–	–	**−3.61E +02**	**−3.72E +02**	**−8.14E +02**	*−3.59E +02*	1.85E+02	–	**−8.43E +00**	**1.64E-03**	−1.72E-04
Precentral R	1218.88	12458.4	**−3.00E +01**	–	–	**1.75E +02**	**4.91E-03**	*1.14E-09*	–	*−1.71E +02*	**−3.15E +02**	**−5.81E +02**	**−4.16E +02**	−1.83E+02	–	**−8.66E +00**	*9.74E-04*	−3.70E-04
Paracentral L	546.86	3926.4	**−8.61E +00**	*8.24E-02*	*−3.40E-03*	−3.87E +01	**1.90E-03**	**8.44E-10**	−1.35E-15	−4.86E +00	**−1.68E +02**	**−3.46E +02**	*−1.48E +02*	4.76E+01	–	*−1.99E +00*	–	–
Paracentral R	561.72	4051.7	**−1.17E +01**	–	–	–	**1.88E-03**	**8.75E-10**	−8.06E-16	**−7.78E +01**	**−2.52E +02**	**−3.48E +02**	–	–	–	–	–	–
Postcentral L	1166.65	10719.0	**−2.16E +01**	*1.89E-01*	*−8.16E-03*	−5.09E +01	**5.19E-03**	4.44E-10	*−4.11E-15*	**−2.00E +02**	**−5.49E +02**	**−7.97E +02**	−2.24E +02	9.51E+01	–	−4.24E +00	–	–
Postcentral R	1124.56	9835.6	**−2.18E +01**	*1.78E-01*	−6.74E-03	−1.09E +02	**4.74E-03**	9.25E-10	−2.49E-15	**−1.93E +02**	**−4.37E +02**	**−6.51E +02**	–	–	−2.37E-04	–	–	–
Supramarginal L	1215.70	10197.9	**−2.68E +01**	*1.67E-01*	−6.96E-03	8.62E +01	**5.71E-03**	1.01E-09	**−7.25E-15**	**−2.82E +02**	**−3.50E +02**	**−3.31E +02**	–	–	–	−3.72E +00	–	–
Supramarginal R	1137.19	9485.4	**−2.38E +01**	*1.77E-01*	*−7.57E-03*	−8.05E +01	**4.80E-03**	**1.41E-09**	−3.10E-15	**−1.48E +02**	**−3.83E +02**	**−4.63E +02**	–	–	–	**−6.60E +00**	–	–
Superior parietal L	1193.70	10490.4	**−2.43E +01**	−3.66E-02	−5.94E-03	**−2.69E +02**	**5.25E-03**	**1.55E-09**	**−4.75E-15**	**−3.04E +02**	*−2.21E +02*	**−7.58E +02**	*−3.63E +02*	**4.48E+02**	–	−3.48E +00	–	–
Superior parietal R	1233.31	11278.6	**−2.42E +01**	−1.13E-01	−6.82E-03	**−2.19E +02**	**5.42E-03**	**1.69E-09**	**−5.18E-15**	**−2.78E +02**	*−2.17E +02*	**−9.42E +02**	**−3.84E +02**	**4.45E+02**	–	**−6.61E +00**	–	–
Inferior parietal L	1382.38	11456.0	**−2.46E +01**	**3.27E-01**	**−1.87E-02**	1.85E +01	**5.50E-03**	*1.24E-09*	–	**−3.52E +02**	**−4.42E +02**	**−6.70E +02**	2.79E+02	**4.21E+02**	–	**−1.01E +01**	*1.18E-03*	−4.13E-04
Inferior parietal R	1553.54	13609.1	**−3.62E +01**	1.92E-01	**−1.48E-02**	**3.25E +02**	**6.13E-03**	**1.94E-09**	–	**−6.26E +02**	**−5.46E +02**	**−1.06E +03**	−3.45E +01	**7.19E+02**	–	**−8.25E +00**	8.19E-04	**−1.03E-03**
Precuneus L	916.22	9288.9	**−2.52E +01**	**2.06E-01**	*−6.05E-03*	2.84E +01	**4.75E-03**	**1.14E-09**	−2.65E-15	**−2.48E +02**	**−2.70E +02**	**−5.17E +02**	**−3.67E +02**	1.43E+02	–	**−6.58E +00**	5.75E-04	−4.24E-04
Precuneus R	987.02	9876.0	**−2.61E +01**	**2.60E-01**	*−7.43E-03*	**1.27E +02**	**4.77E-03**	**1.72E-09**	–	**−2.01E +02**	*−2.06E +02*	**−5.95E +02**	**−5.74E +02**	1.43E+02	–	**−6.63E +00**	*7.35E-04*	*−6.06E-04*
Lingual L	903.45	6400.8	**−1.19E +01**	2.31E-02	**−8.15E-03**	**1.25E +02**	**2.84E-03**	*9.41E-10*	−2.02E-15	*−1.17E +02*	1.20E +00	**−7.55E +02**	*−2.37E +02*	1.62E+02	–	**−5.36E +00**	4.30E-05	**−7.37E-04**
Lingual R	879.52	6634.1	**−1.34E +01**	1.60E-02	*−6.98E-03*	**1.31E +02**	**2.60E-03**	**1.23E-09**	–	2.12E+01	−8.81E +01	**−8.39E +02**	**−4.78E +02**	6.20E+00	–	*−4.18E +00*	−6.70E-05	**−8.89E-04**
Pericalcarine L	385.42	1957.7	**−6.42E +00**	**7.68E-02**	–	1.77E +01	**8.83E-04**	**8.66E-10**	–	1.82E+01	−1.94E +01	**−2.83E +02**	**−1.70E +02**	6.26E+01	–	–	–	–
Pericalcarine R	417.16	2202.0	**−4.43E**	**9.12E-**	*−2.89E-*	3.89E	**1.08E-**	**8.46E-**	–	3.96E+01	*−8.57E*	**−3.31E**	**−1.94E**	3.40E+01	*−2.04E-04*	–	–	–

