impairment as compared to controls. In recent years, a variety of methods have been proposed to differentially classify patients presenting with memory problems. We sought to develop models that would be efficient in classifying individual patients with significant accuracy and ease of use across laboratories and clinical settings. **Methods:** We proposed to return to the basic components of human cognition and their invariable correlative structure. We utilized the CST in a sample of 229 (99 male) normal individuals and 140 (59 male) cognitively impaired (CI) individuals. We evaluated fundamental properties of statistical paradigms for classification of patients with cognitive abnormalities. **Results:** Multivariate statistics provide ample power for detecting and plotting the degree of deficit from the normal population in our study, in essence creating an individualized domain specific cognitive pattern (DSCP). Discriminant analysis provides an effective means for classification of these identified cognitive patterns in individual patients compared to control subjects. **Conclusions:** Domain Specific Cognitive Patterns may provide an accurate means to differentiate between normal, mild cognitive impairment and stages within AD. Importantly, this type of technology may be utilized in differentiating AD or MCI from other types of dementias, trauma or stroke, thereby improving diagnostic accuracy.

P4-098   **POTENTIAL OF SAC (S-ALLYL-L-CYSTEINE), A COMPONENT OF GARLIC, AS A NOVEL DRUG TARGET FOR ALZHEIMER'S DISEASE (AD) BASED ON STUDIES FROM PRIMARY NEURONAL CULTURES AND IN VIVO**

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Background: AD is characterized by amyloid β-peptide (Aβ) plaques and neurofibrillary tangles. Aβ produces reactive oxygen species (ROS) causing neuroinflammation and neuronal damage. Anticholinesterase drugs are predominantly used for AD but they fail to cure AD. Thus, alternative medications should be developed. From ancient times, garlic (*Allium sativum*) is used to treat diabetes and cardiovascular disorders. In AD models, we successfully tested a unique preparation, "Aged Garlic Extract" (AGE). AGE contains DAD (Diallyl disulfide) and SAC **(S-allyl-L-cysteine)**. Here we demonstrate novel property of AGE and SAC in neuroprotection, neuropreservation and synaptic integrity. **Methods:** For neuroprotection, differentiated neuronal PC12 cells were co-treated with 200μM of hydrogen peroxide and either AGE, DAD or SAC. Western immunoblotting and choline acetyltransferase (ChAT) assays were performed with cell lysates. Cells were also fixed with 4% paraformaldehyde for morphology analyses by ICC. For neurorescue experiments, differentiated neuronal cells were pretreated with AGE, DAD or SAC alone for 48 hours and thereafter, posttreated with ROS alone for 24 hours. Cells were harvested and fixed. Further, APP-Tg2576 mice were fed with special diet containing AGE, SAC or isocaloric control diet for 4 months. Animals were sacrificed and brain was dissected, homogenized and brain homogenates were subjected to Western immunoblotting and ELISA. **Results:** We observed significant neuroprotective and neurorescue properties of AGE and SAC independently against ROS- mediated insults to neuronal cells. Both AGE and SAC preserved pre-synaptic proteins (SYPH, SNAP-25) in Alzheimer's APP-Tg mice and ROS-insulted neuronal cells. Notably, AGE increased levels of ChAT activity in ROS-challenge. **Conclusions:** AGE or SAC treatment protects neurons from ROS-mediated oxidative stress and preserves pre-synaptic proteins. AGE treatment reverses ROS-mediated decline in cholinergic function of neuronal cells by increasing neuronal ChAT activity. Synaptic damage from excessive Aβ deposition in APP-Tg mice brain was also prevented by oral AGE or SAC treatment. The pleiotropic effects of AGE and the most active ingredient SAC, can be used as a potential therapeutic agent in treating AD. These findings warrant evaluation of SAC's clinical potency in larger clinical settings.

