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## Robust estimation of sulcal morphology

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12 Abstract

13 While it is well established that cortical morphology differs in relation to a variety of  
14 inter-individual factors, it is often characterized using estimates of volume, thickness,  
15 surface area, or gyrification. Here we developed a computational approach for  
16 estimating sulcal width and depth that relies on cortical surface reconstructions output  
17 by FreeSurfer. While other approaches for estimating sulcal morphology exist, studies  
18 often require the use of multiple brain morphology programs that have been shown to  
19 differ in their approaches to localize sulcal landmarks, yielding morphological  
20 estimates based on inconsistent boundaries. To demonstrate the approach, sulcal  
21 morphology was estimated in three large sample of adults across the lifespan, in  
22 relation to aging. A fourth sample is additionally used to estimate test-retest reliability  
23 of the approach. This toolbox is now made freely available as supplemental to this  
24 paper: <https://cmadan.github.io/calcSulc/>.

25

26 **Keywords:** sulcal width; sulcal depth; age; cortical structure; atrophy; gyrification;  
27 cerebral sulci

## 28 Robust estimation of sulcal morphology

### 29 **1 Introduction**

30 Cortical structure differs between individuals. It is well known that cortical thickness  
31 generally decreases with age (Fjell et al., 2009; Hogstrom et al., 2013; Hutton et al., 2009;  
32 Lemaitre et al., 2012; Madan & Kensinger, 2016, 2018; Madan, 2018; McKay et al., 2014;  
33 Salat et al., 2004; Sowell et al., 2003, 2007); however, a more visually prominent  
34 difference is the widening of sulci, sometimes described as “sulcal prominence”  
35 (Coffey et al., 1992; Drayer, 1988; Jacoby et al., 1980; Laffey et al., 1984; Tomlinson et al.,  
36 1968; Yue et al., 1997). In the literature, this measure has been referred to using a  
37 variety of names, including sulcal width, span, dilation, and enlargement, as well as  
38 fold opening. With respect to aging and brain morphology, sulcal width has been  
39 assessed qualitatively by clinicians as an index of cortical atrophy (Coffey et al., 1992;  
40 Drayer, 1988; Laffey et al., 1984; Pasquier et al., 1996; Scheltens et al., 1997; Tomlinson  
41 et al., 1968). An illustration of age-related differences in sulcal morphology is shown in  
42 Figure 1.

43 Using quantitative approaches, sulcal width has been shown to increase with age  
44 (Kochunov et al., 2005, 2008; Liu et al., 2010, 2013) likely relating to subsequent  
45 findings of age-related decreases in cortical gyrification (Cao et al., 2017; Hogstrom et  
46 al., 2013; Madan & Kensinger, 2016, 2018; Madan, 2018). Sulcal widening has also been  
47 shown to be associated with decreases in cognitive abilities (Liu et al., 2011) and  
48 physical activity (Lamont et al., 2014). With respect to clinical conditions, increased  
49 sulcal width has been found in dementia patients relative to healthy controls  
50 (Andersen et al., 2015; Hamelin et al., 2015; Huckman et al., 1975; Liu et al., 2012; Ming  
51 et al., 2015; Plochanski & Østergaard, 2016; Reiner et al., 2012), as well as with  
52 schizophrenia patients (Largen et al., 1984; Palaniyappan et al., 2015; Rieder et al., 1979)  
53 and mood disorders (Elkis et al., 1995).

54 One of the most common programs for conducting cortical surface analyses is  
55 FreeSurfer (Fischl, 2012). Unfortunately, though FreeSurfer reconstructs cortical