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Table 4 *(continued)*

Region	RMSE	Int	Sociodemographics				Estimated total intracranial volume (eTIV)			Scanner			Interactions					
			Age	Age^2	Age^3	Sex	eTIV	$eTIV^2$	$eTIV^3$	Strength	Manufacturer		GEXMFS	PhilipsXMFS	eTIVXMFS	AgeXSex	eTIVXGE	eTIVXPhilips
						M/F				1.5T/3T	GE/ Siemens	Philips/ Siemens						
			+00	**02**	*03*	+01	**03**	**10**			*+01*	**+02**	**+02**					
Cuneus L	578.02	3961.5	**−1.12E +01**	–	–	4.53E +01	**1.56E-03**	**1.01E-09**	–	–	**−1.56E +02**	**−3.33E +02**	–	–	–	−2.07E +00	–	–
Cuneus R	527.77	3721.1	**−1.13E +01**	–	–	–	**1.88E-03**	**6.72E-10**	−8.64E-16	**1.33E +02**	−7.39E +01	**−3.53E +02**	**−4.10E +02**	−8.89E+01	–	–	2.18E-04	−2.27E-04
Lateral occipital L	1306.69	11522.8	**−1.53E +01**	*−2.38E-01*	**−1.22E-02**	**2.99E +02**	**4.89E-03**	**1.97E-09**	–	**−2.27E +02**	−9.63E +01	**−9.46E +02**	*−4.05E +02*	**3.79E+02**	–	−4.54E +00	2.15E-04	**−9.18E-04**
Lateral occipital R	1363.72	11652.5	**−2.02E +01**	*−2.40E-01*	−7.86E-03	**3.85E +02**	**5.73E-03**	*1.34E-09*	−3.94E-15	−1.33E +02	−1.13E +02	**−9.22E +02**	**−6.09E +02**	**3.49E+02**	–	−4.35E +00	−5.09E-04	**−1.18E-03**
Rostral anterior cingulate L	466.51	3246.7	**−6.43E +00**	**1.12E-01**	–	–	**2.18E-03**	**1.17E-09**	−9.89E-16	**−2.75E +02**	−7.52E +01	−3.71E+01	3.85E+01	**1.65E+02**	−1.96E-04	–	–	–
Rostral anterior cingulate R	416.34	2286.1	**−4.52E +00**	**7.70E-02**	–	–	**1.44E-03**	**9.44E-10**	–	**−1.42E +02**	1.43E +01	*4.37E+01*	–	–	–	–	–	–
Caudal anterior cingulate L	441.35	2991.1	**−7.48E +00**	**1.15E-01**	*−2.72E-03*	−2.54E +01	**1.81E-03**	**9.60E-10**	*−1.37E-15*	**−1.68E +02**	**−1.31E +02**	**−8.96E +01**	*1.09E+02*	**1.44E+02**	*−2.29E-04*	–	–	–
Caudal anterior cingulate R	462.10	2171.6	**−3.33E +00**	**1.17E-01**	*−3.43E-03*	–	**9.44E-04**	–	–	**−1.13E +02**	−2.34E +01	*−7.73E+01*	−5.95E +00	**1.15E+02**	–	–	–	–
Posterior cingulate L	429.20	3265.6	**−7.47E +00**	**1.50E-01**	**−3.60E-03**	**5.77E +01**	**1.59E-03**	2.62E-10	*−1.59E-15*	**−1.81E +02**	**−1.76E +02**	**−1.79E +02**	9.23E+01	*1.01E+02*	–	**−3.03E +00**	–	–
Posterior cingulate R	431.83	3256.1	**−8.24E +00**	**1.09E-01**	−2.46E-03	3.06E +01	**1.71E-03**	**5.56E-10**	−1.12E-15	**−1.29E +02**	−5.99E +01	**−1.34E +02**	*−1.26E +02*	*8.95E+01*	–	**−2.13E +00**	–	–
Isthmus cingulate L	362.56	2559.1	**−6.54E +00**	*5.51E-02*	–	**9.09E +01**	**1.49E-03**	1.58E-10	**−1.83E-15**	**−8.99E +01**	*−7.73E +01*	**−1.78E +02**	−7.31E +01	3.60E+01	–	*−1.68E +00*	–	–
Isthmus cingulate R	357.24	2396.9	**−6.43E +00**	3.70E-02	–	**4.71E +01**	**1.34E-03**	**8.06E-10**	–	–	**−8.94E +01**	**−1.85E +02**	–	–	–	**−1.75E +00**	1.90E-05	*−2.05E-04*
Insula L	486.12	5893.4	**−6.71E +00**	**9.46E-02**	–	**7.22E +01**	**2.66E-03**	**9.62E-10**	–	**−1.02E +02**	**−2.15E +02**	**−1.69E +02**	1.15E+02	7.45E+01	**3.95E-04**	**−3.06E +00**	2.01E-04	**−3.80E-04**
Insula R	517.48	6054.2	**−7.71E +00**	**9.62E-02**	–	**1.02E +02**	**2.61E-03**	**1.06E-09**	–	**−6.78E +01**	**−1.46E +02**	**−1.42E +02**	–	–	*2.83E-04*	**−2.89E +00**	**5.19E-04**	−1.50E-04
Ex vivo entorhinal L	191.01	1136.0	**1.77E +00**	**−7.15E-02**	*−1.39E-03*	**8.62E +01**	**4.13E-04**	−1.13E-10	−4.27E-16	**−1.32E +02**	**−7.72E +01**	**−8.87E +01**	**1.04E +02**	**1.13E+02**	–	–	9.87E-05	*−1.02E-04*
Ex vivo entorhinal R	182.58	1004.4	**1.96E +00**	**−5.22E-02**	*−1.24E-03*	**5.49E +01**	**4.08E-04**	–	–	**−1.54E +02**	**−7.22E +01**	**−1.14E +02**	**9.83E +01**	**1.29E+02**	–	3.47E-01	3.71E-05	**−2.54E-04**
Ex vivo perirhinal L	439.03	2709.3	−7.83E-02	**−9.70E-02**	−2.49E-03	**1.32E +02**	**7.69E-04**	–	–	**−2.86E +02**	−2.22E +01	−1.81E+01	**1.57E +02**	**1.84E+02**	–	–	–	–
Ex vivo perirhinal R	293.74	1924.1	*6.22E-01*	**−9.21E-02**	–	**6.03E +01**	**7.41E-04**	–	–	**−2.72E +02**	−1.37E +01	**−1.08E +02**	**1.30E +02**	**2.08E+02**	–	–	−2.12E-05	**−3.64E-04**

Note. Categories are coded 0 and 1 with reference categories (Female, Siemens, and 3T) coded 0. Age and eTIV are centered by the mean (Age – 47.58; eTIV – 1528926.15). DC: diencephalon, Int: Intercept. RMSE: Root mean square error.
Italic p
<.05; **Bold** *p*
<.01.

