IC-P3-176 WHAT GOES UP, MUST COME DOWN: COMPENSATORY NEURAL ACTIVITY AMONG THE VERY OLD

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Background: Understanding factors that contribute to successful cognitive aging has become increasingly important as a growing portion of the population lives to very old age. Our research has focused on different patterns of cognitive aging by using electrophysiologic and behavioral measures. Previously, we demonstrated (e.g., *NeuroImage,* 2008; 39(1)) that cognitively high-functioning younger-old (y-old) (65-79 y.o.) subjects allocate more neural resources, as measured by the P3 event-related potential, than cognitively high-functioning middle-aged and young subjects and than cognitively average-functioning y-old subjects. Interestingly, although cognitively average-functioning middle-aged subjects appropriate more resources to novel stimuli than cognitively-matched young subjects, cognitively average-functioning y-old subjects exhibit a substantial reduction in novelty P3 amplitude. These findings suggest that age-related compensatory activity may involve increased allocation of capacity-limited controlled resources that persists until capacity limits are exceeded. For cognitively average-functioning adults this may occur by y-old age. We hypothesized that in cognitively high functioning adults this would develop in old-old (o-old) age. Here we have extended our investigations to include o-old individuals ('80 y.o.), and report on preliminary results. **Objective:** To determine whether cognitively high functioning o-old adults continue to exhibit compensatory neural activity and a preference for attending to novelty. **Methods:** Electrophysiologic and behavioral responses to standard, target, and novel visual stimuli were recorded while young, middle-aged, y-old, and o-old individuals performed a subject-controlled variant of the novelty oddball task. **Results:** Cognitively high-functioning o-old adults exhibited a large reduction in their novelty P3, but not until their mid to late 80s. Behaviorally, cognitively high-functioning individuals in their 90s continued to spend more time exploring novel than repetitive standard visual stimuli. **Conclusions:** Our research suggests that age-related compensatory neural activity may not be limited to high-functioning older individuals with substantial cognitive reserve, but also be observed among cognitively average-functioning adults at an earlier stage of the lifespan. Cognitively high-functioning adults appear to have the capacity to appropriate compensatory neural resources at least through their early 80s, and continue to be attracted to novelty, a hallmark of healthy human behavior, at least through their early 90s.

IC-P3-177 AN AUTOMATED METHOD FOR MEASURING LONGITUDINAL VOLUME CHANGES OF THE VENTRICULAR SYSTEM

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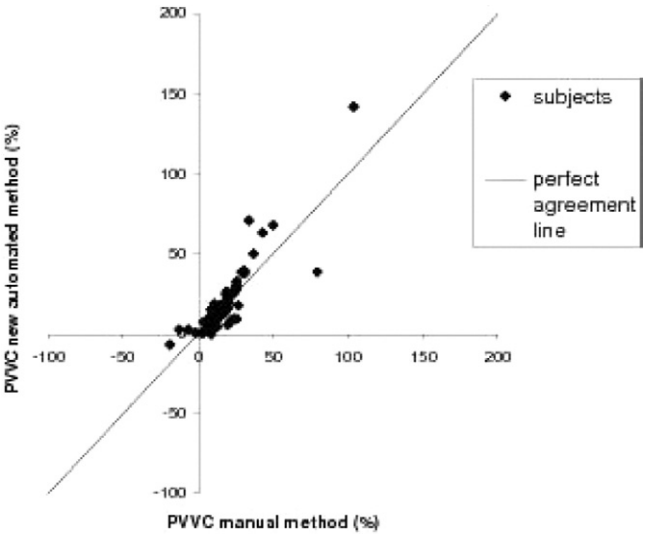
Background: To validate a new automated method for estimating relative volume change of the ventricular system from serial MR data, which would be useful for studying neurodegenerative disorders such as Alzheimer's Disease (AD)[1]. **Methods:** The method is a modification of the SIENA software[2] and completely automated. From a pair of MRI scans, it determines the relative volume change of the ventricular system from the displacement of the boundary between the brain tissue and the ventricular system; this relative movement is converted to a single number: percentage ventricular volume change (PVVC). To validate this method, we compared the resultant PVVC values to the PVVC values obtained by manually outlining the ventricular system, across a number of different MR image types and in two disease groups. We retrospectively selected T1-weighted MR images for a total of 70 subjects, acquired at two time-points (baseline and follow-up); 30 subjects were scanned on a 1.5 Tesla scanner and 40 subjects on a 1.0 Tesla scanner. 3D-MPRAGE images were selected for a "memory clinic group", consisting of 5 patients with probable Alzheimer's disease (AD), 5 patients with mild cognitive impairment (MCI) and 5 controls. Multi-slice 2D MR images were selected from 55 patients with multiple sclerosis (MS). Paired t-tests were used to compare means between methods. Agreement between methods was assessed by the intra-class correlation coefficient (ICC). **Results:** A paired t-test showed no significant difference between the automated measurement (mean±SD) (18%± 32) and the manual measurement (17%± 23; p=.26 across the entire group). The agreement between automated and manual measurement across the entire group was good (ICC=.85). In addition, when we evaluated the performance of SIENA PVVC in the two patient groups separately, we observed a comparable agreement in both groups (memory clinic group: ICC=.88; MS group: ICC=.80). **Conclusions:** These results suggests that this modified version of SIENA can be used to measure relative volume change of the ventricular system in patients with neurodegenerative diseases like AD and MS. We are currently applying this method to a dementia cohort.



