(p<0.01). The $A\beta_{42}/A\beta_{40}$ ratio was significantly lower in AD patients than in all other groups (p <0.001). Differentiating AD from VaD, DLB and non-AD improved when the $A\beta_{42}/A\beta_{40}$ ratio was used instead of $A\beta_{42}$ concentrations alone (p≤0.005). **Conclusions:** In clinically diagnosed patients with dementia the CSF $A\beta_{42}/A\beta_{40}$ ratio improves differentiation of AD patients from VaD, DLB and non-AD patients, when compared to $A\beta_{42}$ alone.

P3-004   CEREBROSPINAL FLUID ALPHA-SYNUCLEIN DOES NOT DISCRIMINATE BETWEEN DEMENTIA DISORDERS

Petra Spies[1], René Melis[1], Magnus Sjögren[1], Marcel Olde Rikkert[1], Marcel Verbeek[1,2], [1]*Radboud University Nijmegen Medical Centre, Nijmegen, Netherlands;* [2]*Donders Institute for Brain, Cognition and Behaviour, Nijmegen, Netherlands. Contact e-mail: p.spies@ger.umcn.nl*

Background: α-Synuclein is the major constituent of Lewy bodies found in neurons in dementia with Lewy bodies (DLB) and might be of diagnostic value as a biomarker for DLB. We hypothesized that, as a consequence of increased accumulation of α-synuclein intraneuronally in DLB, the levels of α-synuclein in cerebrospinal fluid (CSF) of DLB patients would be lower than in other dementias. **Methods:** We analysed the levels of α-synuclein in CSF of 40 DLB patients, 131 patients with Alzheimer's disease, 28 patients with vascular dementia, and 39 patients with frontotemporal dementia. **Results:** We did not find any significant differences in CSF α-synuclein levels between DLB patients and patients with AD, VaD or FTD. **Conclusions:** In clinically diagnosed patients, α-synuclein does not appear to be a useful biomarker for the differentiation between DLB and other types of dementia.

P3-005   SERUM PROGRANULIN IS REDUCED IN GRN MUTATION CARRIERS BUT NOT IN OTHER DEMENTIA

Ging-Yuek R. Hsiung[1], Alice Fok[1], Howard H. Feldman[1], Rosa Rademaker[2], Ian R. A. Mackenzie[1], [1]*University of British Columbia, Vancouver, BC, Canada;* [2]*Mayo Clinic, Jacksonville, FL, USA. Contact e-mail: hsiung@interchange.ubc.ca*

Background: Recent studies have shown that carriers of *GRN* mutation have a significantly lower level of PGRN in plasma than non-carriers and controls. We measured the serum level in a cohort of subjects assessed at a tertiary dementia referral clinic to determine its utility in screening for *GRN* mutation carriers. **Methods:** Blood samples were obtained from subjects with a family history of pathologically proven FTLD-U, as well as patients with cognitive complaints and healthy controls. *GRN* carrier status in "at-risk" family members was determined by direct sequencing of exonic and flanking intronic regions. Serum levels of PGRN were measured using an ELISA assay (Human Progranulin ELISA kit, AdipoGen, Inc, South Korea). PGRN levels among groups were compared by ANOVA with post-hoc SNK tests. We also compared serum and plasma PGRN level in 12 healthy controls using paired t-test. **Results:** *GRN* mutation carriers had significantly lower serum PGRN levels (n=6, 50.5 ± 6.8 ng/mL, range 42.9 to 59.1) compared to other groups (p<10^{-7}). There was no significant difference between non-*GRN* mutation carriers (n=6, 160.5 ± 22.6 ng/mL, range 132 to 187) and other groups (total n=107, 191 ± 57.7 ng/mL, range 97.5 to 364), which include subjects with normal cognition (n=30, 191 ± 59.2 ng/mL), mild cognitive impairment (n=11, 195 ± 36.2 ng/mL), probable AD (n=48, 201 ± 52.5 ng/mL), vascular cognitive impairment (n=4, 196 ± 48.8 ng/mL), other familial FTD (n=8, 165 ± 33.1 ng/mL), FTD with ALS (n=3, 174 ± 13.5 ng/mL), and dementia with Lewy bodies (n=3, 163.8 ± 33.6 ng/mL). The plasma and serum PGRN measurements were comparable (R^2 = 0.946, p=3x10^{-6}). **Conclusions:** This study confirms that *GRN* mutation carriers have significantly lower serum PGRN level than other forms of dementia. Serum and plasma PGRN measurements are quite comparable. Furthermore, it may be a useful initial screening tool to detect *GRN* mutation carriers in patients with dementia. The wide range observed in controls and other dementia subjects suggests that there are other genetic or environmental factors affecting serum PGRN level than just *GRN* genotype.