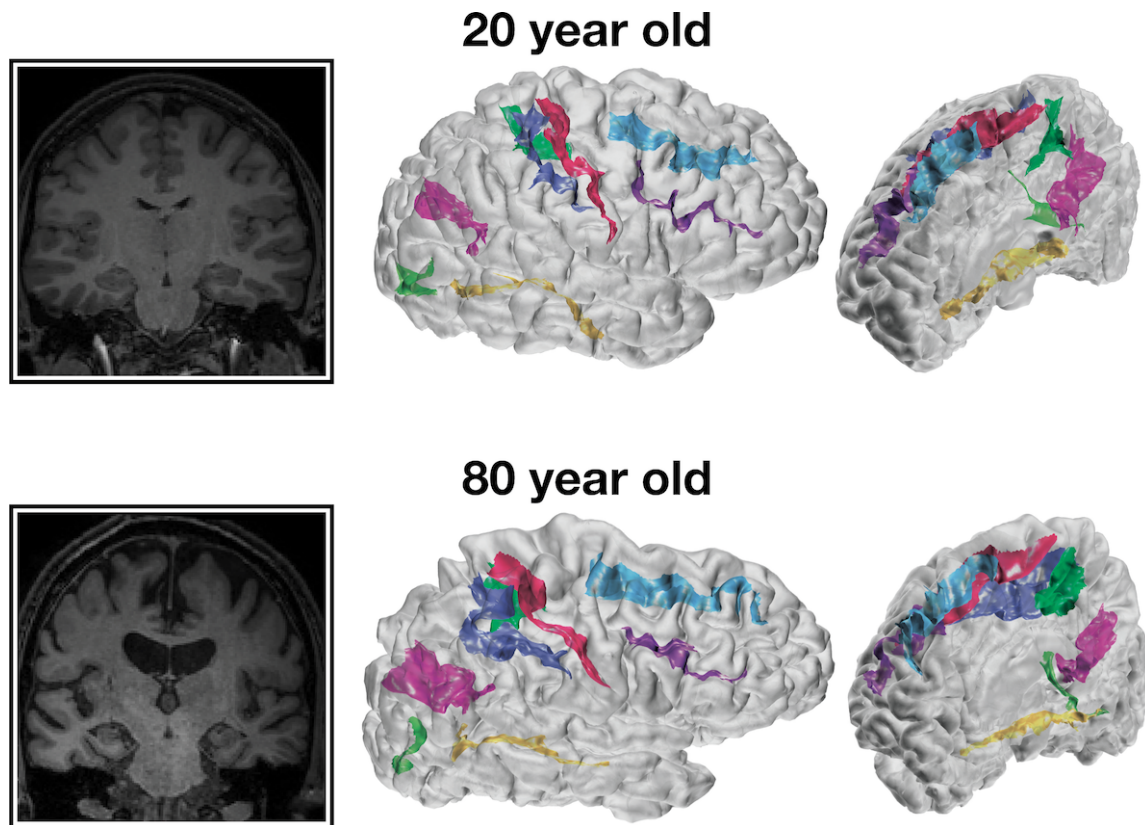


Figure 1. Representative coronal slices and cortical surfaces with sulcal identification for 20- and 80-year-old individuals.

56 surfaces, it does not estimate sulcal width or depth, leading researchers to use  
57 FreeSurfer along with another surface analysis program, BrainVISA (Kochunov et al.,  
58 2012; Mangin, Rivière, et al., 2004; Mangin, Riviere, et al., 2004; Rivière et al., 2002), to  
59 characterize cortical thickness along with sulcal morphology (e.g. Cai et al., 2017;  
60 Lamont et al., 2014; Liu et al., 2011, 2013; Pizzagalli et al., 2017). While this combination  
61 allows for the estimation of sulcal morphology in addition to standard measures such  
62 as cortical thickness, FreeSurfer and BrainVISA rely on different anatomical landmarks  
63 (Mikhael et al., 2018) which can yield differences in their resulting cortical surface  
64 reconstructions (Lee et al., 2006). Admittedly, determining the boundaries for an  
65 individual sulcus and incorporating individual cortical variability is difficult (Campero  
66 et al., 2014; John et al., 2006; Mikhael et al., 2018; Ono et al., 1990; Rhoton, 2007; ten  
67 Donkelaar et al., 2018; Welker, 1990). While an ennumerate amount of other methods  
68 have already been proposed to identify and characterize sulcal morphology (e.g.,

69 Andreasen et al., 1994; Auzias et al., 2015; Beeston & Taylor, 2000; Behnke et al., 2003;  
70 Eskildsen et al., 2005; Im et al., 2010; Jones et al., 2000; Le Goualher et al., 1996, 1998; Le  
71 Troter et al., 2012; Li & Shen, 2011; Li et al., 2010; Lohmann & von Cramon, 2000;  
72 Lohmann et al., 2008; Nowinski et al., 1996; Oguz et al., 2008; Perrot et al., 2011;  
73 Royackkers et al., 1999; Thompson et al., 1996; Vaillant & Davatzikos, 1997; Yang &  
74 Kruggel, 2008; Yun et al., 2013), ultimately these all are again using different landmarks  
75 than FreeSurfer uses for cortical parcellations (i.e., volume, thickness, surface area,  
76 gyrification). Note that, though FreeSurfer itself does compute sulcal maps, these are  
77 computed as normalized depths, not in real-world units (e.g. Kippenhan et al., 2005),  
78 furthermore, these are also independent of sulcal width information.

79 Here we describe a procedure for estimating sulcal morphology and report  
80 age-related differences in sulcal width and depth using three large samples of adults  
81 across the lifespan: two of these datasets are from Western samples, Dallas Lifespan  
82 Brain Study (DLBS) and Open Access Series of Imaging Studies (OASIS), as well as one  
83 East Asian sample, Southwest University Adult Lifespan (SALD), as potential  
84 differences between populations have been relatively understudied (Leong et al., 2017;  
85 Madan, 2017). To further validate the method, test-retest reliability was also assessed  
86 using a sample of young adults who were scanned ten times within the span of a  
87 month (Chen et al., 2015; Madan & Kensinger, 2017b). All four of these datasets are  
88 open-access and have sufficient sample sizes to be suitable for brain morphology  
89 research (Madan, 2017). This procedure has been implemented as a MATLAB toolbox,  
90 `calcSulc`, that calculates sulcal morphology—both width and depth—using files  
91 generated as part of the standard FreeSurfer cortical reconstruction and parcellation  
92 pipeline. This toolbox is now made freely available as supplemental to this paper:  
93 <https://cmadan.github.io/calcSulc/>.

## 94 2 Materials and Methods

### 95 2.1 Datasets

96 **OASIS.** This dataset consisted of 314 healthy adults (196 females), aged 18–94 (see  
97 Figure 2), from the Open Access Series of Imaging Studies (OASIS) cross-sectional  
98 dataset (<http://www.oasis-brains.org>) (Marcus et al., 2007). Participants were  
99 recruited from a database of individuals who had (a) previously participated in MRI  
100 studies at Washington University, (b) were part of the Washington University  
101 Community, or (c) were from the longitudinal pool of the Washington University  
102 Alzheimer Disease Research Center. Participants were screened for neurological and  
103 psychiatric issues; the Mini-Mental State Examination (MMSE) and Clinical Dementia  
104 Rating (CDR) were administered to participants aged 60 and older. To only include  
105 healthy adults, participants with a CDR above zero were excluded; all remaining  
106 participants scored 25 or above on the MMSE. Multiple T1 volumes were acquired  
107 using a Siemens Vision 1.5 T with a MPRAGE sequence; only the first volume was used  
108 here. Scan parameters were: TR=9.7 ms; TE=4.0 ms; flip angle=10°;  
109 voxel size=1.25×1×1 mm. Age-related comparisons for volumetric and fractal  
110 dimensionality measures from the OASIS dataset were previously reported in Madan

