

Davangere Devanand - selected publications

- 1 Devanand, D. P. (2014). Whatever happened to new treatments for Alzheimer's disease? *Journal of Clinical Psychiatry, 75*, 775-776.
- 2 Richard, E., Reitz, C., Honig, L. H., Schupf, N., Tang, M. X., Manly, J. J., Mayeux, R., Devanand, D. P., & Luchsinger, J. A. (2013). Late-life depression, mild cognitive impairment, and dementia. *JAMA Neurology, 70*, 374-382.
Notes: OBJECTIVE: To evaluate the association of late-life depression with mild cognitive impairment (MCI) and dementia in a multiethnic community cohort. DESIGN AND SETTING: A cohort study was conducted in Northern Manhattan, New York, New York. PARTICIPANTS: A total of 2160 community-dwelling Medicare recipients aged 65 years or older were included in the study. METHODS: Depression was assessed using the 10-item version of the Center for Epidemiological Studies Depression scale (CES-D) and defined by a CES-D score of 4 or more. We used logistic regression for cross-sectional association analyses and proportional hazards regression for longitudinal analyses. MAIN OUTCOME MEASURES: Mild cognitive impairment dementia, and progression from MCI to dementia were the main outcome measures. We also used subcategories of MCI (amnesic and nonamnesic), and dementia (probable Alzheimer disease and vascular dementia, including possible Alzheimer disease with stroke). RESULTS: Baseline depression was associated with prevalent MCI (odds ratio, 1.4; 95% CI, 1.1-1.9) and dementia (2.2; 1.6-3.1). Baseline depression was associated with an increased risk of incident dementia (hazard ratio [HR], 1.7; 95% CI, 1.2-2.3) but not with incident MCI (0.9; 0.7-1.2). Persons with MCI and coexisting depression at baseline had a higher risk of progression to dementia (HR, 2.0; 95% CI, 1.2-3.4), especially vascular dementia (4.3; 1.1-17.0), but not Alzheimer disease (1.9; 1.0-3.6). CONCLUSION: The association of depression with prevalent MCI and with progression from MCI to dementia, but not with incident MCI, suggests that depression accompanies cognitive impairment but does not precede it
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- 3 Devanand, D. P. (2013). Psychosis, agitation, and antipsychotic treatment in dementia. *American Journal of Psychiatry, 170*, 957-960.
- 4 Devanand, D. P., Bansal, R., Liu, J., Hao, X., Pradhaban, G., & Peterson, B. S. (2012). MRI hippocampal and entorhinal cortex mapping in predicting conversion to Alzheimer's disease. *NeuroImage, 60*, 1622-1629.
Notes: OBJECTIVE: Using MRI surface morphometry mapping, to evaluate local deformations of the hippocampus, parahippocampal gyrus, and entorhinal cortex in predicting conversion from mild cognitive impairment (MCI) to Alzheimer's disease (AD). METHODS: Baseline brain MRI with surface morphological analysis was performed in 130 outpatients with MCI, broadly defined, and 61 healthy controls followed for an average of 4 years in a single site study. RESULTS: Patients with MCI differed from controls in several regions of the hippocampus and entorhinal cortex, and to a lesser extent in the parahippocampal gyrus. In the MCI sample, Cox regression models were conducted for time to conversion comparing converters to AD (n=31) and non-converters (n=99), controlling for age, sex and education. Converters showed greater atrophy in the head of the hippocampus, predominantly in the CA1 region and subiculum, and in the entorhinal cortex, especially in the anterior-inferior pole bilaterally. When distances of specific points representing localized inward deformation were entered together with the corresponding hippocampal or entorhinal cortex volume in the same Cox regression model, the distances remained highly significant whereas the volumes of the corresponding structures were either marginally significant or not significant. Inclusion of cognitive or memory measures or apolipoprotein E epsilon4 genotype as covariates, or restricting the sample to patients with amnesic MCI (24 converters and 81 non-converters) did not materially change the findings. In the 3-year follow-up sample of patients with MCI, logistic regression analyses using the same measures and covariates yielded similar results.

