Subjective Cognitive Impairment, Neuroticism and Brain Amyloid Load

14th Annual MCI Symposium

January 16, 2016

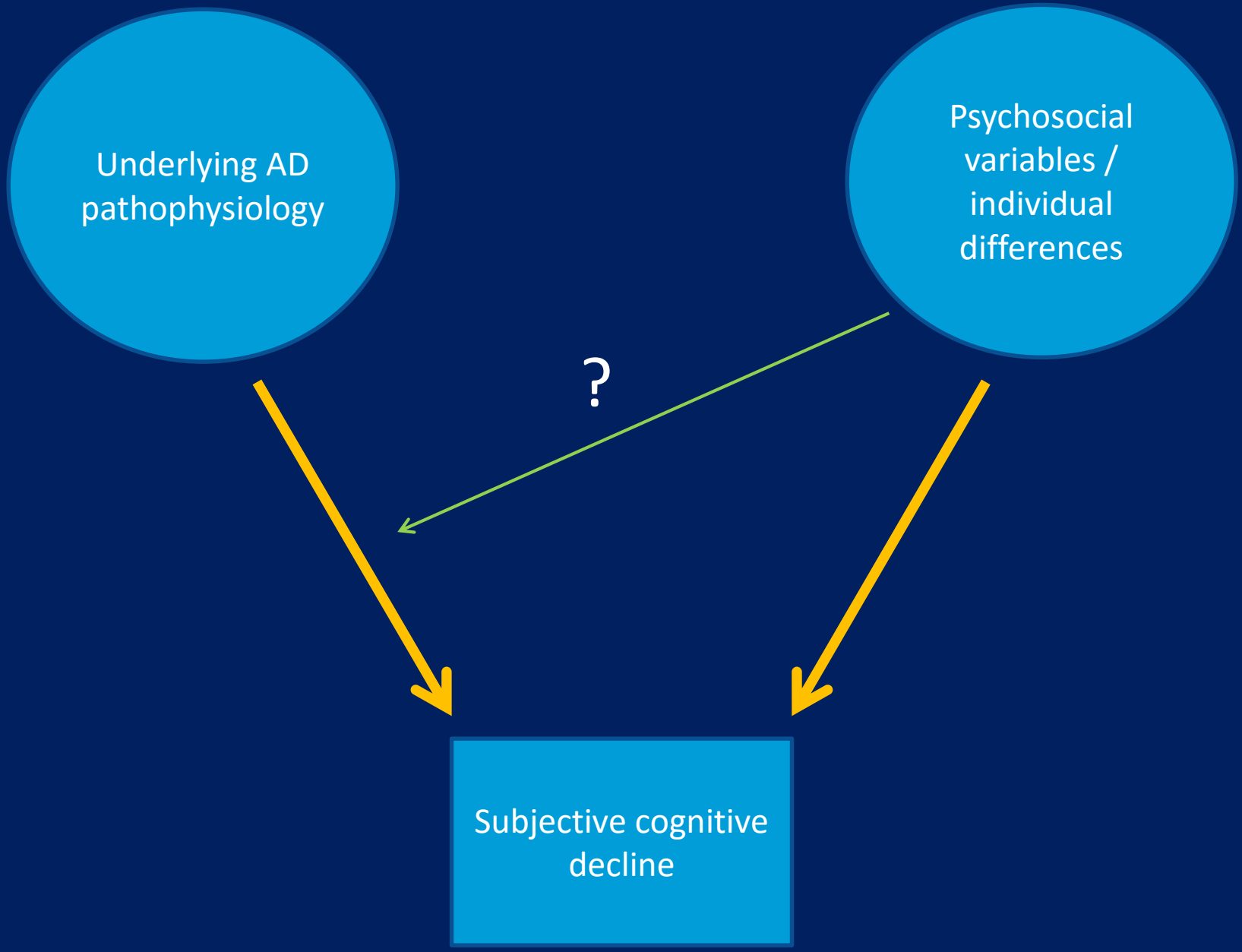
Beth Snitz, PhD
Assistant Professor
Dept. of Neurology, School of Medicine
University of Pittsburgh
Pittsburgh, USA

Subjective memory / cognitive complaints and pre-clinical AD: Biomarker studies

- Post-mortem neuritic & diffuse plaques & NF tangles
  - *Barnes et al., 2006*
- FDG hypometabolism
  - *Mosconi et al., 2008; Scheef, Jessen et al., 2012*
- Hippocampal atrophy
  - *van der Flier et al., 2004; Saykin et al., 2006; Scheef et al., 2012; Perrotin et al., 2015; Cherbuin et al., 2015*
- APOE*4
  - *Small et al., 1999; Zwan et al., 2015*
- Amyloid imaging
  - *Perrotin et al., 2012; Amariglio et al., 2012; Snitz et al., 2015; Zwan et al., 2015*

