

## Neuropsychological profile of milder forms of HIV-associated neurocognitive decline after the antiretroviral era

P. Toro<sup>a</sup>, G. Forno<sup>a</sup>, F. Henríquez<sup>b</sup>, M.E. Ceballos<sup>b</sup>. <sup>a</sup>Department of Psychiatry, Facultad de Medicina, Pontificia Universidad Católica de Chile, Santiago, Chile; <sup>b</sup>Department of Neurology, Facultad de Medicina, Universidad de Chile, Santiago, Chile

**Introduction:** Neuropsychological profile of HIV-Associated Neurocognitive Disorder (HAND) was described before and at the beginning of the highly active antiretroviral therapy (HAART) era by psychomotor slowing, decreased attention, impairment in executive functions and memory (learning and recall) with relatively preserved language, and visuoconstructive abilities, all consistent with a “subcortical” pattern of cognitive impairment. Since the prevalence of severe forms of HAND has decreased because of HAART, the incidence of mild forms of HAND (asymptomatic neurocognitive impairment, ANI and mild neurocognitive disorder, MND) continues to increase. New studies that describe the neuropsychological profile of milder forms of HAND are needed to characterize patients in early stages of cognitive impairment.

**Methods:** 46 HIV patients without history of head injury trauma or opportunistic infections of the CNS were recruited from the HIV clinic, underwent a thorough clinical interview and neuropsychological testing using the Cambridge Neuropsychological Test Automated Battery (CANTAB). The subtests included attention and speeded information processing, episodic memory, working memory, executive function and visuoception. Verbal fluency was examined using FAS.

**Results:** Prevalence of HAND diagnoses were 26.2% for ANI, 33.3% for MND, and 40.5% were diagnosed as cognitive healthy. HAND patients showed impairment in executive functions, episodic memory and verbal fluency, but no significant changes in psychomotor slowing.

**Discussion:** The neuropsychological profile of HAND changed after the HAART era: Mild forms of HAND are characterized principally by executive dysfunction and episodic memory impairment, but not overall psychomotor slowing. This is relevant for early diagnosis and the development of new HAND screening tools.

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### Dementia 1

#### Clinical, neuropsychiatric, and ioflupane SPECT imaging findings in REM sleep behavior disorder

B. Boeve<sup>a</sup>, T. Ferman<sup>b</sup>, M. Irfan<sup>a</sup>, J. Aakre<sup>c</sup>, E.St. Louis<sup>a</sup>, M. Silber<sup>a</sup>, M. Tippmann-Peikert<sup>a</sup>, M. Lipford<sup>a</sup>, M. Junna<sup>a</sup>, J. Graff-Radford<sup>a</sup>, K. Kantarci<sup>d</sup>, V. Lowe<sup>d</sup>. <sup>a</sup>Neurology, Mayo Clinic, Rochester, USA; <sup>b</sup>Psychiatry and Psychology, Mayo Clinic, Jacksonville, USA; <sup>c</sup>Health Sciences Research, Mayo Clinic, Rochester, USA; <sup>d</sup>Radiology, Mayo Clinic, Rochester, USA

**Background:** There is little data regarding which features among those with REM sleep behavior disorder (RBD) predict the eventual phenoconversion to dementia with Lewy bodies (DLB) or Parkinson's disease (PD).

**Methods:** We analyzed findings among subjects with RBD (n = 14) who did not have mild cognitive impairment (MCI), DLB or PD. The Neuropsychiatric Inventory was used to measure neuropsychiatric (NP) burden (sleep domain was excluded). The UPDRS was used to measure parkinsonism. Values  $\leq 2.2$  for the mean putamen to occipital ratio on ioflupane SPECT imaging were categorized as abnormal (DaT+).

**Results:** The sample included 13 (93%) men with a mean age of  $62.3 \pm 8.2$  years, mean Mini-Mental State Examination score of  $29 \pm 1$  and mean UPDRS score of  $0.625 \pm 1$ . Nine subjects had  $\geq 3$  NP features with irritability (n = 8) and apathy (n = 6) being most frequent across all

subjects. Six had subjective cognitive complaints (SCC), 6 had UPDRS  $> 0$ , and 7 were DaT+. Among the 9 subjects with  $\geq 3$  NP features, 6 had SCC, 4 had UPDRS  $> 0$ , and 5 were DaT+. Of the 6 with SCC, all 6 had  $\geq 3$  NP features, 2 had UPDRS  $> 0$ , and 3 were DaT+. Among the 6 subjects with UPDRS  $> 0$ , 4 had  $\geq 3$  NP features, 2 had SCC, and 4 were DaT+. Among the 7 subjects who were DaT+, 5 had  $\geq 3$  NP features, 3 had SCC, and 4 were DaT+. Only 2 subjects had no NP features plus no SCC plus UPDRS = 0, 1 of whom was DaT+.

