



Integrative Analysis of Longitudinal Studies on Aging

Coordinated Analysis of Cross-Sectional and Longitudinal Associations between Physical, Cognitive, and Social Activity and Cognitive Functioning in Later Life

Scott M. Hofer

Piccinin, A.M., Kennison, R., Lindwall, M., Mitchell, M., Cimino, C., Benitez, A., Brown, C.L., Gibbons, L., MacDonald, S.W.S., Robitaille, A., Shirk, S., Atri, A., Zelinski, E., Willis, S., Schaie, K.W., Johansson, B., Dixon, R., Mungas, D.

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Authors claim **“Most Published Research Findings are False”**

Ioannidis (2005); Young, Ioannidis, Al-Ubaydli (2008), www.PloSmedicine.org

- Dramatic or important results are more likely to be false
 - Less dramatic results unpublished or in less prestigious journals
- Why?
 - Competition for “original” contributions: Highly selected studies are overvalued and unrepresentative of true outcomes
 - Bias towards publishing positive results
 - Artificial scarcity; Best journals publish best (i.e., most dramatic) research; excuse for rejection
- Solution: Provide basis for evaluating replicability
 - Publish all research that meets quality threshold

Need for Replication

(e.g., Hendrick, 1990; Park, 2004; Rosenbaum, 2001)

- Essential for a cumulative and innovative science
 - “The fact that a theory has passed one test provides no evidence at all that it will pass a repetition of a test”
(Miller, 1980)
 - “The results in a single study are important primarily as one contribution to a mosaic of study effects” (APA Task Force on Statistical Inference, 1999)
 - “Successful replication provides the basis for further and deeper explanatory studies and theory” (Lindsay & Ehrenberg, 1993)

Replication in Longitudinal Research

- Replication of research based on observational longitudinal data necessary to protect against uncritical acceptance of empirical results.
 - Results from complex data structures and statistical models
 - Extant scientific evidence used to structure, justify and extend research.
- Research findings and conclusions often vary across independent studies addressing the same topic.
 - No one study can control for all extraneous influences
 - Due to unique study characteristics (e.g., sampling, measures, design)
 - Noncomparable results based on different statistical analyses/models
- Between-study variability points to the need for skepticism regarding a single instance of a result and to the importance of multiple replications in the evaluation of scientific findings.

An Evaluation of Analytical Approaches for Understanding Change in Cognition in the Context of Aging and Health

Andrea M. Piccinin,¹ Graciela Muniz,² Catharine Sparks,¹ and Daniel E. Bontempo³

¹Department of Psychology, University of Victoria, Canada.

²MRC Biostatistics Unit, Cambridge, UK.

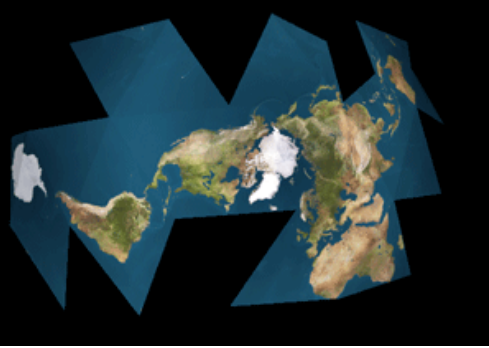
³Schiefelbusch Lifespan Institute, University of Kansas, Lawrence.

Objectives. In this article, we discuss the importance of studying the relationship between health and cognitive function, and some of the methods with which this relationship has been studied.

Methods. We consider the challenges involved, in particular operationalization of the health construct and causal inference in the context of observational data. We contrast the approaches taken, and review the questions addressed: whether health and cognition are associated, whether changes in health are associated with changes in cognition, and the degree of interdependency among their respective trajectories.