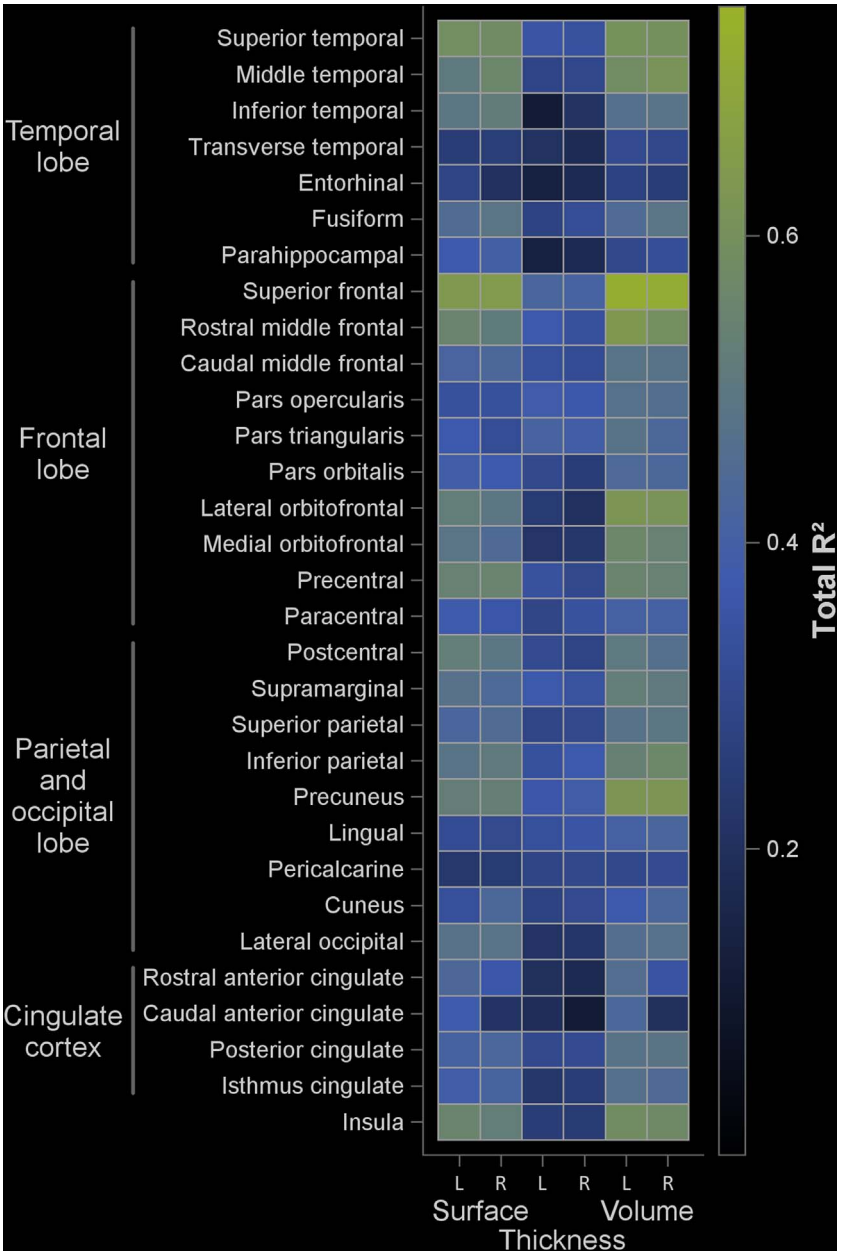

Fig. 1. Total R^2 for the DKT models predicting regional surfaces, thicknesses, and volumes.

mean square error. For example, using formulas for left superior temporal gyrus, a 71 year old male with an eTIV of 1320777 mm^3 (estimation from *FreeSurfer*) scanned on a Philips 1.5T would be expected to have a surface of 4359 mm^2, a thickness of 2.64 mm, and a volume of 13322 mm^3. In the context that the left superior temporal gyrus of this individual has a surface of 4603 mm^2, a thickness of 2.20 mm, and a volume of 10653 mm^3, the difference between the real value (Observed) and the expected normative value (Predicted) divided by the root mean square of the predicting model yields effect size Z scores (Z_{OP}) of 0.61, −2.97, and −1.83, respectively. The Z scores have a mean of 0 and a standard deviation (SD) of 1 and denote that in reference to the normative sample, the individual has a thickness and volume of 3 and nearly 2 SDs below what is expected for his age, sex, and eTIV, respectively. Furthermore, a Microsoft Excel spreadsheet able to compute these Z scores and various statistics including single case significance test of volume abnormality and estimated percentage of the normative population with a smaller volume is provided as supplemental material. In addition, we provide a python script producing normative Z scores for multiple participants using the Desikan-Killiany-Tourville and ex vivo atlases, but also able to use the default cortical and subcortical parcellation protocols (Potvin et al., 2017; Potvin et al., 2016a).

The second objective was to compare the predicting models between the DKT and DK protocols. Despite differences in the labeling protocols, we expected similar normative models including the same predictors and similar explained variance for each region. The results validated these expectations. Like results from the DK atlas (Potvin et al., 2017), those from the DKT atlas showed that for regional cortical surfaces and thicknesses, age, sex and eTIV accounted for nearly all of the total R^2 while MFS and manufacturer accounted for no or negligible amount of variance. The pattern of results between DK and DKT atlases were also identical for cortical thickness; R^2 were substantially smaller than for surfaces and volumes and age was nearly the sole substantial predictor, with MFS and manufacturer explaining a small amount of

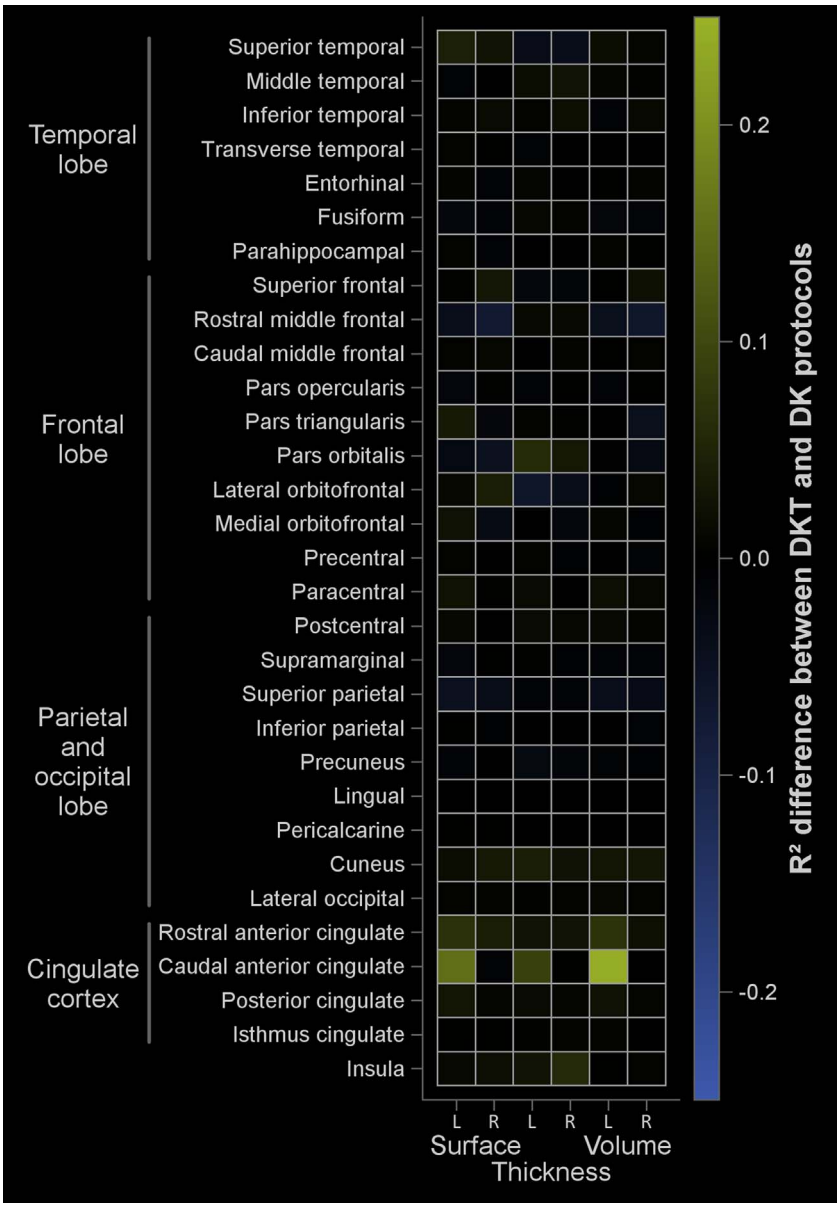

Fig. 2. R^2 difference between the DKT and DK labeling protocols in the models predicting surfaces, thicknesses, and volumes. Green: DKT having higher R^2. Blue: DK having higher R^2.

variance in a few regions (e.g. fusiform, pericalcarine) and sex and eTIV having no or negligible impact. First, there were nearly no difference at all in terms of total R^2, except for the left caudal anterior cingulate. Secondly, the selection of predictors was identical in the vast majority of the models. A few regions showed differences, which were generally the inclusion of sex for one protocol, but not for the other one. In these cases, the total R^2 was generally similar since the protocol omitting sex generally produced a model with eTIV explaining a larger variance. In addition to these minor discrepancies, we observed more substantial differences for the left caudal anterior cingulate since the increased of R^2 for age and eTIV in the DKT protocol did not match a loss of R^2 in other predictors resulting in higher total R^2 in the DKT protocol compared to the DK protocol. As illustrated, in the DKT protocol this region includes substantial parts of the cortex labeled as superior frontal gyrus in the DK protocol.

