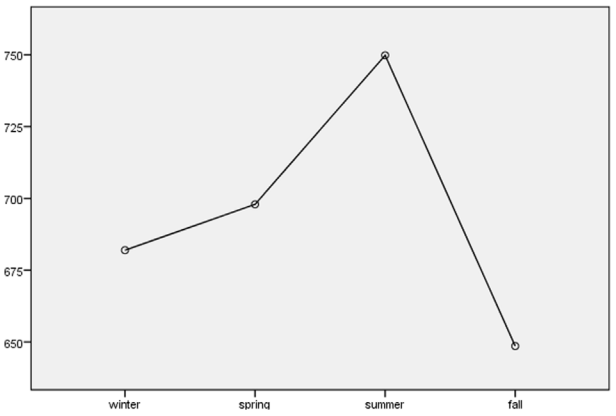
terminal (tau 368 and K9JA). **Results:** Results show that individual antibodies selectively bind to specific tauopathies whilst staining negative to others, confirming a distinct fibril organisation for each tauopathy. Comparing all results to the gold standard for staining of tau pathological inclusions (using AT8 antibody), N-terminal antibodies only stained PiD inclusions and partly GGT. Antibodies targeting the proline rich domain of tau, positively stained the pathological inclusions present in all tauopathies. Finally, C-terminal antibodies positively bound to tangles and to a lesser extent to astrocytic inclusions present in CBD and PSP. **Conclusions:** Here, we report the potential of several tau antibodies to selectively bind to specific forms of tauopathy.



(I) four_seasons	(J) four_seasons	Mean Difference (I-J)	Std. Error	Sig.[b]	95% Confidence Interval for Difference[b]	
					Lower Bound	Upper Bound
winter	spring	-15.980	32.664	.625	-80.232	48.272
	summer	-67.887	35.371	.056	-137.463	1.689
	fall	33.386	35.971	.354	-37.371	104.142
spring	winter	15.980	32.664	.625	-48.272	80.232
	summer	-51.907	31.668	.102	-114.201	10.386
	fall	49.366	32.292	.127	-14.154	112.886
summer	winter	67.887	35.371	.056	-1.689	137.463
	spring	51.907	31.668	.102	-10.386	114.201
	fall	101.273*	35.088	.004	32.254	170.292
fall	winter	-33.386	35.971	.354	-104.142	37.371
	spring	-49.366	32.292	.127	-112.886	14.154
	summer	-101.273*	35.088	.004	-170.292	-32.254

P2-238 SEASONAL EFFECTS ON CEREBROSPINAL FLUID AMYLOID BETA 42 PEPTIDE LEVELS IN A COGNITIVELY NORMAL ELDERLY COHORT FROM NEW YORK CITY

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Background: Seasonal changes affect many features of human physiology including brain function and volume (e.g. performance in neurocognitive tests is significantly better during summer). Cognitive impairment is associated with Alzheimer's disease (AD) pathology. One of the hallmarks of AD is changes in cerebrospinal fluid (CSF) levels of amyloid beta 42 (Aβ42). CSF Aβ42 levels fluctuate diurnally in healthy adults and are influenced by sleep and circadian rhythms. Preliminary evidence has shown seasonal fluctuations in CSF Aβ42 in an elderly cohort from Paris. However, this finding has not been replicated in other geographic locations. In this study, using a substantially increased subject pool size, we tested whether an elderly cohort located in NYC shows similar seasonal rhythmicity. **Methods:** The cohort included cognitively normal elderly. Demographic data, clinical assessments and ApoE4 genotype were collected. Lumbar punctures were performed between 11AM and 1 PM. Using CSF Aβ42 as a continuous variable and a categorical variable for season of the year, defined by using equinox and solstice dates, we performed general linear model to assess the differences in the CSF Aβ42 across seasons. Age, sex, and ApoE4 were considered as covariates. **Results:** We studied 343 subjects with Clinical Dementia Rate=0, Mini-Mental State Examination $\geq$24. The mean$\pm$SD CSF Aβ42 level was 695.9$\pm$229.9. CSF Aβ42 level was rhythmic, peaking during summer ($F=2.9$, $p<.05$) (Figure 1). There was a significant difference between summer and fall (between group comparison $p<.01$). We did not see any other difference between other seasons (Figure 2). Our results are consistent with the study performed in Paris. **Conclusions:** Season of the year had a significant association with CSF Aβ42 levels in a sample of cognitively normal elderly, suggesting the hypothesis that sleep and circadian rhythms are important regulators of Aβ42 production and clearance. Seasonality should be factored in both in clinical diagnosis and in clinical trials that use CSF biomarkers as an outcome variable. We believe this result may also help to generate new treatment options like light therapy.