INTERPRETATION: These findings indicate selective early involvement of the CA1 and subiculum regions of the hippocampus and provide new information on early anterior pole involvement in the entorhinal cortex in incipient AD. Fine-grained surface morphometry of medial temporal lobe structures may be superior to volumetric assessment in predicting conversion to AD in patients clinically diagnosed with MCI

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- 5 Nelson, J. C. & Devanand, D. P. (2011). A systematic review and meta-analysis of placebo-controlled antidepressant studies in people with depression and dementia. *Journal of the American Geriatrics Society*, 59, 577-585.
Notes: OBJECTIVES: To determine the efficacy of antidepressants in people with depression and dementia. DESIGN: A systematic review and meta-analysis based on a literature search of Medline and Cochrane Trials Registry for acute-phase, double-blind, placebo-controlled, parallel-design, random-assignment trials of antidepressants marketed in the United States. SETTING: Outpatient clinics, inpatient units, residential settings. PARTICIPANTS: People with criterion-based diagnoses of dementia and depression. MEASUREMENTS: Numbers of participants randomized; baseline and end point depression scale scores; and response, remission, and discontinuation rates were extracted. Random-effects meta-analyses were performed for response and remission rates, change scores using standardized mean differences, and discontinuation rates. Sensitivity analyses were planned to examine effects of depression diagnosis, severity, and trial duration. RESULTS: Seven trials with 330 participants met selection criteria. The odds ratio (OR) for six trials reporting response rates with antidepressant and placebo was 2.12 (95% confidence interval (CI)=0.95-4.70; Z=1.84, P=.07). The OR for five trials reporting remission rates was 1.97 (95% CI=0.85-4.55; Z=1.59, P=.11). Both analyses demonstrated heterogeneity. The standardized mean difference in trials was 0.29 (95% CI=0.02-0.60, Z=1.86, P=.06). This analysis did not demonstrate significant heterogeneity. Adverse event discontinuation rates (9.0%) were not significantly higher with drug than placebo (6.0%), and were low. CONCLUSION: The evidence for antidepressant treatment of people with depression and dementia, although suggestive, does not confirm efficacy. All of the trials were significantly underpowered to detect differences, resulting in inconclusive findings. Variable trial methods, comorbid conditions, and differences in antidepressants employed further confounded findings
- 6 Devanand, D. P. & Schultz, S. K. (2011). Consequences of antipsychotic medications for the dementia patient. *American Journal of Psychiatry*, 168, 767-769.
- 7 Devanand, D. P., Schupf, N., Stern, Y., Parsey, R., Pelton, G. H., Mehta, P., & Mayeux, R. (2011). Plasma Abeta and PET PiB binding are inversely related in mild cognitive impairment. *Neurology*, 77, 125-131.
Notes: OBJECTIVE: To evaluate the relations between PET Pittsburgh compound B (PiB-PET) binding (amyloid imaging) and plasma Abeta in patients with mild cognitive impairment (MCI) and similarly aged controls. METHODS: In 20 patients with MCI and 19 cognitively intact controls (case-control study), PiB binding potential (BP(nd)) was assessed in 4 regions, and total brain excluding cerebellum, referenced to cerebellar binding. The mean of plasma Abeta levels measured in duplicate was analyzed. RESULTS: Plasma Abeta42/Abeta40 ratio was decreased in MCI compared to controls (mean 0.15 SD 0.04 vs mean 0.19 SD 0.07, p = 0.03) but Abeta40 (p = 0.3) and Abeta42 (p = 0.06) levels did not differ between the 2 groups. PiB BP(nd) was increased in MCI compared to controls in the cingulate (p = 0.02), parietal (p = 0.02), and total brain (p = 0.03), but not in prefrontal cortex (p = 0.08) or parahippocampal gyrus (p = 0.07). Linear regression analyses adjusting for age, sex, and cognitive test scores showed that low Abeta42/Abeta40 ratio was associated with high cingulate, parietal, and total brain PiB binding ($0.01 < p \leq 0.05$). These associations between PiB binding and the Abeta42/Abeta40 ratio were strongest in PiB-positive subjects and within the MCI group. CONCLUSIONS: Though cross-sectional, the findings support the "sink" hypothesis that increased brain Abeta is accompanied by lower peripheral levels of