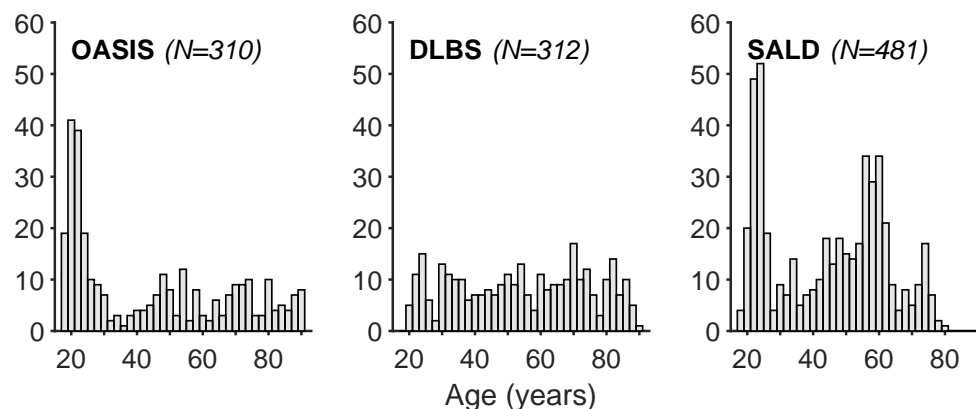


Figure 2. Histogram of age distribution for the three aging datasets: OASIS, DLBS, and SALD, only for participants included in the sulcal morphology analyses. Each bar corresponds to a two-year age-range bin.

111 and Kensinger (2017a), Madan and Kensinger (2018), and Madan (2019) <sup>1</sup>.

112 **DLBS.** This dataset consisted of 315 healthy adults (198 females), aged 20–89 (see  
113 Figure 2), from wave 1 of the Dallas Lifespan Brain Study (DLBS), made available  
114 through the International Neuroimaging Data-sharing Initiative (INDI) (Mennes et al.,  
115 2013) and hosted on the Neuroimaging Informatics Tools and Resources Clearinghouse  
116 (NITRC) (Kennedy et al., 2016)

117 ([http://fcon\\_1000.projects.nitrc.org/indi/retro/dlbs.html](http://fcon_1000.projects.nitrc.org/indi/retro/dlbs.html)).

118 Participants were screened for neurological and psychiatric issues. No participants in  
119 this dataset were excluded *a priori*. All participants scored 26 or above on the MMSE.  
120 T1 volumes were acquired using a Philips Achieva 3 T with a MPRAGE sequence. Scan  
121 parameters were: TR=8.1 ms; TE=3.7 ms; flip angle=12°; voxel size=1×1×1 mm. See  
122 Kennedy et al. (2015) and Chan et al. (2014) for further details about the dataset.

123 Age-related comparisons for volumetric and fractal dimensionality measures from the  
124 DLBS dataset were previously reported in Madan and Kensinger (2017a), Madan and  
125 Kensinger (2018), and Madan (2019) <sup>1</sup>.

126 **SALD.** This dataset consisted of 483 healthy adults (303 females), aged 19–80 (see  
127 Figure 2), from the Southwest University Adult Lifespan Dataset (SALD) (Wei et al.,  
128 2018), also made available through INDI and hosted on NITRC

129 ([http://fcon\\_1000.projects.nitrc.org/indi/retro/sald.html](http://fcon_1000.projects.nitrc.org/indi/retro/sald.html)). No  
130 participants in this dataset were excluded *a priori*. T1 volumes were acquired using a  
131 Siemens Trio 3 T with a MPRAGE sequence. Scan parameters were: TR=1.9 s;  
132 TE=2.52 ms; flip angle=9°; voxel size=1×1×1 mm.

133 **CCBD.** This dataset consisted of 30 healthy adults (15 females), aged 20–30, from the  
134 Center for Cognition and Brain Disorders (CCBD) at Hangzhou Normal University  
135 (Chen et al., 2015). Each participant was scanned for 10 sessions, occurring 2–3 days

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<sup>1</sup>Note that analyses reported in these previous papers were based on preprocessing in FreeSurfer 5.3.0, rather than FreeSurfer 6.0.



136 apart over a one-month period. No participants in this dataset were excluded *a priori*.  
137 T1 volumes were acquired using a SCANNER with a FSPGR sequence. Scan  
138 parameters were: TR=8.06 ms; TE=3.1 ms; flip angle=8°; voxel size: 1×1×1 mm. This  
139 dataset is included as part of the Consortium for Reliability and Reproducibility  
140 (CoRR) (Zuo et al., 2014) as HNU1. Test-retest comparisons for volumetric and fractal  
141 dimensionality measures from the CCBD dataset were previously reported in Madan  
142 and Kensinger (2017b)<sup>1</sup>.