Psychosocial correlates of subjective memory complaints

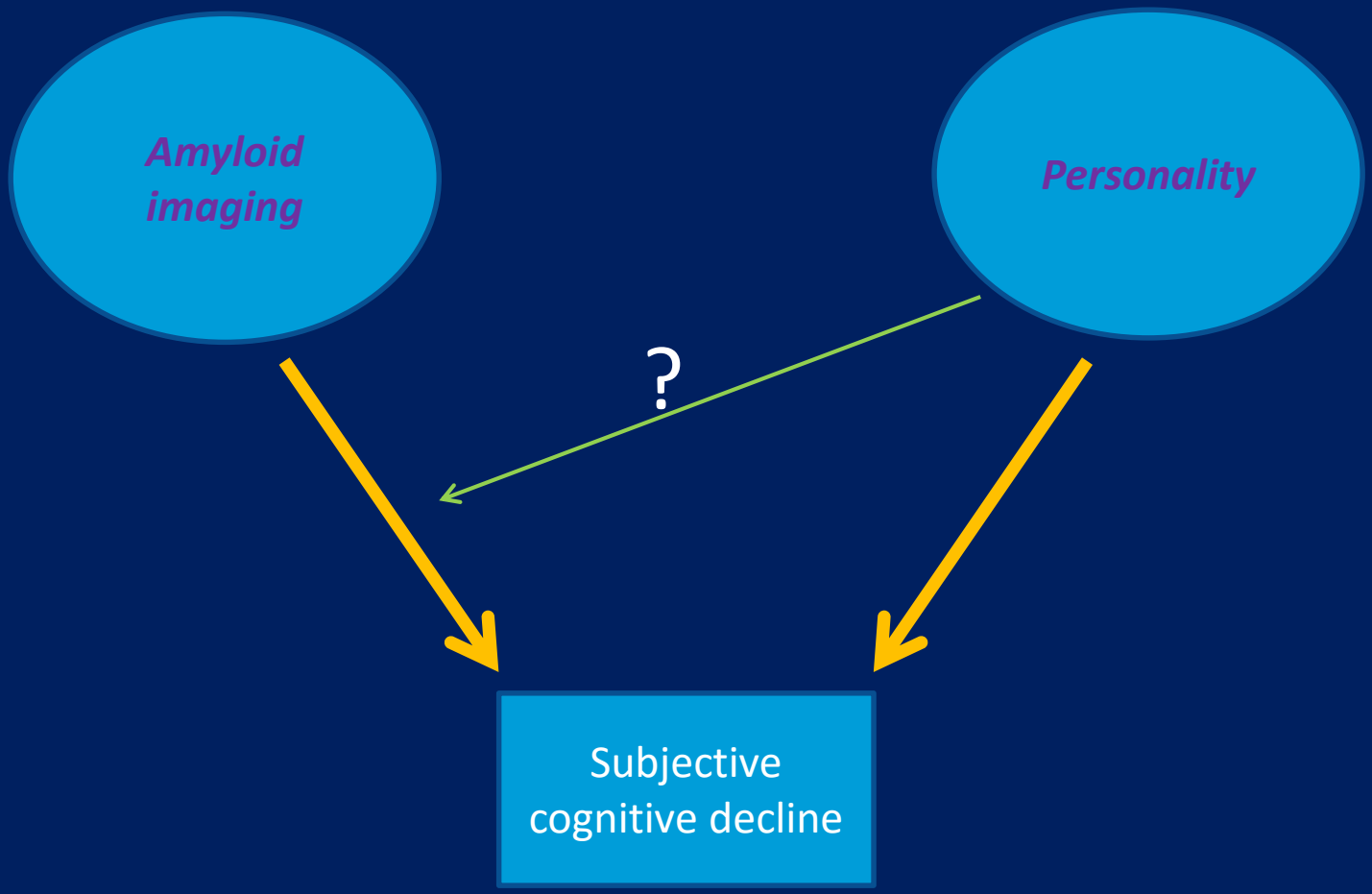
- Depressive symptoms & anxiety
  - *Reid & MacLullich, 2006 review; Schofield et al, 1997; Jungwirth et al., 2004; Pearman et al., 2004; Kliegel et al., 2005; Minett et al., 2005; Slavin et al., 2010; Buckley et al., 2013*
- Personality
  - High neuroticism, low conscientiousness, high somatic complaints
  - *Hänninen et al., 1994; Comijs et al., 2002; Jorm et al., 2004; Pearman & Storandt, 2004; Pearman & Storandt, 2005; Slavin et al., 2010; Steinberg et al., 2013*
- Stress / cortisol
  - *Wolf et al., 2005; Elfgren et al., 2005; Metternich et al, 2009*
- Illness perception/ personal relevance / fear of Alzheimer Disease
  - *Hurt et al., 2011; French et al., 2012*
- Sampling / recruitment / study setting
  - *Rodriguez-Gomez et al., 2015; Archer et al., 2015*


Underlying AD pathophysiology
Psychosocial variables / individual differences
?
Subjective cognitive decline

Subjective Cognitive Complaints, Personality and Brain Amyloid-beta in Cognitively Normal Older Adults

Beth E. Snitz, Ph.D., Lisa A. Weissfeld, Ph.D., Ann D. Cohen, Ph.D., Oscar L. Lopez, M.D., Robert D. Nebes, Ph.D., Howard J. Aizenstein, M.D., Ph.D., Eric McDade, D.O., Julie C. Price, Ph.D., Chester A. Mathis, Ph.D., William E. Klunk, M.D., Ph.D.

