

Searching for Mediators in Preventive Interventions: What Should We Look For? Where Should We Look?

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Three Parts and Take-Home Messages

- Part I: What to Look For: Emotion Regulation and Coping with Stress
- Part II: Evidence of Long Term Mediation
 - Effects of Family Group Cognitive Behavioral Preventive Intervention
 - Candidate Mediators: Parenting and Emotion Regulation/ Coping
- Part III: Where to Look: Depression and Medical Comorbidities
 - Major Depressive Disorder and Medical Conditions
 - Example: Huntington's Disease

Part I: Emotion Regulation and Coping With Stress

Emotion Regulation and Coping with Stress

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Coping, Emotion Regulation, and Psychopathology in Childhood and Adolescence: A Meta-Analysis and Narrative Review

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In this meta-analytic and narrative review, we examine several overarching issues related to the study of coping, emotion regulation, and internalizing and externalizing symptoms of psychopathology in childhood and adolescence, including the conceptualization and measurement of these constructs. We report a quantitative meta-analysis of 212 studies ($N = 80,850$ participants) that measured the associations between coping and emotion regulation with symptoms of internalizing and externalizing psychopathology. Within the meta-analysis we address the association of broad *domains* of coping and emotion regulation (e.g., total coping, emotion regulation), intermediate *factors* of coping and emotion regulation (e.g., primary control coping, secondary control coping), and specific coping and emotion regulation *strategies* (e.g., emotional expression, cognitive reappraisal) with internalizing and externalizing symptoms. For cross-sectional studies, which made up the majority of studies included, we examine 3 potential moderators: age, measure quality, and single versus multiple informants. Finally, we separately consider findings from longitudinal studies as these provide stronger tests of the effects. After accounting for publication bias, findings indicate that the broad domain of emotion regulation and adaptive coping and the factors of primary control coping and secondary control coping are related to lower levels of symptoms of psychopathology. Further, the domain of maladaptive coping, the factor of disengagement coping, and the strategies of emotional suppression, avoidance, and denial are related to higher levels of symptoms of psychopathology. Finally, we offer a critique of the current state of the field and outline an agenda for future research.

Keywords: adolescents, children, coping, emotion regulation, psychopathology



Annual Review of Psychology

Psychological Resilience: An Affect-Regulation Framework

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Keywords

resilience, adversity, stress and coping, emotion, emotion regulation, affect regulation, psychological health

Abstract

Part I: Emotion Regulation and Coping with Stress

- Conceptualization
 - Defining emotion regulation
 - Defining coping with stress
- Paradigms
 - Controlled laboratory experiments
 - Reports from individuals and other informants
- Measurement
 - Emotions (the result of efforts to regulate)
 - Strategies to regulate emotions
 - Verbal reports of lab processes
 - Questionnaires

Emotion Regulation and Coping with Stress

- Troy et al. (2023)
 - “Exposure to adversity (e.g., poverty, bereavement) is a robust predictor of disruptions in psychological functioning.”
 - “However, people vary greatly in their responses to adversity; some experience severe long-term disruptions, others experience minimal disruptions or even improvements.”
 - “We refer to the latter outcomes—faring better than expected given adversity—as psychological resilience.”
 - “Psychology’s understanding of resilience is incomplete, for two reasons: **(a) We lack conceptual clarity, and (b) two major approaches to resilience—the stress and coping approach and the emotion and emotion-regulation approach—have limitations and are relatively isolated from one another.**”
 - “We offer an integrative affect-regulation framework that capitalizes on complementary strengths of both approaches.”
 - “This framework advances our understanding of resilience by integrating existing findings, highlighting gaps in knowledge, and guiding future research.”

Emotion Regulation and Coping with Stress

- Emotion Regulation and Coping: Different Wine, Different Bottles?
- Or: Same Wine, Different Bottles?



Emotion Regulation and Coping with Stress

- **Conceptualization and Definitions**
- **Coping:** Behavioral and cognitive strategies used to manage stressors and stress responses (Troy et al., 2023)
- **Emotion regulation:** Strategies used to alter one's emotions, including attempts to change subjective experience, cognition, behavior, physiology, or the environment (Troy et al., 2023)
- **Coping:** Conscious and volitional efforts to regulate emotion, cognition, behavior, physiology, and the environment in response to stressful events or circumstances." (Compas et al., 2001, 2017)
- **(Executive functions:** Higher order cognitive processes including attentional/inhibitory control, working memory/updating, and shifting/cognitive flexibility)