IC-P3-178 MULTI-COMPONENT RELAXOMETRY AND MYELIN WATER FRACTION IMAGING WITH GRADIENT RECALLED ACQUISITION IN THE STEADY STATE

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Background: An emerging hypothesis of AD is that clinical symptoms are precipitated by a decrease in myelination of longer developing neural circuits. Histopathological studies show a loss of the densely packed myelin structure in AD, with splits in the lamellae of the myelin sheaths and an increase in interstitial water and astrocytes. Unfortunately, few in vivo imaging studies have addressed this hypothesis directly, due to the difficulty of non-invasive, whole-brain myelin quantification. Currently, multi-component relaxometry (MCR) is the most direct means of quantifying myelin volume, however, established approaches suffer lengthy acquisition times and limited volume coverage. Here we describe a new MCR method, termed multi-component driven equilibrium single pulse observation of T1 and T2 (mcDESPOT). **Methods:** MCR decomposes the measured MRI signal into contributions from two exchanging water pools. In brain tissue, these correspond to the intra/extra cellular pool and water trapped between the myelin sheaths. The spoiled and balanced steady-state

free-precession (SPGR and SSFP) signals arising from two pools have been modeled previously and include pool-specific T1 and T2 values (T1,F, T1,S, T2,F, T2,S) and volume fractions (fF, fS) as free parameters, allowing their estimation from multi-flip angle SPGR and SSFP data. For in vivo demonstration, whole-brain data were acquired of 4 healthy volunteers on a 1.5T Siemens Sonata clinical scanner. Imaging parameters were: 22cm2 × 16cm field of view, 256x160x118 matrix, SPGR: TE/TR = 3.1ms/6.5ms, angles 2° through 18° in 2° increments; SSFP: TE/TR = 2.3ms/4.6ms, angles 6° though 70° in 8° increments. **Results:** Images through the T1,F, T1,S, T2,F, T2,S and myelin fraction maps are shown in Fig. 1. Mean values obtained from different brain regions are shown in Fig. 2 and agree well with previous literature reports.

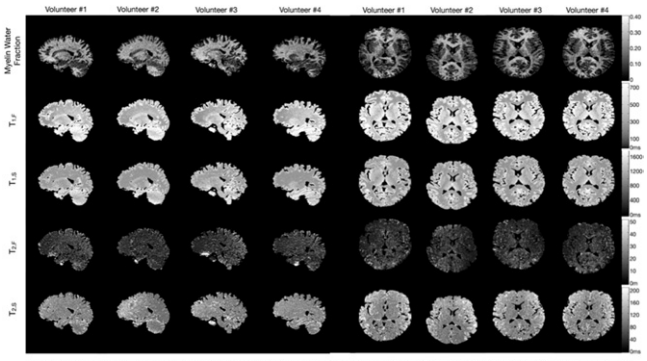

Figure 1: Representative sagittal and axial slices through the water pool-specific T_1 and T_2 values and myelin water fraction volume maps calculated for each volunteer.

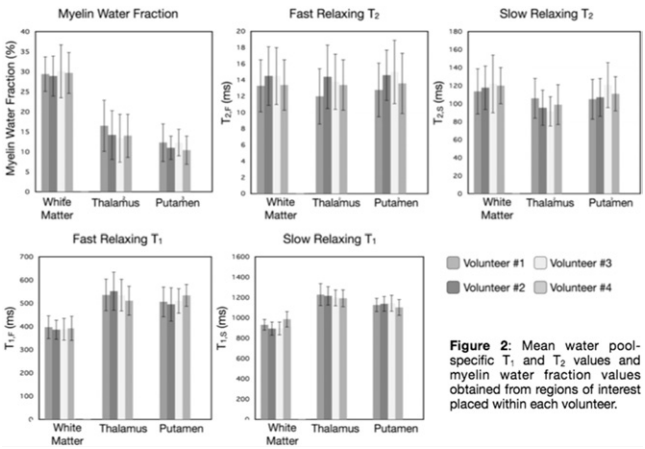

Figure 2: Mean water pool-specific T_1 and T_2 values and myelin water fraction values obtained from regions of interest placed within each volunteer.

