The Colorado Adoption/Twin Study of Lifespan Behavioral Development and Cognitive Aging (CATSLife): An Introduction

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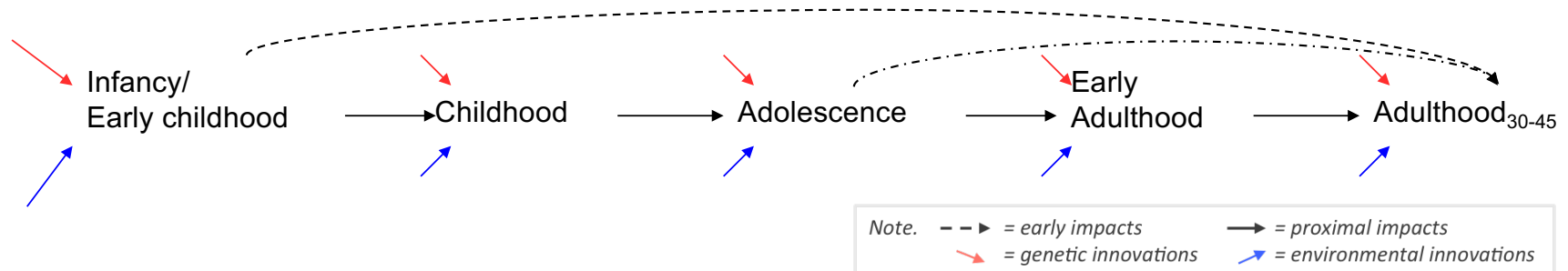
University of Colorado **Boulder**

King's College London

Early origins

"Cognitive health begins at conception."[1] This implies that early influences accumulate over the life course to impact how well we age[2].

If early life origins exist, do cognitive growth patterns in early childhood & adolescence uniquely impact adult functioning beyond proximal influences?

Infancy/Early childhood → Childhood → Adolescence → Early Adulthood → Adulthood$_{30-45}$

Note. - - ▶ = early impacts   ⟶ = proximal impacts
↘ = genetic innovations   ↗ = environmental innovations

1. Barnett JH, Hachinski V, Blackwell AD. Cognitive health begins at conception: addressing dementia as a lifelong and preventable condition. BMC Med 2013;11:246.
2. Liu S, Jones R, Glymour M. Implications of Lifecourse Epidemiology for Research on Determinants of Adult Disease. Public Health Reviews 2010;32:489-511.

CATSLife Aims

I. Conduct genetically sensitive study of behavioral & cognitive changes at cusp of middle adulthood.

II. Map individual differences in growth and maintenance of cognitive abilities.

III. Evaluate physical factors and health behaviors associated with sustaining cognitive performance.

IV. Trace biochemical and gene pathways important to sustaining cognitive performance.

V. Track environmental factors that decrease, sustain or boost cognitive performance.

cognition & neural function

- Episodic memory
- Executive functioning
- Processing speed
- fMRI (via MH063207, Friedman & Hewitt)

biochemical & gene pathways

- Lipids/Cholesterol (e.g., LDL; *APOE*)
- Synaptic plasticity, cell signaling (e.g. BDNF)
- Polygenic scores (e.g., AD risk, BMI)

health behaviors & environment

- BMI, diet, sleep
- Substance use
- Physical, Social, Cognitive activities
- Geographic/neighborhood factors

CAP & LTS → CATSLife

◦ Colorado Adoption Project (CAP)
  ◦ Initiated in 1975
  ◦ 245 adoptive and 245 matched "control" families

◦ Longitudinal Twin Study (LTS)
  ◦ Initiated in 1985
  ◦ 483 twin pairs

	Planned	As of May 2017
Adoptive		
Probands	175	81
Siblings	182	53
Total Adoptive	**357**	**134**
Non-Adoptive		
Probands	198	79
Siblings	221	70
Total Non-Adoptive	**419**	**149**
Total CAP	**776**	**283**
Twins		
MZ	438	199
DZ	386	185
Total Twins	**824**	**384**
Total individuals	**1600**	**667**

CAP & LTS: Longitudinal Coverage

Domains & exemplars	Parent	1	2	3	4	7	9	10	11	12	13	14	15	16	17	21-22	30-35
Cognition																	
Standardized Tests (IQ)	CT	CT	CT	CT	CT	CT				CT				CT		C	C
Specific Cognitive Abilities	CT			C	CT	CT	CT	CT		CT		CT		CT		C	C
Executive Function															T	T	
'Environmental' Variables																	
Home/Neighborhood		CT	CT	CT		CT	CT	CT	CT	CT	CT	CT	CT			C	
Life Events						CT	CT	CT	CT	CT	CT	CT	CT				
Health & Health Behaviors																	
Substance Use										CT	CT	CT	CT	CT	CT	CT	
Height/Weight	CT	CT	CT	CT	CT	CT	CT	CT	CT	CT	CT	CT	CT	CT	CT	CT	C
Health Ratings, Illnesses		CT	CT	CT	CT	CT	CT	CT	CT	CT	CT	CT	CT	C		C	C
Interests/Activities	CT					CT	CT	CT	CT	CT				CT		C	
Personality/Socioemotional																	
Depression/Anxiety							CT	CT	CT	CT	CT	CT	CT	CT	CT	CT	
Social Support										T	CT	CT	CT	CT			
Temperament(CCTI/EASI)	CT	CT	CT	CT	CT	CT	CT	CT	CT	CT	CT	CT	CT	CT	CT	CT	C