Emotion Regulation and Coping with Stress

- **Paradigms** (from Troy et al., 2023; Compas et al., 2017)
- Emotion regulation:
 - Emphasis on controlled laboratory contexts
 - Greater reliance on laboratory studies with experimental manipulations of emotion regulation
 - Greater emphasis on shorter-term causal effects of emotion regulation and examinations of temporally fine-grained dynamic processes
- Coping with stress:
 - Naturalistic emphasis
 - Greater reliance on surveys and correlational methods to assess coping
 - Greater emphasis on longer-term relationships between coping and resilience
 - Greater ecological validity and lower internal validity

Emotion Regulation and Coping with Stress

- Measurement
- **Emotion regulation:**
 - Laboratory instructions to engage in specific ER strategies
 - fMRI studies of cognitive reappraisal (Gross and colleagues)
 - Emotion Regulation Questionnaire (Gross & John)
 - **Cognitive Reappraisal**
 - Suppression of Expression of Emotions
 - Trait-level
- **Coping with stress**
 - Relatively few laboratory studies
 - Multiple different measures
 - Example: Responses to Stress Questionnaire (Connor-Smith et al.)
 - Three factors of coping
 - Most relevant: **Secondary control coping (acceptance, cognitive reappraisal)**
 - Stressor or domain specific

Emotion Regulation and Coping with Stress

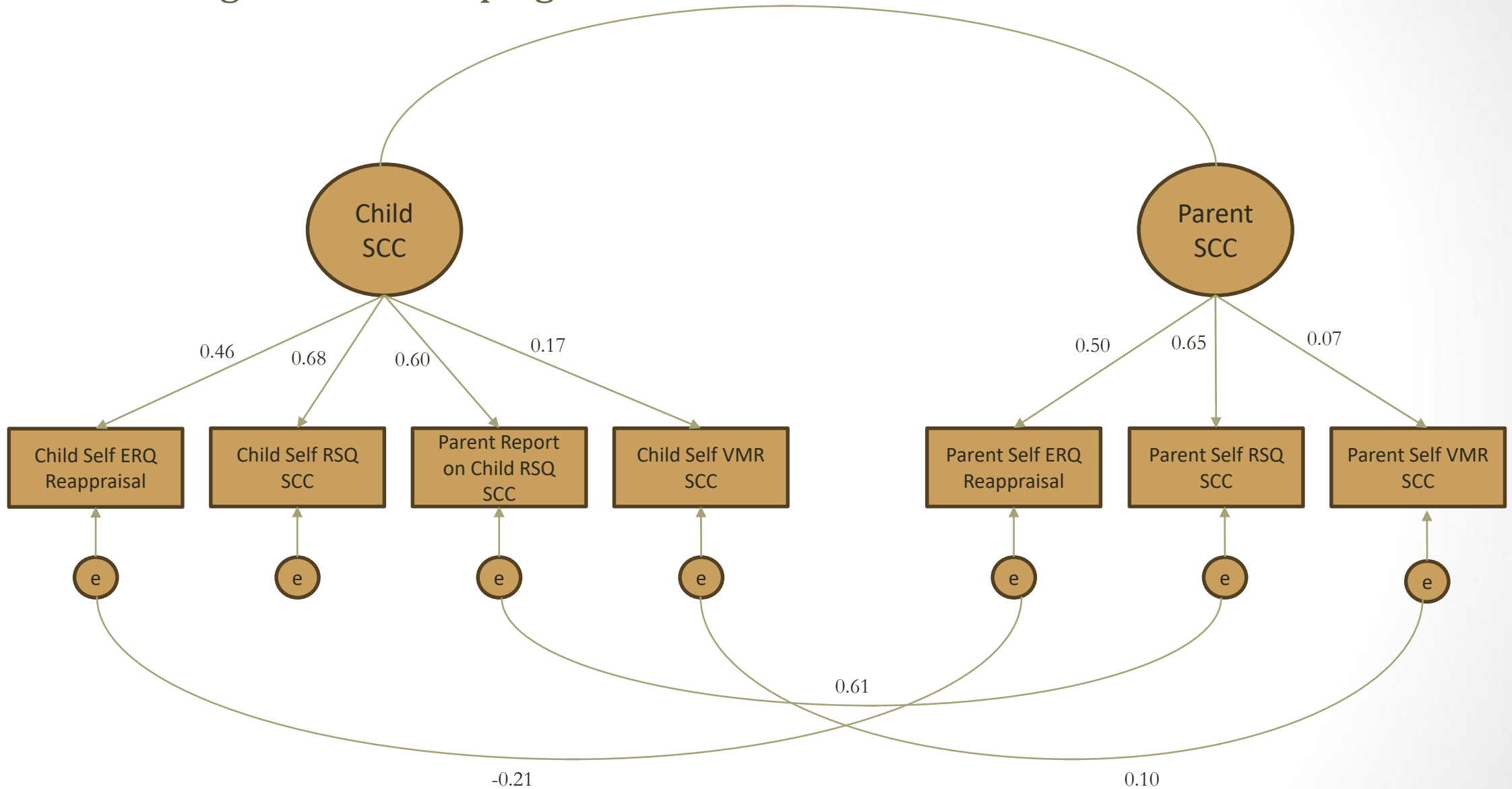
- **Testing a Measurement Model of ER and Coping**
- Measurement of emotion regulation and coping with stress in adolescents (age 10-15 years) and their parents (Anderson, Ciriegio, Cole.... & Compas, 2023)
- Multi-method and multi-informant
- Adolescents
 - Self report of ER (ERQ) (reappraisal)
 - Self report of Coping (RSQ) (secondary control coping)
 - Parent report on Adolescent Coping (RSQ) (secondary control coping)
 - Video-mediated recall (coded for secondary control coping)
- Parents
 - Self report of ER (ERQ) (reappraisal)
 - Self report of Coping (RSQ) (secondary control coping)
 - Video-mediated recall (coded for secondary control coping)