## 143 **2.2 Procedure**

144 Data were analyzed using FreeSurfer v6.0  
145 (<https://surfer.nmr.mgh.harvard.edu>) on a machine running Red Hat  
146 Enterprise Linux (RHEL) v7.4. FreeSurfer was used to automatically volumetrically  
147 segment and parcellate cortical and subcortical structures from the T1-weighted  
148 images (Fischl, 2012; Fischl & Dale, 2000) FreeSurfer's standard pipeline was used (i.e.,  
149 `recon-all`). No manual edits were made to the surface meshes, but surfaces were  
150 visually inspected. Cortical thickness is calculated as the distance between the white  
151 matter surface (white-gray interface) and pial surface (gray-CSF interface) .  
152 Gyrification was also calculated using FreeSurfer, as described in Schaer et al. (2012).  
153 Cortical regions were parcellated based on the Destrieux et al. (2010) atlas, also part of  
154 the standard FreeSurfer analysis pipeline.

## 155 **3 Calculation**

156 Here we outline a novel, simple yet robust, automated approach for estimating sulcal  
157 width and depth, based on intermediate files generated as part of the standard  
158 FreeSurfer analysis pipeline. This procedure and functionality has been implemented  
159 in an accompanying MATLAB toolbox, `calcSulc`. The toolbox is supplemental  
160 material to this paper and is made freely available:  
161 <https://cmadan.github.io/calcSulc/>.



162 For each individual sulcus (for each hemisphere and participant), the following  
163 approach was used to characterize the sulcal morphology. The procedure has been  
164 validated and is supported for the following sulci: central, post-central, superior  
165 frontal, inferior frontal, parieto-occipital, occipito-temporal, middle occipital and  
166 lunate, and marginal part of the cingulate (`S_central`, `S_postcentral`,  
167 `S_front_sup`, `S_front_inf`, `S_parieto_occipital`,  
168 `S_oc-temp_med&Lingual`, `S_oc_middle&Lunatus`, `S_cingul-Marginalis`).  
169 All of the sulci are labeled in Figure 3.

170 First the pial surface and Destrieux et al. (2010) parcellation labels were read into  
171 MATLAB by using the FreeSurfer-MATLAB toolbox provided alongside FreeSurfer  
172 (`calcSulc_load`), this consists of the `?h.pial` (FreeSurfer cortical surface mesh)  
173 `?h.aparc.a2009s.annot` (FreeSurfer parcellation annotation) files. Using this, the  
174 faces associated with the individual sulcus were isolated as a 3D mesh  
175 (`calcSulc_isolate`).

176 The width of each sulcus (`calcSulc_width`) was calculated by determining  
177 which vertices lay on the boundary of the sulcus and the adjacent gyrus. An iterative  
178 procedure was then used to determine the 'chain' of edges that would form a  
179 contiguous edge-loop that encircle the sulcal region (`calcSulc_getEdgeLoop`). This  
180 provided an exhaustive list of all vertices that were mid-way between the peak of the

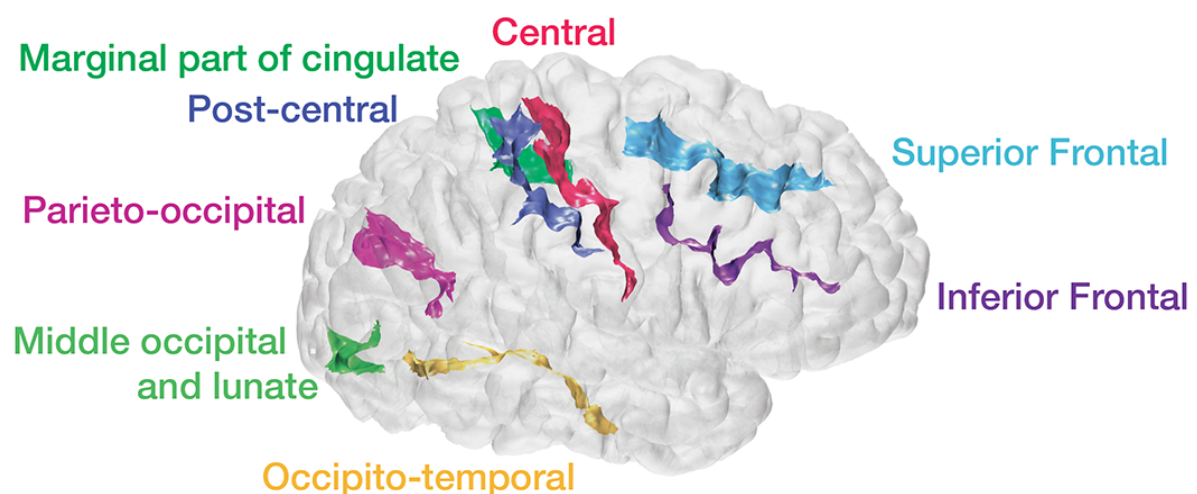


Figure 3. Example cortical surface with estimated sulci identified and labelled.