Abeta, particularly the Abeta42/Abeta40 ratio in patients with MCI. The association between PiB binding and the plasma Abeta42/Abeta40 ratio suggests possible use of plasma Abeta combined with PiB binding as a risk biomarker with potential clinical application
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- 8 Sneed, J. R., Culang, M. E., Keilp, J. G., Rutherford, B. R., Devanand, D. P., & Roose, S. P. (2010). Antidepressant medication and executive dysfunction: a deleterious interaction in late-life depression. *American Journal of Geriatric Psychiatry*, 18, 128-135.
Notes: OBJECTIVES: To determine whether there is differential response to placebo or citalopram among older patients with and without deficient response inhibition (DRI). DESIGN: This is an 8-week, double-blind, placebo-controlled trial. SETTING: Outpatient psychiatry. PARTICIPANTS: Unipolar depressed patients aged 75 years and older. INTERVENTION: Citalopram (20-40 mg/day) or placebo pill. MEASUREMENTS: Baseline Stroop Color-Word Test and weekly 24-item Hamilton Rating Scale for Depression assessments. RESULTS: Citalopram-treated patients with DRI did significantly worse than placebo-treated patients with DRI. Conversely, citalopram-treated patients without DRI did significantly better than placebo-treated patients without DRI. CONCLUSION: Patients with late-life depression and DRI respond worse to selective serotonin reuptake inhibitor (SSRI) than placebo. These findings suggest that there may be a deleterious interaction between DRI and antidepressant medication in late-life depression and that the mechanism of SSRI and placebo response is different
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- 9 Devanand, D. P., Mikhno, A., Pelton, G. H., Cuasay, K., Pradhaban, G., Dileep Kumar, J. S. et al. (2010). Pittsburgh compound B (11C-PIB) and fluorodeoxyglucose (18 F-FDG) PET in patients with Alzheimer disease, mild cognitive impairment, and healthy controls. *Journal of Geriatric Psychiatry and Neurology*, 23, 185-198.
Notes: Amyloid load in the brain using Pittsburgh compound B ((11)C-PIB) positron emission tomography (PET) and cerebral glucose metabolism using fluorodeoxyglucose ((18)F-FDG) PET were evaluated in patients with mild Alzheimer disease (AD, n = 18), mild cognitive impairment (MCI, n = 24), and controls (CTR, n = 18). (11)C-PIB binding potential (BP(ND)) was higher in prefrontal cortex, cingulate, parietal cortex, and precuneus in AD compared to CTR or MCI and in prefrontal cortex for MCI compared to CTR. For (18)F-FDG, regional cerebral metabolic rate for glucose (rCMRGlu) was decreased in precuneus and parietal cortex in AD compared to CTR and MCI, with no MCI-CTR differences. For the AD-CTR comparison, precuneus BP(ND) area under the receiver operating characteristic (ROC) curve (AUC) was 0.938 and parietal cortex rCMRGlu AUC was 0.915; for the combination, AUC was 0.989. (11)C-PIB PET BP(ND) clearly distinguished diagnostic groups and combined with (18)F-FDG PET rCMRGlu, this effect was stronger. These PET techniques provide complementary information in strongly distinguishing diagnostic groups in cross-sectional comparisons that need testing in longitudinal studies
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- 10 Devanand, D. P., Liu, X., Tabert, M. H., Pradhaban, G., Cuasay, K., Bell, K. et al. (2008). Combining early markers strongly predicts conversion from mild cognitive impairment to Alzheimer's disease. *Biological Psychiatry*, 64, 871-879.
Notes: BACKGROUND: The utility of combining early markers to predict conversion from mild cognitive impairment (MCI) to Alzheimer's Disease (AD) remains uncertain. METHODS: Included in the study were 148 outpatients with MCI, broadly defined, followed at 6-month intervals. Hypothesized baseline predictors for follow-up conversion to AD (entire sample: 39/148 converters) were cognitive test performance, informant report of functional impairment, apolipoprotein E genotype, olfactory identification deficit, and magnetic resonance imaging (MRI) hippocampal and entorhinal cortex volumes. RESULTS: In the 3-year follow-up patient sample (33/126 converters), five of eight hypothesized predictors