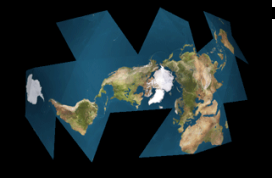
Results. A variety of approaches for understanding the association between cognition and health in aging individuals have been used. Much of the literature on cognitive change and health has relied on methods that are based at least in part on the reorganization of between-person differences (e.g., cross-lag analysis) rather than relying more fully on analysis of within-person change and joint analysis of individual differences in within-person change in cognition and health.

Discussion. We make the case for focusing on the interdependency between within-person changes in health and cognition and suggest methods that would support this.



IALSA: Integrative Analysis of Longitudinal Studies on Aging

- The IALSA network is currently comprised of over 35 longitudinal studies on aging, spanning eight countries.
 - Mix of population representative, volunteer, and special population samples, aged from birth to 100 years (focus 50+), with birth cohorts ranging from 1880 to 1980, assessed during historical periods from 1946 to the present. Between-occasion intervals range from 6 months to 17 years (the majority 1-5 years), with up to 32 (typically 3-5) measurement occasions spanning 4 to 48 years of within-person assessment.
- Primary goal: To facilitate new longitudinal research in ways that permit direct comparison of findings and cumulative knowledge from a within-person perspective
 - Direct involvement of PIs and research teams



IALSA Approach

Harmonization

- Goal: Obtain comparable answers to key questions
- Levels of Harmonization
 - Research Questions
 - Statistical Models
 - Measurements
- Harmonization permits synthesis of results
 - Account of how other variables/processes, country and other sampling differences, initial representativeness, attrition, historical period, age range sampled, etc. relate to differences across studies.

Integrative Data Analysis Through Coordination of Measurement and Analysis Protocol Across Independent Longitudinal Studies

Scott M. Hofer and Andrea M. Piccinin
Oregon State University

Replication of research findings across independent longitudinal studies is essential for a cumulative and innovative developmental science. Meta-analysis of longitudinal studies is often limited by the amount of published information on particular research questions, the complexity of longitudinal designs and the sophistication of analyses, and practical limits on full reporting of results. In many cases, cross-study differences in sample composition and measurements impede or lessen the utility of pooled data analysis. A collaborative, coordinated analysis approach can provide a broad foundation for cumulating scientific knowledge by facilitating efficient analysis of multiple studies in ways that maximize comparability of results and permit evaluation of study differences. The goal of such an approach is to maximize opportunities for replication and extension of findings across longitudinal studies through open access to analysis scripts and output for published results, permitting modification, evaluation, and extension of alternative statistical models and application to additional data sets. Drawing on the cognitive aging literature as an example, the authors articulate some of the challenges of meta-analytic and pooled-data approaches and introduce a coordinated analysis approach as an important avenue for maximizing the comparability, replication, and extension of results from longitudinal studies.

Keywords: longitudinal, integrative data analysis, meta-analysis, data pooling, longitudinal studies



Coordinated Analysis

- Interactive development of research protocol
 - Aim: Maximize data value from each study while making results as comparable as possible
- Evaluation of alternative models
- Complete reporting of results permits direct comparison across studies and variations in models
 - Analysis scripts and extended results available on IALSA site
 - Direct and interactive evaluation of complex hypotheses across longitudinal studies on aging
 - Emphasis on cross-culture, cross-study comparisons
- Communication: Publication models
 - Joint authorship of single paper
 - Series of independent reports, submitted together or independently
 - Possible introduction and consensus paper
 - e.g., analysis of two studies using common statistical approach



- Developing and established researchers
 - Methods & practice
 - Collaborative research & manuscript production
- 2010 -
- Four IALSA-affiliated studies with PIs
 - Coordinated analysis with focus on associations between activities (cognitive, physical, social) and change in cognitive abilities

Longitudinal Studies & PIs

- Origins of Variance in the Oldest-Old (OCTO-Twin)
 - Boo Johansson, Magnus Lindwall
- Long Beach Longitudinal Study
 - Elizabeth Zelinski, Robert Kennison
- Seattle Longitudinal Study
 - K. Warner Schaie, Sherry Willis
- Victoria Longitudinal Study
 - Roger Dixon, Stuart MacDonald

Questions

1. Is baseline cognitive *performance* associated with cognitive, physical, or social activity?
2. Are baseline cognitive, physical, or social activity associated with subsequent cognitive *changes*?
3. Are cognitive *changes* associated with *changes* in cognitive, physical, or social activity?

