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## A database of age-appropriate average MRI templates

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### Abstract

This article summarizes a life-span neurodevelopmental MRI database. The study of neurostructural development or neurofunctional development has been hampered by the lack of age-appropriate MRI reference volumes. This causes misspecification of segmented data, irregular registrations, and the absence of appropriate stereotaxic volumes. We have created the “Neurodevelopmental MRI Database” that provides age-specific reference data from 2 weeks through 89 years of age. The data are presented in fine-grained ages (e.g., 3 months intervals through 1 year; 6 months intervals through 19.5 years; 5 year intervals from 20 through 89 years). The base component of the database at each age is an age-specific average MRI template. The average MRI templates are accompanied by segmented partial volume estimates for segmenting priors, and a common stereotaxic atlas for infant, pediatric, and adult participants. The database is available online (<http://jerlab.psych.sc.edu/NeurodevelopmentalMRIDatabase/>).

### Keywords

Neurodevelopmental MRI Database; lifespan MRI; average MRI templates; brain development

### Age-appropriate MRI reference templates

There are changes in the brain that occur over the entire lifespan. The study of brain structural development has been aided by the application of Magnetic Resonance Imaging (MRI) of participants at a wide range of ages. However, the study of brain development with MRI has been hampered by a lack of precise tools to measure brain structure in typically developing humans. Voxel-based morphometry (VBM; Ashburner & Friston, 2000) and functional MRI (fMRI) use MRI reference volumes to normalize participants’ brains to a common MRI space. However, the normalization of pediatric populations to adult reference volumes is problematic in several respects (Richards & Xie, 2015). These include misclassification of brain tissue in pediatric samples, more variable contours and local/

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global structural changes in pediatric brains, spurious age differences when there was a disparity between the age of the participant and the reference volume, and incorrect tissue (GM, WM) brain distribution. These issues are most often studied in pediatric populations, but may also be relevant for older adults. A solution to these problems is the creation of age-appropriate MRI reference templates with fine-grained age intervals. We present a database of MRI reference volumes that include average MRI templates, segmented partial volume estimates for segmentation, and a common stereotaxic atlas for all ages. These reference volumes may be used for studies of brain structural development (e.g., VBM) but also will be useful for studies of brain functional development (e.g., fMRI, EEG/ERP, fNIRS). We recently reviewed this work in Richards and Xie (2015).

Structural and functional MRI studies require a standardized reference volume. Both VBM and fMRI methods register a participant MRI to a standard template MRI in order to combine MRIs from different participants, and VBM uses reference-segmented priors to help construct segmented MRI volumes on individual participants. Initial work used the Talairach atlas that was based on a system that related similar structural areas with proportional distances (Talairach & Tournoux, 1988). Quantitative MRI studies required a reference MRI volume (Mandal et al., 2012). The contemporary reference system for quantitative MRI work is the “Montreal Neurological Institute” (MNI) standard space, which is based on young adult participants (MNI, Mazziota, Toga, Evans, Fox, & Lancaster, 1995; Evans, Collins, & Milner, 1992; Evans, Collins, Mills, Brown, Kelly, & Peters, 1993). Studies of young children (or older adults) have been performed using the MNI template based on young adult participants, as the reference data. However, there have been several studies that have shown that problems exist with aligning child brains to adult reference templates. These issues are reviewed in Richards and Xie (2015). They include misclassification of brain tissue, differential brain growth during specific developmental periods, local and global macrostructural differences between adult and child brains, and more variable contours of the cortex in young participants. These problems also may exist when using young adult data as reference volumes when studying older adults (Huang et al., 2010; Richards & Xie, 2015).

The problem of using age-inappropriate reference templates has been solved by the construction of average MRI reference data from pediatric populations (see Richards & Xie, 2015). These include templates for specific ages (e.g., infants: Akiyama et al., 2013, Altaye et al., 2008, Shi et al., 2010, 2011; 8 year olds, Yoon et al., 2009) and templates for wide age ranges (Fonov et al., 2011; Wilke et al., 2008). Of particular note in this regard is the work of Fonov et al. (2011). They used the National Institutes of Health longitudinal study data (NIHPD; Evans, 2006). The provided templates with six age ranges with a width of 4 to 6 years each that were grouped according to estimated pubertal status: 4.5–8.5 years, pre-puberty; 7.0–11.0 years, pre- to early- puberty; 7.5–13.5 years, pre- to mid-puberty; 10.0–14.0 years, early to advanced puberty; and 13.0–18.5 years, mid- to post- puberty.

