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Influence of thickening of the inner skull table on intracranial volume measurement in older people

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ABSTRACT

Introduction: It is generally assumed that intracranial volume (ICV) remains constant after peaking in early adulthood. Thus ICV is used as a 'proxy' for original brain size when trying to estimate brain atrophy in older people in neuroimaging studies. However, physiological changes in the skull, such as thickening of the frontal inner table, are relatively common in older age and will reduce ICV. The potential influence that inner table skull thickening may have on ICV measurement in old age has yet to be investigated.
Methods: We selected 60 (31 males, 29 females) representative older adults aged 71.1–74.3 years from a community-dwelling ageing cohort, the Lothian Birth Cohort 1936. A semi-automatically derived current ICV measurement obtained from high resolution T1-weighted volume scans was compared to the estimated original ICV by excluding inner skull table thickening using expert manual image processing.
Results: Inner table skull thickening reduced ICV from an estimated original 1480.0 ml to a current 1409.1 ml, a median decrease of 7.3% ($Z = -6.334$; $p<0.001$), and this reduction was more prominent in women than men (median decrease 114.6 vs. 101.9 ml respectively). This led to potential significant underestimations of brain atrophy in this sample by 5.3% ($p<0.001$) and obscured potential gender differences.
Conclusions: The effects of skull thickening are important to consider when conducting research in ageing, as they can obscure gender differences and result in underestimation of brain atrophy. Research into reliable methods of determining the estimated original ICV is required for research into brain ageing.

1. Introduction

Head size is strongly influenced by brain growth in childhood and reaches maximum size by early adulthood [1]. It is generally assumed that head size, and therefore intracranial volume (ICV), remains the same from early adulthood to old age. However, age-related skull changes, such as an increase in the thickness of the inner table and overall size of the cranium, have been found [2,3]. Physiological changes of the skull such as hyperostosis frontalis interna (HFI), thickening of the inner table of the frontal region of the skull, have also long been documented in the medical literature [4]. Whereas it is commonly observed by radiologists in older adults, skull thickening is not often mentioned in ageing research, possibly due to the benign nature of the changes [5]. Although the process is benign, some research suggests that, where the increase is very pronounced, dural irritation and pressure atrophy may occur [6]. Case studies of hydrocephalic children [7] and adults with severe brain atrophy [8] suggest that thickening of the inner skull table may occur in response to the reduction in brain volume caused by atrophy or changes in intracranial pressure. A cause of this sporadic thickening is thought to be hormonal as it is most prominently found in post-menopausal women and some studies have found endocrine abnormalities coincidental with HFI [9,4].

In neuroimaging studies, ICV is used as an estimate of peak prior adult brain volume [10–12]. Because it is thought that ICV is not influenced by disease or age-related changes, it is therefore often used to estimate brain atrophy. However, the influence that thickening of the inner skull table may have on measures of ICV, and hence on estimates of brain atrophy and its correlations, have yet to be investigated. In this paper, we investigated the potential influence of inner table skull thickening on measurement of ICV and estimates of brain atrophy in a cohort of community-dwelling older adults.

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2. Method

2.1. Subjects

We randomly selected 60 participants from the Lothian Birth Cohort 1936 [13] who had, on visual inspection, a range of inner skull table thickening from significant to little or no thickening. Study participants (31 males and 29 females) were non-demented, community-dwelling older individuals who underwent cognitive tests and brain MRI between 8th November 2007 and 29th June 2010 at 71.1 to 74.3 years of age (mean 72.7, standard deviation (SD) 0.7 years).

2.2. Image acquisition

Structural brain MRI data were obtained from a GE Signa HDxt 1.5 T MRI clinical scanner (GE Healthcare, Milwaukee, WI, USA) using a self-shielding gradient set with maximum gradient strength of 33 m/Tm, and an 8-channel phased-array head coil. The examination included a high resolution T1-weighted (T1W) volume scan, and whole brain T2- (T2W), T2*- (T2*W) and FLAIR-weighted sequences. Full details of the imaging protocol are provided in Wardlaw et al. [14].

2.3. Measurement method

All analyses were performed blind to subject details, including gender, on anonymised scans. The scans were aligned to the anterior-posterior commissure (AC-PC) line to improve reproducibility.