Am. J. Geriatric Psychiatry, 23:9, Sep, 2015



Study goals

1. Replication of previous findings of association between amyloid burden – SCC in healthy CN older adults
    - Perrotin et al., 2012; Amariglio et al., 2012

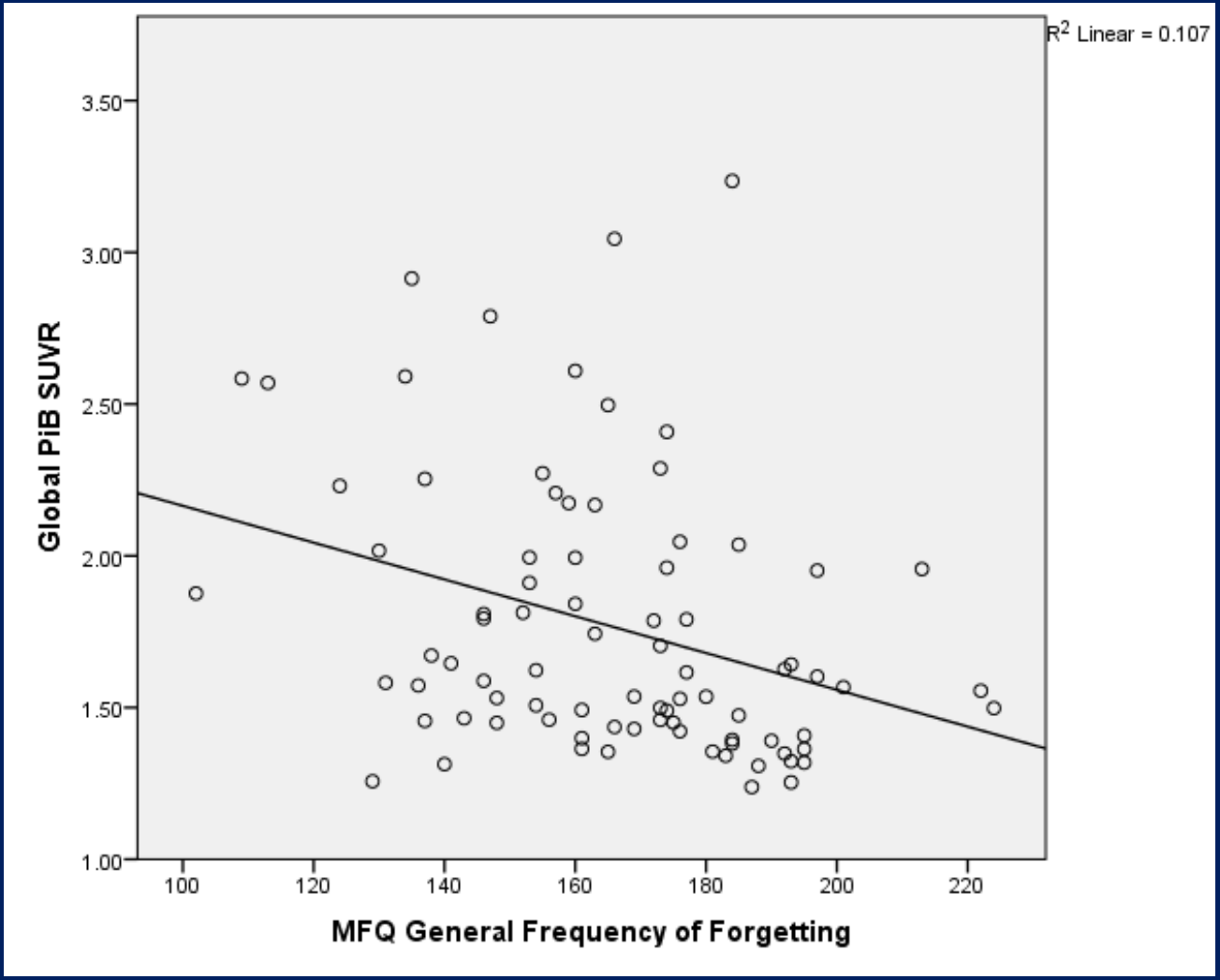
2. Explore five-factor personality as moderating variables
    - Openness, Conscientiousness, Extraversion, Agreeableness, Neuroticism
    - Neuroticism hypotheses:

    "Worried well" vs. "Negative-affect-risk"

Methods

- Add-on to two ongoing PiB-PET imaging studies
  - (Klunk, PI; P01 AG025204; Klunk R37 AG025516)
  - PiB-PET 50-70 minutes; SUVR cerebellum reference; global SUVR = average of 5 cortical regions (precuneus, anterior cingulate, frontal parietal, lateral temporal)
- Sample
  - **n = 89** cognitively normal (CN) participants, based on NP battery
  - mean age 80.8 (SD 8.4) years; IQR = 74 to 86 years
  - mean educ. 16.6 (SD 9.6) years
  - 48% female; 90% white
- Detailed self-report measures at time of neuroimaging
  - Memory Functioning Questionnaire (Zelinski et al., 1990; 64 items; 4 factors)
  - Cognitive Failures Q'nnaire (Broadbent et al., 1982; 25 items; some tap "trait" absent-mindedness)
  - Subjective Memory Scale (Ganguli et al.,2004)
  - Geriatric Depression Scale (Yesavage et al., 1982)
  - NEO-FFI (McCrae & Costa, 2007; 60 items; five-factor personality inventory)
  - MMPI-2-RF (Ben-Porath & Tellegen, 2008; 30 items; L-r & Fs: under-reporting & over-reporting indicators)

Frequency of subjective memory failures & PiB retention



"*How often do these present a problem for you…*"

-names
-faces
-appts.
-where put things
-words
-dates
-phone numbers
-etc.