Emotion Regulation and Coping with Stress

- **Video-mediated recall**

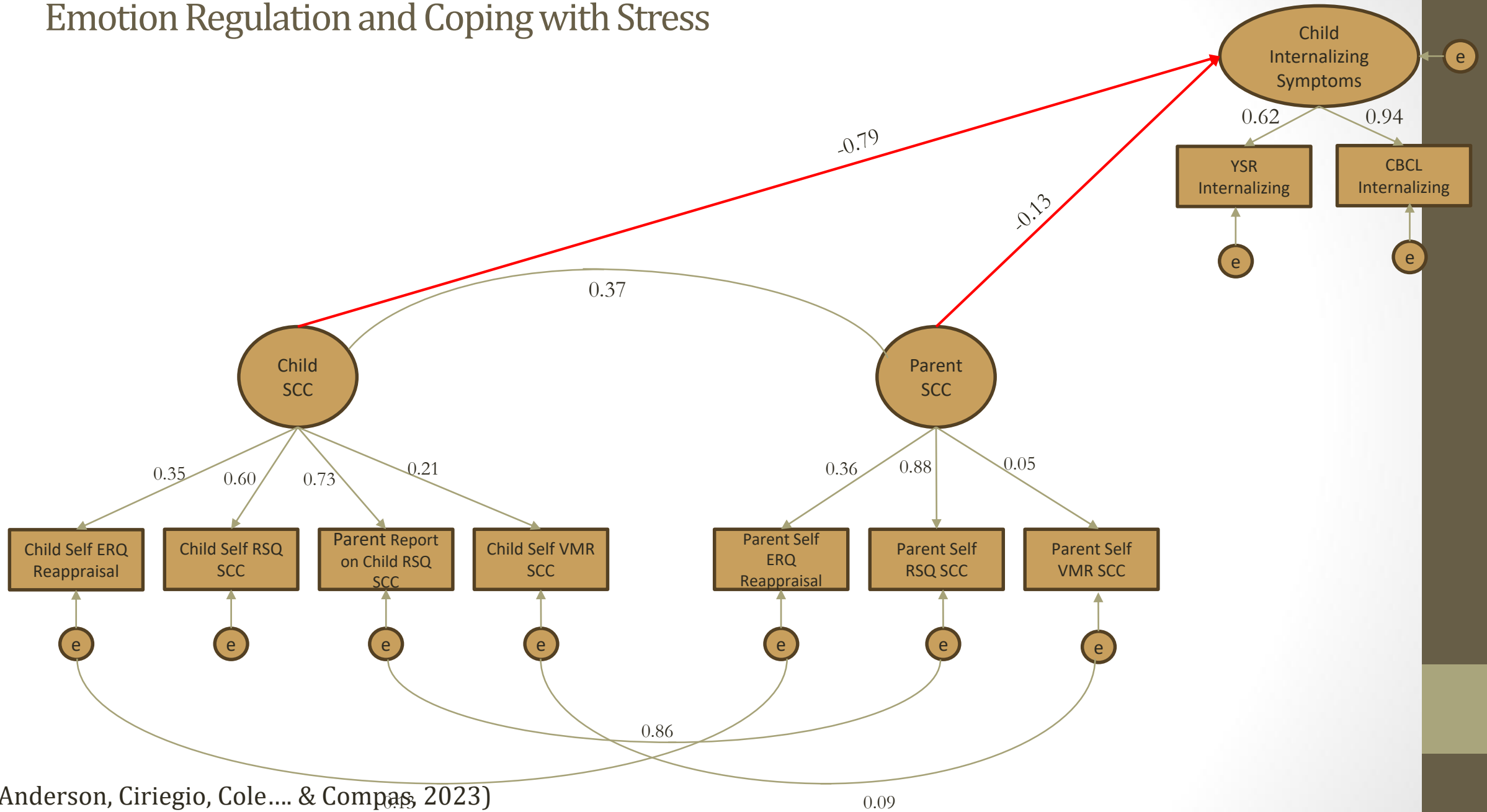
- 10-minute parent-adolescent discussion about current source of stress and conflict in their relationship
- Continuous measures of ANS physiology (skin conductance and heart rate variability) (Siciliano et al., 2023)
- Parent and adolescent separately view video after interaction
 - Continuous rating of their emotions over the 10-minutes (CARMA) (Henry et al. 2023)
 - Recall of ER-related thoughts every 30-seconds for middle 4 minutes of interaction
 - Coded for secondary control coping strategies
 - Rating scale after interaction regarding specific coping/ER strategies