We contributed to this body of knowledge by creating fine-grained average MRI templates for a wide range of ages with discrete age intervals. To this end, we created average MRI templates for ages 2 weeks through 4 years in 1.5-month, 3-month, or 6-month increments (Sanchez et al., 2011), for ages 4.5 years to 20 years in 6-month-increments (Sanchez et al.,

2012), and adult reference volumes from 20 years through 89 years in 5-year increments (Fillmore et al., 2014; Phillips-Meek & Richards, 2014). The average MRI templates come from a database of over 4000 participants obtained from open-access and local sources for whom we have T1-weighted MRIs. We found in our studies that an external validation group showed a closer registration to the age-appropriate template than to typical young adult templates (Fillmore et al., 2014, 2015; Sanchez et al., 2012; Xie et al. 2014b). In addition to average MRI volumes, we also generated segmented partial volume estimates of GM, WM, and T2W-derived CSF (Fillmore et al., 2015; Phillips-Meek & Richards, 2013; Sanchez et al., 2011, 2012) and a common stereotaxic atlas for infants, children, adolescents, and adults (e.g., for infants see Fillmore et al., 2014; Phillips et al., 2013).

The result of this work is the “Neurodevelopmental MRI Database”. This database consists of average MRI templates, segmented priors, and stereotaxic atlases. The database is available online (<http://jerlab.psych.sc.edu/NeurodevelopmentalMRIDatabase/>). A fuller description of the rationale and characteristics of the database may be found in Richards and Xie (2015). Details of the construction of the MRI averages and segmented partial volume estimate volumes may be found in the original papers (Fillmore et al., 2015; Phillips-Meek & Richards, 2014; Sanchez et al., 2011, 2012). A description of the procedures for the stereotaxic atlas for infants is found in Fillmore et al., 2014.

An important contribution of the Neurodevelopmental MRI Database is its applicability to the measurement of brain activity in pediatric populations. The quantitative analysis of brain function requires reference MRI volumes in order to normalize brain differences across participants (e.g., for fMRI analysis). Additionally, the study of brain activity with external measurement of scalp electrical activity (EEG and ERP) requires age-appropriate scalp electrode measurement and age-appropriate head models. The “Neurodevelopmental MRI Database” is a unique resource for the study of such brain activity, and should be useful in the study quantitative studies of developmental brain functioning.

## Purpose of database

The goal for constructing the database was to make available a series of age-appropriate average MRI reference templates and associated files in order to provide more precise representations of the brain across lifespan development. This database serves as a unique resource for the study of brain development in which the templates are done separately by age for a large number of ages across the lifespan. Each template was constructed using identical procedures to facilitate comparisons across the lifespan. The database includes average MRI templates, segmented partial volume estimate volumes for GM, WM, T2W-derived CSF, and stereotaxic atlas volumes. The data is also separated into brain-based and head-based averages (Fillmore et al., 2015; Phillips-Meek et al., 2013; Sanchez et al., 2011, 2012). Table 1 contains the age-increments for the average MRIs, numbers of scans, the materials that are available at each age, and the sources of the scans at each age. The age-increment of the average templates are 1.5 months from 3 to 7.5 months, 3 months from 9 to 18 months, half-year increments from 2 to 19–5 years, and 5-year increments from 20 through 89 years (Table 1). The data are organized in the database according to infants (2 weeks through 12 months), preschool (15 months through 4 years), children (4.5 through

10.5 years), adolescents (11 through 17.5 years), and adults (18 through 89 years). There is also a ‘young adult’ template generated from participants from 20 to 24 years of age. This average was constructed to create an adult comparison template similar to the ages of the MNI and ICBM templates (Collins, Neelin, Peters, & Evans, 1994; Evans, Brown, Kelly, & Peters, 1994; Evans et al., 1993; Joshi, Davis, Jomier, & Gerig, 2004; Mazziotta et al., 2001).