While DK and DKT protocols produced a few notable discrepancies, it is hard to favor one or the other at moment. The DKT protocol has the advantage of removing a few regions that have less distinct anatomical boundaries (i.e. temporal and frontal poles, banks of the superior temporal sulcus), which likely improves the automatic labeling procedure and the reliability of manual edits in neighboring regions (Klein and Tourville, 2012). On the other hand, the DK protocol relies on a training set of individuals that covers a larger age range and atrophy variability than the DKT protocol, since it comprises older adults and individuals with AD (Desikan et al., 2006). The results of the present study highlight the need for harmonized segmentation protocols for the whole brain. Such initiative was done for several medial temporal lobe regions (Boccardi et al., 2015; Frisoni et al., 2015; Yushkevich et al., 2015) and could be highly beneficial for the remaining of the cortex.

The third objective was to compare the entorhinal cortical measure between the three protocols (DK, DKT, and ex vivo). Our results showed very little difference in a group of individuals with AD and the correlations between measures were relatively high, especially between DK and DKT measures. Thus, the choice of atlas for this brain region does not appear to have a notable impact.

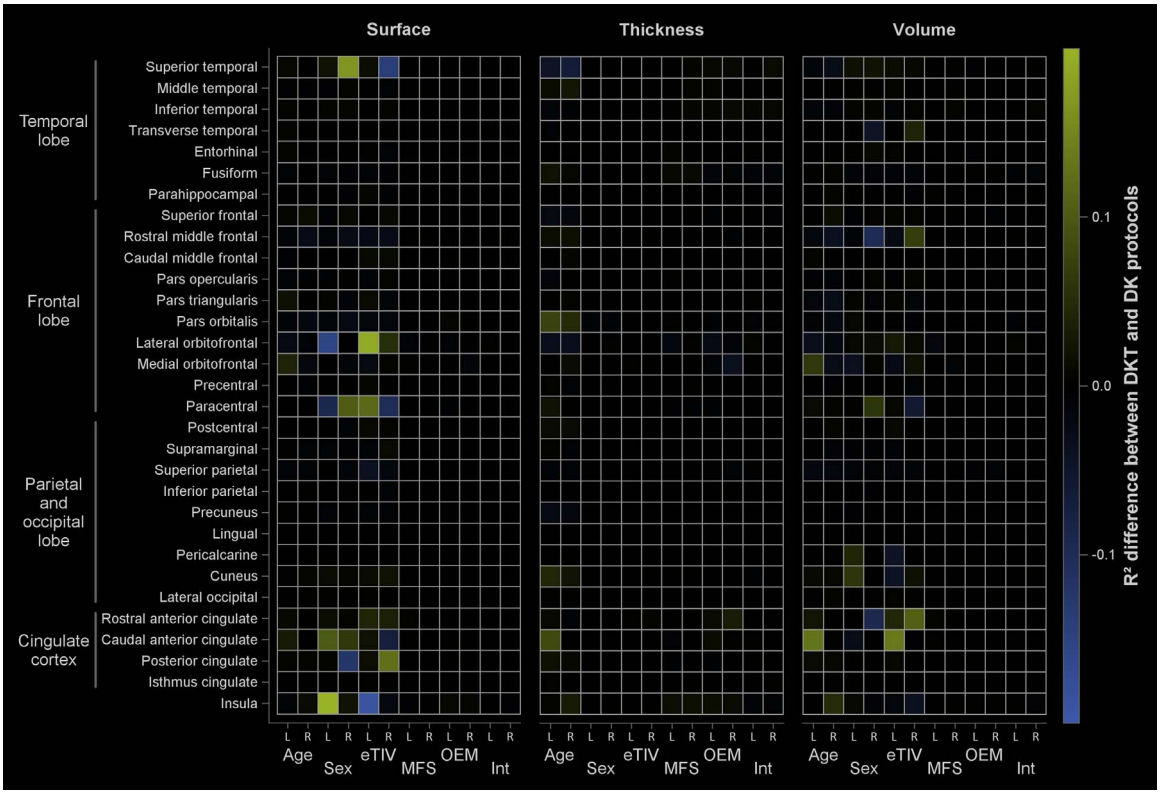

Fig. 3. Predictors R^2 difference between the DKT and DK labeling protocols in the models predicting surfaces, thicknesses, and volumes. Green: DKT having higher R^2. Blue: DK having higher R^2. eTIV: Estimated intracranial volume. MFS: Magnetic field strength. OEM: Original equipment manufacturer.

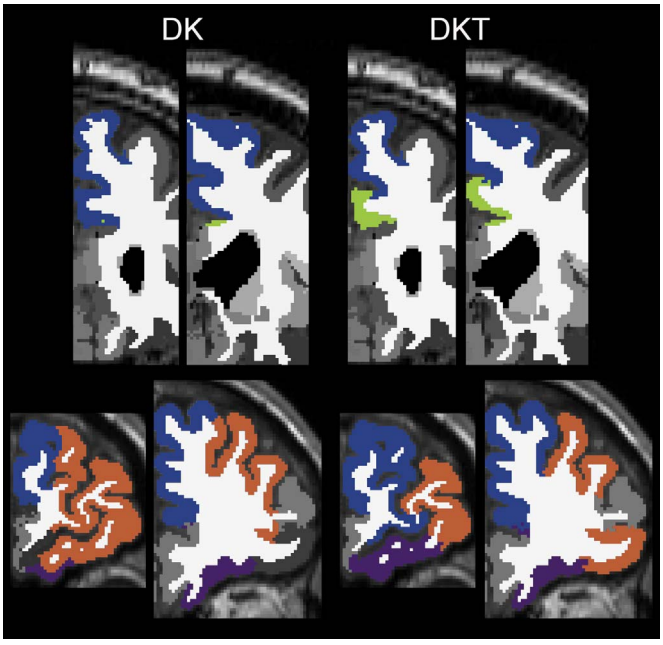

Fig. 4. Illustration of the labeling of the largest R^2 discrepancies between DK and DKT protocols. Top row: left caudal anterior cingulate in green and superior frontal gyrus in blue. Bottom row: left rostral middle frontal gyrus in orange, lateral orbitofrontal gyrus in violet, and superior frontal gyrus in blue. Regions in gray belong to other labels.

