of limited knowledge of brain membrane lipids. Therefore, we studied glycerophospholipids (GP) and sphingolipids (SP) that constitute the major lipid component of membranes and are precursors of inflammatory or apoptotic molecules in CSF fractions. **Results:** GPs are differentially metabolized in nanoparticle (NP) membrane and supernatant fluid (SF) fractions of cerebrospinal fluid (CSF). Most GPs and molecular species from cognitively healthy participants with pre-symptomatic AD, based on abnormal CSF $A\beta_{42}$/Tau levels (CH-PAT, pre-symptomatic), were increased compared to those of cognitively healthy with normal $A\beta_{42}$/Tau (CH-NAT) and AD participants. Plasmalogen-containing phosphatidylethanolamine was decreased the most in AD and was the only GP species that was reduced in CH-PAT compared with CH-NAT. In SF, sphingomyelin (SM) decreased in CH-PAT and AD compared with CH-NAT and this corresponded with an increase in ceramide (CM) and dihydroceramide (dhCM). In contrast to the SF fraction, there is an increase in SM in the NP fraction from CH-PAT, decease in CM and dhCM, and an increase in the ratio SM/CM. On investigating the mechanism for the lipid changes in AD, we observed that phospholipase A_2 (PLA_2) activity increased in AD, but not in the preclinical stages. Considering external influences on lipids, the clinical groups did not differ in their fasting blood lipids or intake of dietary lipids, consistent with the CSF lipid changes originating from brain pathophysiology. **Conclusions:** The lipid accumulation that we report in preclinical AD identifies perturbation of lipid metabolism and disturbances in APP/Aß as early events in AD pathophysiology. Our results identify increased lipid turnover in preclinical AD switching to a predominantly lipolytic state in dementia, knowledge that may be useful for targeting and testing AD treatments.

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GENE-BRAIN STRUCTURE NETWORKING ANALYSIS IN ALZHEIMER'S DISEASE USING THE PIPELINE ENVIRONMENT

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Background: This article uses subjects from the Alzheimer's Disease Neuroimaging Initiative (ADNI) to investigate and understand dementia-related late-onset cognitive impairment using neuroimaging and genetics biomarkers. **Methods:** The 1,245 subjects implemented using ADNI 1, ADNI GO and ADNI 2 were divided into three groups: those with Alzheimer's disease (AD), those with mild cognitive impairment (MCI), and those in the normal control (NC) group. Two hundred twenty eight of the subjects qualified for AD diagnosis at the baseline; 684 had MCI; and 333 were included in the NC group. The structural ADNI data were parcellated using FreeSurfer metrics, and all the SNPs for the 1,245 subject were extracted using Plink and the Pipeline environment. Network analyses were applied for all the subjects. **Results:** Our previous study for the AD, MCI and NC subjects (using ADNI 1 - 808 subjects), indicated the significant associations between the SNPs and the neuroimaging phenotypes for the AD, MCI and NC subjects. The previous findings included that the set of 140 genes chosen (from 416 SNPs with $p <$ 0.00005) represented commonly appearing genes in known AD gene networks. So we expect that we can get more meaningful result from the 1,245 subjects implemented using ADNI 1, ADNI GO and ADNI 2, because more big data have built up. **Conclusions:** We expect the significant correlations between the SNPs and the neuroimaging phenotypes in the 1,245 subjects in terms of neuroimaging genetics networking analyses. These analyses may explain some of the differences among the AD, MCI and NC groups.

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ANALYSIS OF VOICES RECORDED THROUGH A MOBILE APPLICATION RUNNING IN THE WILD FOR THE ASSESSMENT OF COGNITIVE IMPAIRMENT

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Background: As various types of cognitive disorders present with language dysfunctions, computational speech analysis methods have been proposed aiming at detection of dementia and mild cognitive impairment (MCI) at earlier stages. The speech analysis is expected to be useful as a non-invasive, affordable screening tool in daily lives. However, as previous studies have mostly investigated voices recorded in clinical interviews or laboratory settings, little is known about the effectiveness of these methods for voices recorded in realistic daily life situations. **Methods:** 158 participants (80 males, 78 females), aged 56-88 years (mean=73.1, SD=7.6), performed immediate verbal recall tasks on a commercially-available smartphone at home (33 in assisted living, 125 at normal home). The participants included patients with dementia (n=44) and MCI (n=63) as well as healthy controls (n=51). The tasks were presented among a series of cognitive exercises implemented on a smartphone application. Speech analysis models exploited acoustic, fluency, and lexical features. The ratio of successfully-recorded voice samples was also tested to examine if the participants could perform the tasks without human instructions. **Results:** There were significant differences in acoustic (e.g., jitter and shimmer) and lexical (e.g., recall rate) features between MCI vs. control and dementia vs. control ($p<.01$ for both). No significant differences were found in fluency features (e.g., pauses and hesitations). The area under the ROC curve (AUC) of logistic regression models were 0.857 for MCI vs. control, 0.612 for dementia vs. MCI, and 0.892 for dementia vs. control. The ratio of successfully-recorded voice samples was 42.1%, 46.2%, and 90.0% for dementia, MCI, and control, respectively. A logistic regression model based on the same set of features could classify successfully-recorded and useless voice samples with AUC of 0.894. **Conclusions:** The results showed that the speech analysis can be effective for dementia and MCI screening even when voices are recorded through a smartphone application in daily life situations. A computational model could also be used to sort out voice samples to input to the screening models, which implies a fully-automated personal screening application can be built on a standard smartphone by combining the two types of models.