There are occasional updates of the averages. For the most part, the data on the database are stable. However, specific ages are being updated as more participants are obtained (e.g., 4 years and 12 years have 3T studies in progress). We envision the data to be available on the web site for at least 7 years (through 2022), and at the end of this time will be transferred to a long-term data storage system (e.g., LONI Image Data Archive, <https://ida.loni.usc.edu>; DATABRARY, [databr.org](http://databr.org); Adolph, Gilmore, Freeman, Sanderson, & Millman, 2012).

### Site of Individual MRIs, Participants, Image Modalities

The database consists of average templates (T1W and T2W), segmenting priors, and stereotaxic atlases. The average MRI templates were drawn from a total database of over 4000 participants from open-access databases or scans performed at the McCausland Center for Brain Imaging (MCBI). These sources include open-access database such as the NIHPD Object 2 data (Almli et al., 2007, [http://www.bic.mni.mcgill.ca/nihpd/info/data\\_access.html](http://www.bic.mni.mcgill.ca/nihpd/info/data_access.html)), NIHPD Objective 1 data (Waber et al., 2007), Autism Brain Imaging Data Exchange (ABIDE; Di Martino et al., 2013; [http://fcon\\_1000.projects.nitrc.org/indi/abide/](http://fcon_1000.projects.nitrc.org/indi/abide/)), Information Extracted from Medical Images database (IXI; Ericsson, Aljabar, & Rueckert, 2008; Heckemann, et al., 2003; <http://biomedic.doc.ic.ac.uk/brain-development/index.php?n=Main.Datasets>), and Open Access Series of Imaging Studies (OASIS; Marcus, Fotenos, Csernansky, Morris, & Buckner, 2010; Marcus, et al., 2007; : <http://www.oasis-brains.org>). We also have obtained a number of scans from other sites, which are used in collaborative studies (e.g., Center for Brain and Cognitive Development, Lloyd-Fox et al., 2014). The scans from the NIHPD data set included some participants who were scanned at more than one age (see Sanchez & Richards, 2011, 2012 for the numbers of repeated scans; Almli et al., 2007, and Waber et al., 2007 for the sampling protocol). Otherwise the scans came from individuals scanned at a single age. A brief description of the scan sequences is presented in Table 2. The details of the MRI sequences can be found in the publications that describe the database averages (Fillmore et al., 2015; Phillips-Meek & Richards, 2014; Sanchez et al. 2011, 2012) and in the open-access sites (www sites listed above).

All participants making up the templates were typically developing individuals, whose MRIs were specifically acquired as typically developing (e.g., NIHPD) or as controls for children/adults with neurodevelopmental disorders (e.g., ABIDE controls for ADHD participants). There are approximately equal numbers of males and females. The gender of the participants making up each age-appropriate average is not provided on the database, but is available in the publications (Fillmore et al., 2015; Phillips-Meeks & Richards, 2014; Sanchez et al., 2011, 2012). We have MRI volumes from more than 4000 participants, and selected 2762 for the averages. The other participants have neurodevelopmental disabilities (e.g., PKU, FXS, ASD, siblings of ASD, ADHD), other nationalities (Chinese), or other data not used

(e.g., ABIDE control males not matched with female participants; MRIs from collaborations with sharing restrictions). We consider these participants part of the Neurodevelopmental MRI Database (Richards & Xie, 2015), but they are not shared on the site. We have used these scans for other related projects (e.g., volumetric comparison of Chinese children head/brain development with the US participants, Xie et al, 2014a; placement of NIRS optodes on the scalp and underlying brain areas, Lloyd-Fox et al, 2014; average MRI templates for Chinese children and adolescents, Xie et al., 2014b). We encourage others to contribute MRI scans to our database and are open to collaborations based on the average MRI templates.