Limitations

The main limitations of the present study are mainly related to the sample. First, while the sample used has several advantages including being one of the largest used in such studies, encompassing a large spectrum of age and geographical areas (11 countries), it was not recruited using a probability sampling method and is not necessarily representative of the healthy adult-population. Second, the design was cross-sectional and age effects may therefore encompass cohort biases such as brain developments discrepancies between older and younger participants due to environmental differences. Finally, automated cortical labeling is not an easy task since neocortical landmarks might not be as apparent as that for other regions (e.g. hippocampus). In order to assure that the labeling protocol is applied correctly, it is essential that the segmentation procedure yielded adequate results, otherwise mislabeling is likely to occur. For example, a portion of the hippocampus segmented as neocortex, will likely produce larger entorhinal cortex volume and surface area, as well as affect entorhinal cortical thickness. One should note that since cortical thickness of a region is a mean of the thickness, this measure will always be more robust to segmentation error compared to cortical volume and surface.

Conclusions

The present study provides formulas to produce cortical morphometric normative values when using *FreeSurfer* with the DKT labeling protocol. Deviations from the normative sample can be computed for new individuals based on their characteristics and the characteristics of the scanner. Supplementary materials are provided to easily compute these statistics.

Conflict of interest

O.P. and L.D. declare no competing financial interests. S.D. is officer and shareholder of True Positive Medical Devices inc.

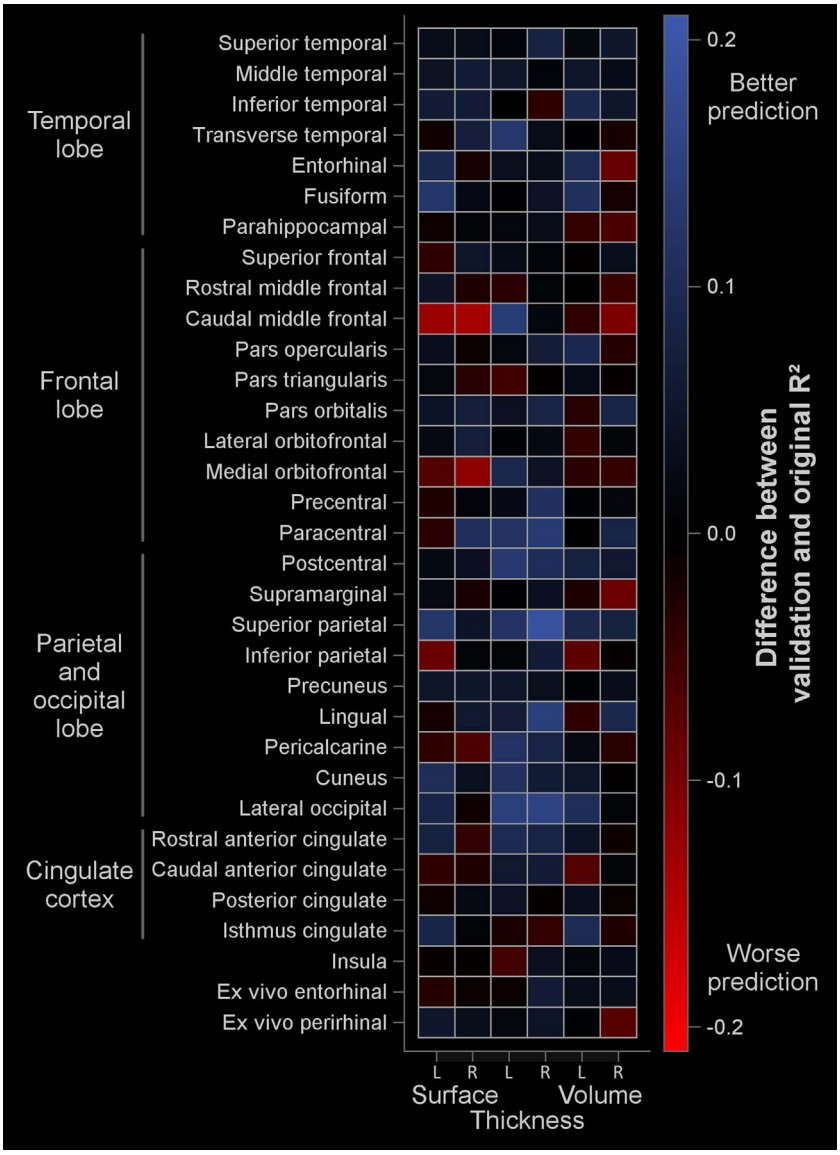

Fig. 5. Difference between validation and original R^2 for each cortical morphometric measure of the DKT and ex vivo protocols.

Acknowledgments

We gratefully acknowledge financial support from the Alzheimer's Society of Canada (#13-32), the Canadian Foundation for Innovation (#30469), the Fonds de recherche du Québec – Santé/Pfizer Canada – Pfizer-FRQS Innovation Fund (#25262), and the Canadian Institute for Health Research (#117121). S.D. is a Research Scholar from the Fonds de recherche du Québec – Santé (#30801).

This study comprises multiple samples of healthy individuals. We wish to thank all principal investigators who collected these datasets and agreed to let them accessible.

Autism Brain Imaging Data Exchange (ABIDE): Primary support for the work by Adriana Di Martino was provided by the NIMH (K23MH087770) and the Leon Levy Foundation. Primary support for the work by Michael P. Milham and the INDI team was provided by gifts from Joseph P. Healy and the Stavros Niarchos Foundation to the Child Mind Institute, as well as by an NIMH award to MPM (R03MH096321). http://fcon_1000.projects.nitrc.org/indi/abide/.

Alzheimer's Disease Neuroimaging Initiative (ADNI): Funded by the ADNI (National Institutes of Health Grant U01 AG024904) and DOD ADNI (Department of Defense award number W81XWH-12-2-0012). ADNI is funded by the National Institute on Aging, the National Institute of Biomedical Imaging and Bioengineering, and through generous contributions from the following: AbbVie, Alzheimer's Association; Alzheimer's Drug Discovery Foundation; Araclon Biotech; BioClinica, Inc.; Biogen; Bristol-Myers Squibb Company; CereSpir, Inc.; Eisai Inc.; Elan Pharmaceuticals, Inc.; Eli Lilly and Company; EuroImmun; F. Hoffmann-La Roche Ltd and its affiliated company Genentech, Inc.; Fujirebio; GE Healthcare; IXICO Ltd.; Janssen Alzheimer Immunotherapy Research & Development, LLC.; Johnson & Johnson Pharmaceutical Research & Development LLC.; Lumosity; Lundbeck; Merck & Co., Inc.; Meso Scale Diagnostics, LLC.; NeuroRx Research; Neurotrack Technologies; Novartis Pharmaceuticals Corporation; Pfizer Inc.; Piramal Imaging; Servier; Takeda Pharmaceutical Company; and Transition Therapeutics. The Canadian Institutes of Health Research is providing funds to support ADNI clinical sites in Canada. Private sector contributions are facilitated by the Foundation for the National Institutes of Health (www.fnih.org). The grantee organization is the Northern California Institute for Research and Education, and the study is coordinated by the Alzheimer's Disease Cooperative Study at the University of California, San Diego. ADNI data are disseminated by the Laboratory for Neuro Imaging at the University of Southern California. http://adni.loni.usc.edu/.