P3-006   MARKERS OF ALZHEIMER'S DISEASE IN A NATURALISTIC POPULATION ATTENDING A MEMORY CLINIC

Annapaola Prestia[1], Giovanni B. Frisoni[1], Orazio Zanetti[1], **Samantha Galluzzi**[1], Melissa Romano[1], Maria Cotelli[3], Massimo Gennarelli[1,2], Giuliano Binetti[1], Luisella Bocchio[1], Barbara Paghera[3], Giovanni Amicucci[4], Matteo Bonetti[5], Luisa Benussi[1], Roberta Ghidoni[1], Cristina Geroldi[1], [1]*IRCCS, Centre "S. Giovanni di Dio", Fatebenefratelli, Brescia, Italy;* [2]*University of Brescia, Brescia, Italy;* [3]*Spedali Civili of Brescia, Brescia, Italy;* [4]*S.Orsola-Fatebenefratelli Hospital, Brescia, Italy;* [5]*Istituto Clinico Città di Brescia, Brescia, Italy. Contact e-mail: sgalluzzi@fatebenefratelli.it*

Background: New marker-based criteria for the diagnosis of Alzheimer's disease (AD) have been recently proposed. We describe their operational translation in consecutive patients referred to our Memory Clinic. **Methods:** Patients were 12 with subjective memory complaints (SMC, MMSE 28.0±1.1), 37 with mild cognitive impairment (MCI, MMSE 25.1±3.6), 55 with AD (MMSE 21.1±3.5), and 40 with non-AD dementia (MMSE 21.6±5.5). Hippocampal volumetry on MRI, visual rating of cortical glucose hypometabolism on PET, and concentration of total tau and Abeta1-42 on cerebrospinal fluid were assessed. **Results:** The sensitivity for AD of individual biomarkers is higher (43 to 71%) than for MCI (18 to 31%). Their specificity versus SMC and non-AD dementias is good to moderate (83% and 69%). Positivity to at least 1 marker increases the probability of belonging to the AD group of 34 times (p<.0001). **Conclusions:** The new diagnostic criteria can be operationalized in the clinic. Longitudinal studies of MCI patients are needed to assess their prognostic value.

P3-007   BINDING FORM OF CURCUMIN DERIVATIVES TO β-AMYLOID AGGREGATES

Daijiro Yanagisawa[1,2], Nobuaki Shirai[3], Tomone Amatsubo[1,2], Hiroyasu Taguchi[1], Koichi Hirao[3], Makoto Urushitani[1], Shigehiro Morikawa[1], Toshiro Inubushi[1], Masanari Kato[4], Kyuya Morino[4], Hirohiko Kimura[4], Ichiro Nakano[4], Chikako Yoshida[4], Takashi Okada[4], Mitsuo Sano[4], Ikuo Tooyama[1], [1]*Shiga University of Medical Science, Otsu, Japan;* [2]*JST Innovation Satellite Shiga, Otsu, Japan;* [3]*Industrial Research Center of Shiga Prefecture, Ritto, Japan;* [4]*Central Research Institute, Ishihara Sangyo Kaisya Ltd., Kusatsu, Japan. Contact e-mail: daijiroy@belle.shiga-med.ac.jp*

Background: Curcumin is a yellow-orange pigment derived from the turmeric, which was found to bind β-amyloid (Aβ) protein. Chemically, curcumin possesses a 1,6-heptadiene-3,5-dione (α,β-unsaturated β-diketone) moiety, which implies that it can exist in two tautomers, a keto form and an enol. The aim of this study was to assess the involvement of keto-enol tautomerism in the binding activity to Aβ fibrils/aggregates. **Methods:** We synthesized curcumin derivatives F-H-Cur and F-Mecar-Cur. Further, we synthesized a keto form analogue of curcumin derivatives F-diMe-Cur. UV-visible spectrophotometric analysis performed between 250 and 750 nm. Distinction between the keto and the enol forms was assessed in 19F- and 13C-NMR analysis. The binding affinity of curcumin derivatives to Aβ aggregates was measured and expressed in the half maximal inhibitory concentration (IC50) in thioflavin T fluorescence assay. **Results:** F-H-Cur and F-Mecar-Cur consist of four forms, that is, keto form with phenolic hydroxy group, keto form with phenolic anion, enol form with phenolic hydroxy group, and enol form with phenolic anion. On the other hand, F-diMe-Cur possesses only keto forms. Each form displayed a unique UV-visible absorption spectrum, color and fluorescence. The thioflavin T fluorescence assay for the binding affinity of chemicals to Aβ aggregates demonstrated that IC50 values of F-H-Cur and F-Mecar-Cur were 0.26 μM and 0.44 μM, respectively. While, the IC50 value of F-diMe-Cur was 23 μM, indicating that a keto form of curcumin derivatives little binds to Aβ aggregates. F-Mecar-Cur in phosphate buffer (pH 7.5) showed yellow color that was resulted from the keto forms. When Aβ aggregates were added into the solution, the color of the solution containing F-Mecar-Cur turned into reddish orange from yellow. NMR analysis and UV-visible spectrophotometry showed that reddish color was resulted from enol forms of F-Mecar-Cur.