P4-099   **PROTECTIVE ROLES OF S-NITROSOGLUTATHIONE (GSNO) IN RAT CHRONIC CEREBRAL HYPOPERFUSION-INDUCED MILD COGNITIVE IMPAIRMENT**

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Background: Early decrease in cerebral blood perfusion featuring in most Alzheimer's disease (AD) cases has documented as a critical risk for AD. **Methods:** Because loss of cerebral vascular function is critical for development of AD pathologies under chronic cerebral hypoperfusion (CCH) conditions, we examined if S-nitroso-glutathione (GSNO) is able to improve damaged learning-memory function and Aβ accumulation in the brains of aged rats treated with bilateral common carotid artery occlusion (BCCAO), an animal model for human CCH. GSNO is a most abundant low molecular weight S-nitrosothiol and has been regarded as an important endogenous NO source exerting anti-inflammatory and vasoprotective activities. **Results:** We here report that long-term administration of GSNO (50μg/kg/day for 4 months) improved learning and memory functions of BCCAO treated rats with reducing brain Aβ levels. GSNO inhibited proinflammatory signaling in bEnd3 brain endothelial cells and thus reduced gene expression related to endothelial inflammation (i.e. ICAM-1, VCAM, and MMP-9). In addition, GSNO increased uptake of Aβ by cultured bEnd3 cell with increasing S-nitrosylation of dynamin-2 protein, a protein regulating cellular endocytosis activity. **Conclusions:** Taken together, these data first time document a potential therapeutic activity of GSNO on neurovascular pathologies involved in CCH and AD.

P4-100   **SMALL MOLECULE INHIBITOR OF AMYLOID BETA-PROTEIN OLIGOMERIZATION REDUCES BRAIN ABETA LOAD IN AN ALZHEIMER'S DISEASE MOUSE MODEL**

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Background: Cognitive dysfunction and brain atrophy seen in Alzheimer's disease (AD) are believed to be results of a cascade of events beginning with self-assembly of amyloid beta-protein (Abeta) leading to synaptic injury. Formation of Abeta oligomers is mediated by specific electrostatic and hydrophobic interactions that can be targeted to prevent neurotoxicity. **Methods:** We have identified a small molecule, termed CLR01, that complexes with Abeta and competes for the molecular interactions controlling initial Abeta folding and assembly. We used a variety of in vitro and in vivo assays to test the efficacy of CLR01. **Results:** Dot blot experiments with the Abeta oligomer specific antibody, A11, show inhibition of oligomer formation and cell culture experiments show significant protection against Abeta-induced toxicity upon administration of CLR01. Initial in vivo experiments have been performed in triple-transgenic and double-transgenic mouse models of AD. These experiments show significant brain-Abeta load reduction and improvement of spatial working memory following 28 days of subcutaneous CLR01 administration. **Conclusions:** These data support CLR01 as a promising lead for disease-modifying AD therapy.

P4-101   **DIAGNOSTIC DISCRIMINATION OF MILD COGNITIVE IMPAIRMENT, ALZHEIMER'S DISEASE, AND OTHER DEMENTIA GROUPS USING THE COGSTATE CLINIC BATTERY**

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Background: Computerized testing has become increasingly common as a cognitive evaluation method in clinical trials and other settings for both healthy controls and clinical populations. Despite this prevalence, the literature on diagnostic utility is not extensive and the discriminative abilities of computerized batteries examining different dementias are not currently known. The CogState computerized battery is an example of a measure that has been used in multiple clinical trials and is administered to patients as an early identification of mild cognitive impairment (MCI). We report here the results of a study comparing CogState performance across groups of healthy controls, MCI, Alzheimer's disease (AD), Lewy Body dementia (DLB), and Fronto-temporal dementia (FTD). **Methods:** Participants were 106 individuals (23 healthy controls; 19 MCI; 45 AD; 9 DLB; 10 FTD) seen through the University of Michigan Alzheimer's Disease Research Center, with diagnoses established by clinician consensus. Participants were administered the CogState Clinic battery consisting of subtests measuring speed and accuracy of responses on measures of simple reaction time (Detection), choice reaction time (Identification), working memory (One-Back), incidental learning (One-Card Learning), divided attention (Monitoring), and associative learning (Associate Learning). **Results:** ANOVAs indicated that all variables comprising the CogState battery discriminated dementia groups (AD, DLB, FTD) from MCI and controls, such that the dementia groups performed worse than the MCI and control groups. MCI participants performed significantly worse than controls on only the working memory speed and accuracy tasks (One-Back). Whereas no differences were noted between AD and other dementias, the DLB group performed worse than the other dementia groups on response speed to the working memory task (One-Back) and simple reaction time (Detection). **Conclusions:** This CogState Clinic battery appears to be effective in discriminating normal and sub-threshold clinical groups from dementia groups, but not as effective in differentiating healthy controls and MCI or between dementia groups. The results with One-Back suggest particular sensitivity to variable cognitive performance, and it may be especially useful in clinical trials. For enhanced discrimination among dementias clinically, other CogState measures emphasizing executive ability, such as Mazes, may be more sensitive to differences among patient subgroups and should be considered in future clinical trials.