(RED = CAP only; BLUE = Twin only; PURPLE = both samples)

CATSLife Testing (Target *N* = 1600)

ONLINE QUESTIONNAIRE

Environments — Education, Work, Religion, Neighborhood Demographics, Life Events, Financial Distress

Health — Health, Diet, Sleep, Activity

Attitudes, interests & feelings — EASI, SWLS, RYFF, MASQ, BIS, PWSQ, BFI, ASRS, RRS

Social Life — Relationship Status, DAS, Family Relationship Quality, Friends/Social Support

IN PERSON TESTING: 7 HOURS

Testing mainly done at IBG, or travel to participants

I. Cognitive assessments
◦ WAIS III, Specific Cognitive Ability Battery (short)
◦ Executive functioning

II. Physical assessments, saliva & blood samples
◦ Weight, waist/hip, grip strength, spirometry
◦ Assays: lipid panel, BDNF, DNA extraction
◦ Genotyping: *APOE*, Affymetrix Precision Medicine

III. Brief questionnaire and interview
◦ Activity, sleep, caffeine use
◦ Address history
◦ DIS modules

Current projects: snapshots

FOR MORE, IAGG 2017 SAN FRANCISCO

Geocoding: features related to behavioral health

Last known US address plotted in ArcGIS with points jiggled for de-identification. (AK & HI not shown)

Coding of distances to parks and trails (Boulder exemplars). Parks within ¼ mile are "walkable"
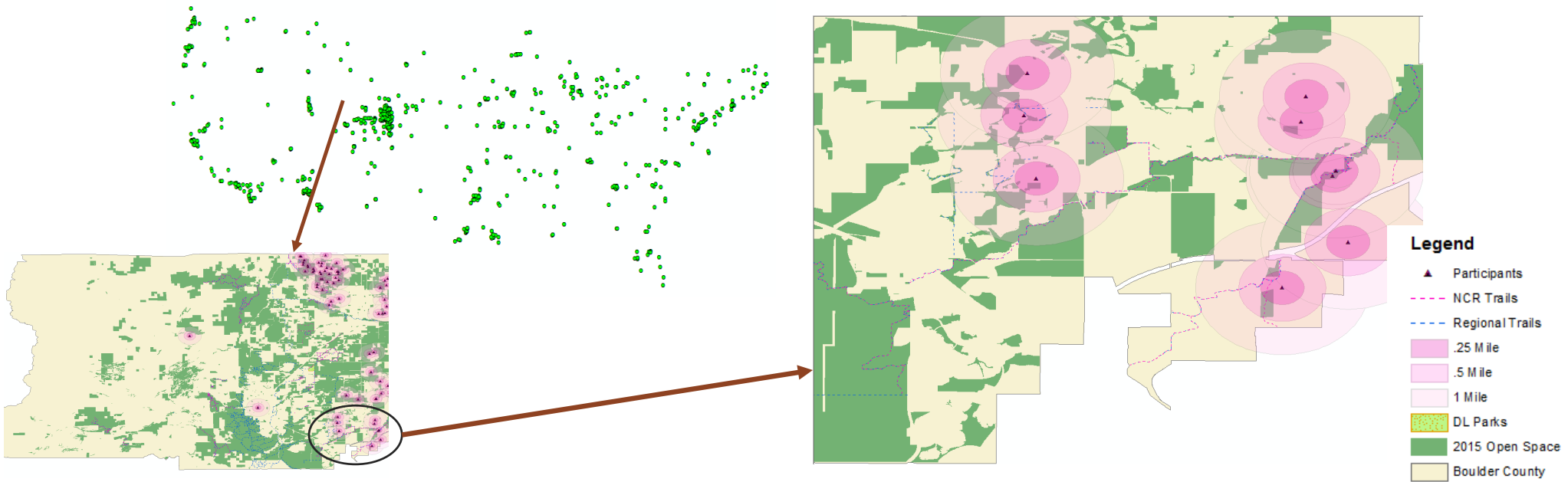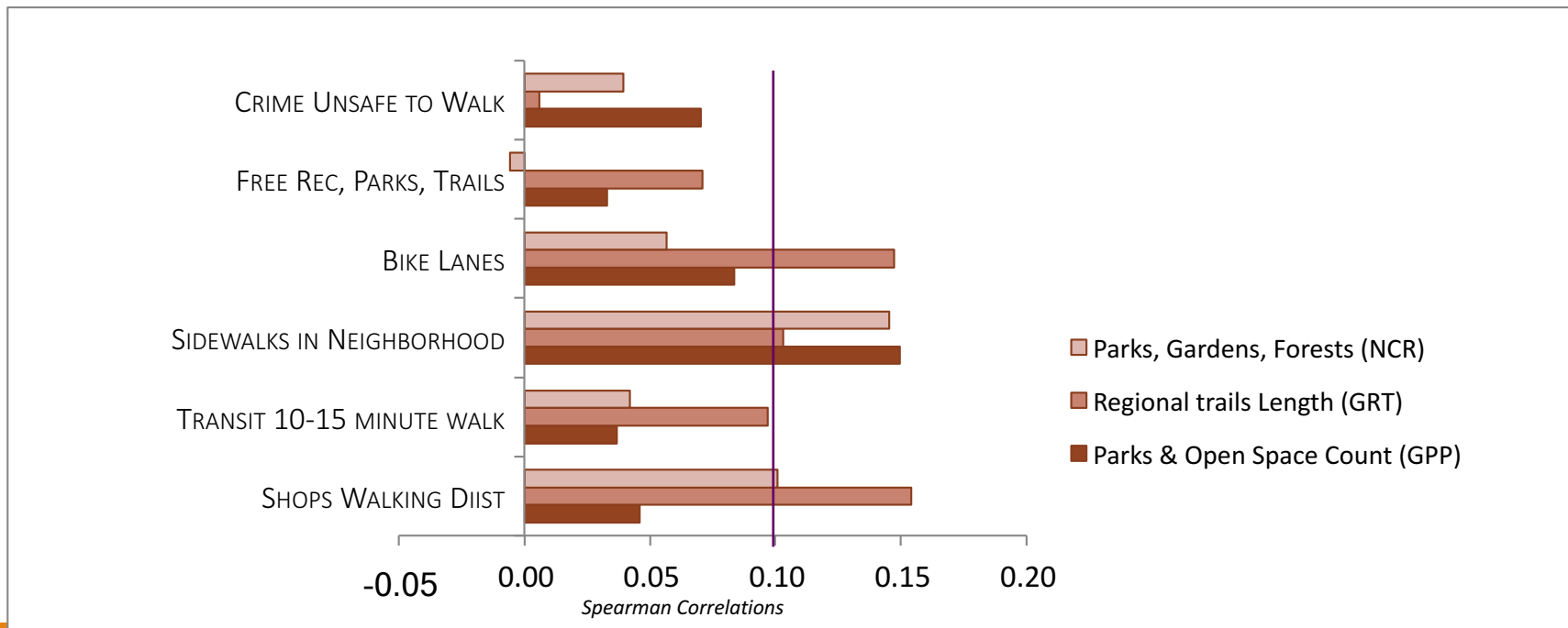

