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Variation in longitudinal trajectories of regional brain volumes of healthy men and women (ages 10 to 85 years) measured with atlas-based parcellation of MRI

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ABSTRACT

Numerous cross-sectional MRI studies have characterized age-related differences in regional brain volumes that differ with structure and tissue type. The extent to which cross-sectional assumptions about change are accurate depictions of actual longitudinal measurement remains controversial. Even longitudinal studies can be limited by the age range of participants, sex distribution of the samples, and scan intervals. To address these issues, we calculated trajectories of regional brain volume changes from T1-weighted (SPGR) MRI data, quantified with our automated, unsupervised SRI24 atlas-based registration and parcellation method. Longitudinal MRIs were acquired at 3 T in 17 boys and 12 girls, age 10 to 14 years, and 41 men and 41 women, age 20 to 85 years at first scan. Application of a regression-based correction function permitted merging of data acquired at 3 T field strength with data acquired at 1.5 T from additional subjects, thereby expanding the sample to a total of 55 men and 67 women, age 20 to 85 years at first scan. Adjustment for individual supratentorial volume removed regional volume differences between men and women due to sex-related differences in head size. Individual trajectories were computed from data collected on 2 to 6 MRIs at a single field strength over a ~1 to 8 year interval. Using linear mixed-effects models, the pattern of trajectories over age indicated: rises in ventricular and Sylvian fissure volumes, with older individuals showing faster increases than younger ones; declines in selective cortical volumes with faster tissue shrinkage in older than younger individuals; little effect of aging on volume of the corpus callosum; more rapid expansion of CSF-filled spaces in men than women after age 60 years; and evidence for continued growth in central white matter through early adulthood with accelerated decline in senescence greater in men than women.

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Introduction

Numerous cross-sectional MRI studies have characterized age-related differences in regional brain volumes that differ with structure and tissue type. In general, these brain imaging studies are consistent in reporting larger cerebrospinal fluid (CSF) filled volumes (ventricles and sulci), smaller brain tissue volumes, more prominent in cortical and allocortical gray matter than in centrum semiovale or corpus callosum white matter, and thinner cortices (e.g., Blatter et al., 1995; Courchesne et al., 2000; Good et al., 2001; Jernigan et al., 2001; Pfefferbaum et al., 1994; Raz et al., 2004a; Sowell et al., 2007; Sullivan et al., 2004; Walhovd et al., 2011); (reviewed by Raz and Kennedy, 2009; but see Burgmans et al., 2009). Age-related shrinkage of selective subcortical structures is controversial (e.g., Jack et al., 2000; Jernigan et al., 2001; Luft et al., 1999; Raz et al., 2003; Sullivan et al., 2004, 2005). One of the largest cross-sectional samples analyzed 1143 healthy men and women, age 18 to 94 years, from seven imaging centers and measured cortical thickness and regional volumes acquired on different 1.5 T MRI systems with a single method (FreeSurfer) (Fjell et al., 2009b). This analysis revealed small but significant sex differences in white matter, CSF, and the pallidum, suggesting more rapid age effects in older men than women; however, caution is required for data based on the pallidum measure because it was the least reliable of those used (Pfefferbaum et al., 2012). The extent to which cross-sectional assumptions about change reflect true longitudinal measurement, however, remains controversial (cf., Lindenberger et al., 2011; Rabbitt, 2011; Raz and Lindenberger, 2011; Salthouse, 2011). Statistical modeling has identified notable shortcomings in making longitudinal inferences about change from cross-sectional data, even in instances where cross-sectional measures correlate well with longitudinal change (e.g., Lindenberger et al., 2011).