Study Characteristics

Study	"Baseline" # Waves	Intervals (years)	Span (years)	Mean Age	Education (years)	% Female	
OCTO-Twin	1991	5	2	8	83	7.2	65
LBLS	1994*	4	3	9	74	13.7	51
SLS	1984*	4	7	21	67	14.6	52
VLS	1986	7	3	18	69	14.9	64

* To maximize similarity of measures

Retention in Follow-up Waves

	2	3	4	5	6	7
OCTO-Twin	82	77	76	71	—	—
LBLS	52	49	70	—	—	—
SLS	56	48	41	—	—	—
VLS	73	79	72	69	72	57

Cognitive Performance Measures

	Reasoning	Fluency	Memory	Semantic knowledge
Octo-Twin	WAIS Block design	--	Prose recall	WAIS information task
LBSL	STAMAT Letter and Word Series	Word fluency for letter "s"	Immediate recall of 20 words studied for 3.5 min.	Recognition Vocabulary of 50 items
SLS	STAMAT Word Series	Word fluency for letter "s"	Immediate recall of 20 words studied for 3.5 min.	ETS Advanced Vocabulary of 36 items in 4 min.
VLS	Letter Series	Similar meaning as target words for 6 min.	Immediate recall of 30 words in 5 semantic categories	ETS Recognition Vocabulary of 54 items

Activity Measures

Study	Cognitive	Physical	Social
OCTO-Twin	Games, crosswords, reading, writing, research, other, and "train memory/keep mind active"	Present/previous effort to train body/keep fit	"How many people do you see?"
LBLS	Educational, reading, music, writing, games, cultural	Walking, outdoor hobbies, fitness, sports	Volunteering, cards, phone, visiting, dancing, partying
SLS	(same)	(same)	(same)
VLS	Communication (e.g., writing), Computation (e.g., balancing checkbook) & Conundrum (e.g., cross-words) factors	Gardening, jogging, tennis, sailing	restaurants, visit, give dinner party, attend church, club /service organization meetings

Analytic Approach

- Mixed effects models
 - Time varying covariates
 - Does change in activity predict change in cognition?
 - Covariates in level 1 of regression equation
 - Estimator: Restricted maximum likelihood (REML)
 - Random intercepts and slopes
 - Unrestricted covariance matrix
- Models fit to each of the four cognitive measures and each of the studies

Statistical Model

- Model Covariates:
 - Linear Time (mean centered)
 - Baseline Age (mean centered)
 - Years of education (mean centered)
 - Sex (coded: 0 = male; 1 = female)
 - Baseline Activity
 - Activity change (time-varying covariate)
 - Two-way interactions
- Final models included 12 terms
 - Original models included 19 terms
 - Non-significant terms obtained across the set of models were eliminated

Cognitively Stimulating Activities: Effects on Cognition across Four Studies with up to 21 Years of Longitudinal Data

Meghan B. Mitchell,¹ Cynthia R. Cimino,² Andreana Benitez,³
 Cassandra L. Brown,⁴ Laura E. Gibbons,⁵ Robert F. Kennison,⁶ Steven D. Shirk,¹
 Alireza Atri,¹ Annie Robitaille,⁴ Stuart W. S. MacDonald,⁴ Magnus Lindwall,^{7,8}
 Elizabeth M. Zelinski,⁹ Sherry L. Willis,¹⁰ K. Warner Schaie,⁵
 Boo Johansson,⁸ Roger A. Dixon,¹¹ Dan M. Mungas,¹²
 Scott M. Hofer,⁴ and Andrea M. Piccinin⁴