Quality control procedures were used both on the individual scans. The open access data had specific protocols for insuring quality of the scans (see online sites above). For the MCBI scans we followed the NIHPD quality control procedure (e.g., [http://www.bic.mni.mcgill.ca/nihpd/info/quality\\_control.html](http://www.bic.mni.mcgill.ca/nihpd/info/quality_control.html)). This included automatic biasfield inhomogeneity correction with a N4 bias field correction procedure (Avants et al., 2011; Tustison et al., 2010) and image cropping. The MCBI scans had brain extraction done with the procedure recommended by FSL's VBM protocol and each brain was visually inspected and manually edited if necessary. All scans were also visually inspected according to the NIHPD protocol for movement artifacts, intensity homogeneity after correction, GM / WM / CSF contrast, MRI volume orientation, or any other artifacts. Scans were accepted only if these categories were acceptable. Additionally, since the scans came from different recording sites and scanners, we did a bias-field inhomogeneity correction on all scans and transformed the voxel intensity so that the peak of the GM histogram was normed to 100 (Sanchez et al., 2011). This allowed the data from different sites to be normalized to the same voxel value range and resolution.

The scans were used to create average reference templates. These include templates with combined 1.5T and 3.0T scan strengths, only 1.5T scan strengths, and only 3.0T scan strengths. Separate averages were done for the head and the brain, and separate averages for T1-weighted and T2-weighted scans. The steps for the averaging procedure are listed in Table 3. Details of the averaging procedure may be found in Sanchez et al. (2011, 2012) and Fillmore et al. (2015). Figure 1 shows representative scans for ages from the 6–0Months3T through the 85–89Years templates. Figures representing all the other ages may be found in the original articles (Fillmore et al., 2015; Sanchez et al, 2011, 2012). The averages were visually inspected at each iteration to insure that the ICBM-152 orientation remained stable and were rigidly rotated to that average template if necessary. The averages were also inspected for obvious inhomogeneity or irregularity. These occurred occasionally because an individual MRI volume had poor quality, and those individual MRI volumes were removed. Otherwise, the averaging process was not manually adjusted. The preparation of the individual participant volumes (bias-field inhomogeneity correction, GM intensity normalization) allowed some correction for the scans coming from different sites and scanners. The transformation of the MRIs into the ICBM-152 step resulted in initial participant MRI orientations that were similar for the first averaging step and preserved the relative size of the head or brain (see Fonov et al., 2011; Mandal et al., 2012; Mazziotta et al., 2001; Sanchez et al., 2011). The initial rigid rotation results in initial average templates that are loosely oriented to the ICBM-152 average MRI template. The nonlinear registration

in the procedure preserves the fine details in the average MRI and the iterative procedure avoids biasing the templates to adult reference data.

Some of the ages have both 1.5T and 3.0T scans. We have separate average MRI templates for the 1.5T scans, the 3.0T scans, and a combined 1.5T and 3.0T scan. The 1.5T scans for the templates from 2–0Weeks through 19–5Years were only from the NIHPD data, so their quality (scan strength, 2D or 3D, resolution, quality control) are similar. The 3.0T scans come primarily from the MCBI and ABIDE data, and have comparable scan quality (scan strength, 3D scans, voxel resolution, comparable “modern” scanners). The scans for the combined averages have different resolution due to the scanner strength or spatial resolution, and come from different sites. We recommend the use of the 3.0T templates where available. Additionally, the 3.0T templates have associated stereotaxic atlases.

Average segmenting priors and stereotaxic atlases were made for each age. A segmenting method (e.g., FSL’s FAST; Zhang, Brady, & Smith, 2001) was used to segment the original T1W images into GM and WM, and a threshold procedure was used to identify CSF in the T2W image. Each participant T1W scan was registered (linear-FLIRT; and non-linear-ANTS) to the average template to which it contributed, the GM, WM, and T2W-derived CSF were warped into the average space, and partial volume probabilities were constructed for each segmented material for each average.

The stereotaxic atlases were constructed from manually segmented lobar atlas for selected averages (e.g., all first year; and 6, 12, 18, and 20–24 year average 3T templates), with image fusion methods (e.g., majority vote, Gousias et al., 2008; joint fusion, Wang et al., 2013) for the LONI LPBA40 (LONI Probabilistic Brain Atlas, LPBA40, Shattuck et al., 2008) and the IXI Hammers (Hammers atlases; Hammers et al., 2003; Heckemann, Hajnal, Aljabar, Rueckert, & Hammers, 2006; Heckemann et al., 2003) atlases for all 3T average templates (4 years through 30–34 year templates; e.g., for infant templates see Phillips et al., 2013, and Fillmore et al., 2014).