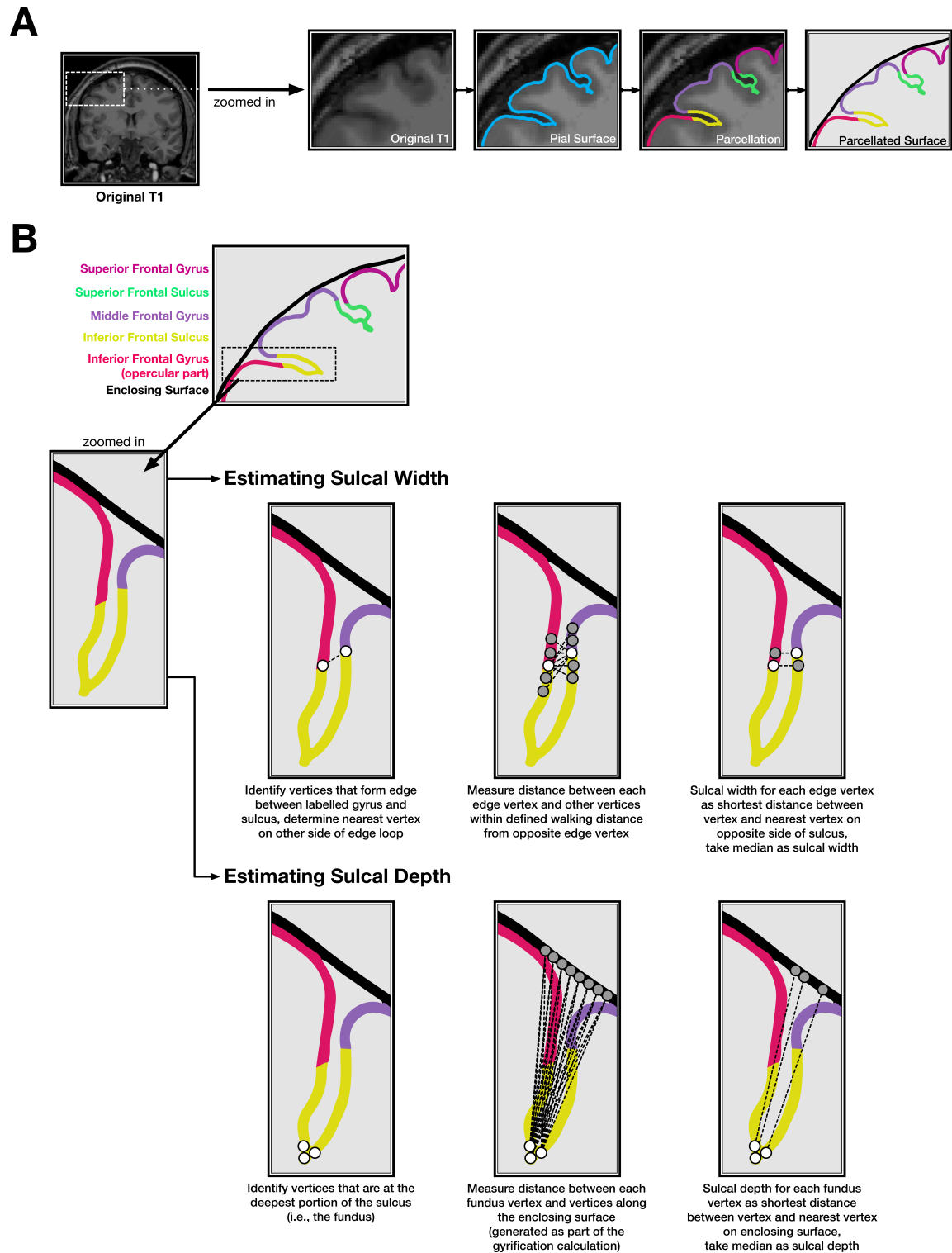


Figure 4. Illustration of the sulcal morphology method. (A) Cortical surface estimation and sulcal identification, as output from FreeSurfer. (B) Sulcal width and depth estimation procedure. Note that the surface mesh and estimation algorithm use many more vertices than shown here.

181 respective adjacent gyri and depth of the sulcus itself. For each vertex in this edge-loop,  
182 the nearest point in 3D space that was *not* neighbouring in the loop was determined,  
183 with the goal of finding the nearest vertex in the edge that was on the opposite side of  
184 the sulcus—i.e., a line between these two vertices would ‘bridge’ across the sulcus. Since  
185 these nearest vertices in the edge loop are not necessarily the nearest vertex along the  
186 opposite sulcus wall, an exhaustive search (walk) was performed, moving up to a 4  
187 edges from the initially determined nearest vertex (configurable as  
188 `options.setWidthWalk`). The sulcal width was then taken as the median of these  
189 distances that bridged across the sulcus.

190 The depth of each sulcus (`calcSulc_depth`) additionally used FreeSurfer’s  
191 sulcal maps (`?h.sulc`) to determine the relative inflections in the surface mesh, which  
192 would be in alignment with the gyral crown. The deepest points of the sulcus, i.e., the  
193 sulcal fundus, were taken as the 100 vertices within the sulcus with the lowest values  
194 in the sulcal map. For these 100 vertices, the shortest (i.e., Euclidean) distance to the  
195 smoothed enclosing surface was calculated (generated by FreeSurfer’s built-in  
196 gyrification analysis [`?h.pial-outer-smoothed`], Schaer et al., 2012), and the  
197 median of these was then taken as the sulcal depth. While the use of a Euclidean  
198 distance here underestimates the true sulcal depth, it is nonetheless robust (as  
199 demonstrated in the present work) and does not markedly differ from other  
200 algorithmic approaches for estimating sulcal depth for much of the cortex (see Yun et  
201 al., 2013, for a comparison).

202 Sulcal morphology, width and depth, was estimated for eight major sulci in each  
203 hemisphere: central, post-central, superior frontal, inferior frontal, parieto-occipital,  
204 occipito-temporal, middle occipital and lunate, and marginal part of the cingulate  
205 (`S_central`, `S_postcentral`, `S_front_sup`, `S_front_inf`,  
206 `S_parieto_occipital`, `S_oc-temp_med&Lingual`, `S_oc_middle&Lunatus`,  
207 `S_cingul-Marginalis`). Preliminary analyses additionally included superior and  
208 inferior temporal sulci and intraparietal sulcus but these were removed from further  
209 analysis when the sulci width estimation was found to fail to determine a closed

210 boundary edge-loop at an unacceptable rate ( $> 10\%$ ) for at least one hemisphere. This  
211 edge boundary determination failed when parcellated regions were labeled by  
212 FreeSurfer to comprise at least two discontinuous regions, such that they could not be  
213 identified using a single edge loop. Nonetheless, sulcal measures failed to be estimated  
214 for some participants, resulting in final samples of 310 adults from the OASIS dataset,  
215 312 adults from the DLBS dataset, 481 adults from the SALD dataset, and 30 adults  
216 from the CCBD dataset (see Figure 2).