**Conclusions:** Varying degrees of cognitive complaints, NP burden, parkinsonism and ioflupane SPECT findings were present among RBD subjects. Longitudinal assessment of RBD subjects using clinical and imaging measures may predict subsequent phenoconversion of RBD to MCI/DLB versus PD.

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### Dementia 1

#### Mitochondria-targeted therapeutics for Alzheimer's disease

E. Trushina<sup>a</sup>, L. Zhang<sup>a</sup>, S. Zhang<sup>a</sup>, S. Trushin<sup>a</sup>, D. Hua<sup>b</sup>. <sup>a</sup>Neurology, Mayo Clinic, Rochester, USA; <sup>b</sup>Pharmacology, Kansas State University, Manhattan, USA

We have previously demonstrated that alterations in mitochondrial dynamics precede the onset of memory phenotype and the development of amyloid plaques in three transgenic animal models of familial Alzheimer's disease (FAD). The objective of the study was to develop a treatment to restore mitochondrial dynamics and function. Here we provide evidence that treatment with CP2, a member of a family of tricyclic pyrone compounds, restores axonal trafficking *in vivo*, and averts cognitive and motor deficit in multiple animal models of AD (APP, PS1 and APP/PS1) *in vivo*. Animals were administered CP2 *via* drinking water. Cognitive and behavior tests were applied at the end of a lifetime treatment (13 months) or short-term treatments (2 and 4 months). Changes in mitochondrial dynamics and function *in vivo* and *in vitro* were evaluated using real-time imaging of mitochondrial motility; an XF24 Seahorse Extracellular Flux Analyzer; the activity of OXFOS Complexes I–V was done using enzymatic reactions; and metabolic changes were measured using LC- and GC–MS-based metabolomics. Behavior and memory functions were detected with a battery of tests. Alleviation of the motor and memory phenotype was accompanied with partial reduction in amyloid burden. Investigation of the molecular mechanism revealed that CP2 modulates mitochondria energetics and activates a cascade of events protecting mitochondrial dynamics. Our findings, for the first time, demonstrate that restoration of mitochondrial trafficking protects against cognitive dysfunction in AD. Our data validate mitochondrial motility as an early therapeutic target for AD and poise CP2 as a promising therapeutic compound.

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### Dementia 1

#### Prevalence of dementia among older people from rural Hmong and non-Hmong communities living in Vangvieng, Lao People's Democratic Republic

M. Guerchet<sup>a</sup>, X. Bouapao<sup>b</sup>, F. Quet<sup>b</sup>, S. Auriacombe<sup>c</sup>, J.F. Dartigues<sup>c</sup>, P.M. Preux<sup>a</sup>. <sup>a</sup>INSERM U1094 Tropical Neuroepidemiology, University

of Limoges, Limoges, France; <sup>b</sup>BP 9519, Institut de la Francophonie pour la Médecine Tropicale, Vientiane, Laos; <sup>c</sup>Victor Segalen Bordeaux II University, INSERM U897, Bordeaux, France

**Background:** The global prevalence of dementia has been estimated at 44.35 million in 2013 and is expected to rise to 135.46 million by 2050. Southeast Asia will not be spared by this epidemic as the proportionate increase of affected people will be one of the highest, reaching 340% (Prince et al., 2013).

**Aim:** The aim of this study was to estimate the prevalence of dementia among older people in Lao PDR and investigate the factors associated with dementia in those communities.

**Methods:** A cross sectional 2-stage study among people aged 65 years old and over living in Vangvieng (province of Vientiane) was carried out. Socio-demographic data and medical history were collected. Participants were screened using the Community Screening Instrument for Dementia (CSI-D), those who obtained a poor

performance were assessed by a neurologist and performed further psychometrical tests. Diagnosis of dementia followed the DSM-IV criteria.

This study was approved by the Ethics Committee of the Ministry of Health of Lao PDR.

**Results:** In total, 471 elderly were included in this study, with a mean age of  $74.1 \pm 6.9$  years. After neurological assessment, the prevalence of dementia was estimated at 9.1% (95% CI [6.7–12.1]) in this rural area of Laos, and wasn't different between Hmong (9.2%, 95% CI [5.8–13.7]) and non-Hmong (9.1%, 95% CI [5.8–13.4];  $p = 0.976$ ) ethnic groups.

**Conclusion:** This first population-based study in Lao PDR showed a high crude prevalence of dementia, close to the estimates for other Asian or LMIC countries.

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