¹Edith Nourse Rogers Memorial Veterans Hospital, Geriatric Research, Education and Clinical Center, Massachusetts General Hospital, Harvard Medical School, 200 Springs Road, Bedford, MA 01730, USA

²Departments of Psychology and Department of Neurology, University of South Florida, 4202 E. Fowler Avenue, Tampa, FL 33620, USA

³Center for Biomedical Imaging, Medical University of South Carolina, 68 President Street, MSC 120, Charleston, SC 29425, USA

⁴Department of Psychology, University of Victoria, P.O. Box 3050 STN CSC, Victoria, BC, Canada V8W 3P5

⁵Division of General Internal Medicine, University of Washington, P.O. Box 359780, Harborview Medical Center, 325 Ninth Avenue Seattle, WA 98104, USA

⁶Department of Psychology, California State University-Los Angeles 5151 State University Drive, Los Angeles, CA 90032, USA

⁷Department of Food and Nutrition, and Sport Science, Department of Psychology, University of Gothenburg, P.O. Box 100, SE-405 30 Gothenburg, Sweden

⁸Department of Psychology, University of Gothenburg, Box 500, SE 405 30, Gothenburg, Sweden

⁹Ethel Percy Andrus Gerontology Center, Leonard Davis School of Gerontology, University of Southern California, Los Angeles, CA 90089-0191, USA

¹⁰University of Washington, 180 Nickerson, Suite 206, Seattle, WA 98109, USA

¹¹Department of Psychology, University of Alberta, P217 Biological Sciences Building, Edmonton, AB, Canada T6G 2E9

¹²Lawrence J. Ellison Ambulatory Care Center, University of California, Davis, 4860 Y Street, Ste 0100, Sacramento, CA 95817, USA

Correspondence should be addressed to Meghan B. Mitchell, mbmitchell@partners.org

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Engagement in cognitively stimulating activities has been considered to maintain or strengthen cognitive skills, thereby minimizing age-related cognitive decline. While the idea that there may be a modifiable behavior that could lower risk for cognitive decline is appealing and potentially empowering for older adults, research findings have not consistently supported the beneficial effects of engaging in cognitively stimulating tasks. Using observational studies of naturalistic cognitive activities, we report a series of mixed effects models that include baseline and change in cognitive activity predicting cognitive outcomes over up to 21 years in four longitudinal studies of aging. Consistent evidence was found for cross-sectional relationships between level of cognitive activity and cognitive test performance. Baseline activity at an earlier age did not, however, predict rate of decline later in life, thus not supporting the concept that engaging in cognitive activity at an earlier point in time increases one's ability to mitigate future age-related cognitive decline. In contrast, change in activity was associated with relative change in cognitive performance. Results therefore suggest that change in cognitive activity from one's previous level has at least a transitory association with cognitive performance measured at the same point in time.

Results – Cognitive Activity

Cognitive Outcome	OCTO	LBLS	SLS	VLS
Reasoning				
CogAct-> Cognitive	Y	N	Y	Y
CogAct-> Cog Change	N	N	N	N/Y*
CogAct Change -> Cog Change	Y	N	Y	Y
Memory				
CogAct-> Cognitive	Y	N	N	Y
CogAct-> Cog Change	N	N	N	N
CogAct Change -> Cog Change	Y	Y	Y	Y/N~
Fluency				
CogAct-> Cognitive	—	Y	Y	Y
CogAct-> Cog Change	—	N	N	N
CogAct Change -> Cog Change	—	N	Y	Y
Semantic Knowledge				
CogAct-> Cognitive	Y	N	Y	Y
CogAct-> Cog Change	N	N	N	N
CogAct Change -> Cog Change	Y	Y	Y	Y