## Data Sharing, Online Access

The “Neurodevelopmental MRI Database” is available online (<http://jerlab.psych.sc.edu/NeurodevelopmentalMRIDatabase/>). These are publicly available to researchers for clinical and experimental studies of normal and pathological brain development. The data is shared under a Creative Commons Attribution-NonCommercial-NoDerivs 3.0 Unported License (CC BY-NC-ND 3.0; [http://creativecommons.org/licenses/by-nc-nd/3.0/deed.en\\_US](http://creativecommons.org/licenses/by-nc-nd/3.0/deed.en_US)). Data access is limited to scientific professionals for research purposes. Interested users should contact John E. Richards (richards-john@sc.edu) for access with a request detailing the purpose of the work, the number of people using the data, the ages to which access is desired, and a statement agreeing to the terms of use (<http://jerlab.psych.sc.edu/NeurodevelopmentalMRIDatabase/request.html>). The terms of use state, “The MRI templates from this database are freely available and distributed for scientific work. The CC BY-NC-ND 3.0 license allows sharing but users should inform JER of any sharing. These should not be modified or used in commercial applications. Publications from this work should cite the publications for the data upon which these templates are based. JER retains

all copyrights to the templates.” To date there are 120 sites (individual user, or laboratory) that have requested access to the database, and 277 users (individual users, or laboratory personnel).

The online data consist of the average MRI templates, segmented priors, and stereotaxic atlases. The template volumes are in compressed NIFTI format (<http://nifti.nimh.nih.gov/>). The data are on a file server that may be accessed with the Secure Shell (SSH) file transfer protocols (SCP or SFTP), with instructions for how to access the data (<http://jerlab.psych.sc.edu/NeurodevelopmentalMRIDatabase/access.html>). Instructions are given on the site for a SCP copy of the entire database, or SFTP may be used to access individual components. The original, individual MR brain scans and behavioral data from the NIHPD can be obtained from their website (<https://nihpd.crbs.ucsd.edu/nihpd/info/index.html>). The original individual MR brain scans for the ABIDE ([http://fcon\\_1000.projects.nitrc.org/indi/abide/](http://fcon_1000.projects.nitrc.org/indi/abide/)), IXI (database <http://biomedic.doc.ic.ac.uk/brain-development/index.php?n=Main.Datasets>) and OASIS (<http://www.oasis-brains.org>) are available at those websites for public access.

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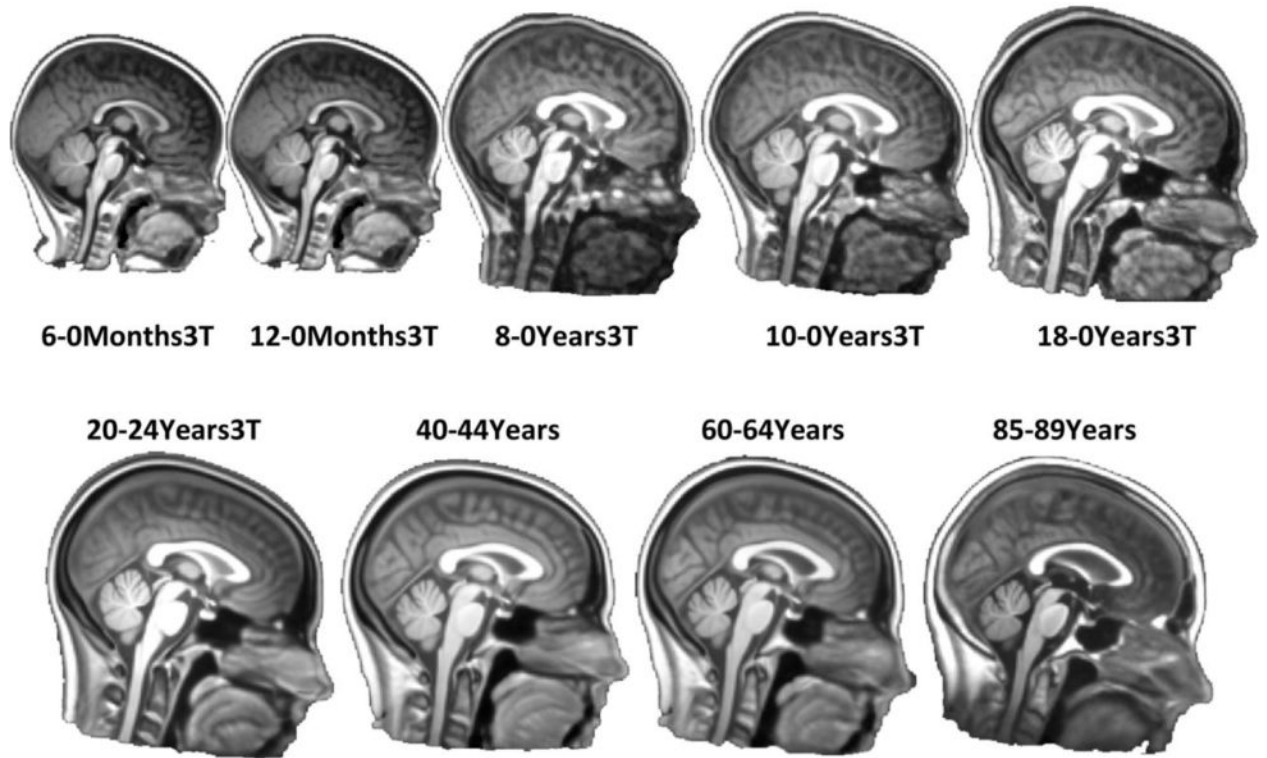
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**Figure 1.** Whole head T1-Weighted average MRI templates for selected average templates from 6–0Months3T through 80–89Years. The MRI volumes are shown displayed at the mid-sagittal slice.