Emotion Regulation and Coping with Stress 0.38

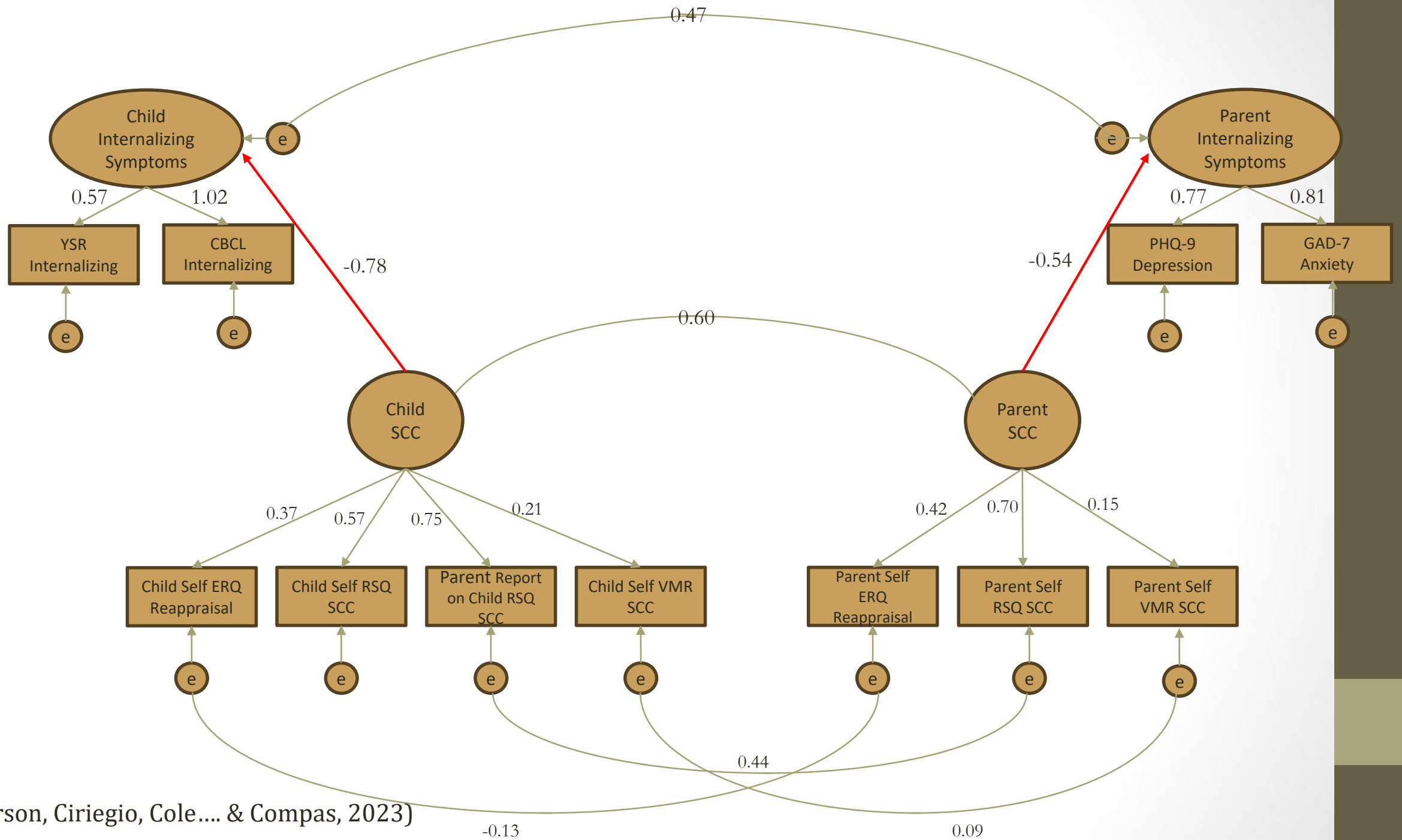


(Anderson, Ciriegio, Cole.... & Compas, 2023)

Emotion Regulation and Coping with Stress



(Anderson, Ciriegio, Cole.... & Compas, 2023)



(Anderson, Ciriegio, Cole.... & Compas, 2023)

Part II: Family Group Cognitive Behavioral Prevention in Families of Depressed Parents: Mediators of Effects at 18- and 24-Months

Part II: Mediators of Family Group Cognitive Behavioral Preventive Intervention

- **Family Group Cognitive Behavioral (FGCB) Preventive Intervention**
- Efficacy studies
 - Compas et al. (2015)
 - Lochner et al. (2023)
- Compas et al.: Two site RCT
 - Mediators measured at 6-months:
 - Direct observations and coding of parenting behaviors
 - Adolescent and parent reports of adolescents' secondary control coping
 - Adolescent internalizing and externalizing problems and depression symptoms measured at 18- and 24-months

Part II: Mediators of Family Group Cognitive Behavioral Preventive Intervention

- FGCB
- Four families per group
 - Block randomization: 8 families per block randomized to group or written information comparison
- 8 weekly sessions, 4 monthly booster sessions
- Three components:
 - Educate families about depression, stress and effects on families
 - Teach parenting skills
 - Increase parental warmth
 - Increase structure
 - Teach coping skills to adolescents
 - Secondary control coping skills (ADAPT)
 - Acceptance
 - Cognitive Reappraisal/Positive Thinking
 - Distraction

Part II: Mediators of Family Group Cognitive Behavioral Preventive Intervention

	Baseline	2- months	6- months	12- months	18- months	24- months
CES-D	---	.06	.14	.26*	.04	.22*
YSR A/D	---	.25†	.45***	.41**	.38**	.27*