(1 – 7, "*always*" to "*never*")

- 33 items
- higher = better functioning

r = .32, p <.05

Only MFQ associated with global PiB SUVR retention in adjusted models

TABLE 2. Regression Model Predicting Global PiB Retention

A. Using MFQ total score and covariates

	Unstandardized Coefficients		Standardized Coefficients		
	B	Std. Error	Beta	t	p
Constant	1.233	0.566		2.178	0.032
Age	0.016	0.006	0.323	2.825	0.006
Sex	−0.038	0.101	−0.045	−0.379	0.706
GDS	−0.002	0.012	−0.019	−0.175	0.861
MFQ total score	−0.003	0.001	−0.230	−2.029	0.046

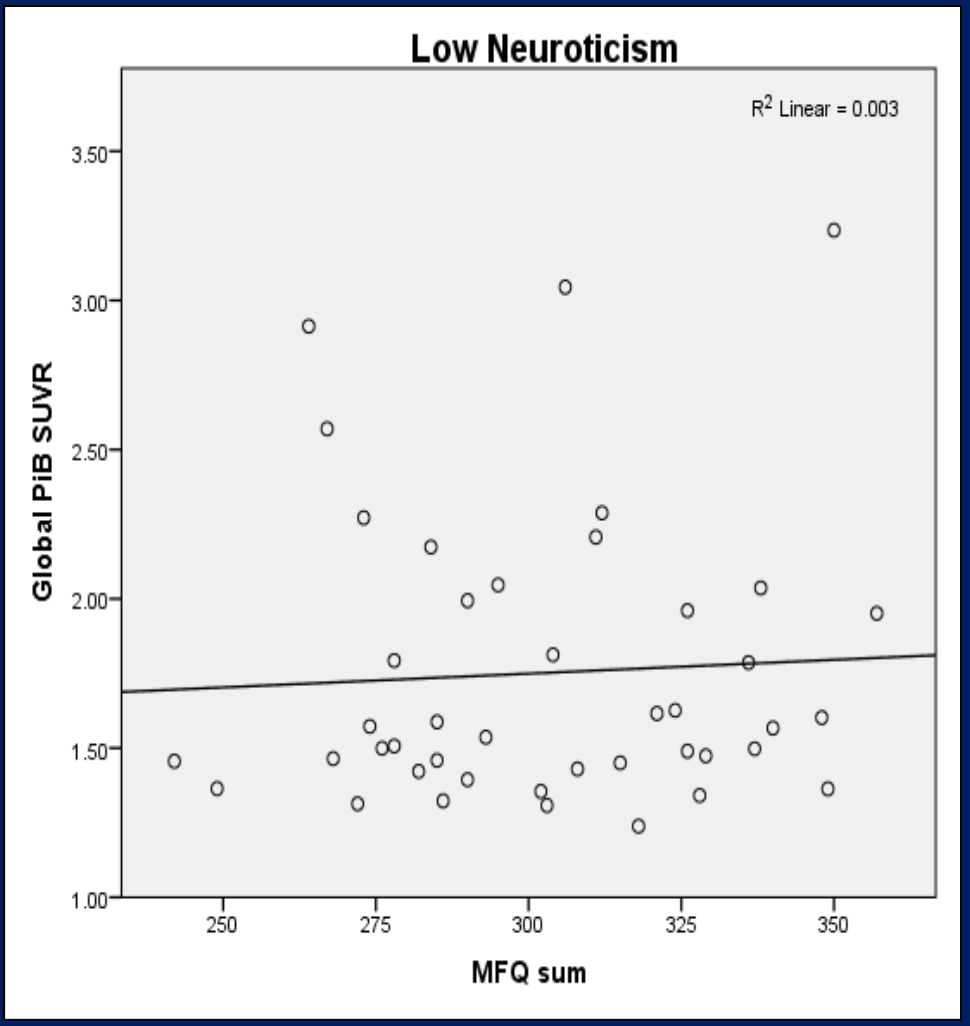
Notes: Model $R^2 = 0.145$; Model $F_{(4,77)} = 3.264$, $p = 0.016$.

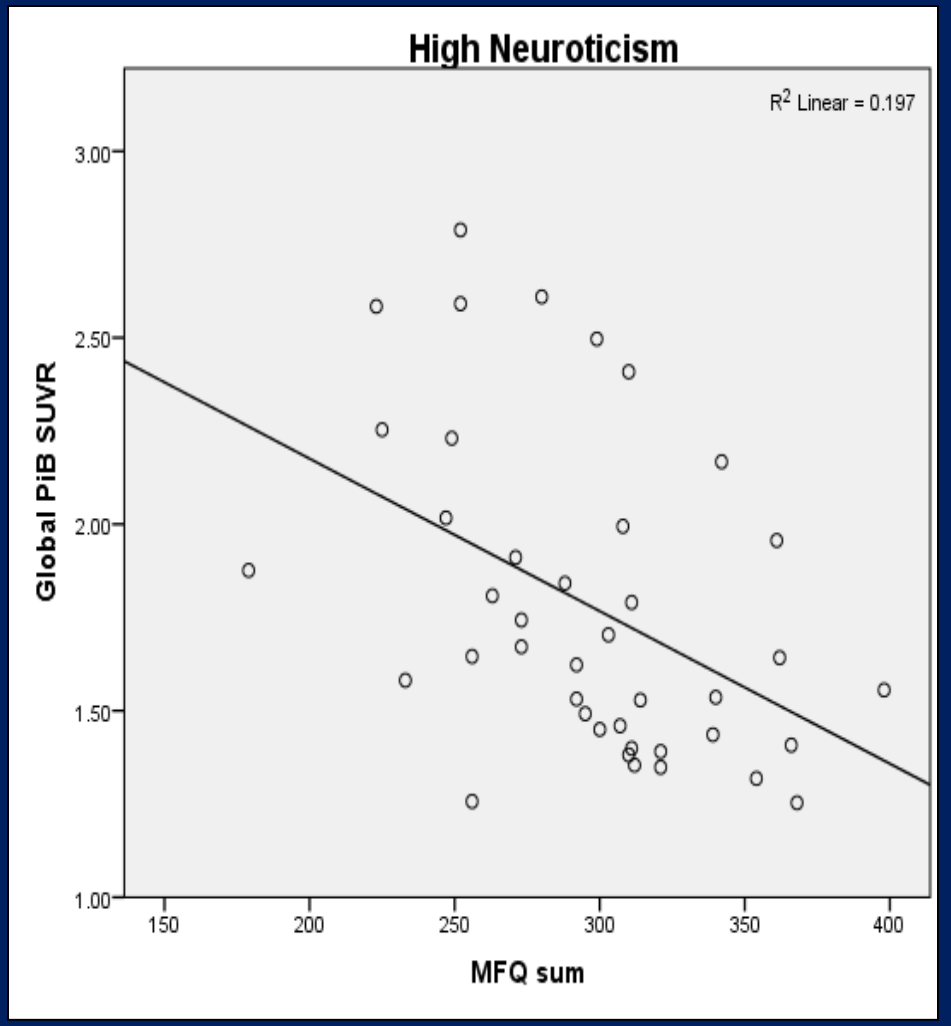
B. Using MFQ 'General Frequency of Forgetting' factor and covariates