* Computation

~ Conundrums

Summary Cognitive Activity: Baseline Activity

- Baseline *activity level* predicted baseline cognitive performance in all studies except LBLS reasoning and memory
 - Higher levels of cognitive activity associated with better cognitive performance
- Baseline activity did not predict change in cognitive performance, with one exception:
 - VLS computation reasoning

Summary Cognitive Activity: Activity Change

- Change in *activity level* predicted change in cognitive performance, except:
 - LBLS reasoning and fluency; VLS conundrums reasoning and memory
- Steeper declines in activity level were associated with steeper declines in cognitive performance

Dynamic Associations of Change in Physical Activity and Change in Cognitive Function: Coordinated Analyses of Four Longitudinal Studies

Magnus Lindwall,¹ Cynthia R. Cimino,² Laura E. Gibbons,³ Meghan B. Mitchell,⁴ Andreana Benitez,⁵ Cassandra L. Brown,⁶ Robert F. Kennison,⁷ Steven D. Shirk,⁴ Alireza Atri,⁴ Annie Robitaille,⁶ Stuart W. S. MacDonald,⁶ Elizabeth M. Zelinski,⁸ Sherry L. Willis,⁹ K. Warner Schaie,⁹ Boo Johansson,¹⁰ Marcus Praetorius,¹⁰ Roger A. Dixon,¹¹ Dan M. Mungas,¹² Scott M. Hofer,⁶ and Andrea M. Piccinin⁶

¹Department of Food and Nutrition, and Sport Science and Department of Psychology, University of Gothenburg, P.O. Box 300, 405 30 Gothenburg, Sweden

²Department of Psychology and Neurology, University of South Florida, 4202 East Fowler Avenue, Tampa, FL 33620, USA

³General Internal Medicine, Harborview Medical Center, University of Washington, 325 Ninth Avenue, P.O. Box 359780, Seattle, WA 98104, USA

⁴Massachusetts General Hospital, Harvard Medical School, ENRM Bedford VA Hospital, 200 Springs Road, Bedford, MA 01730, USA

⁵Center for Biomedical Imaging, Medical University of South Carolina, 68 President Sreet, MSC 120, Charleston, SC 29425, USA

⁶Department of Psychology, University of Victoria, P.O. Box 3050 STN CSC, Victoria, BC, Canada V8W 3P5

⁷Department of Psychology, California State University, Los Angeles, 5151 State University Drive, Los Angeles, CA 90032, USA

⁸Andrus Gerontology Center, Leonard Davis School of Gerontology, University of Southern California, Los Angeles, CA 90089, USA

⁹Department of Psychiatry and Behavioral Sciences, University of Washington, 180 Nickerson, Suite 206, Seattle, WA 98109, USA

¹⁰Department of Psychology, University of Gothenburg, P.O. Box 100, 405 30 Gothenburg, Sweden

¹¹Department of Psychology, University of Alberta, Edmonton, AB, Canada T6G 2E9

¹²Davis Lawrence J. Ellison Ambulatory Care Center, University of California, 4860 Y Street, Ste 0100, Sacramento, CA 95817, USA

Correspondence should be addressed to Magnus Lindwall, magnus.lindwall@psy.gu.se and Andrea M. Piccinin, piccinin@uvic.ca

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The present study used a coordinated analyses approach to examine the association of physical activity and cognitive change in four longitudinal studies. A series of multilevel growth models with physical activity included both as a fixed (between-person) and time-varying (within-person) predictor of four domains of cognitive function (reasoning, memory, fluency, and semantic knowledge) was used. Baseline physical activity predicted fluency, reasoning and memory in two studies. However, there was a consistent pattern of positive relationships between time-specific changes in physical activity and time-specific changes in cognition, controlling for expected linear trajectories over time, across all four studies. This pattern was most evident for the domains of reasoning and fluency.