**Table 1**  
**Ages and templates, number of MRIs, and information on database**

Age and number of scans for the 1.5T, 3.0T, and Combined average MRI templates. The “Combined” column represents the total number of scans in the combined (1.5T + 3.0T) atlas, which includes all 1.5T MRIs and part or all of the 3.0T MRIs, as in the original publications (Fillmore et al., 2015; Phillips-Meek & Richards, 2013; Sanchez et al., 2011, 2012). The NIHPD scans (1.5T, ages 2 weeks through 18 years) include scans from some participants at more than one age, the other scans were from participants scanned at only one age. All average MRI templates are accompanied by segmented partial volume estimates (GM, WM, and when available, T2W-derived CSF). The atlases are based on the 3.0T average MRI template when 3.0T scans exist (Atlas-3.0T), or based on the 1.5T average MRI template when no 3.0T scans exist (Atlas-1.5T).

<b>Infants</b>				
<b>Age</b>	<b>1.5T</b>	<b>3.0T</b>	<b>Combined</b>	<b>Notes</b>
2–0 Weeks	23			
3–0Months	22	14	36	Separate 1.5, 3.0T, Combined, Atlas-3.0T
4–5Months		12	12	3–0T only, Atlas-3.0T
6–0 Months	32	14	46	Separate 1.5, 3.0T, Combined, Atlas-3.0T
7–5 Months		11	11	3–0T only, Atlas-3.0T
9–0 Months	29	12	34	Separate 1.5, 3.0T, Combined, Atlas-3.0T
12–0 Months	25	12	35	Separate 1.5, 3.0T, Combined, Atlas-3.0T
<b>Preschool</b>				
<b>Age</b>	<b>1.5T</b>	<b>3.0T</b>	<b>Combined</b>	<b>Notes</b>
15–0 Months	32		32	
18–0 Months	32		32	
2–0 Years	27		27	Atlas-1.5T
2.5 Years	32		32	
3–0 Years	22		22	Atlas-1.5T
4–0 Years	19	10	19	Separate 1.5, 3.0T, Combined is 1.5T only, Atlas-3.0T
<b>Children</b>				
<b>Age</b>	<b>1.5T</b>	<b>3.0T</b>	<b>Combined</b>	<b>Notes</b>
4–5 Years	9		9	
5–0 Years	14		14	
5–5 Years	17		17	
6–0 Years	27	10	37	Separate 1.5, 3.0T, Combined, Atlas-3.0T
6–5 Years	36		36	
7–0 Years	27		27	
7–5 Years	44		44	
8–0 Years	46	19	56	Separate 1.5, 3.0T, Combined, Atlas-3.0T
8–5 Years	40	12	40	Separate 1.5, 3.0T, Combined is 1.5T only, Atlas-3.0T
9–0 Years	46		46	
9–5 Years	41	10	41	Separate 1.5, 3.0T, Combined is 1.5T only, Atlas-3.0T
10–0 Years	62	16	72	Separate 1.5, 3.0T, Combined, Atlas-3.0T
10–5 Years	52		52	

