

Papers recently published using NACC data

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Example publications, 2016-2017

NACC data used	Author	Year
UDS	Kielb et al	2017
NP + UDS	Sposato et al	2017
MRI + UDS	Lange et al	2016

Kielb et al (2017)

Subjective cognitive decline (SCD): Cognitive complaint within “normal” range on standard clinical assessments

SCD assessed in UDS Form B9:

- **“Does the subject report decline in memory relative to previously attained abilities?”**

Kielb (2017) - Hypotheses

Baseline SCD associated with:

1. Subtle weaknesses in functional abilities
2. Subtle weaknesses in longitudinal performance – episodic memory, psychomotor speed
3. Higher prevalence of progression to MCI/dementia

Kielb (2017) - Sample

- **UDS participants (through Nov 2013):**
 - >65 years old
 - Version 2 UDS neuropsychological battery
 - Normal cognition dx, MMSE \geq 27, CDR=0 at initial visit
 - Non-missing APOE data
 - At least 2 visits
 - Did not endorse more than 7 GDS symptom
- **Final sample, n=3,915 (19.5% with SCD)**

Kielb (2017) – Methods

- **T-tests and chi-square tests:**
 - Demographics
 - Family history of dementia
 - APOE e4 status
 - Functional Assessment Scale ratings
 - Final clinical status (MCI/dementia vs no MCI/dementia)
- **Linear mixed models:** compared longitudinal change in neuropsychological test scores

Kielb (2017) - Results

- Similar demos, family hx, APOE4 by SCD status
- Neither group had functional impairment
 - However, worse baseline Functional Assessment Scale rating in SCD+ versus SCD- (0.40 vs 0.16, $p < 0.001$)

Kielb (2017) - Results

- Worse scores over time in SCD+ vs SCD- in:
 - Episodic memory (Log Mem Immed & Delayed)*
 - Psychomotor speed (DS, Trail A, Trail B)
 - Language (BNT)
 - No interaction between APOE e4 and SCD
- Later MCI/dementia more common in SCD+ vs SCD-

* Specifically, less practice effects in SCD+ group

Kielb (2017) - Conclusions

- Although detected subtle differences between SCD+ and SCD-, were within “normal” score range
- More sensitive measures needed to recognize SCD+ individuals later developing MCI/dementia

Sposato et al (2017)

- **Previous studies:**
association between heart failure (HF) / atrial fibrillation (AF) and clinical AD
- **Aim:** Are HF and AF associated with more severe AD neuropath?

Sposato (2017) - Sample

- **Restricted to UDS participants with:**
 - Primary AD neuropath dx
 - No contributing CVD neuropath
- **Final sample, n=1,593**
 - HF, n=129 (8%)
 - AF, n=250 (16%)

Sposato (2017) – Defining HF & AF

- **AF and HF:**
 - Recent/remote history reported, any UDS visit
- **4 clinical phenotypes:**
 - No HF, no AF
 - AF without HF
 - HF without AF
 - HF and AF

Sposato (2017) – AD severity

- **AD severity:**
 - Severe: Braak V/VI
 - Milder: Braak III/IV

Sposato (2017) – Methods

- **Multiple logistic regression:**
 - Outcome: AD pathology severity
 - Predictors: HR and AF
 - Covariates: age, sex, hypertension, hyperlipidemia, smoking, diabetes, stroke/TIA
- **Network analysis** (not reported here)
 - Relating demos, risk factors, comorbidities, neuropath

Sposato (2017) - Results

- <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5592781/figure/F2/>

Sposato (2017) – Regression results

- Age and HR x AF inversely related to AD severity
 - 1-year age increase, 5% lower odds of severe AD
 - Both HF & AF, 39% lower odds of severe AD
- Posthoc analyses: Severe AD resulted in 3-fold increased risk of younger death (<72 yrs)

Sposato (2017) – Conclusions

- Individuals with more benign AD course:
 - Live longer into older ages
 - More likely to develop HR and AF
- HF and AF individuals had more CVD neuropath
 - Lower threshold for dementia (and thus had less severe AD)

Lange et al (2016)

White Matter Hyperintensities (WMH):

- WM lesions due to demyelination and axonal loss
- Common in older adults

Lange (2016) - Hypothesis

- WMH associated with SCD, MCI, dementia
 - However, WMH severity and cognition associations often weak
- Irregularly shaped WMH may have stronger association with cognition than smooth/spherical WMH
- **Hypothesis:** WMH shape provides information above and beyond lesion volume

Lange (2016) - Methods

iDSS study sample, n=87

- Germany, prospective neuroimaging study
- MRI from 7 days before to 9 days after neuropsych
- Cog. impaired, various etiologies (eg., AD, CVD)

NACC sample, n=198

- Dx of VaD, MRI & neuropsych available
- Dx of primary probable AD or NC, MRI \pm 100 days from neuropsych testing

Lange (2016) - Methods

- Confluency Sum Score (COSU):
 - Quantitative summary of WMH shape irregularity
 - WMH lesion auto-segmentation of FLAIR images
 - For each lesion:
 - $\text{confluency}_i = [1/(36\pi) \cdot \text{surface}_i^3 / \text{volume}_i^2]^{1/3} - 1.$
 - For all lesions ≥ 100 voxels:
 - COSU – summed confluency over all WMH clusters

Lange (2016) - Methods

- iDSS: CERAD-plus battery; NACC: UDS battery
- Age, sex, education adjusted z-scores for each test
- Spearman test correlation: COSU/WMH volume and z-scores
 - Restricted to WMH loads ≥ 13.5 mL
- Partial correlation for association with TMT-A, based on bivariate findings
 - Controlled for MMSE, dx, MRI to test interval, magnetic strength, voxel volume in FLAIR

Lange (2016) - Conclusions

- WMH shape irregularity more strongly correlated with mental speed/fluid abilities (Trail Making A) than WMH volume
 - Suggests that COSU provides additional information beyond total WMH volume
 - Pathophysiological reasons unclear
 - Diffusion tensor tractography or resting state functional MRI may help tease apart observed findings

References

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Few other highlighted papers

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