	Unstandardized Coefficients		Standardized Coefficients		
	B	Std. Error	Beta	t	p
Constant	1.479	0.591		2.503	0.014
Age	0.014	0.006	0.277	2.462	0.016
Sex	−0.047	0.100	−0.056	−0.476	0.636
GDS	−0.004	0.012	−0.032	−0.297	0.768
MFQ General Frequency of Forgetting factor	−0.005	0.002	−0.278	−2.425	0.018

Notes: GDS: Geriatric Depression Scale; MFQ: Memory Functioning Questionnaire. Model $R^2 = 0.163$; Model $F_{(4,77)} = 3.754$; $p = 0.008$.

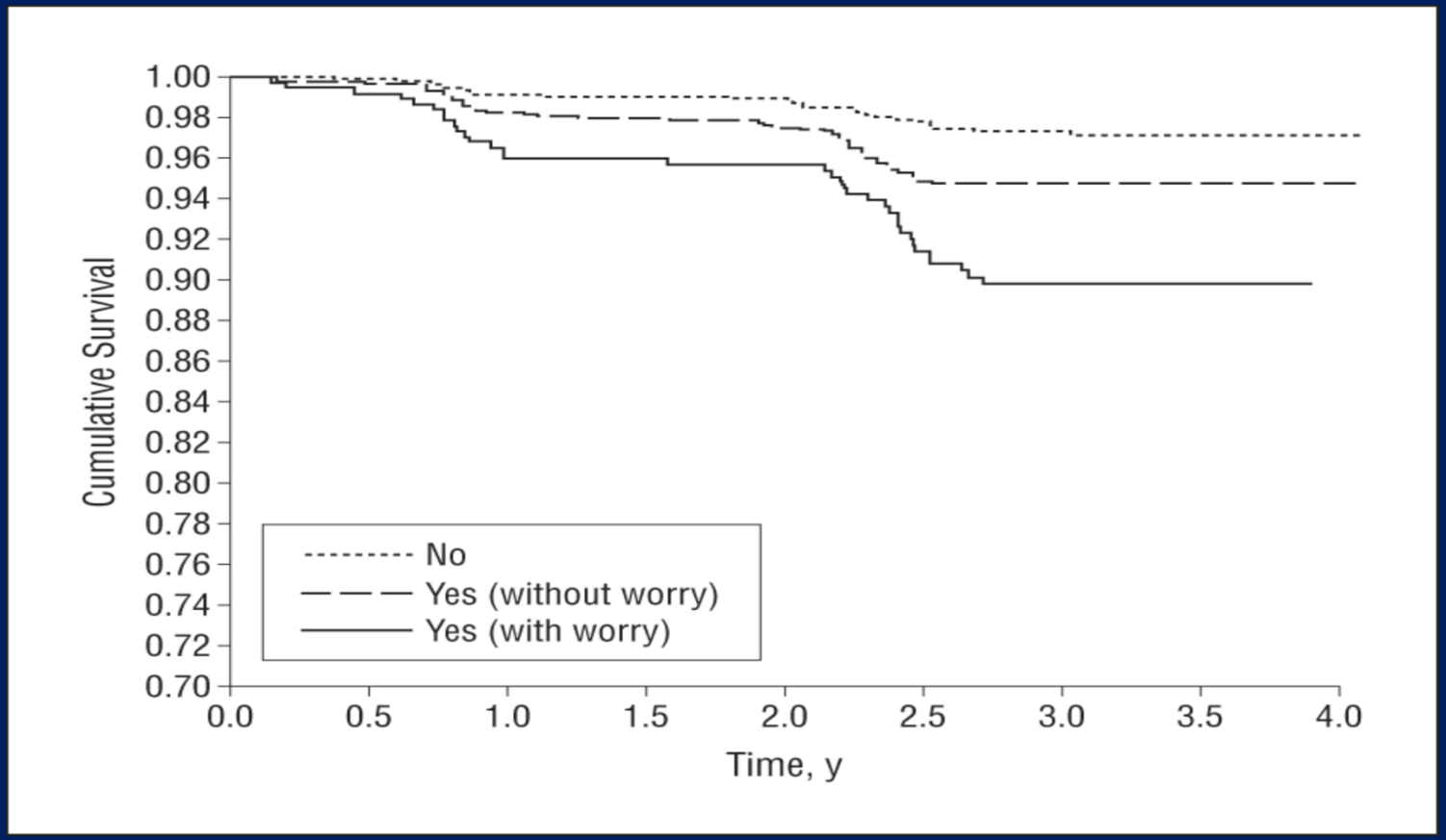
Neuroticism moderates the association





- No other personality factor was a moderator

Effect of “worry” about one’s memory on risk for AD



Kaplan-Meier survival curves showing the conversion to dementia in Alzheimer disease relative to the presence of subjective memory impairment with or without worry at baseline.

Jessen et al. *Arch Gen Psychiatry*. 2010;67(4):414-422.

NEUROLOGY 2003;61:1479–1485

Articles

Proneness to psychological distress is associated with risk of Alzheimer's disease

R.S. Wilson, PhD; D.A. Evans, MD; J.L. Bienias, ScD; C.F. Mendes de Leon, PhD; J.A. Schneider, MD; and D.A. Bennett, MD

ELSEVIER

Alzheimer's & Dementia ■ (2013) 1–8

Alzheimer's & Dementia

Personality and risk of Alzheimer's disease: New data and meta-analysis