### 217 **3.1 Test-retest reliability**

218 Test-retest reliability was assessed as intraclass correlation coefficient (*ICC*), which can  
219 be used to quantify the relationship between multiple measurements (Asendorpf &  
220 Wallbott, 1979; Bartko, 1966; Chen et al., 2018; Hallgren, 2012; Koo & Li, 2016; Madan &  
221 Kensinger, 2017b; Rajaratnam, 1960; Shrout & Fleiss, 1979). McGraw and Wong (1996)  
222 provide a comprehensive review of the various *ICC* formulas and their applicability to  
223 different research questions. *ICC* was calculated as the one-way random effects model  
224 for the consistency of single measurements, i.e., *ICC*(1, 1). As a general guideline,  
225 *ICC* values between .75 and 1.00 are considered 'excellent,' .60–.74 is 'good,' .40–.59 is  
226 'fair,' and below .40 is 'poor' (Cicchetti, 1994).

## 227 **4 Results & Discussion**

### 228 **4.1 Age-related differences in sulcal morphology**

229 Scatter plots showing the relationships between each individual sulcal width and  
230 depth and age, for the OASIS dataset, are shown in Figure 5; the corresponding  
231 correlations for all datasets are shown in Tables 1 and 2. The width and depth of the  
232 central and post-central sulci appear to be particularly correlated with age, with wider  
233 and shallower sulci in older adults. Age-related differences in sulcal width and depth  
234 and generally present in other sulci as well, but are generally weaker.

235 Age-related relationships for each sulcus were relatively consistent between the

236 two Western lifespan datasets (OASIS and DLBS), but age-related differences in sulcal  
237 width (but not depth) were markedly weaker in the East Asian lifespan dataset (SALD).  
238 This finding will need to be studied further, but may be related to gross differences in  
239 anatomical structure (Kochunov et al., 2003; Longstreth et al., 2000; Tang et al.,  
240 2010)—and motivates the need to aging in samples that vary in ethnicity/race and are  
241 otherwise not of a so-called WEIRD (Western, Educated, Industrialized, Rich, and  
242 Democratic) demographic (Madan, 2017). Additionally, there did not appear to be a  
243 significant influence of field strength (i.e., 1.5 T for the OASIS dataset vs. 3 T for the  
244 DLBS dataset) on estimates of sulcal morphology. Importantly, test-retest reliability,  
245  $ICC(1, 1)$ , was particularly good for the sulcal depth across individual sulci.

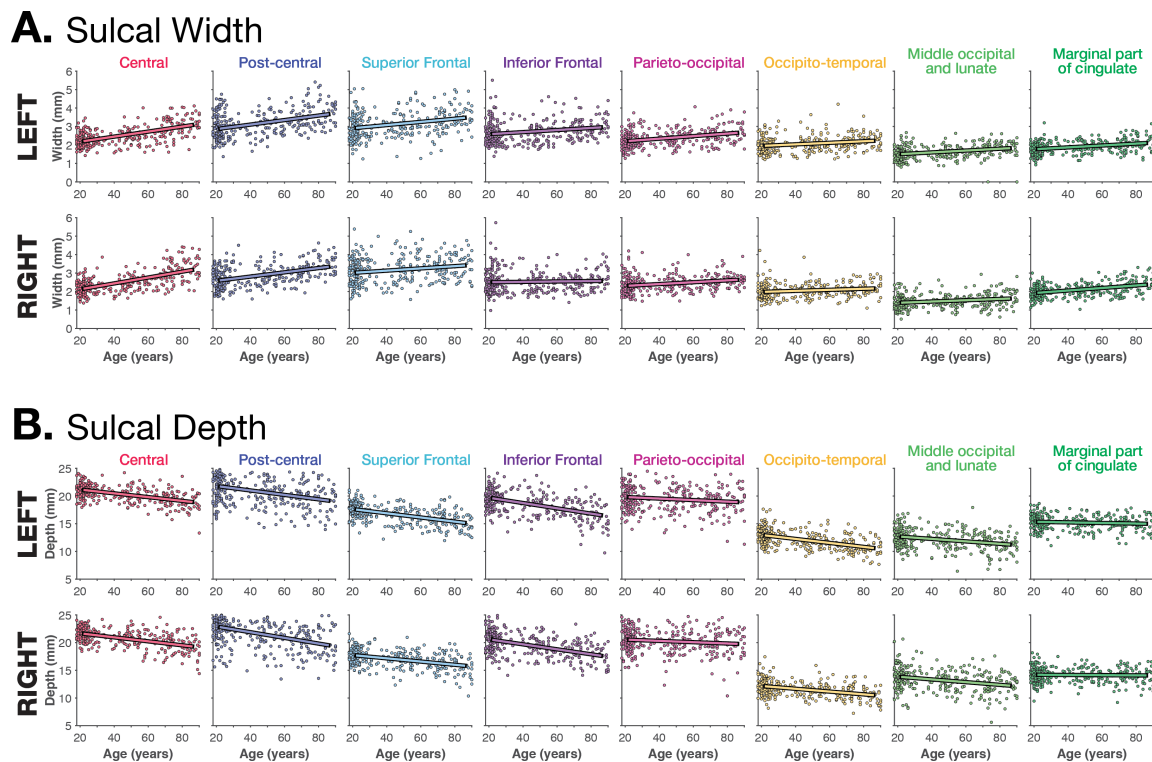


Figure 5. Relationship between (A) sulcal depth and (B) width for each of the sulci examined, based on the OASIS dataset.