<b>Infants</b>				
<b>Age</b>	<b>1.5T</b>	<b>3.0T</b>	<b>Combined</b>	<b>Notes</b>
<b>Adolescents</b>				
Age	1.5T	3.0T	Combined	Notes
11–0 Years	31		31	
11–5 Years	40		40	
12–0 Years	37	15	47	Separate 1.5, 3.0T, Combined, Atlas-3.0T
12–5 Years	30		30	
13–0 Years	34	11	34	Separate 1.5, 3.0T, Combined is 1.5T only, Atlas-3.0T
13–5 Years	29	19	29	Separate 1.5, 3.0T, Combined is 1.5T only, Atlas-3.0T
14–0 Years	32	30	42	Separate 1.5, 3.0T, Combined, Atlas-3.0T
14–5 Years	30		30	
15–0 Years	32		32	
15–5 Years	23		23	
16–0 Years	34	13	44	Separate 1.5, 3.0T, Combined, Atlas-3.0T
16–5 Years	28		28	
17–0 Years	25		25	
17–5 Years	25		25	
<b>Adults</b>				
Age	1.5T	3.0T	Combined	Notes
18–0 Years	18	20	28	Separate 1.5, 3.0T, Combined, Atlas-3.0T
18–5 Years	12	23	29	Separate 1.5, 3.0T, Combined, Atlas-3.0T
19–0 Years	10	17	23	Separate 1.5, 3.0T, Combined, Atlas-3.0T
19–5 Years	5	21	22	Separate 1.5, 3.0T, Combined, Atlas-3.0T
20–24 Years	157	108	244	Separate 1.5, 3.0T, Combined, Atlas-3.0T
25–29 Years	86	24	101	Separate 1.5, 3.0T, Combined, Atlas-3.0T
30–34 Years	63	34	79	Separate 1.5, 3.0T, Combined, Atlas-3.0T
35–39 Years	50		50	
40–44 Years	61		61	
45–49 Years	65		65	
50–54 Years	57		57	Atlas-1.5T
55–59 Years	73		73	
60–64 Years	83		83	
65–69 Years	89		89	
70–74 Years	101		101	
75–79 Years	61		61	
80–84 Years	62		62	
85–89 Years	36		36	Atlas-1.5T
<b>Totals</b>	<b>2275</b>	<b>487</b>		
<b>Sources</b>				<b>Included in Templates</b>
NIHPD	1258			2–0Weeks through 20–24Years
MCBI		325		3–0Months3T through 35–39Years3T
ABIDE		132		8–0Years3T through 19–5Years3T

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<b>Infants</b>				
<b>Age</b>	<b>1.5T</b>	<b>3.0T</b>	<b>Combined</b>	<b>Notes</b>
IXI	543	30		20–24Years through 85–89Years
OASIS	474			20–24Years through 85–89Years
	2275	487		

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**Table 2**

A brief description of the scan sequences. See Fillmore et al. (2015), Phillips-Meeks and Richards (2014), and Sanchez et al. (2011, 2012) for details.