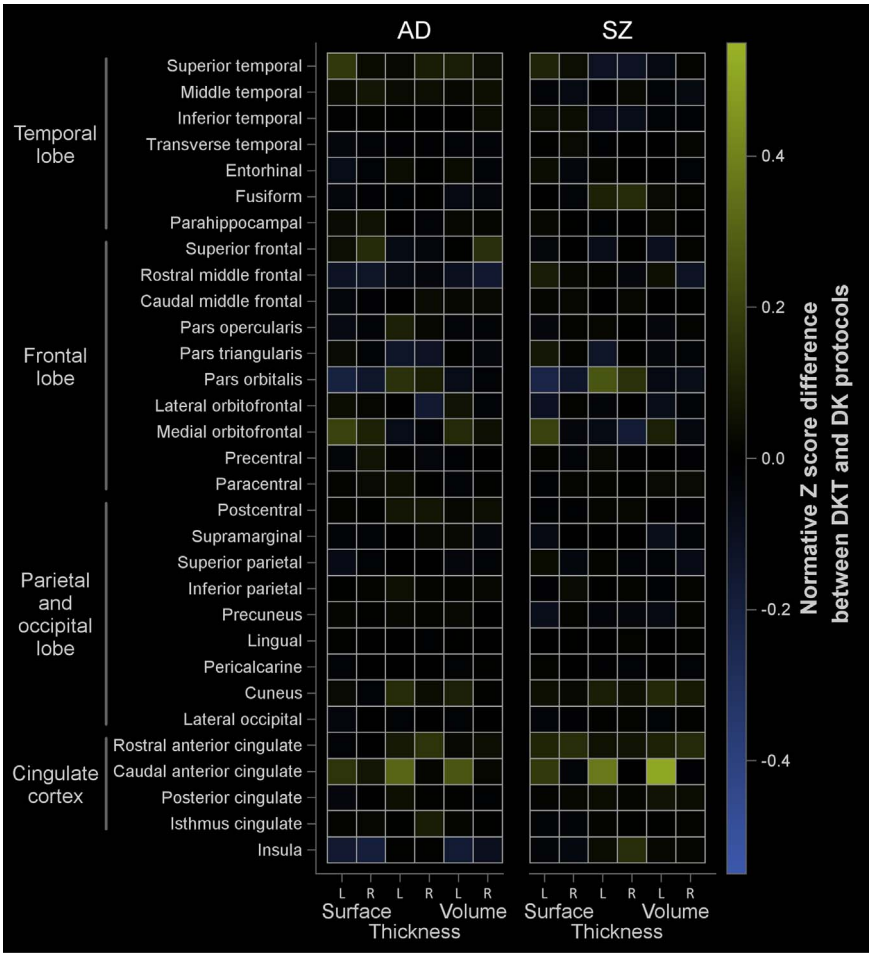

Fig. 6. Normative Z scores difference between the DKT and DK labeling protocols in individuals with Alzheimer's disease (AD) and schizophrenia (SZ). Green: DKT having higher Z score. Blue: DK having higher Z score.

Australian Imaging Biomarkers and Lifestyle flagship study of ageing (AIBL): Part of the data used in this study was obtained from the Australian Imaging Biomarkers and Lifestyle flagship study of ageing (AIBL) funded by the Commonwealth Scientific and Industrial Research Organisation (CSIRO) which was made available at the ADNI database (www.loni.usc.edu/ADNI). The AIBL researchers contributed data but did not participate in analysis or writing of this report. AIBL researchers are listed at www.aibl.csiro.au.

BMB – Berlin Mind and Brain (Margulies, Villringer). Zuo, X.N., et al. (2014). An open science resource for establishing reliability and reproducibility in functional connectomics. Scientific data, 1, 140049. doi: http://dx.doi.org/10.1016/j.neuron.2008.09.00610.1038/sdata.2014.49. http://fcon_1000.projects.nitrc.org/indi/CoRR/html/bmb_1.html.

Cleveland Clinic (Cleveland CCF): Funded by the National Multiple Sclerosis Society. http://fcon_1000.projects.nitrc.org/indi/retro/ClevelandCCF.html.

Center of Biomedical Research Excellence (COBRE): The imaging data and phenotypic information was collected and shared by the Mind Research Network and the University of New Mexico funded by a National Institute of Health COBRE: 1P20RR021938-01A2. http://fcon_1000.projects.nitrc.org/indi/retro/cobre.html.

DS-108. Wager et al. (2008). Prefrontal-subcortical pathways mediating successful emotion regulation. Neuron, 59(6):1037–50. doi: http://dx.doi.org/10.1016/j.neuron.2008.09.006. This data was obtained from the OpenfMRI database. NSF Grant OCI-1131441 (R. Poldrack, PI). Poldrack et al. (2013). Toward open sharing of task-based fMRI data: the OpenfMRI project. Frontiers in neuroinformatics, 7, 12. doi: http://dx.doi.org/10.3389/fninf.2013.00012. https://openfmri.org/dataset/ds000108/.

DS-170. Learning and memory: motor skill consolidation and intermanual transfer. This data was obtained from the OpenfMRI database. NSF Grant OCI-1131441 (R. Poldrack, PI). Poldrack et al. (2013). Toward open sharing of task-based fMRI data: the OpenfMRI project. *Frontiers in neuroinformatics, 7*, 12. doi: http://dx.doi.org/10.3389/fninf.2013.00012. https://openfmri.org/dataset/ds000170/.

Functional Biomedical Informatics Research Network (FBIRN): Provided by the Biomedical Informatics Research Network under the following support: U24-RR021992, by the National Center for Research Resources at the National Institutes of Health, U.S.A. http://www.birncommunity.org/resources/data/.

FIND lab sample. Funded by the Dana Foundation; John Douglas French Alzheimer's Foundation; National Institutes of Health (AT005733, HD059205, HD057610, NS073498, NS058899). http://fcon_1000.projects.nitrc.org/indi/retro/find_stanford.html.

International Consortium for Brain Mapping (ICBM). http://www.loni.usc.edu/ICBM/.

Information eXtraction from Images (IXI): Data collected as part of the project: EPSRC GR/S21533/02 - http://www.brain-development.org/.

F.M. Kirby Research Center neuroimaging reproducibility data (KIRBY-21). Landman, B.A. et al. “Multi-Parametric Neuroimaging Reproducibility: A 3T Resource Study”, NeuroImage. (2010) NIHMS/PMC:252138 doi: http://dx.doi.org/10.1016/j.neuroimage.2010.11.047 http://mri.kennedykrieger.org/databases.html.

