Analysis of White Matter Hyperintensities and Ventricular Enlargement in an Elderly Cohort

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Summary

White matter hyperintensities (WMH) are lesions that appear brightly on magnetic resonance images (MRI) that are commonly associated with elderly individuals and cognitive decline. There are four interconnected cavities in the brain called ventricles. Particularly large ventricles have been connected to Alzheimer’s Disease. This study explores the relationship between white matter hyperintensities and ventricular enlargement in an elderly cohort. Previous literature has suggested that ventricular enlargement is directly caused by the white matter degeneration around it, and this study sought to find out if that was true. 65 subjects were included in this study, and data was provided from a cohort of elderly individuals participating in a longitudinal study conducted by the Layton’s Aging and Alzheimer’s Disease Center. A voxel based analysis was conducted based on longitudinal MRI images. The results showed that the lateral ventricles in the brain did not grow where white matter hyperintensities previously were. This is significant because it provides insight into the validity of these as biomarkers for disease.

Research Question

To what extent does the growth of white matter hyperintensities affect ventricular enlargement?

Background

White Matter Hyperintensities (WMHs) are lesions that appear on Magnetic Resonance Images (MRI) that are commonly associated with elderly individuals and cognitive decline. They often grow in areas of demyelination and axonal degeneration. There are four interconnected cavities in the brain called ventricles. The ventricles are filled with cerebrospinal fluid (CSF) which circulates around the brain and assists to dispose toxins and other waste matter into the brain. Patients with clinically diagnosed Alzheimer’s disease have significantly larger volumes of ventricles than subjects without (Ott et al, 2010). As they age, their ventricles in their brain usually grow pretty significantly. What is left unclear though is what is driving this ventricular enlargement. A common consensus in literature is that ventricular enlargement is occurring as a result of its surrounding White Matter (WM) tissue atrophy (Cou tout et al, 2018, Raj et al, 2011). More longitudinal analyses must be performed to confirm which neurodegeneration is occurring first to begin determining if this relationship is a correlation or a causation. Additionally literature has previously found that a larger amount of global WMHs are linked to higher ventricular volume (Wang et al, 2014, Godlin et al, 2009).

Subjects

The subjects used in this study were from the a cohort of elderly individuals participating in a longitudinal study conducted by the Layton’s Aging and Alzheimer’s Disease Center. The original scan log data included 120 subjects. 55 subjects were excluded from this project because they failed to have more than one valid MRI scan. A total of 65 subjects were used in the study. In that group, 25 were male and 40 were female. Their ages ranged from 66.2 to 102 (mean = 85.0). They all received a range of 2-6 MRI scans (median=3). The time in between a subject’s visits ranged from 0.6-4.9 years (mean=1.36). In relation to cognition, subjects had a mean MMSE score of 28.6, and a mean CDR score of .045.

Methodology

Before the start of this study, computerized algorithms had been used to segment white matter hyperintensities, ventricles, and the skull-striped brain. A fluid-attenuated inversion recovery (FLAIR) image is shown in Figure 1 where you can clearly see the white matter hyperintensities and the lateral ventricles. Each subject also had a T1 MRI image for every visit they had (Figure 2), a white matter hyperintensity mask, and a ventricle mask.

All masks made for this project were made through computer scripting. To start, combined ventricle and WMH masks were created using the 3dcalc function. The voxel intensity was labeled corresponding to the subject’s visit number. Next, another mask was created also using the 3dcalc function to show the amount of voxels that were labeled 2 on the combined ventricle mask, and 1 on the combined white matter hyperintensity mask. The function 3dBrickstat was used to count the amount of voxels that were in that generated mask. The same process was repeated for voxels labeled 3 on the combined ventricle mask and 2 on the combined WMH mask. This technique was also used to create and count

Results

The comparison of the ventricle graph is shown below. Out of the total ventricle growth an average of 4.21% could be accounted for ventricles growing in the WMHs, and an average of 95.8 % could be accounted to ventricles growing into other parts of the brain.

Conclusions

Patients with clinically diagnosed Alzheimer’s Disease have significantly larger volumes of ventricles then subjects without (Ott et al., 2010). Additionally, the initial hypothesis relating to ventricular enlargement was incorrect. The areas where WMHs previously were did not affect the direction of where the ventricles are going to grow. The graphs show that a large portion of ventricular enlargement is accounted for growth into areas that were not previously white matter hyperintensities.

Limitations

Limitations include not having more visits per subjects. Additionally the variance in the amount of time in between the subjects’ visits could’ve caused inconsistencies in the results. Furthermore, the manual code used to transform the data could hold inaccuracies. This is due to the fact that the flirt command of ‘nearestneighbor’ was used in the transformation, and all the values generated that were below 0.35 were exempt.

Further Research

Further studies of interest include learning more about what exactly is driving ventricular enlargement, and the spatial arrangement of what is physically happening in the brain. A question of interest is “If the ventricles are not growing where the white matter hyperintensities used to be, where are they growing into?” A variable to consider for that analysis could be hippocampal atrophy. Another area for further exploration is the root cause of ventricular enlargement. Literature has proposed various ideas on these topics, but more discovery can still be made. It would also be beneficial to analyze more covariates surrounding this topic such as hypertension and diabetes, to gain a more complete understanding of the issue.