Antonio Terracciano[a,b,*], Angelina R. Sutin[a,b], Yang An[a], Richard J. O'Brien[c], Luigi Ferrucci[a], Alan B. Zonderman[a], Susan M. Resnick[a]

[a]National Institute on Aging, National Institutes of Health, Baltimore, MD, USA
[b]Florida State University College of Medicine, Tallahassee, FL, USA

Open Access Research

BMJ open

Common psychosocial stressors in middle-aged women related to longstanding distress and increased risk of Alzheimer's disease: a 38-year longitudinal population study

Lena Johansson,[1] Xinxin Guo,[1] Tore Hällström,[1,2] Maria C Norton,[3] Margda Waern,[1] Svante Östling,[1] Calle Bengtsson,[4] Ingmar Skoog[1]

Pilot Study:
14 SCD patients presenting in a memory disorder clinic

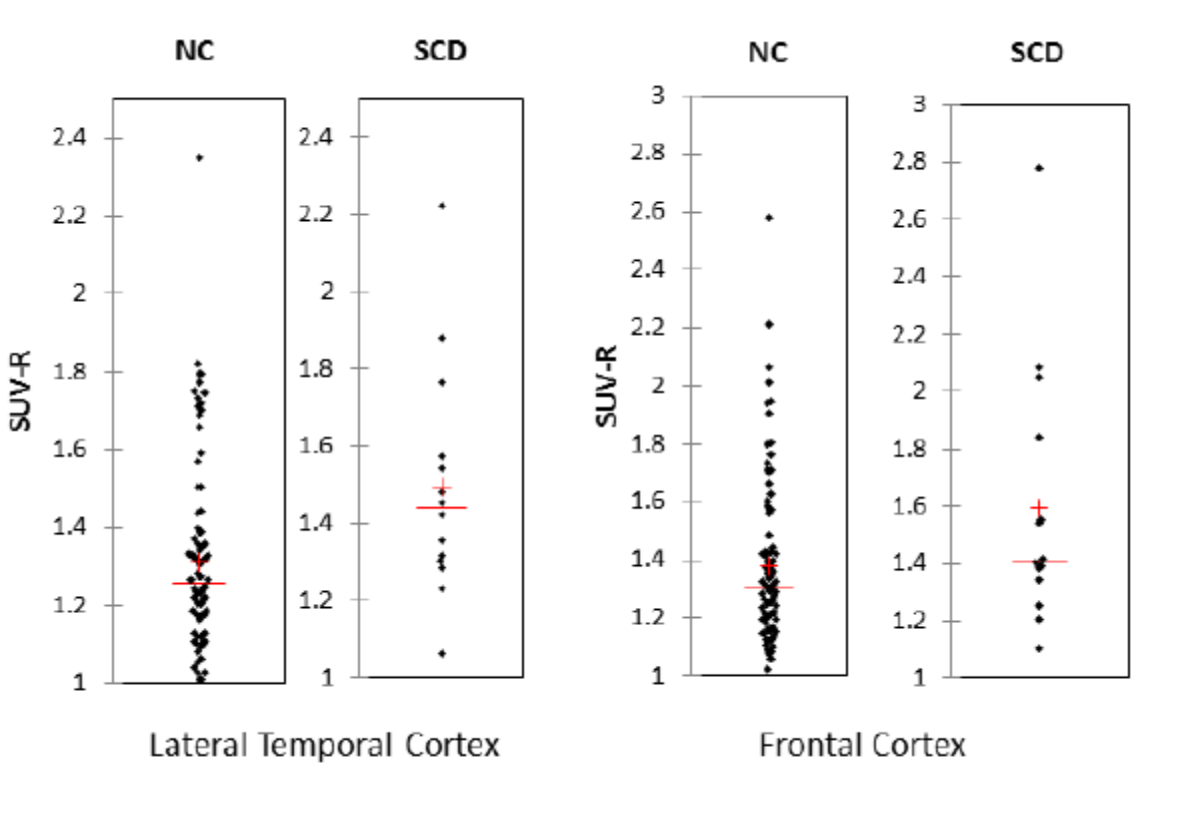
Case #	Age (years)	Sex	Education (years)	APOE	MMSE	CERAD WLL DR (max=10)	mR-O Copy (max=24)	Animal Fluency	Trails B (sec)	PiB status
1	70	M	20	33	30	6	23	17	40	+
2	66	F	20	33	29	10	23	30	78	+
3	65	F	18	34	30	8	21	23	57	+
4	69	F	20	33	30	8	24	25	45	-
5	74	F	16	33	29	9	23	30	68	-
6	67	F	16	34	29	6	23	28	64	-
7	65	F	17	34	28	7	22	19	58	+
8	70	M	20	34	30	8	24	22	60	+
9	63	M	16	33	27	8	24	21	64	-
10	76	F	16	---	29	*	19	15	80	-
11	69	F	13	33	28	8	24	24	62	+
12	69	M	18	33	29	7	22	17	68	-
13	69	F	18	33	30	7	23	34	89	+
14	61	M	18	23	30	8	24	17	69	+