were selected by backward and stepwise logistic regression: Pfeffer Functional Activities Questionnaire (FAQ; informant report of functioning), University of Pennsylvania Smell Identification Test (UPSIT; olfactory identification), Selective Reminding Test (SRT) immediate recall (verbal memory), MRI hippocampal volume, and MRI entorhinal cortex volume. For 10% false positives (90% specificity), this five-predictor combination showed 85.2% sensitivity, combining age and Mini-Mental State Examination (MMSE) showed 39.4% sensitivity; combining age, MMSE, and the three clinical predictors (SRT immediate recall, FAQ, and UPSIT) showed 81.3% sensitivity. Area under ROC curve was greater for the five-predictor combination (.948) than age plus MMSE (.821; $p = .0009$) and remained high in subsamples with MMSE $\geq 27/30$ and amnesic MCI. CONCLUSIONS: The five-predictor combination strongly predicted conversion to AD and was markedly superior to combining age and MMSE. Combining the clinically administered measures also led to strong predictive accuracy. If independently replicated, the findings have potential utility for early detection of AD

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- 11 Devanand, D. P., Habeck, C. G., Tabert, M. H., Scarmeas, N., Pelton, G. H., Moeller, J. R. et al. (2006). PET network abnormalities and cognitive decline in patients with mild cognitive impairment. *Neuropsychopharmacology*, 31, 1327-1334.

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Temporoparietal and posterior cingulate metabolism deficits characterize patients with Alzheimer's disease (AD). A H₂(15)O resting PET scan covariance pattern, derived by using multivariate techniques, was previously shown to discriminate 17 mild AD patients from 16 healthy controls. This AD covariance pattern revealed hypoperfusion in bilateral inferior parietal lobule and cingulate; and left middle frontal, inferior frontal, precentral, and supramarginal gyri. The AD pattern also revealed hyperperfusion in bilateral insula, lingual gyri, and cuneus; left fusiform and superior occipital gyri; and right parahippocampal gyrus and pulvinar. In an independent sample of 23 outpatients with mild cognitive impairment (MCI) followed at 6-month intervals, the AD pattern score was evaluated as a predictor of cognitive decline. In this MCI sample, an H₂(15)O resting PET scan was carried out at baseline. Mean duration of follow-up was 48.8 (SD 15.5) months, during which time six of 23 MCI patients converted to AD. In generalized estimating equations (GEE) analyses, controlling for age, sex, education, and baseline neuropsychological scores, increased AD pattern score was associated with greater decline in each neuropsychological test score over time (Mini Mental State Exam, Selective Reminding Test delayed recall, Animal Naming, WAIS-R digit symbol; $P < 0.01-0.001$). In summary, a resting PET covariance pattern previously reported to discriminate AD patients from control subjects was applied prospectively to an independent sample of MCI patients and found to predict cognitive decline. Independent replication in larger samples is needed before clinical application can be considered

- 12 Devanand, D. P. (1995). Role of neuroleptics in treatment of behavioral complications. In B.A.Lawlor (Ed.), *Behavioral complications in Alzheimer's disease* (pp. 131-151). Washington,DC: American Psychiatric Press.