Minimal Interval Resonance Imaging in Alzheimer's Disease (MIRIAD): The MIRIAD investigators did not participate in analysis

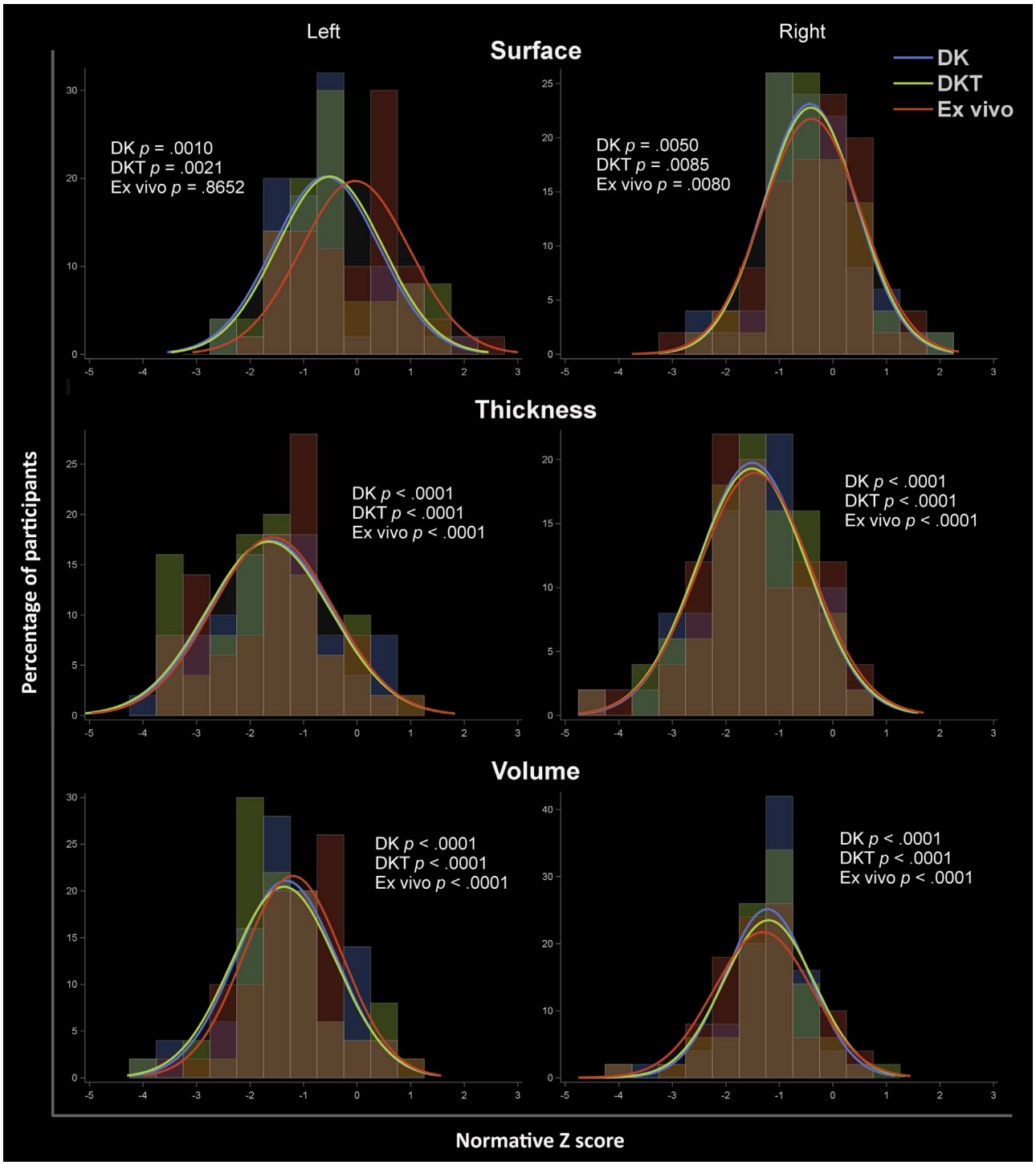

Fig. 7. Normative Z score distributions of the entorhinal cortex for the DK, DKT and ex vivo atlases in participants with Alzheimer's disease. *p*-values represents the difference between true and normative expected values for each atlas.

or writing of this report. The MIRIAD dataset is made available through the support of the UK Alzheimer's Society (RF116). The original data collection was funded through an unrestricted educational grant from GlaxoSmithKline (6GKC). http://miriad.drc.ion.ucl.ac.uk.

Nathan Kline Institute Rockland (NKI-R) sample (phase 1) and (phase 2): Principal support for the enhanced NKI-RS project is provided by the NIMH BRAINS R01MH094639-01. Funding for key personnel also provided in part by the New York State Office of Mental Health and Research Foundation for Mental Hygiene. Funding for the decompression and augmentation of administrative and phenotypic protocols provided by a grant from the Child Mind Institute (1FDN2012-1). Additional personnel support provided by the Center for the Developing Brain at the Child Mind Institute, as well as NIMH R01MH081218, R01MH083246, and R21MH084126. Project support also provided by the NKI Center for Advanced Brain Imaging (CABI), the Brain Research Foundation, the Stavros Niarchos Foundation and the NIH P50 MH086385-S1 (phase 1). http://fcon_1000.projects.nitrc.org/indi/pro/nki.html http://fcon_1000.projects.nitrc.org/indi/enhanced/.

Open access series of imaging studies (OASIS): The OASIS Project was funded by Grants P50 AG05681, P01 AG03991, R01 AG021910,

P50 MH071616, U24 RR021382, and R01 MH56584. http://www.oasis-brains.org/.

POWER: This database was supported by NIH R21NS061144 R01NS32979 R01HD057076 U54MH091657 K23DC006638 P50 MH71616 P60 DK020579-31, McDonnell Foundation Collaborative Action Award, NSF IGERT DGE-0548890, Simon's Foundation Autism Research Initiative grant, Burroughs Wellcome Fund, Charles A. Dana Foundation, Brooks Family Fund, Tourette Syndrome Association, Barnes-Jewish Hospital Foundation, McDonnell Center for Systems Neuroscience, Alvin J. Siteman Cancer Center, American Hearing Research Foundation grant, Diabetes Research and Training Center at Washington University grant. http://fcon_1000.projects.nitrc.org/indi/retro/Power2012.html.

Parkinson's Progression Markers Initiative (PPMI): PPMI – a public-private partnership – is funded by the Michael J. Fox Foundation for Parkinson's Research and funding partners, including Abbvie, Avid Radiopharmaceuticals, Biogen Idec, Bristol-Myers, Covance, GE Healthcare, Genentech, GlaxoSmithKline, Eli Lilly and Company, Lundbeck, Merck, Meso Scale Discovery, Pfizer, Piramal, Roche, and UCB. See http://www.ppmi-info.org for further details.

TRAIN-39: Data collected at the Biomedical Imaging Center at the Beckman Institute for Advanced Science and Technology at UIUC. Funded by the Office of Naval Research (ONR): N00014-07-1-0903. http://fcon_1000.projects.nitrc.org/indi/retro/Train-39.html.

University of Wisconsin, Madison (Birn, Prabhakaran, Meyerand) CoRR sample (UWM). Zuo, X.N., et al. (2014). An open science resource for establishing reliability and reproducibility in functional connectomics. Scientific data, 1, 140049. doi: http://dx.doi.org/10.1038/sdata.2014.49.

http://fcon_1000.projects.nitrc.org/indi/CoRR/html/samples.html.

Appendix A. Supplementary material

Supplementary data associated with this article can be found in the online version at doi: 10.1016/j.neuroimage.2017.04.035.