Results – Physical Activity

<u>Cognitive Outcome</u>	<u>OCTO</u>	<u>LBLS</u>	<u>SLS</u>	<u>VLS</u>
Reasoning				
PhysAct-> Cognitive	Y	N	N	N
PhysAct-> Cog Change	N	N	N	N
PhysAct Change -> Cog Change	Y	Y	Y	Y
Memory				
PhysAct-> Cognitive	Y	N	N	Y
PhysAct-> Cog Change	N	N	N	N
PhysAct Change -> Cog Change	Y	N	N	Y
Fluency				
PhysAct-> Cognitive	—	N	Y	N
PhysAct-> Cog Change	—	N	Y	Y
PhysAct Change -> Cog Change	—	N	Y	Y
Semantic Knowledge				
PhysAct-> Cognitive	N	N	N	N
PhysAct-> Cog Change	N	N	N	N
PhysAct Change -> Cog Change	Y	N	N	N

Summary Physical Activity: Baseline Activity

- Higher physical activity at baseline associated with higher scores on reasoning in OCTO-Twin, memory in OCTO-Twin and VLS and fluency in SLS.
- For semantic knowledge in LBLS and SLS, the association with physical activity at baseline was stronger for people with less education
- Baseline activity did not predict change in cognitive performance, with two exceptions:
 - Fluency in VLS and SLS

Summary Physical Activity: Activity Change

- Change in *activity level* predicted change in cognitive performance in:
 - (a) reasoning in all four studies;
 - (b) fluency in two (VLS and SLS) of three studies;
 - (c) memory in two studies (OCTO-Twin and VLS);
 - (d) semantic knowledge in one study (OCTO-Twin).
- Steeper declines in activity level were associated with steeper declines in cognitive performance

Social Activity and Cognitive Functioning Over Time: A Coordinated Analysis of Four Longitudinal Studies

Cassandra L. Brown,¹ Laura E. Gibbons,² Robert F. Kennison,³ Annie Robitaille,¹ Magnus Lindwall,^{4,5} Meghan B. Mitchell,⁶ Steven D. Shirk,⁶ Alireza Atri,⁶ Cynthia R. Cimino,⁷ Andreana Benitez,⁸ Stuart W. S. MacDonald,¹ Elizabeth M. Zelinski,⁹ Sherry L. Willis,¹⁰ K. Warner Schaie,¹⁰ Boo Johansson,⁵ Roger A. Dixon,¹¹ Dan M. Mungas,¹² Scott M. Hofer,¹ and Andrea M. Piccinin¹

¹ Department of Psychology, University of Victoria, P.O. Box 3050 STN CSC, Victoria, BC, Canada V8W 3P5

² Harborview Medical Center and General Internal Medicine, University of Washington, Box 359780, 325 Ninth Avenue, Seattle, WA 98104, USA

³ Department of Psychology, California State University, Los Angeles, 5151 State University Drive, Los Angeles, CA 90032, USA

⁴ Department of Food and Nutrition, and Sport Science and Department of Psychology, University of Gothenburg, P.O. Box 100, SE 405 30 Gothenburg, Sweden

⁵ Department of Psychology, University of Gothenburg, P.O. Box 500, SE 405 30 Gothenburg, Sweden

⁶ Bedford Veterans Affairs Medical Center, Massachusetts General Hospital, Harvard Medical School, 200 Springs Rd, Bedford, MA 01730, USA

⁷ Department of Psychology and Neurology, University of South Florida, 4202 E. Fowler Avenue, Tampa, FL 33620, USA

⁸ Center for Biomedical Imaging, Medical University of South Carolina, 68 President St, MSC 120, Charleston, SC 29425, USA

⁹ Andrus Gerontology Center and Leonard Davis School of Gerontology, University of Southern California, Los Angeles, CA 90089-0191, USA

¹⁰ Department of Psychiatry and Behavioral Sciences, University of Washington, 180 Nickerson, Suite 206, Seattle, WA 98109, USA

¹¹ Department of Psychology, University of Alberta, P-217 Biological Sciences Building, Edmonton, AB, Canada T6G 2E9