Fig 2a. Parks and trails layers: Boulder Co

Legend

- ▲ Participants
- NCR Trails
- Regional Trails
- .25 Mile
- .5 Mile
- 1 Mile
- DL Parks
- 2015 Open Space
- Boulder County

Perceived Distance/Availability & Parks and Trails within ¼ mile (Colorado only)

PhenX Activity. Think about the different facilities in and around your neighborhood; by this we mean the area ALL around your home that you could walk to in 10-15 minutes. (Strongly Disagree to Strongly Agree)
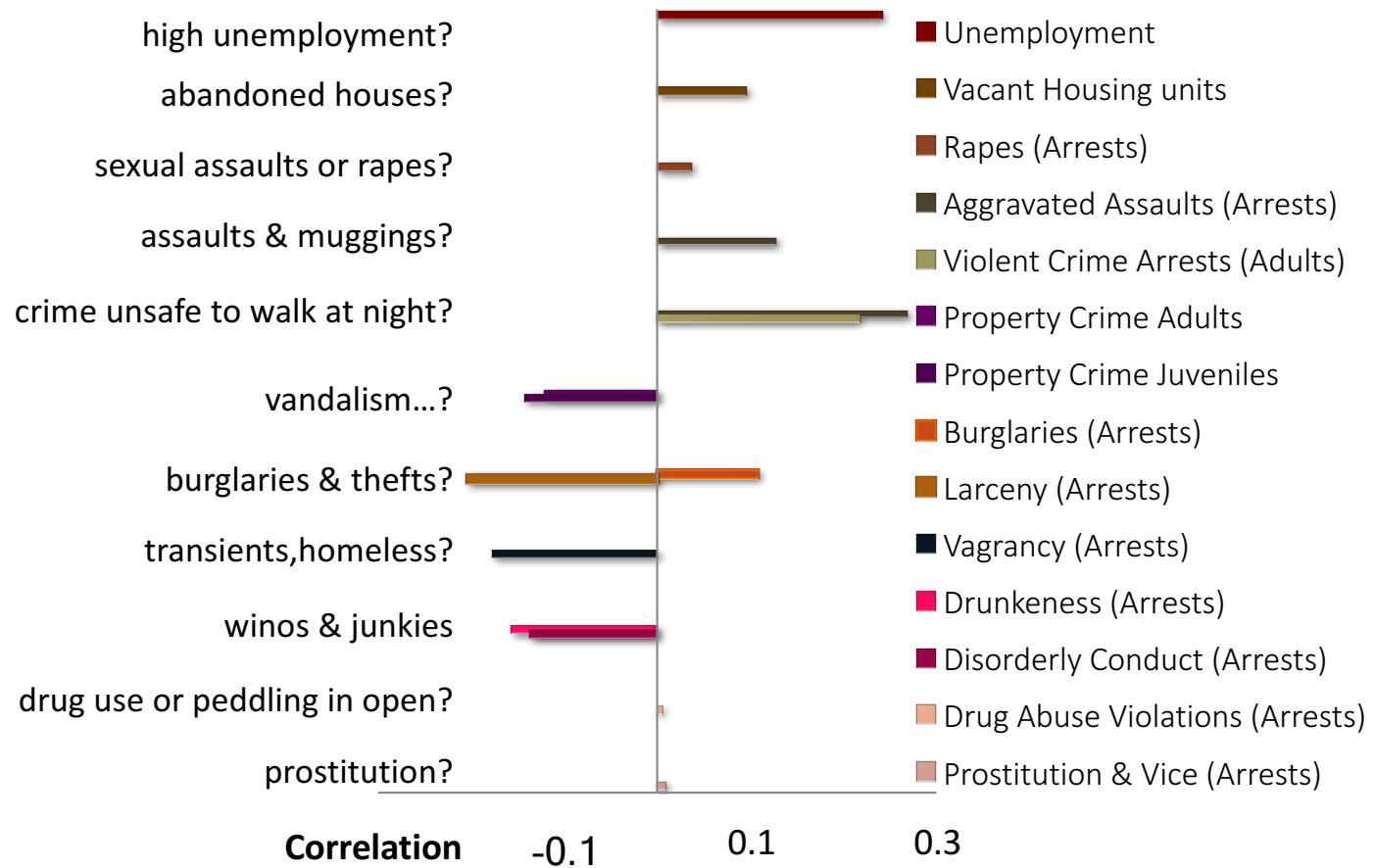