Measurements of current ICV were obtained using the T2*W sequence by a validated method [14]. The inferior limit of the intracranial cavity was defined as the axial slice that was superior to the tip of the odontoid peg at the foramen magnum (Fig. 1), and excluding the cavernous and extradural sinuses. To define the limits of the current ICV, we placed a seed-point in the axial slice at the midpoint where the orbits showed the optic nerve and selected the optimal threshold as the intensity value that separated the optic nerve from the rest of the brain tissue. The Object Extraction Tool (OET) in Analyze 9.0 that applies morphological erosion, dilation, region growing steps and thresholding, was used automatically to segment the ICV. The software then automatically extracted the ICV, creating a current ICV volume mask where the outer limit was the dural lining of the inner skull table. The current ICV mask was visually assessed and manually edited where necessary to exclude erroneous tissue using the MCMxxxVI multispectral segmentation tool [15] (http://sourceforge.net/projects/bric1936/). The MCMxxxVI method uses the colour combination of T2*W and FLAIR in the red/green colour spectrum, which facilitates easier identification of the brain boundaries in difficult areas. This method also determines cerebrospinal fluid (CSF) volume.

We estimated the original ICV, denoted as 'estimated original' ICV, excluding the effects of inner table skull thickening by editing the current ICV mask slices throughout the skull vault, extending its boundaries to include the inner skull table thickening. The inferior boundary for the measurement of inner table skull thickening was identified as the supraorbital ridge, which is the most prominent point in the midline sagittal view [16]. This landmark was used as it is an easily identifiable point and separates the vault where most of the inner table thickening occurs from the frontal sinuses and orbits where there is little thickening and the boundaries which are also more difficult to measure. Using multiplanar display software (MRIcro; www.cabiatl.com/mricro/mricro/index.html; Fig. 1), the sagittal view was selected and the location of the supraorbital ridge was highlighted to indicate which axial slice was the most inferior limit of the region. Then, for all slices showing ICV and inner table skull thickening superior to the supraorbital ridge, the edge of the current ICV mask was extended by manually tracing along the line where the original skull table was thought to be, as shown in Fig. 2. The inferior slices remained the same as those in the current ICV mask. The entire mask was re-measured providing an estimate of original ICV measurement without the effects of inner table skull thickening.

Finally, the current brain volume was measured in all subjects and brain atrophy determined by calculating the total brain tissue volume as a percentage of both current and estimated original ICV.

2.4. Statistical analysis

The sample was not normally distributed (Shapiro-Wilk normality test) for either the current ($W = 0.902$, $p = 0.001$) or estimated original ICV ($W = 0.919$, $p = 0.001$). The Wilcoxon Signed Ranks test

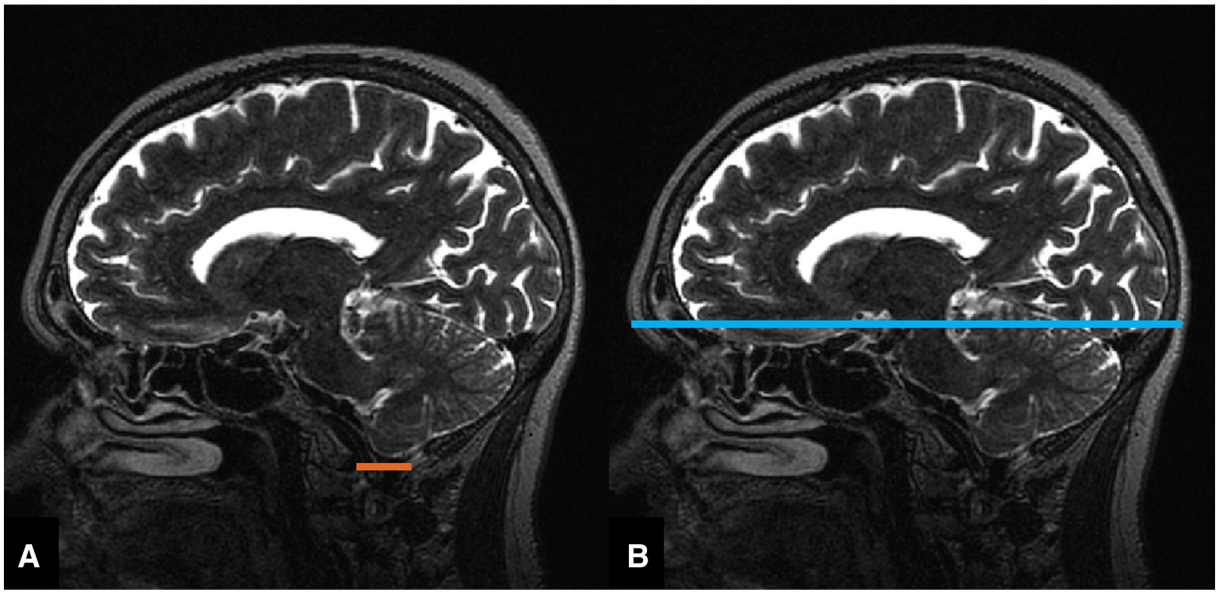

Fig. 1. (A) sagittal slice from a T2W MRI sequence showing the inferior limit of the intracranial volume at the foramen magnum (orange). (B) identification of the inferior boundary using the upper edge of the supraorbital ridge (blue).