¹² Davis Lawrence J. Ellison Ambulatory Care Center, University of California, 4860 Y Street, Ste 0100, Sacramento, CA 95817, USA

Correspondence should be addressed to Cassandra L. Brown, clb@uvic.ca and Andrea M. Piccinin, piccinin@uvic.ca

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Social activity is typically viewed as part of an engaged lifestyle that may help mitigate the deleterious effects of advanced age on cognitive function. As such, social activity has been examined in relation to cognitive abilities later in life. However, longitudinal evidence for this hypothesis thus far remains inconclusive. The current study sought to clarify the relationship between social activity and cognitive function over time using a coordinated data analysis approach across four longitudinal studies. A series of multilevel growth models with social activity included as a covariate is presented. Four domains of cognitive function were assessed: reasoning, memory, fluency, and semantic knowledge. Results suggest that baseline social activity is related to some, but not all, cognitive functions. Baseline social activity levels failed to predict rate of decline in most cognitive abilities. Changes in social activity were not consistently associated with cognitive functioning. Our findings do not provide consistent evidence that changes in social activity correspond to immediate benefits in cognitive functioning, except perhaps for verbal fluency.

Results – Social Activity

Cognitive Outcome	OCTO	LBLS	SLS	VLS
Reasoning				
SocAct-> Cognitive	Y	N	N	Y
SocAct-> Cog Change	N	N	Y	N
SocAct Change -> Cog Change	Y	N	Y	Y
Memory				
SocAct-> Cognitive	Y	N	Y	Y
SocAct-> Cog Change	N	N	N	N
SocAct Change -> Cog Change	Y	N	Y	Y
Fluency				
SocAct-> Cognitive	—	Y	N	N
SocAct-> Cog Change	—	N	N	N
SocAct Change -> Cog Change	—	Y	N	Y
Semantic Knowledge				
SocAct-> Cognitive	Y	N	Y	N
SocAct-> Cog Change	N	N	Y	N
SocAct Change -> Cog Change	Y	N	N	N

Conclusions / Implications

- Between-person differences in baseline activity not “protective” against subsequent decline
- Within-person changes more important than between person differences
 - Whether activity level *changed* was more important than how active someone was relative to others

Issues: Causal Inference

- Direction of influence?
 - Activity → Cognition:
 - Isolation, lack of stimulation/challenge; fitness
 - Cognition → Activity:
 - Inability to exercise due to health issues that also affect cognition
 - Withdrawal from activity due to memory loss
- Causation?
 - Experimental v Observational

Can We Improve Our Physical Health by Altering Our Social Networks?

Sheldon Cohen and Denise Janicki-Deverts

Carnegie Mellon University

- Experimental/interventions studies are needed
 - Randomly assign people to “improved” network versus ... current network conditions.
 - Sufficient to capture long-term nature of causal effect?

IALSA Approach

- Evaluate evidence and refine theory from within-person change perspective
 - Integrate health, psychosocial and demographic factors in models of aging-related changes in cognitive and functional outcomes, personality, and emotional well-being.
- Evaluate result sensitivity to measurement and analysis/modeling decisions
 - Evaluate and report alternative models on same data
- Accumulate knowledge from replicated evidence
 - Open, direct and immediate comparison and contrast of results across independent studies
 - Availability of analysis protocol, scripts, and results