- Parks, Gardens, Forests (NCR)
- Regional trails Length (GRT)
- Parks & Open Space Count (GPP)

Spearman Correlations

Trubenstein, Munoz, Corley, Wadsworth & Reynolds for CATSLife

Self-report neighborhood problems vs geographic data

Social Explorer

Uniform Crime Reporting

Colorado Participants (N=405-415)

How big a problem do you think your neighborhood has with...

- high unemployment?
- abandoned houses?
- sexual assaults or rapes?
- assaults & muggings?
- crime unsafe to walk at night?
- vandalism...?
- burglaries & thefts?
- transients, homeless?
- winos & junkies
- drug use or peddling in open?
- prostitution?

Correlation   -0.1   0.1   0.3

- Unemployment
- Vacant Housing units
- Rapes (Arrests)
- Aggravated Assaults (Arrests)
- Violent Crime Arrests (Adults)
- Property Crime Adults
- Property Crime Juveniles
- Burglaries (Arrests)
- Larceny (Arrests)
- Vagrancy (Arrests)
- Drunkeness (Arrests)
- Disorderly Conduct (Arrests)
- Drug Abuse Violations (Arrests)
- Prostitution & Vice (Arrests)

Trubenstein, Munoz, Corley, Wadsworth & Reynolds for CATSLife

Neighborhood Stress & Cognition

"HOW BIG OF A PROBLEM DO YOU THINK YOUR NEIGHBORHOOD HAS WITH… "
- Unemployment
- Vandalism
- Abandoned houses
- Assaults and muggings
- +17 other problems
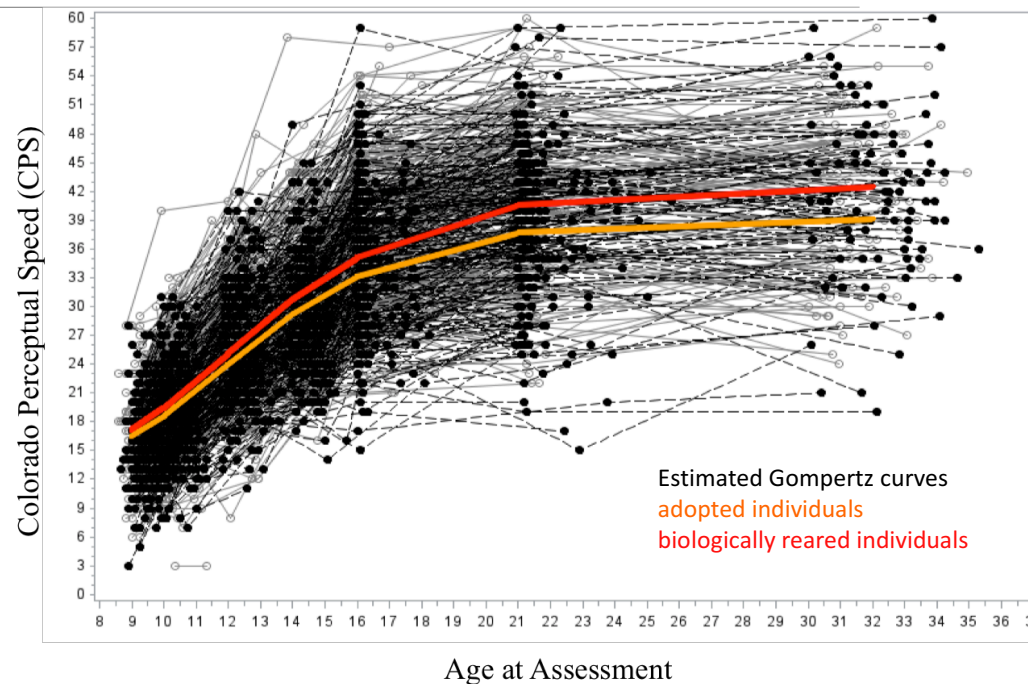
Correlations with CATSLife Cognitive Performance:

Problems	r
Spatial	**-0.11**
Verbal	0.00
Memory	0.01
Speed	**-0.10**
WAIS total	-0.07
WAIS verbal	-0.04
WAIS performance	*-0.07*

NEIGHBORHOOD PROBLEMS PREDICT LOWER SPEED AND SPATIAL SCORES

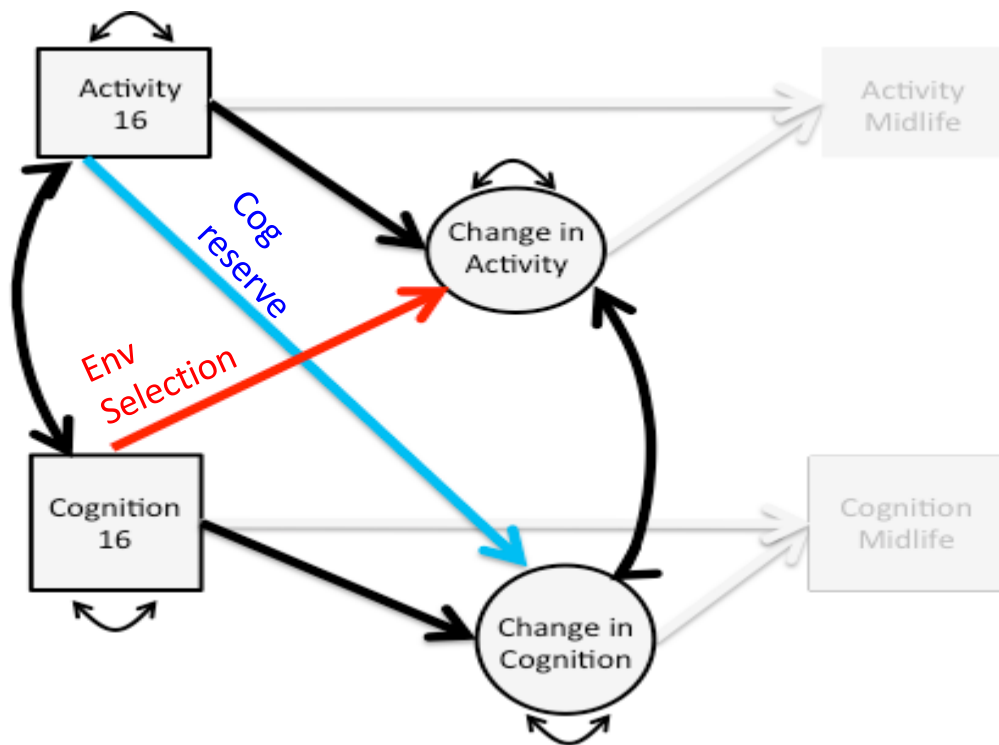Munoz, Corley, Wadsworth & Reynolds
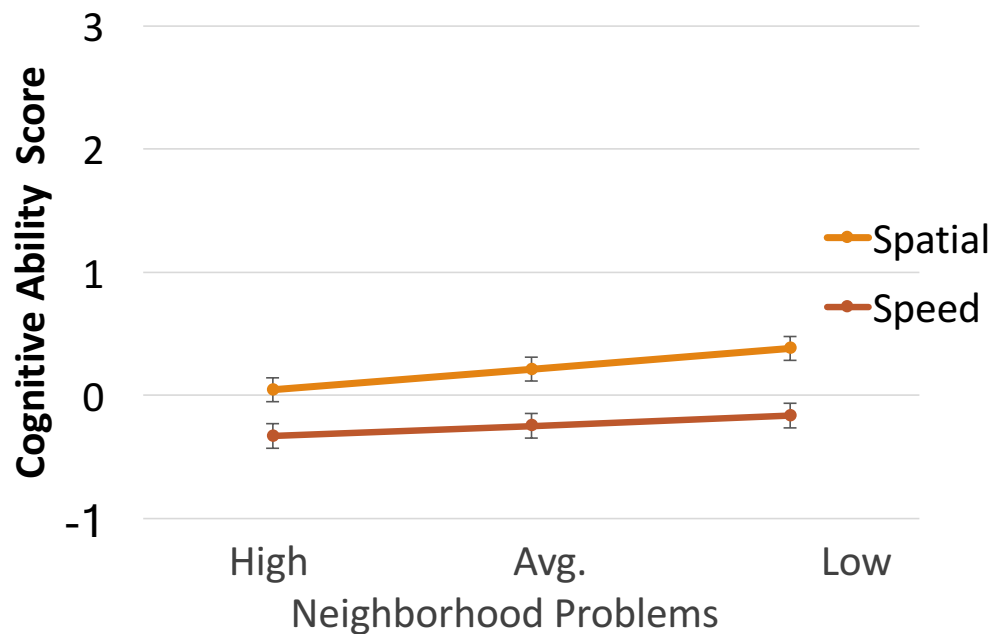
Earlier Life Stress & Memory and Speed trajectories (CAP)