P2-239 POTENTIAL DIAGNOSTIC VALUE OF RED BLOOD CELLS α-SYNUCLEIN HETEROAGGREGATES IN ALZHEIMER'S DISEASE

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Background: A plethora of complex misfolded protein combinations have been found in Alzheimer disease (AD) brains besides the classical pathological hallmarks. Recently, α-synuclein (α-syn) and its heterocomplexes with amyloid-β (Aβ) and tau have been suggested to be involved in the pathophysiological processes of neurodegenerative diseases. These pathological features are not limited to the brain, but can be also found in peripheral fluids. In this respect, Red Blood Cells (RBCs) have been suggested as a good model to investigate the biochemical alterations of neurodegeneration. Our aim is to find whether RBC concentrations of α-syn and its heterocomplexes (i.e., α-syn/Aβ and α-syn/tau) were different in AD patients compared with healthy controls (HC)

and to assess their potential diagnostic accuracy in discriminating AD from HC individuals. **Methods:** The levels of homo- and hetero-aggregates of α-syn, Aβ and tau were analysed in a cohort of AD patients at early stage either with dementia or prodromal symptoms (N=39) and age-matched HC (N=39). All AD patients showed a typical hippocampal phenotype and received a biomarker-based diagnosis (low cerebrospinal fluid levels of Aβ peptide combined with high cerebrospinal fluid concentrations of total-tau and/or phospho-tau proteins; alternatively, a positivity to cerebral amyloid-PET scan). **Results:** We found lower concentrations of α-syn and its heterocomplexes (i.e., α-syn/Aβ and α-syn/tau) in RBCs of AD patients compared to HC. RBC α-syn/Aβ as well as RBC α-syn/tau heterodimers discriminated AD participants from HC with fair accuracy (Area under receiver operating characteristic, AUROC=0.76, 0.72, respectively), whereas RBC α-syn concentrations differentiated poorly the two groups (AUROC=0.63). RBC Aβ and RBC α-syn/Aβ heterocomplex moderately correlated with CSF Aβ (ρs=0.435 and 0.368, respectively; *P*=0.015 and 0.042) in a subset of 32 AD patients. **Conclusions:** Although additional investigations are required, these data suggest α-syn heteroaggregates in RBCs as potential tool in the diagnostic work-up of early AD diagnosis. Finally, RBCs may represent interesting peripheral *in vivo* models of neurodegeneration since they likely to be involved in the accumulation and clearance of the misfolded proteins.

P2-240 NEUROPHYSIOLOGICAL CORRELATES OF *PSEN1* MUTATION-RELATED SPASTIC PARAPARESIS

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Background: A subset of *PSEN1* mutations can cause disabling spastic paraparesis (SP). The neurophysiological changes associated with this atypical manifestation are poorly understood with limited prior publications suggesting diffuse ultrastructural change in white matter. In the current study we aimed to characterize the function of callosal and corticomotor circuitry in persons with *PSEN1*-related SP. **Methods:** We performed clinical tests and collected transcranial magnetic stimulation measures on 17 persons with or known to be at 50% for inheriting the A431E mutation in *PSEN1*or the V717I mutation in *APP* (n = 1). Leg spasticity was characterized using the Ashworth Scale (0 – 4). TMS was performed over the motor area of the abductor pollicis brevis and tibialis anterior to quantify central motor conduction times (CMCT), transcallosal conduction time (TCT), interhemispheric inhibition (IHI), and cortical silent period (CSP) for both the upper and lower extremities. As spastic paraparesis was symmetric, values of these measures were averaged between the two hemispheres and Pearson's correlations calculated between Ashworth scores and TMS measures. **Results:** Sixteen subjects were carriers and one is pending. Among subjects, 7 were asymptomatic (CDR = 0), 4 had very mild (CDR = 0.5), 4 had mild (CDR = 1), and 2 had moderate (CDR = 2). Seven subjects had Ashworth scores of 0, 6 had scores of 1, 3 had scores of 2, and 1 had a score of 4. There were significant correlations between Ashworth scores and lower extremity CSP (n = 17, r = 0.50, p = 0.041), TCT (n = 16, r = 0.76, p < 0.001), and IHI (n = 16, r = -0.55, p = 0.029). **Conclusions:** Increased spasticity was associated with greater cortical inhibition, as evidenced by increased cortical silent period. These results may reflect the fact that our TMS measurements were taken from tibialis anterior which is antagonist to the more commonly affected gastrocnemius. Increased spasticity is also associated with increased TCT and decreased IHI. These measures are indicative of reduced function and demyelination of the corpus callosum associated with spastic paraparesis in autosomal dominant AD. This project was funded by U01 AG051218 and P50 AG05142

P2-241 GUT MICROBIAL METABOLITES IN CEREBROSPINAL FLUID ARE ASSOCIATED WITH BIOMARKERS OF ALZHEIMER'S DISEASE PATHOLOGY

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Background: Prior studies suggest that enteric microbiota may modulate neurological and psychiatric disorders. Recently we reported that cognitively unimpaired (CU) patients and those with Alzheimer's Disease (AD) dementia harbor divergent fecal bacterial communities, and that several bacterial taxa abundances associate with AD pathology measured via cerebrospinal fluid (CSF) (Vogt et al. 2017). With preliminary associations between AD and dysbiosis, here we tested whether gut flora-associated metabolites are measurable in CSF, and secondarily whether they are differentially present across the AD spectrum and associated with AD biomarkers. **Methods:** CSF was collected via lumbar puncture from participants in the Wisconsin Registry for Alzheimer's Prevention and the Wisconsin Alzheimer's Disease Research Center [CU (N=334), AD mild cognitive impairment (MCI) (N=35), AD