References

Augustinack, J.C., Huber, K.E., Stevens, A.A., Roy, M., Frosch, M.P., van der Kouwe, A.J., Wald, L.L., Van Leemput, K., McKee, A.C., Fischl, B., Alzheimer's Disease Neuroimaging, I., 2013. Predicting the location of human perirhinal cortex, Brodmann's area 35, from MRI. NeuroImage 64, 32–42.

Boccardi, M., Bocchetta, M., Ganzola, R., Robitaille, N., Redolfi, A., Duchesne, S., Jack, C.R., Jr., Frisoni, G.B., Segmentation, E.-A.W.Go. T.H.Pf.M.H., for the Alzheimer's Disease Neuroimaging, I., 2015. Operationalizing protocol differences for EADC-ADNI manual hippocampal segmentation. Alzheimers Dement. 11, 184–194.

Buckner, R.L., Head, D., Parker, J., Fotenos, A.F., Marcus, D., Morris, J.C., Snyder, A.Z., 2004. A unified approach for morphometric and functional data analysis in young, old, and demented adults using automated atlas-based head size normalization: reliability and validation against manual measurement of total intracranial volume. Neuroimage 23, 724–738.

Crawford, J.R., Garthwaite, P.H., Denham, A.K., Chelune, G.J., 2012. Using regression equations built from summary data in the psychological assessment of the individual case: extension to multiple regression. Psychol. Assess. 24, 801–814.

Desikan, R.S., Segonne, F., Fischl, B., Quinn, B.T., Dickerson, B.C., Blacker, D., Buckner, R.L., Dale, A.M., Maguire, R.P., Hyman, B.T., Albert, M.S., Killiany, R.J., 2006. An automated labeling system for subdividing the human cerebral cortex on MRI scans into gyral based regions of interest. Neuroimage 31, 968–980.

Ellis, K.A., Bush, A.I., Darby, D., De Fazio, D., Foster, J., Hudson, P., Lautenschlager, N.T., Lenzo, N., Martins, R.N., Maruff, P., Masters, C., Milner, A., Pike, K., Rowe, C., Savage, G., Szoeke, C., Taddei, K., Villemagne, V., Woodward, M., Ames, D., Group, A.R., 2009. The Australian Imaging, Biomarkers and Lifestyle (AIBL) study of aging: methodology and baseline characteristics of 1112 individuals recruited for a longitudinal study of Alzheimer's disease. Int. Psychogeriatr. 21, 672–687.

First, M.B., Spitzer, R.L., Gibbon, M., Williams, J.B.W., 1996. Structured Clinical Interview for DSM-IV Axis I Disorders (SCID), (Clinician version). American Psychiatric Press, Washington D.C.

Fischl, B., Stevens, A.A., Rajendran, N., Yeo, B.T., Greve, D.N., Van Leemput, K., Polimeni, J.R., Kakunoori, S., Buckner, R.L., Pacheco, J., Salat, D.H., Melcher, J., Frosch, M.P., Hyman, B.T., Grant, P.E., Rosen, B.R., van der Kouwe, A.J., Wiggins, G.C., Wald, L.L., Augustinack, J.C., 2009. Predicting the location of entorhinal cortex from MRI. NeuroImage 47, 8–17.

Frisoni, G.B., Jack, C.R., Jr., Bocchetta, M., Bauer, C., Frederiksen, K.S., Liu, Y., Preboske, G., Swihart, T., Blair, M., Cavedo, E., Grothe, M.J., Lanfredi, M., Martinez, O., Nishikawa, M., Portegies, M., Stoub, T., Ward, C., Apostolova, L.G., Ganzola, R., Wolf, D., Barkhof, F., Bartzokis, G., DeCarli, C., Csernansky, J.G., deToledo-Morrell, L., Geerlings, M.I., Kaye, J., Killiany, R.J., Lehericy, S., Matsuda, H., O'Brien, J., Silbert, L.C., Scheltens, P., Soininen, H., Teipel, S., Waldemar, G., Fellgiebel, A., Barnes, J., Firbank, M., Gerritsen, L., Henneman, W., Malykhin, N., Pruessner, J.C., Wang, L., Watson, C., Wolf, H., deLeon, M., Pantel, J., Ferrari, C., Bosco, P., Pasqualetti, P., Duchesne, S., Duvernoy, H., Boccardi, M., Volumetry, E.-A.W.Go.T.H.Pf.M.H., for the Alzheimer's Disease Neuroimaging, I., 2015. The EADC-ADNI Harmonized Protocol for manual hippocampal segmentation on magnetic resonance: evidence of validity. Alzheimers Dement. 11, 111–125.

Hastie, T., Tibshirani, R., Friedman, J., 2008. The Elements of Statistical Learning. Data Mining, Inference, and Prediction. Springer.

Klein, A., Tourville, J., 2012. 101 labeled brain images and a consistent human cortical labeling protocol. Front. Neurosci. 6, 171.

McKhann, G., Drachman, D., Folstein, M., Katzman, R., Price, D., Stadlan, E.M., 1984. Clinical diagnosis of Alzheimer's disease: report of the NINCDS-ADRDA Work Group under the auspices of Department of Health and Human Services Task Force on Alzheimer's Disease. Neurology 34, 939–944.

Potvin, O., Dieumegarde, L., Duchesne, S., 2017. Normative morphometric data for cerebral cortical areas over the lifetime of the adult brain. Neuroimage (submitted for publication).

Potvin, O., Mouiha, A., Dieumegarde, L., Duchesne, S., 2016a. Normative data for subcortical regional volumes over the lifetime of the adult human brain. NeuroImage 137, 9–20.

Potvin, O., Mouiha, A., Dieumegarde, L., Duchesne, S., 2016b. FreeSurfer subcortical normative data. Data in Brief 9, 732–736.

Sheikh, J.I., Yesavage, J.A., 1986. Geriatric Depression Scale (GDS): Recent Evidence and Development of a Shorter Version. Clinical Gerontology: A Guide to Assessment and Intervention. The Haworth Press, New York, 165–173.

Yushkevich, P.A., Amaral, R.S., Augustinack, J.C., Bender, A.R., Bernstein, J.D., Boccardi, M., Bocchetta, M., Burggren, A.C., Carr, V.A., Chakravarty, M.M., Chetelat, G., Daugherty, A.M., Davachi, L., Ding, S.L., Ekstrom, A., Geerlings, M.I., Hassan, A., Huang, Y., Iglesias, J.E., La Joie, R., Kerchner, G.A., LaRocque, K.F., Libby, L.A., Malykhin, N., Mueller, S.G., Olsen, R.K., Palombo, D.J., Parekh, M.B., Pluta, J.B., Preston, A.R., Pruessner, J.C., Ranganath, C., Raz, N., Schlichting, M.L., Schoemaker, D., Singh, S., Stark, C.E., Suthana, N., Tompary, A., Turowski, M.M., Van Leemput, K., Wagner, A.D., Wang, L., Winterburn, J.L., Wisse, L.E., Yassa, M.A., Zeineh, M.M., Hippocampal Subfields, G., 2015. Quantitative comparison of 21 protocols for labeling hippocampal subfields and parahippocampal subregions in in vivo MRI: towards a harmonized segmentation protocol. Neuroimage 111, 526–541.