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Quantifying the trajectory of gyrification changes in the aging brain (Commentary on Madan, 2021)

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As the brain ages, it changes shape. The gross changes in the brain are very obvious. The brain appears to shrink within the skull and the ventricles enlarge, meaning that the space in the head occupied by brain tissue is smaller than in a younger person. These changes begin at roughly the age of 25, and continue for the remaining lifespan. Figure 1 shows a comparison between an older person's brain and that of someone in the middle years. As well as the large-scale changes in the morphology of the brain, there are associated changes in the thickness of the cortical sheet (Fjell et al., 2015; Thambisetty et al., 2010).

FIGURE 1 HERE

The most striking feature of the brain it its pattern of gyrification. The organisation of the gyri of the brain is astonishingly consistent across people, and even within and between animal species. This consistency hints at a developmental process, and it is reasonably well established that a combination of genetic and physical factors interact during gestation to 'crumple' the brain into a consistent shape (see Ronan & Fletcher, 2015 for a review of the different models). While there is considerable interest in understanding the mechanisms of brain gyrification in early-life development, it is also important to understand morphological change in the aging brain. These changes do not result from a reversal of the mechanisms that operate in the developing foetus, so must relate to changes that occur during maturity. In understanding these changes, it is helpful to have measures that capture the changes with sufficient sensitivity that individual differences can be explored.

Madan (2021) tackles this problem by looking at the gradients of gyrification across the brain. Madan uses a gyrification index (GI) that captures the smoothness of the brain at each point on its surface (Schaer et al., 2012; Zilles et al., 1988). The GI is a ratio of the surface area of the brain to the convex hull that encloses the brain volume. A more deeply folded brain surface will have a greater surface area compared to this outer surface, so giving a higher GI than a less 'crumpled' brain. Previous studies have used cross-sectional data to infer age-related changes in GI, finding that gyrification decreases during aging. Here, Madan (2021) uses longitudinal data to examine within-subject trajectories (LaMontagne et al., 2019). The main finding here is that the changes in gyrification are not uniform across the brain. Gyrification decreases in this longitudinal series, as demonstrated in previous, cross-sectional, studies. However there is a more prominent decrease in GI in the parietal cortex, which is a relatively more folded region. Madan (2021) extends this analysis by showing that the change in GI is driven by changes in the morphology of the sulci, becoming shallower and wider as the brain ages (see also Madan, 2019). These changes to the sulci are obvious in the slices in Figure 1, which are taken roughly through the regions with the greatest GI change in Madan's analysis.

What does this analysis add to our understanding of the aging brain? Madan shows that the age-related gyrification changes are most obvious in the parietal cortex, and the posterior parts of the frontal lobe. Gyrification changes in these areas correlate with cognitive abilities and with genetic factors (in cross-sectional studies, Fjell et al., 2015; Gregory et al., 2016), suggesting causal relationships among these measures. These regions are also associated with complications of vascular disorders such as hypertension (Raz et al., 2007), suggesting a role for lifestyle factors in predicting structural and cognitive changes.

The shape of the brain affects how neuroscientists interact with the brain in health and in disease. Localising the sources of functional activity in the brain, for example with EEG, requires a detailed knowledge of brain shape. For example, event-related EEG components may differ in their amplitude or computed source location according to age (Tsolaki et al., 2015). Similarly, aging-related changes affect the BOLD signal used in functional MRI (Liu et al., 2017). In a different modality, the variance of brain morphology predicts the distribution of energy induced by non-invasive brain stimulation such as TMS or tDCS (Bikson et al., 2016; Davis, 2021). So the changes in gyrification identified by Madan (2021) will help to understand safety and efficacy in stimulating the brain of the older person (Davis, 2017a, 2017b).

A deeper understanding of the relationship between brain structure and brain function will aid our understanding of how efficient cognitive processing relates to a physically healthy brain. Moreover, this will lead to more sensitive biomarkers for the early signs of progressive brain disorders, and will aid scientists in developing tools to track and to treat these disorders.

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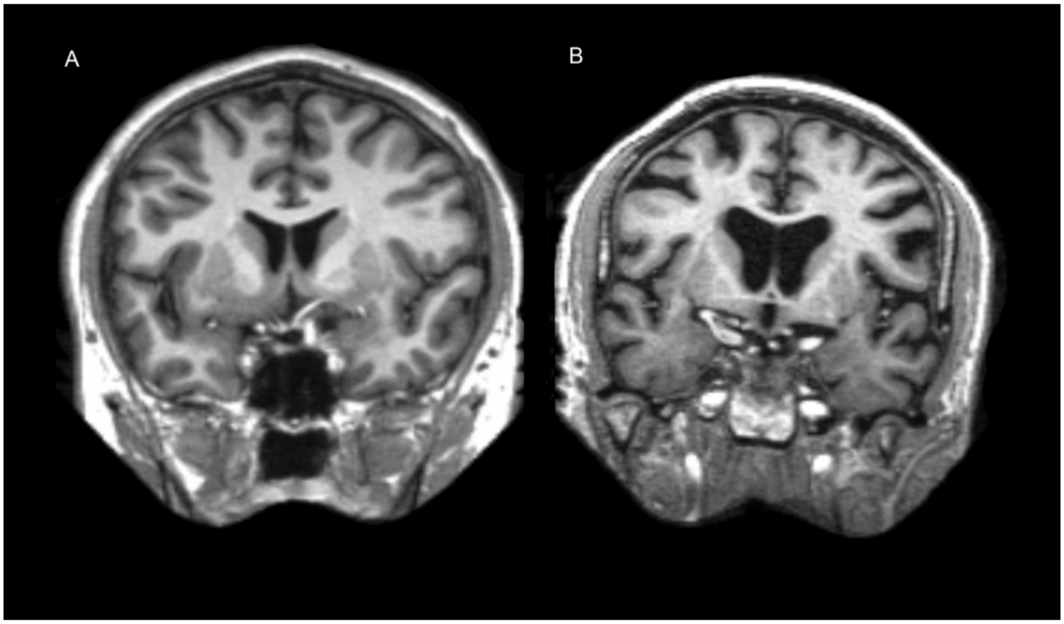
FIGURE 1. Two brain images taken from two right-handed male participants, aged 30 years (A) and 80 years (B). The difference in the shape of the brain within the skull is evident in these coronal slices. In the older person's image, the brain appears to have shrunk within the skull, and the ventricles appear enlarged. A measure such as the gyrification index (GI) captures the relationship between the surface area of the cortical sheet and the volume that encloses it. Shallower and wider sulci in the older brain (B) lead to a lower GI than that of the younger brain (A).



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