246 To obtain a coarse summary measure across sulci, we averaged the sulcal width  
247 across the 16 individual sulci for each individual, and with each dataset, and examined  
248 the relationship between mean sulcal width with age. These correlations, shown in  
249 Table 1, indicate that the mean sulcal width was generally a better indicator of

Sulci Name	FreeSurfer Label†	Hemi.	OASIS	DLBS	SALD	CCBD	
			<i>r</i> (Age)	<i>r</i> (Age)	<i>r</i> (Age)	ICC(1,1)	95% CI of ICC
Central	S_central	L	.586	.486	.322	.858	[ 0.785, 0.918]
		R	.632	.523	.294	.842	[ 0.764, 0.908]
Post-central	S_postcentral	L	.413	.391	.198	.764	[ 0.660, 0.858]
		R	.460	.436	.213	.864	[ 0.794, 0.922]
Superior Frontal	S_front_sup	L	.281	.421	.055	.797	[ 0.703, 0.880]
		R	.205	.291	.035	.843	[ 0.764, 0.909]
Inferior Frontal	S_front_inf	L	.217	.323	-.037	.775	[ 0.675, 0.865]
		R	.043	.222	-.036	.831	[ 0.748, 0.901]
Parieto-occipital	S_parieto_occipital	L	.348	.279	.145	.616	[ 0.486, 0.753]
		R	.257	.357	.213	.682	[ 0.561, 0.802]
Occipito-temporal	S_oc-temp_med&Lingual	L	.227	.270	-.055	.660	[ 0.535, 0.786]
		R	.168	.189	.017	.692	[ 0.572, 0.808]
Middle occipital and lunate	S_oc_middle&Lunatus	L	.306	.271	.145	.605	[ 0.474, 0.744]
		R	.212	.177	.023	.625	[ 0.496, 0.760]
Marginal part of cingulate	S_cingul-Marginalis	L	.340	.275	.075	.783	[ 0.685, 0.871]
		R	.430	.382	.161	.757	[ 0.651, 0.853]
<i>Mean</i>			.636	.592	.227	.907	[ 0.856, 0.947]

Table 1

*Correlations between sulcal width and age for each sulci and hemisphere, for each of the three lifespan datasets examined. Test-retest reliability, ICC(1, 1), is also included from the CCBD dataset. †FreeSurfer labels in version 6.0; labels are named slightly different in version 5.3.*

*ICC values between .75 and 1.00 are considered ‘excellent,’ .60–.74 is ‘good,’ .40–.59 is ‘fair,’ and below .40 is ‘poor’ (Cicchetti, 1994).*

250 age-related differences in sulcal morphology than individual sulci, and had increased  
 251 test-retest reliability. Mean sulcal depth was similarly more sensitive to age-related  
 252 differences than for an individual sulcus (e.g., it is unclear why the relationship  
 253 between age and width of the central sulcus differed between samples) and the  
 254 magnitude of this relationship was more consistent across datasets. Reliability was  
 255 even higher for mean sulcal depth than mean sulcal width.

## 256 4.2 Comparison with other age-related structural differences

257 Within each dataset, mean sulcal depth and width correlated with age, as shown in  
 258 Tables 1 and 2. Of course, other measures of brain morphology also differ with age,  
 259 such as mean (global) cortical thickness [OASIS:  $r(308) = -.793, p < .001$ ; DLBS:  
 260  $r(310) = -.759, p < .001$ ; SALD:  $r(479) = -.642, p < .001$ ]. and volume of the third  
 261 ventricle (ICV-corrected) [OASIS:  $r(308) = .665, p < .001$ ; DLBS:  $r(310) = .677, p < .001$ ;



Sulci Name	FreeSurfer Label†	Hemi.	OASIS	DLBS	SALD	CCBD	
			<i>r</i> (Age)	<i>r</i> (Age)	<i>r</i> (Age)	ICC(1,1)	95% CI of ICC
Central	S_central	L	-.517	-.205	-.346	.848	[ 0.772, 0.912]
		R	-.505	-.256	-.348	.860	[ 0.789, 0.919]
Post-central	S_postcentral	L	-.371	-.264	-.268	.965	[ 0.944, 0.981]
		R	-.436	-.246	-.330	.890	[ 0.831, 0.937]
Superior Frontal	S_front_sup	L	-.523	-.454	-.397	.899	[ 0.844, 0.943]
		R	-.413	-.465	-.444	.886	[ 0.825, 0.935]
Inferior Frontal	S_front_inf	L	-.517	-.490	-.491	.932	[ 0.893, 0.962]
		R	-.496	-.480	-.490	.915	[ 0.868, 0.952]
Parieto-occipital	S_parieto_occipital	L	-.145	-.093	-.241	.979	[ 0.966, 0.989]
Occipito-temporal	S_oc-temp_med&Lingual	R	-.124	.059	-.229	.970	[ 0.952, 0.984]
		L	-.509	-.323	-.263	.953	[ 0.926, 0.974]
Middle occipital and lunate	S_oc_middle&Lunatus	R	-.404	-.316	-.281	.913	[ 0.864, 0.951]
		L	-.290	-.167	-.150	.949	[ 0.919, 0.972]
Marginal part of cingulate	S_cingul-Marginalis	R	-.288	-.120	-.132	.922	[ 0.879, 0.956]
		L	-.092	-.035	-.268	.952	[ 0.925, 0.974]
		R	-.032	-.017	-.156	.918	[ 0.872, 0.954]
<i>Mean</i>			-.465	-.645	-.600	.972	[ 0.955, 0.985]