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Author Manuscript	<p><u>NIHPD Objective 2, templates 2–0Months through 4–0Years (Sanchez et al., 2011).</u>          Axial scan, 2D T1-weighted spin echo, T2-weighted 2D Fast Turbo spin echo          Nominal 1×1×3 mm resolution (1×1×3 or 0.97×0.97×3), 46 to 66 slices in axial plane          Siemens Medical Systems (Sonata, Magnetom), GE (Signa Excite), 1.5T</p>
Author Manuscript	<p><u>USC-MCBI Infant scans, templates 3–0Months through 12–0Months (Sanchez et al, 2011)</u>          Sagittal scan, 3D T1-weighted “MPRAGE” RF-spoiled rapid flash          Axial scan, 2D T2/PD-weighted multi-slice Fast Turbo spin-echo          1×1×1 mm resolution, 144 sagittal slices (T1-weighted)          1×1×2.5 mm resolution, 50 axial slices (T2/PD-weighted)          Siemens Medical Systems (Tim Trio), 3.0T</p>
Author Manuscript	<p><u>NIHPD Objective 1, templates 4.5Years through 20–24Years (Sanchez et al., 2012)</u>          Sagittal scan, 3D T1-weighted spoiled gradient recalled (SPGR) echo          Alternate protocol, sagittal scan, 2D T1-weighted spin echo sequence          Axial scan, 2D T2/PD-weighted Fast Turbo spin echo          1×1×1 mm resolution, 160–180 sagittal slices (T1-weighted)          1×1×3 mm resolution, 192 sagittal slices (alternate protocol, T1-weighted)          1×1×1 mm resolution, 224 axial slices (T2-weighted)          Siemens Medical Systems (Sonata, Magnetom), GE (Signa Excite), 1.5T</p>
Author Manuscript	<p><u>USC-MCBI Child-through-Adult scans, templates 4–0 Years through 30–34Years (Sanchez et al, 2011 for children to young adults; Fillmore et al., 2015, for adults)</u>          Sagittal scan, 3D T1-weighted “MPRAGE” RF-spoiled rapid flash          Sagittal scan, 3D T2-weighted multi-slice Fast Turbo spin-echo          1×1×1 mm resolution, 160–212 sagittal slices          Siemens Medical Systems (Tim Trio), 3.0T</p>
Author Manuscript	<p><u>ABIDE Child through adolescent scans, templates 4–0Years through 18–0Years</u>          Sagittal scan, 3D T1-weighted MPRAGE RF-spoiled rapid flash          1×1×1 mm resolution, 160–208 sagittal slices          Siemens Medical Systems (Magenetom Tim Trio, Magnetom Verio, Magnetom Allegra)          GE (MR750, Signa); Phillips Medical Systems (Achieva, Intera)</p>
Author Manuscript	<p><u>OASIS Adult scans, templates 20–24Years through 85–89Years (Fillmore et al., 2015)</u>          Sagittal scan, 3D T1-weighted MPRAGE RF-spoiled rapid flash          1×1×1 mm resolution, 162–182 sagittal slices          Siemens Medical Systems (Magnetom Vision), 1.5T</p>
Author Manuscript	<p><u>IXI Adult scans, templates 20–24Years through 88–89Years (Fillmore et al., 2015)</u>          Sagittal scan, 3D T1-weighted spin echo, T2-weighted Fast Turbo spin-echo          0.9375×0.9375×1.2 mm resolution, 140–150 sagittal slices          Phillips Medial Systems (Intera 3T, Gyroscan Intera 1.5T), GE (1.5T)</p>

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**Table 3**

Steps for the average MRI templates. See Fillmore et al. (2015), Phillips-Meeks and Richards (2014), and Sanchez et al. (2011, 2012) for details.

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1—Individual MRI volume preparation.

- Bias-field inhomogeneity correction (Avants et al., 2011; Tustison et al., 2010)
- Segmenting of MRIs in GM/WM with FAST (Zhang et al., 2001)
- Threshold of T2W for CSF segmented volume
- GM histogram intensity normed to 100 (Sanchez et al., 2011)
- Rigid affine registration (rotation, translation) to ICBM-152 (Mandal et al., 2012)
- Transformation (rotation, translation) of MRI into the ICBM-152 orientation

2—Initial average

- All T1W MRI for age-range were averaged into a single MRI volume
- Separate averages were done for brain and head
- Separate averages for T1-weighted and T2-weighted scans

3—Iterative nonlinear averaging procedure

- Non-linear registration of individual MRIs in age-range to average MRI (Avants, et al., 2008, 2011).
- Non-linear transformation of individual MRI to average MRI space
- Average of the transformed individual MRIs to create a new average
- Steps continue until RMS between subsequent averages is minimized

4—Construction of segmenting priors

- Non-linear transformation of segmented GM/WM/CSF volume into average space using the registration parameters from the final iteration of step 3.
  - Average of transformed segmented volumes for segmented priors.
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