Longitudinal studies are better suited to address conflicts emerging from cross-sectional investigation (cf., Lindenberger et al., 2011;

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Weiner et al., 2012). Such studies report ventricular enlargement or brain tissue volume decline detectable over 1 year (Adalsteinsson et al., 2000; Fjell et al., 2009a) to several years (e.g., Cook et al., 2004; Marcus et al., 2010; Pfefferbaum et al., 1998; Raji et al., 2009; Raz et al., 2005; Resnick et al., 2003; Rusinek et al., 2003; Scahill et al., 2003; Sullivan et al., 2004, 2010; Taki et al., 2011b; Tang et al., 2001), with the longest follow-up to date being 10 years (Driscoll et al., 2009). Brain regional volumes commonly identified as exhibiting the greatest aging effects are prefrontal cortex, medial temporal lobe structures, and lateral ventricles. As with cross-sectional studies, these longitudinal studies provide only inconsistent evidence for sex differences in rates of change. The series of analyses by Raz and colleagues on trajectories of local volume decline in striatum (Raz et al., 2003), entorhinal cortex, hippocampus (Raz et al., 2004b; Rodrigue and Raz, 2004), and cerebellum (Raz et al., 2005) culminated in an analysis comparing rates of change in these and other brain structures, examined three times on a 1.5 T MRI system over a 30-month interval in 40 participants, age 49 to 85 years, and subjected to manual delineation of target brain structures (Raz et al., 2010). Adjusted for variation in intracranial volume, areas especially vulnerable to aging were the lateral prefrontal cortex, prefrontal white matter, hippocampus, putamen, and cerebellar hemispheres; the least affected were the primary visual cortex, corpus callosum, and ventral pons; the only sex difference reported was for the pons, where women showed greater shrinkage than men. Another study of 3 measurements over 4 years in 92 men and women, age 59 to 85 years, revealed widespread white matter volume decline with local gray matter volume decline, which was most prominent in inferior and orbital frontal, inferior parietal, insular and cingulate cortices, and ventricular enlargement with little evidence for sex differences in rates of change (Resnick et al., 2003). A 6-year longitudinal study in 381 community-dwelling men and women, age 28 to 89 years, reported greater annual declines in gray matter-to-intracranial volume ratios in older men and women relative to younger women (Taki et al., 2011a).

Cross-sectional developmental studies focused on adolescence have revealed a curvilinear function of cortical gray matter with an increase from birth to about 10 years of age followed by a continuous decline through adulthood to old age (Blanton et al., 2001; Carne et al., 2006; Courchesne et al., 2000; Giedd et al., 1996; for reviews Giedd et al., 2010; Gogtay et al., 2004; Jernigan et al., 2001; Lange et al., 1997; Lu et al., 2007; Pfefferbaum et al., 1994; Raz and Rodrigue, 2006; Reiss et al., 1996; Sowell et al., 2002, 2007; Stiles and Jernigan, 2010; Tisserand et al., 2002). Longitudinal studies are consistent with this depiction of regional brain volumetric change when regional brain volumes obtained over time are expressed as individual trajectories (Giedd et al., 1996; Raznahan et al., 2011b; Shaw et al., 2008). These analyses characterized heterochronicity in trajectories by brain region and sex (Brain Development Cooperative Group, 2012; Giedd et al., 1999; Lenroot et al., 2007; Raznahan et al., 2011a, 2011b; Shaw et al., 2008; Sowell et al., 2004). Brains of boys can be 10% larger than those of girls (Dekaban and Sadowsky, 1978; Goldstein et al., 2001), but growth starts and ends earlier in girls than boys, peaking at 10.5 years in girls compared with 14.5 years in boys and declining thereafter in both (Lenroot et al., 2007).