Normal cognitive test scores …

… Elevated scores on SCC scales, depression, neuroticism
(= dysphoric mood)

Case #	MFQ (higher=better)	CFQ (higher=worse)	SCCS (higher=worse)	GDS	Neuroticism (T-score)	PiB status
1	257	52	6	16	57	+
2	228	50	9	---	50	+
3	262	51	10	11	55	+
4	230	37	9	9	58	-
5	265	50	15	15	71	-
6	269	48	8	2	50	-
7	229	51	16	8	59	+
8	219	54	15	10	46	+
9	277	44	11	7	44	-
10	242	40	8	11	46	-
11	249	64	10	26	75	+
12	299	34	6	3	39	-
13	193	59	12	6	50	+
14	243	62	12	5	39	+

Pilot study:
14 SCD patients presenting in a memory disorder clinic



Elevated PiB retention in two cortical areas

Snitz et al. , *J. of Alzheimer's Dis*, 48, Sep, 2015

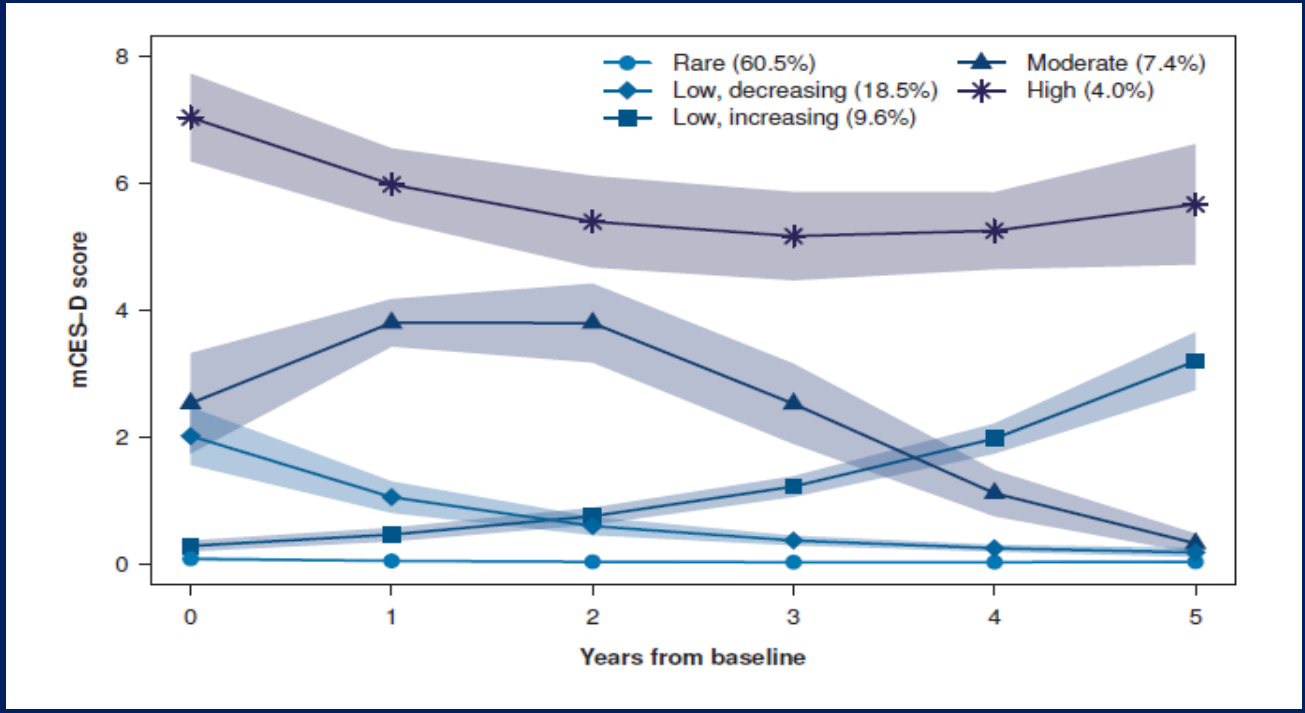
Accepted Manuscript

Dual Trajectories of Depression and Cognition: A Longitudinal Population-Based Study

Julie A. Graziane, M.D., Joanne C. Beer, M.S., Beth E. Snitz, Ph.D., Chung-Chou H. Chang, Ph.D., Mary Ganguli, M.D., M.P.H.