Table 2

*Correlations between sulcal depth and age for each sulci and hemisphere, for each of the three lifespan datasets examined. Test-retest reliability, ICC(1, 1), is also included from the CCBD dataset. †FreeSurfer labels in version 6.0; labels are named slightly different in version 5.3. ICC values between .75 and 1.00 are considered ‘excellent,’ .60–.74 is ‘good,’ .40–.59 is ‘fair,’ and below .40 is ‘poor’ (Cicchetti, 1994).*

262 SALD:  $r(479) = .328, p < .001$ ]. Previous studies have demonstrated that both of these  
 263 measures are robust estimates of age-related differences in brain structure (Fjell et al.,  
 264 2009; Hogstrom et al., 2013; Hutton et al., 2009; Lemaitre et al., 2012; Madan &  
 265 Kensinger, 2016, 2017a; Madan, 2018; McKay et al., 2014; Salat et al., 2004; Sowell et al.,  
 266 2003, 2007; Walhovd et al., 2011).

267 To test if these mean sulcal measures served as distinct measures of age-related  
 268 differences in brain morphology, beyond those provided by other measures, such as  
 269 mean cortical thickness and volume of the third ventricle, we conducted partial  
 270 correlations that controlled for these two other measures of age-related atrophy. Mean  
 271 sulcal width [OASIS:  $r_p(306) = .188, p < .001$ ; DLBS:  $r_p(308) = .177, p = .002$ ; SALD:  
 272  $r(477) = .003, p = .96$ ] and depth [OASIS:  $r_p(306) = -.443, p < .001$ ; DLBS:  
 273  $r_p(308) = -.397, p < .001$ ; SALD:  $r_p(477) = -.534, p < .001$ ] both explained unique  
 274 variance in relation to age. Thus, even though more established measures of



275 age-related differences in brain morphology were replicated here, the additional sulcal  
276 measures captured aspects of aging that are not accounted for by these extant  
277 measures, indicating that these sulcal measures are worth pursuing further and are not  
278 redundant with other measures of brain structure. Providing additional support for  
279 this, mean sulcal width and depth were only weakly related to each other [OASIS:  
280  $r(308) = -.192, p < .001$ ; DLBS:  $r(310) = .092, p = .104$ ; SALD:  $r(479) = .119, p = .009$ ].

281 As with the individual sulci measures, we did observe a difference between  
282 samples where some age-related measures were less sensitive in the East Asian lifespan  
283 sample (SALD), here in the ventricle volume correlation and the unsurprisingly weaker  
284 age relationship in the partial correlation using sulcal width. These sample differences  
285 are puzzling, though there is a general correspondence between the two Western  
286 samples. Given that much of the literature is also based on Western samples, we think  
287 further research with East Asian samples, and particularly comparing samples with the  
288 same analysis pipeline, is necessary to shed further light on this initial finding.

## 289 5 Conclusion

290 Differences in sulcal width and depth are quite visually prominent, but are not often  
291 quantified when examining individual differences in cortical structure. Here we  
292 examined age-related differences in both sulcal measures as a proof-of-principle to  
293 demonstrate the utility of the calcSulc toolbox that accompanies this paper and is  
294 designed to closely compliment the standard FreeSurfer pipeline. This allows for the  
295 additional measurement of sulcal morphology, to add to the extant measures of brain  
296 morphology such as cortical thickness, area, and gyrification. Critically, this approach  
297 uses the same landmarks and boundaries as in the Destrieux et al. (2010) parcellation  
298 atlas, in contrast to all previous approaches to characterize sulcal features. This toolbox  
299 is now made freely available as supplemental to this paper:

300 <https://cmadan.github.io/calcSulc/>.

301 Using this approach, here we demonstrate age-related differences in sulcal width  
302 and depth, as well as high test-retest reliability. Since individual differences in sulcal

303 morphology are sufficiently distinct from those characterized by other brain  
304 morphology measures, this approach should complement extant work of investigating  
305 factors that influence brain morphology, e.g., see Figure 3 of Madan and Kensinger  
306 (2018). Given the flexibility in the methodological approach, these measures can be  
307 readily applied to other samples after being initially processed with FreeSurfer.

### 308 **Acknowledgments**

309 MRI data used in the preparation of this article were obtained from several sources,  
310 data were provided in part by: (1) the Open Access Series of Imaging Studies (OASIS)  
311 (Marcus et al., 2007); (2) wave 1 of the Dallas Lifespan Brain Study (DLBS) led by Dr.  
312 Denise Park and distributed through INDI (Mennes et al., 2013) and NITRC (Kennedy  
313 et al., 2016); (3) the Southwest University Adult Lifespan Dataset (SALD) (Wei et al.,  
314 2018), also made available through INDI and hosted on NITRC; and (4) the Center for  
315 Cognition and Brain Disorders (CCBD) (Chen et al., 2015) as dataset HNU1 in the  
316 Consortium for Reliability and Reproducibility (CoRR) (Zuo et al., 2014).

### 317 **Competing Interests**

318 The author declares that they have no competing interests.

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