- Perceived Stress during middle childhood (9 to 12 years) and adolescence (ages 13 to 16 years).
  - Brooks-Gunn Life Events Scale

- Stress did not predict differential cognitive gains in either period, adjusting for parental education & occupation, child sex and adoption status.

- Differences in perceptual speed trajectories between non-adopted and adopted individuals were observed.
  - adopted individuals showing smaller gains

Estimated Gompertz curves
adopted individuals
biologically reared individuals

Age at Assessment

$\chi^2 (3) = 25.82, p = 1.04E\text{-}05$

Ricker, Corley, DeFries, Wadsworth & Reynolds, in press

Activity engagement & Episodic Memory change

$\Delta\chi^2 (2) = 7.32$, $p = 0.026$

Trubenstein, Haberstick, Corley, Wadsworth, & Reynolds
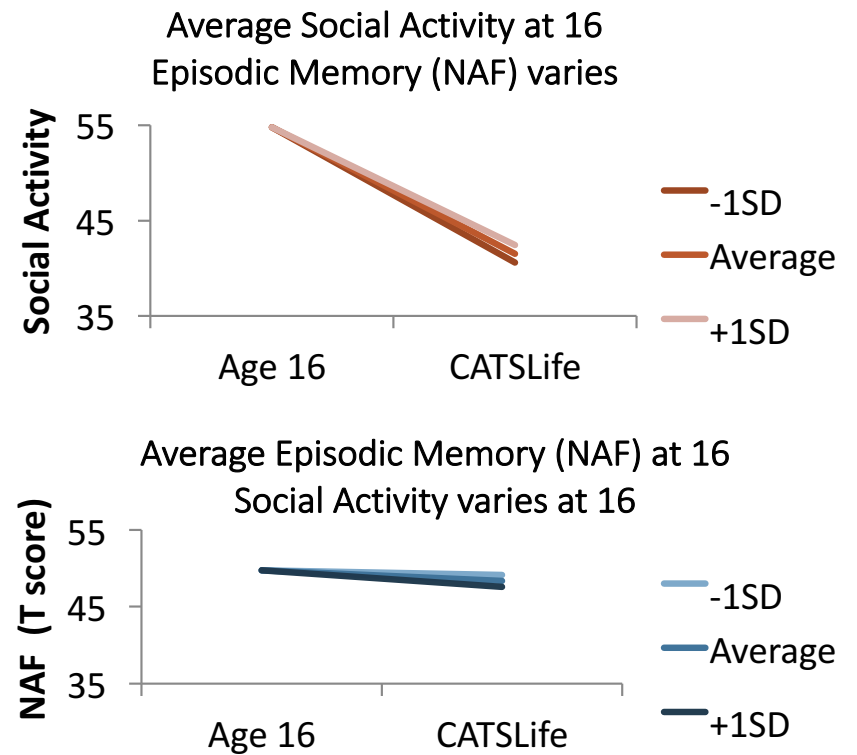
APOE & Episodic Memory Trajectories