Conclusions: The ability to derive multi-component T1 and T2 and myelin volume fraction information from rapidly acquired steady-state imaging data may have significant implications for identifying and assessing tissue change associated with neuro-degenerative disorders, such as AD, and investigating the role myelin degeneration plays in the disorder's pathogenesis. With a scan time of 20 minutes, the method may easily be implemented in a clinical setting.

IC-P3-179 QUANTIFYING METABOLIC ASYMMETRY IN ALZHEIMER'S DISEASE USING BOTH MR AND PET IMAGING

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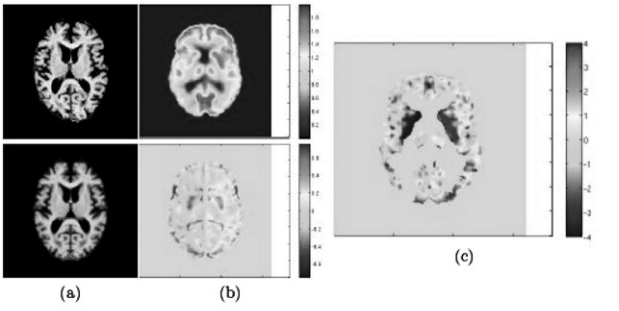
Background: Some of the earliest studies of FDG-PET in Alzheimer's disease (AD) noticed that patients sometimes had predominant left or right hemisphere hypometabolism. Currently, asymmetry in clinical brain scans is interpreted using only visual inspection. Quantifying metabolic asymmetry is difficult because mirroring values about the midsagittal plane does not necessarily align homologous structures in the left and right hemispheres. The objective of this research is to automatically quantify statistically significant areas of metabolic asymmetry in AD, while removing the confounding effects of structural asymmetry. **Methods:** We constructed an atlas of normative metabolic asymmetry from 10 normal control subjects from the Alzheimer's Disease Neuroimaging Initiative (ADNI) and quantified the metabolic asymmetry of an AD subject compared to the normative atlas. A symmetric structural image for each subject was computed using an unbiased average image from the original MRI and the MRI mirrored about the midsagittal plane. The PET image was mapped onto this structurally symmetric image, and an asymmetry image was computed as the difference of the left minus the right side. Since this is done in structurally symmetric coordinates, metabolism was compared across homologous structures of each hemisphere. Next, we built a structurally symmetric atlas of the 10 control subjects from an unbiased average of their symmetric MR images. The mean and standard deviation of the population's metabolic asymmetry was computed in the symmetric atlas coordinates. Finally, we registered the asymmetry image from an AD subject to the normal atlas and computed a pixel-by-pixel z-score of metabolic asymmetry. **Results:** Average normal asymmetry was in the range -0.15 to 0.15 relative to pons, with a maximal standard deviation of 0.35. The asymmetry z-score map of the AD patient shown in the figure showed significant ($z > 3$) asymmetry, which verifies and quantifies the asymmetry found by visual inspection. **Conclusions:** Structurally symmetric image coordinates are an effective approach to locating and quantifying asymmetry of glucose metabolism in AD. Acknowledgements: Supported in part by the Center for Alzheimer's Care, Imaging and Research and NIH grant AG024904. References: Fletcher, et al., *IPMI* 2007, pp. 346-358.



Shown in (a) are original MRI scan (top) and the associated structurally symmetric image (bottom) of a subject with AD. Shown in (b) top is the subjects PET scan. Shown in the (b) bottom is the metabolic asymmetry image mapped in to the atlas space. Shown in (c) is the image of the statistical significance of metabolic asymmetry as compared to the normative atlas.

IC-P3-180 CHANGES IN CEREBRAL BLOOD FLOW MEASURED BY ASL-PERFUSION MRI IN DIFFUSE LEWY BODY DISEASE: COMPARISON TO NORMAL AGING AND ALZHEIMER'S DISEASE

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Background: Advances in functional neuroimaging have improved early detection and differential diagnosis of dementia. Moreover, these methods may be useful for study of the underlying pathophysiology of dementia, and may ultimately guide development of new therapies for dementia. Previous studies in patients with severe DLB have identified decreased metabolism or blood flow in the occipital cortex relative to AD, and this pattern of decreased function has been proposed to be diagnostic for DLB. **Methods:** In this study, comparison of regional cerebral blood flow (rCBF) was made between subjects with mild diffuse Lewy body disease (DLB), age-matched controls, and subjects with mild Alzheimer's disease (AD). Diagnosis of AD or DLB was made by experienced clinicians using established clinical criteria.