MRI studies report that the neocortex follows a curvilinear trajectory (Gogtay et al., 2004; Lenroot et al., 2007; Shaw et al., 2008), whereas allocortex and medial temporal structures follow a linear path (Gogtay et al., 2004). Growth is earlier in anterior than posterior cortical regions in both sexes (Shaw et al., 2008). Examination of regional cortical thickness over 2-year intervals revealed continued gray matter thinning of cortical language areas associated with vocabulary scores and probably language development (Sowell et al., 2004). The largest longitudinal study of brain development examined 647 individuals, age 3 to 30 years over approximately 2-year intervals (Raznahan et al., 2011b). Developmental trajectories for regional cortical volumes and surface area analysis revealed curvilinear growth and sexual dimorphism varying by cortical, allocortical, and subcortical tissue structures and developmental stage (also see Raznahan et al., 2010, 2011a). Recently, we reported that longitudinal MRI assessment using robust, atlas-based parcellation methods was sufficiently sensitive to identify regional brain changes over a ~6-month interval in boys and girls in early adolescence. Supratentorial and CSF volumes increased, while cortical gray matter volumes declined in anterior (lateral and medial frontal, anterior cingulate, precuneus, and parietal) but not posterior (occipital, calcarine) cortical regions, whereas subcortical structures did not show consistent changes (Sullivan et al., 2011).

Despite power to detect change, longitudinal studies can be limited by the age range of participants recruited for examination. For example, some studies focus on healthy seniors (age 60 years and older), who had served as the comparison group for age-related dementing disorders, or use data taken from publicly available data sources, such as the Alzheimer's Disease Neuroimaging Initiative (ADNI) (e.g., Fjell et al., 2009a; Weiner et al., 2012). Restricting the age range of subjects to the elderly for the purpose of detecting and modeling the effects of aging, however, can potentially introduce a bias in modeling brain structural changes, especially in structures with developmental changes best described by higher-order rather than linear functions. Even longitudinal studies that use restricted age ranges comprise both the obvious longitudinal component, which provides a metric of rate and trajectory of change, and a cross-sectional component, which is related to the age at initial observation. The cross-sectional component can affect the levels of dependent measures and may exert cohort effects (cf., Schaie and Hofer, 2001). These cross-sectional influences have been characterized as the "selection–maturation interaction" (Nesselroade, 1986), where "selection" refers to the age at study entry and "maturation" refers to the ages over which an individual was studied and the course of maturation over that period. According to Schaie and Hofer (2001), this interaction can be measured and even accounted for by examining multiple, parallel samples. Analysis of simple slopes of the longitudinal component describing change per individual does not fully address the cross-sectional component, which can potentially affect the initial level of trajectories. Thus, we assert that a statistical model incorporating both components should be employed to analyze data collected in the typical mixed longitudinal design.

Most studies of normal aging have been conducted at 1.5 T field strength (e.g., Fjell et al., 2009b; Raz et al., 2010; Weiner et al., 2012). Studies at higher field strength, typically 3 T and based on smaller samples, are now emerging (e.g., Sullivan et al., 2011). Recognizing the worth to longitudinal studies of merging data collected at different field strengths, a growing number of studies have attempted to combine data across MRI systems, typically 1.5 T and 3 T field strengths (Goodro et al., 2012; Han et al., 2006; Jovicich et al., 2009; Keihaninejad et al., 2010). To do so requires adjustment to minimize regional susceptibility to field effects that differentially influence tissue signal and border conspicuity (e.g., Bammer et al., 2007; Boss et al., 2007; Fushimi et al., 2007; Stankiewicz et al., 2011; Zhu et al., 2011). Recently, we showed that application of a regression-based linear correction function derived from 3 T data and applied to 1.5 T data on regional brain volumes determined from our SRI24 atlas-based registration and parcellation method (Rohlfing et al., 2010) significantly improved correspondence between volumes and enabled T1-weighted MRI data at both field strengths to be combined into a single analysis (Pfefferbaum et al., 2012).

The aims of the present study were to measure longitudinal changes in regional brain volumes in terms of trajectories over the full adult to senescent age range. Given the wide age range in combining longitudinal data collected over a 1 to 8 year interval in adults whose initial MRI age varied from 20 to 85 years, our analysis used a linear mixed-effects model, designed to handle mixed cross-sectional and

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