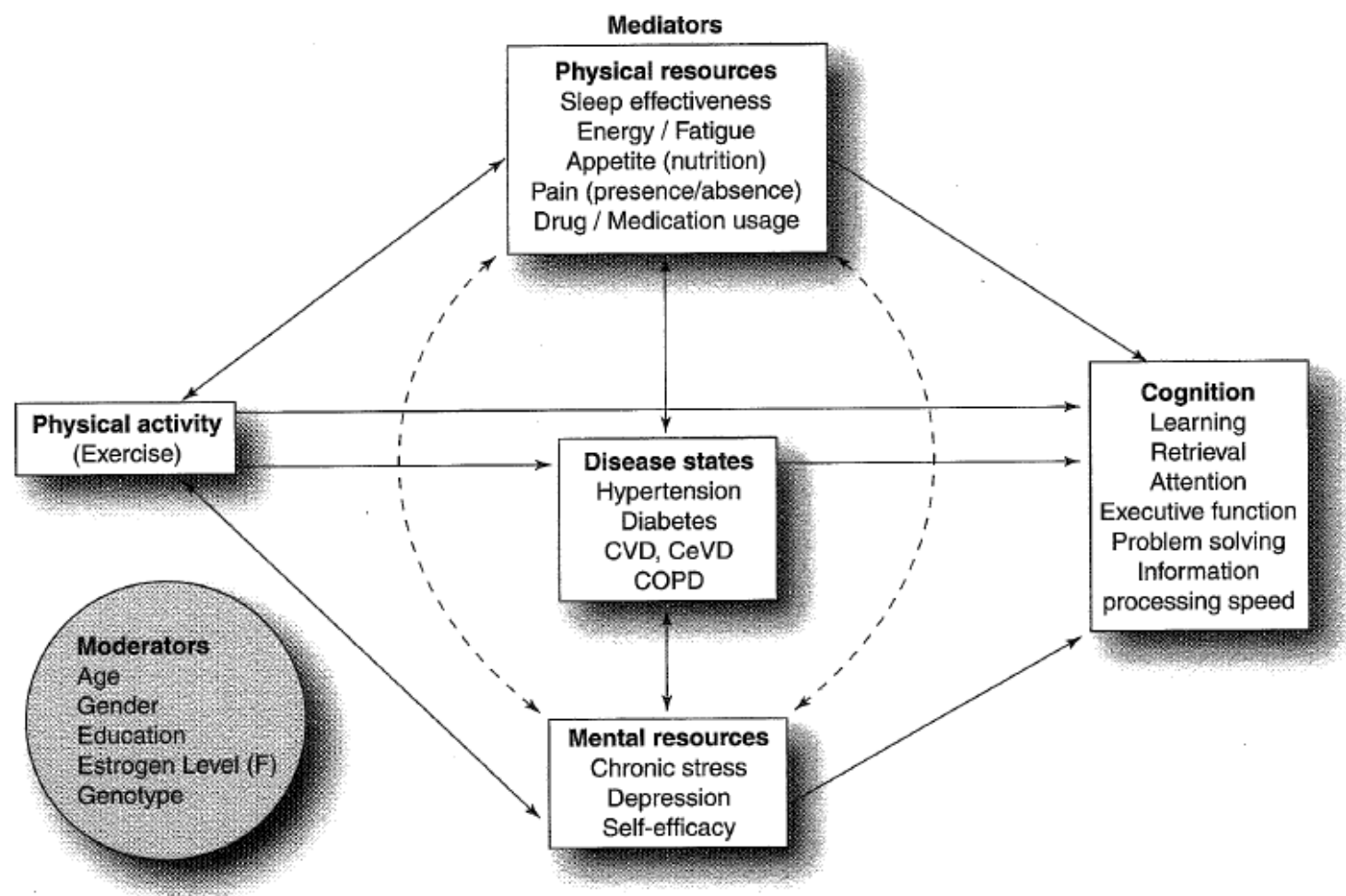


Figure 1.1 Working model of the role of mediators in exercise effects on cognition. F = female; CVD = cardiovascular disease; CeVD = cerebrovascular disease; COPD = chronic obstructive pulmonary disease.

Spirduso WW, Poon LW, Chodzko-Zajko W. Using resources and reserves in an exercise-cognition model. In: Spirduso WW, Poon LW, Chodzko-Zajko WJ, eds. Exercise and its mediating effects on cognition Champaign, IL, US: Human Kinetics, 2008:3-11.

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