CAP			LTS		
APOE	*N*	*freq*	*APOE*	*N*	*freq*
e22	5	1.01	e22	9	1.03
e23	51	10.26	e23	105	12.07
e24	15	3.02	e24	16	1.84
e33	295	59.36	e33	536	61.61
e34	121	24.35	e34	197	22.64
e44	10	2.01	e44	7	0.80
Current N	497			870	
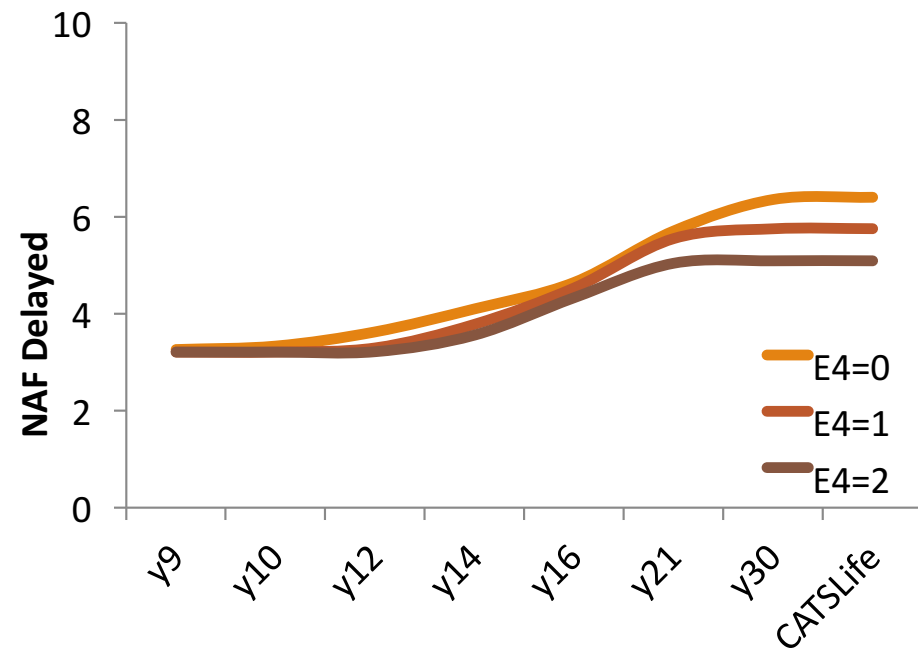
Gompertz model shown. *APOE* E4 effects: $\chi^2(3) = 21.13$, p = 0.0001. For each E4 allele, a lower asymptote (p=.02) and faster rate of change to the asymptote (p=.000). Adjusted for *APOE* E2, sex, study (CAP/LTS), practice and mode of administration.

Reynolds, Smolen, Haberstick, DeFries, & Wadsworth

Current & Future Directions

- Geocoding across all 50 states
  - e.g., Distance to parks & trails, open space, hospitals, schools, etc.

- Polygenic risk scores
  - Awaiting first results of Precision Medicine Affymetrix chip
  - Informed by TEDS work, e.g., whether genetic risks for traits relevant to older-aged populations are related to individual differences in cognitive phenotypes across development (Selzam, Plomin et al).

- Health-cognition associations
  - BMI-cognition dynamics
  - Biomarker associations with cognitive and health phenotypes (e.g., lipids, BDNF, BMI).

Acknowledgements

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[MPIs, Chandra A. Reynolds (Contact), Sally J. Wadsworth]

The content of this presentation is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.
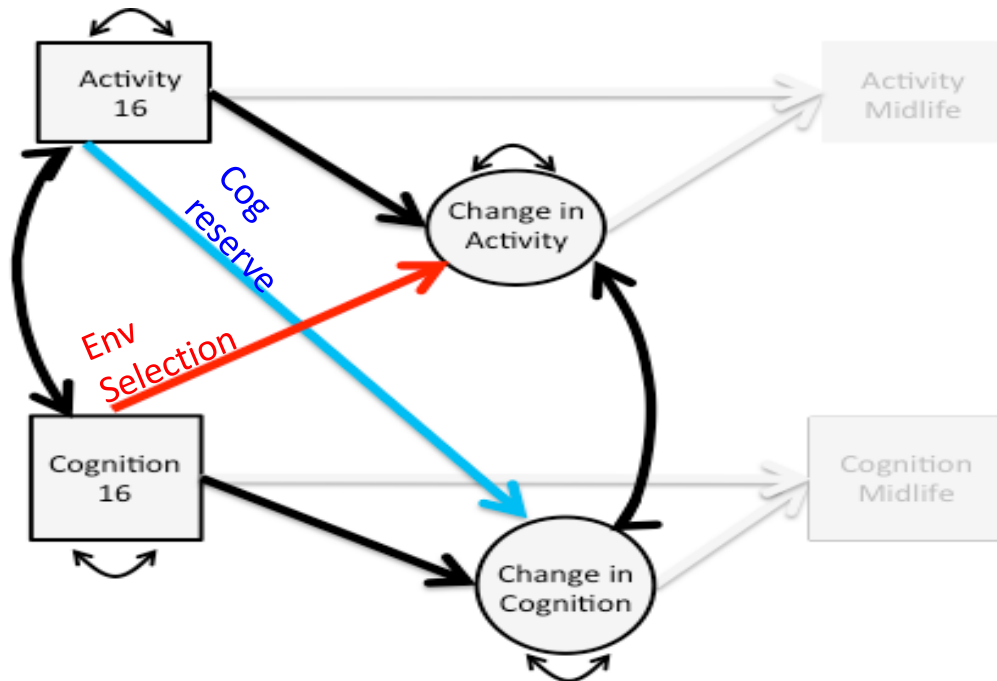
CATSLife Team