P4-102 **ANOSOGNOSIA IN AMNESTIC MCI AND AD: DECREASED FUNCTIONAL CONNECTIVITY OF CORTICAL MIDLINE STRUCTURES**

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Background: Awareness of memory impairment is variable in aMCI and AD. This study tested our overarching hypothesis that aMCI and AD patients with mnemonic anosognosia show reduced functional connectivity in cortical midline structures. **Methods:** Our participants included 10 aMCI patients, 5 AD patients and 11 cognitively-healthy older adults. Our a priori seed regions of interest included the posterior cingulate and the medial prefrontal cortex For each seed region, we computed the Pearson's product-moment correlation coefficient between the regional mean of seed region time courses and the time course for each voxel in the whole brain; these correlation maps were converted to z' values. Group level random effects statistical analyses assessed: 1) test-retest reliability of functional connectivity; 2) group differences in cortical midline functional connectivity, and 3) regression analysis examining the relationship between mnemonic anosognosia and cortical midline functional connectivity in the patient groups. **Results:** Analysis of test-retest reliability in controls revealed high reliability (for map using MPFC seed, ICC = .83; for PCC map, ICC = .74). Results of the 2 group t test showed that compared to controls, the MCI and AD patients showed decreased MFC-PCC functional connectivity, and connectivity covaried with anosognosia. **Conclusions:**

Consistent with prior reports in the literature, patients with MCI and AD show decreased BOLD functional connectivity in two regions that are vulnerable to Alzheimer's disease - the posterior cingulate cortex and the medial frontal lobe. In addition, we found that aMCI and AD patients with mnemonic anosognosia showed reduced functional connectivity in cortical midline structures.

P4-103 **OLFACTORY IMPAIRMENT IN JAPANESE ALZHEIMER'S DISEASE PATIENTS USING ODOR STICK IDENTIFICATION TEST**

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Background: the purpose of the present study was to clarify the olfactory functions of Japanese patients with Alzheimer's disease(AD) using the odor stick identification test for Japanese(OSIT-J) for cunstuction of their suitable treatment and care. **Methods:** Fifty-nine AD patients (22 men and 37 women), ranging in age from 48 to 90 years (70.0 ± 8.9 years). They were diagnosed using history, neurological findings, MMSE, RBMT, FAB, MRI(volumetric study; VSRAD) and IMP-SPECT(3D-SSP analysis). 50 age and gender muched healthy controles who reported having no olfactory complains were enrolled. OSIT-J consisted of 12 odorants familiar to Japanese subjects. Each subject sniffed each odor that was applied to paraffin paper. Next the subject chose 1 of 6 answeres: 4 pictures associated with the odors labeled with their names, one of which was correct, and 2 other ones ("unknown" and "not deteced"). **Results:** The number of correct answers was significantly lower in AD group than in control group. Total score of OSIT-J was correlated with tolal score of MMSE and decrease score of the hippocampal comples on VSRAD analysis. **Conclusions:** The present study demonstrated that Japanese smell identification ability of AD patients was impaired associated demented degree on the OSIT-J.

P4-104 **EVOLUTION OF BRAIN Aβ OLIGOMERS INTERACTOMES DURING THE COURSE OF ALZHEIMER'S DISEASE**

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Background: Over the past decade, soluble oligomeric forms of Amyloid-beta (Aβ) have been suggested to underlie neuronal dysfunction in Alzheimer's disease (AD). However, due to the lack of tools to measure each oligomeric Aβ species, the relative contribution of specific brain Aβ oligomers to AD progression in humans remains a matter of intense debate. **Methods:** To address this crucial problem, we used 89 well-characterized human brain tissues from the Religious Order Study and analyzed cerebral expression of 34 proteins using a co-expression network analysis (WGCNA). **Results:** Briefly, we found that i) co-expressed synaptic protein networks, called interactomes, are remodeled during disease progression, ii) disease-related proteins invaded physiological brain networks beginning in the asymptomatic phase of AD, iii) each Aβ oligomer (dimers, trimers and Aβ*56) impacts different synaptic interactomes during disease progression. Finally, using this approach, we identified two novel receptors for Aβ oligomers. **Conclusions:** Distinct Aβ oligomers are involved in different phases of synaptic network evolution during the course of Alzheimer's disease.