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Markers of Neurodegeneration Associate with Worse Performance of Complex Daily Tasks

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OBJECTIVES/GOALS: In preclinical Alzheimer disease (AD), biomarkers such as amyloid protein, decreased hippocampal volume, and weaker network connections are apparent in the brain, but memory symptoms assessed by paper and pencil tests have not yet appeared. Performance tests of complex daily tasks may be more sensitive and detect early functional impairment. METHODS/STUDY POPULATION: This is a cross-sectional analysis of an ongoing cohort study. Cognitively normal (CN) older adults completed 3 standardized complex daily tasks from the Performance Assessment of Self-Care Skills (PASS) in their home. Biomarkers of AD were assessed within 2-3 years of an individuals completion of the PASS and include: amyloid accumulation, hippocampal volume, and resting-state functional connectivity (rs-fc) signature. Associations between performance on PASS tasks and the biomarkers of AD were quantified by Pearson point-biserial correlations, as biomarker data was normally distributed and PASS scores fell between two categories (acceptable or optimal quality of performance). Correlations with a 95% confidence interval (CI) that did not include 0 were considered significant. RESULTS/ANTICIPATED RESULTS: 161 CN participants (mean age 74.3 years, 55% female) were included. Mean score on the 3 PASS tasks ranged from 2.67 [standard deviation (SD): .47] to 2.90 (SD: .16) out of 3. Mean amyloid PET on Centiloid scale was 23.8 (SD: 34.8); mean partial volume corrected hippocampal volume was 7448.5 (SD: 909.8); mean rs-fc signature was .805 (SD: .164). After controlling for age and gender, worse performance of complex daily activities was associated with smaller hippocampal volumes (Pearsons r: 0.302, p=.02, 95% CI: .179 to .416) and weaker rs-fc network connections (Pearsons r: 0.276, p=.03, 95% CI: .078 to .453), but not amyloid accumulation. DISCUSSION/SIGNIFICANCE: This study suggests that worse performance of complex daily tasks may be associated with markers of neurodegeneration. These findings could lead to a better understanding of functional changes that may occur during the preclinical stage of AD.

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A Bacterial Serine Protease Inhibitor, Ecotin Inhibits Neutrophil Elastase in Cystic Fibrosis Airway Samples

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OBJECTIVES/GOALS: Ecotin is a potent periplasmic serin protease inhibitor that was first described in Escherichia coli (E. coli). Ecotin is known to inhibit a broad range of serine proteases including NE. Therefore, we hypothesized that ecotin can inhibit the NE activity present in CF clinical sputum samples. METHODS/STUDY POPULATION: To investigate the function of ecotin on CF sputum, orthologues from Campylobacter rectus and Campylobacter showae were recombinantly expressed and purified from E. coli to generate C. rectus ecotin, C. showae ecotin, and E. coli ecotin. Ecotin was added to CF sputum supernatant samples at various concentrations and NE enzymatic activity was measured by a fluorometric assay kit. In addition, CF sputum and healthy sputum was added to PMNs isolated from healthy donors for 3.5 hours and NE was measured with immunofluorescence staining. The sputum was washed two times prior to measuring NE released and on the PMNs, and PBMCs was used as a control. RESULTS/ANTICIPATED RESULTS: Our results indicate a clear inhibition of NE activity in CF sputum supernatant. C. showae ecotin showed the greatest inhibitory effect on NE activity in CF sputum supernatant. We also saw that CF sputum supernatant causing healthy PMNs to release more NE suggesting that NE in the CF airway may trigger more NE release from newly incoming PMNs to the lung. Our next steps will be to determine if ecotin can inhibit NE on the PMN surface and released from PMNs. DISCUSSION/SIGNIFICANCE: Neutrophil elastases are produced by PMNs to kill microbial pathogens in the lung, however in CF, the pathogens are unable to be killed by NE and instead causes severe lung damage. PMNs and NE has been shown to be elevated in the sputum of CF patients and there is currently no NE therapeutic inhibitor that has been effective in these patients.

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Factors Associated with Primary Care Provider (PCP) Use Among Home Dialysis Patients

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OBJECTIVES/GOALS: Patients utilizing dialysis receive fewer primary care services, especially during the time of initiation of dialysis. This project aims to identify clinical or demographic factors that are associated with either initiation or continuity of PCP use after initiating home dialysis. METHODS/STUDY POPULATION: Using Medicare claims data from the United States Renal Data System (USRDS), we analyzed PCP use for patients aged 67 years or older. We included patients who initiated either peritoneal or home-hemodialysis between 2008-2014. Patients were followed for 2 years: 1 year before and after home dialysis initiation. We used a multivariable logistic model to control for various demographic and clinical factors believed to be confounders and to ascertain factors (i.e. age, race/ethnicity, area of residence, comorbidities, frailty scores) associated with initiation of PCP use or continuity of PCP use. RESULTS/ANTICIPATED RESULTS: Among the 9,854 patients analyzed, 68% of patients used PCP after dialysis initiation. 85% of patients who used PCP before dialysis continued PCP use after home dialysis initiation. Only 29% of patients who had not used PCP before dialysis initiated PCP use after. Employment (vs. unemployment) and use of home-hemodialysis (vs peritoneal) were associated with lower odds of PCP continuity of care. Diabetes and pre-dialysis nephrology care were associated with greater odds of PCP continuity of care. Black race (vs White) and high frailty scores were associated with lower odds of PCP initiation. Those with cardiovascular disease, residence in the South (vs the Northeast), and residence in more urban areas (vs low urban) were associated with greater odds of PCP initiation. DISCUSSION/SIGNIFICANCE: This study highlights the prevalence of PCP use, as well as the factors and subgroups that are associated with lower PCP use among patients receiving home dialysis. These findings will guide future research, interventions and policies in order to improve our understanding of the barriers to PCP use in that population.

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