<u>Pictured above</u>. From left to right: Amy Ledbetter, Brett Haberstick, John DeFries, Liz Muñoz Diaz, Paige Trubenstein, Corinne Gunn, Chandra Reynolds, John Hewitt, Sally Wadsworth, Mike Stallings, Naomi Friedman, Robin Corley, Soo Rhee, Andy Smolen
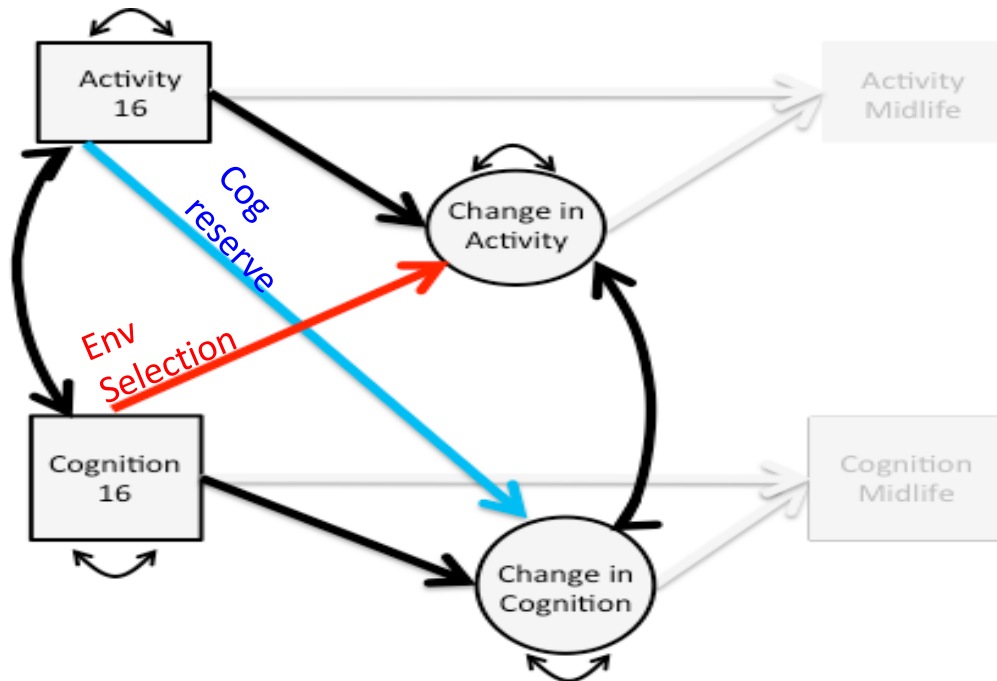<u>Pictured below</u>. From left to right: Saskia Selzam, Robert Plomin

http://www.colorado.edu/ibg/human-research-studies/catslife

Activity engagement & Episodic Memory change

How many hours per week do you spend……
- sitting around with friends?
- taking part in an organized sport or recreation program?
- reading for fun?
- talking on the telephone?
- working out as part of a personal exercise program?
- just sitting around listening to music?
- playing pickup games like basketball, touch football…?
- doing thing with your family?
- just sitting around doing nothing?
- practicing different physical activities?
- taking care of younger family members?
- doing household chores?
- doing things with a club?
- spending time on a hobby?
- going out with friends or dating?
- watching television?

Trubenstein, Haberstick, Corley, Wadsworth, & Reynolds
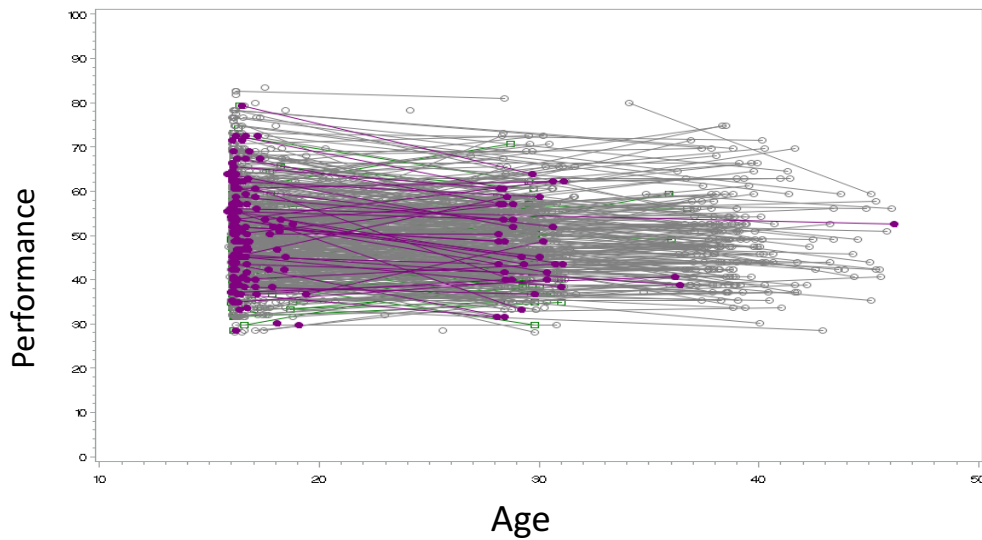
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Trubenstein, Haberstick, Corley, Wadsworth, & Reynolds

Individual Differences in Names and Faces Performance by Social Activity

FULL SAMPLE

HIGH (+1*SD*) VS LOW (-1*SD*) SOCIAL ACTIVITY

Names and Faces Change

Names and Faces

Performance

Age

Performance

Age

Trubenstein, Haberstick, Corley, Wadsworth, & Reynolds