Population – based cohort: MYHAT Study (Ganguli, PI)

- Age-stratified random sampling
- Small-town Southwest PA
- N=1982



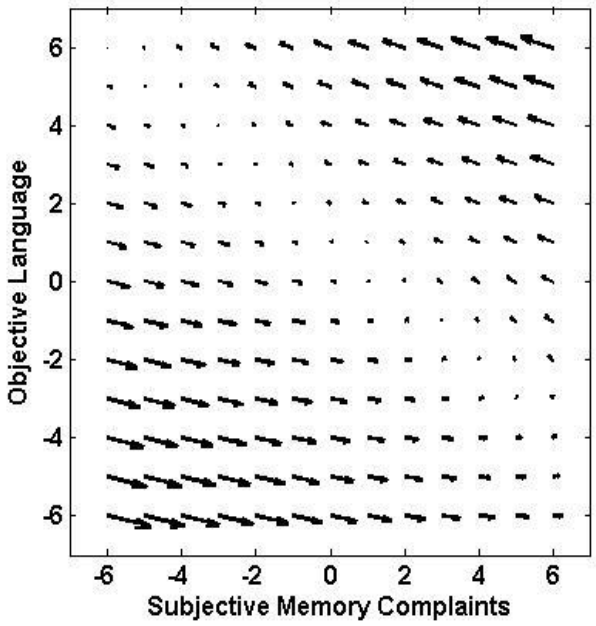
Journal of the International Neuropsychological Society (2015), **21**, 732–742.

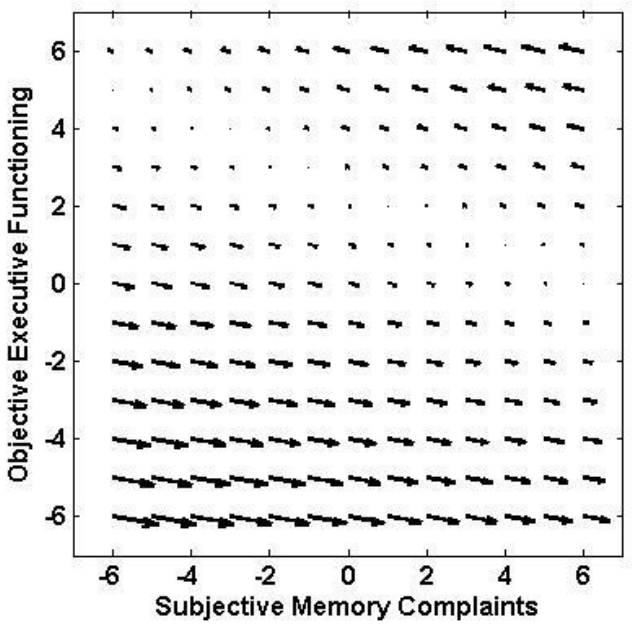
doi:10.1017/S1355617715000922

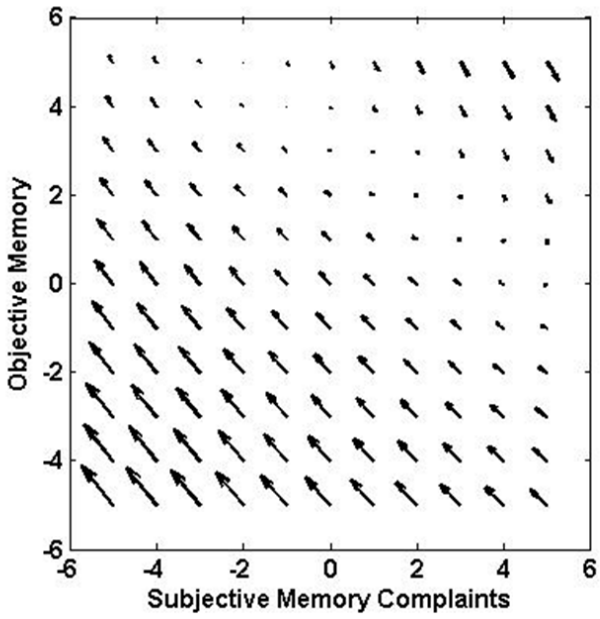
Do Subjective Memory Complaints Lead or Follow Objective Cognitive Change? A Five-Year Population Study of Temporal Influence

Beth E. Snitz,[1] Brent J. Small,[2] Tianxiu Wang,[1] Chung-Chou H. Chang,[1] Tiffany F. Hughes,[1] AND Mary Ganguli[1]
[1]University of Pittsburgh, Pittsburgh, Pennsylvania
[2]University of South Florida, Tampa, Florida

- How do subjective memory complaints relate to objectively assessed cognition, across 5 annual study visits ?
- What is the sequence of change across time – subjective complaints leading objective cognition, or vice versa, or both pathways important ?
    - Bivariate latent change score modeling
        - Does *objective* cognition at time 1 predict *subjective* cognition at time 2 ?
        - Does *subjective* cognition at time 1 predict *objective* cognition at time 2 ?
    - Broad spectrum of cognition at baseline (17% CDR 0.5)







- MEMORY temporal dynamics different than other two domains
- Poor insight at lower objective memory performance

- Meaning & prognostic value of subjective memory complaints nuanced & *complex* – here dependent on starting point of objectively assessed memory function

Snitz, Small, Wang, Chang, Hughes & Ganguli, *JINS*; 2015