CSF from head CT using probabilistic, atlas-based classification. Feasibility and utility were evaluated by comparing MRI-only to CT-only segmentations in 10 older adults [mean (μ) ± standard deviation (σ) of age = 65 ± 7 yrs; 5 females] from whom both MRI and CT scans were acquired within an eight-week period. Segmentation similarity was quantified using the Dice coefficient (DC), a robust measure of inter-modality tissue classification agreement. Results: Comparison of MRI vs. CT segmentations yielded normally-distributed DCs [ μ ± σ across participants: 85.5% ± 4.6% (WM), 86.7% ± 5.6% (GM) and 91.3% ± 2.8% (CSF)], indicating satisfactory ability to calculate brain volumetrics from the CT scans of the participants, relative to MRI measurements. For this sample, bootstrapping suggests that the tissue classification method is sufficiently sensitive to estimate WM, GM and CSF volumes within ~5%, ~4% and ~3% of their MRI-based values, respectively. Compared to MRI, volumes computed from CT displayed no evidence of systematic over- or under-estimation [ t (9) = 0.89, p > 0.80]. Conclusions: Our contribution broadens the ability to integrate CT imaging findings with other research on brain aging in health and disease, and complements other methodologies for the study of brain volumetrics in neurodegenerative diseases, including AD.

CSF CHOLINERGIC INDEX, A NEW BIOMEASURE OF TREATMENT EFFECT IN PATIENTS WITH ALZHEIMER’S DISEASE

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Background: Alzheimer’s disease (AD) is a progressive disease with extensive loss of central cholinergic functions. Currently, three of four AD drugs disease act by inhibiting the acetylcholine (ACh) degrading enzyme, acetylcholinesterase (AChE). However, efficacy of these drugs also depends on amount of ACh available for synaptic release. In turn ACh is biosynthesized by choline acetyltransferase (ChAT). Thus we investigated whether treatment with the cholinesterase-inhibitor, galantamine alters the relative ACh-biosynthesizing to -degrading capacities, (defined as Cholinergic Index) and whether this index correlates with clinical and paraclinical measures in patients. Methods: Activities of ChAT and AChE were measured by colorimetric assays in cerebrospinal fluids of 18 patients with mild AD prior to and after 3 months of treatment with galantamine or placebo, as well as after 9 months galantamine treatment in all patients. The cholinergic index was calculated as the ratio of ChAT to AChE activities in CSF, and evaluated in relation to the in vivo AChE inhibition in the brain (assessed by 11C-PMP-PET) as well as different cognitive measures. Results: At 3-months, the cholinergic index was significantly increased after the galantamine (60% ± 14) compared to baseline (p < 0.0023) or the placebo-group (p < 0.0004), in which this index remained unchanged (6% ± 13). At 12-months, the cholinergic index remained high in the galantamine-group compared to baseline (54% ± 11). Interestingly, the cholinergic index showed a similar increase when the placebo-group were on galantamine for 9 months (44% ± 14 compared to baseline, 48% ± 10 compared to 3 months).

Furthermore, the in vivo brain AChE inhibition (assessed by PET) correlated significantly with the CSF cholinergic index at 12 months (r = 0.98, p < 0.001). More on, the CSF cholinergic index correlated with; MMSE Score, ADAS-Cog, Memory Domain and Visuospatial Domain at 12 months. Conclusions: This is the first study assessing a CSF Cholinergic index in relation to treatment with a cholinesterase inhibitor. The treatment-specific increase in this index suggested that inhibition of ACh degradation by galantamine also resulted in an increase in the acetylcholine-biosynthesis capacity in the patients. Further studies with other cholinesterase inhibitors are warranted to determine the usage of CSF Cholinergic index to detect therapeutic effect or disease progression while on treatment.