CBCL A/D	---	.30†	.23	.27†	.21	.23
YSR Int	---	.21	.36**	.43***	.39**	.19
CBCL Int	---	.33**	.25	.28†	.26	.23
YSR Ext	---	.00	.20	.29*	.41***	.28*
CBCL Ext	---	.25	.26	.16	.25	.20

Number Significant Effects: 1/7 2/7 4/7 3/7 3/7

Note. N = 242. Effects reported as Cohen's d 's; * $p < .05$; ** $p < .01$; *** $p < .001$; all two-tailed

13/35 total effects (37%)

Compas, Forehand et al. (2015)

Part II: Mediators of Family Group Cognitive Behavioral Preventive Intervention

Löchner et al. *BMC Psychiatry* (2023) 23:455
<https://doi.org/10.1186/s12888-023-04926-2>

BMC Psychiatry

RESEARCH

Open Access



A randomized controlled trial of a preventive intervention for the children of parents with depression: mid-term effects, mediators and moderators

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Abstract

Background In a parallel randomized controlled trial the effectiveness of the family- and group-based cognitive-behavioural “Gug-Auf” intervention in preventing depression in children of depressed parents was evaluated. We hypothesized that the intervention would be associated with reduced incidence of depression at 15 months as well as with reduced symptom severity at 6, 9, and 15 months. We also explored the role of a number of mediators and moderators.

Methods Families were included if a parent (n = 100, mean age = 46.06, 61% female) had experienced depression and children (n = 135, aged 8–17 years, 53% female) had no mental illness. Families (91.5% German) were randomly allocated (50:50 block-wise; stratified by child age and parental depression) to the 12-session “GuG-Auf” intervention or no intervention. Outcomes were assessed (on an intention-to-treat basis) at 0-(T1), 6-(T2), 9-(T3) and 15-months (T4) after baseline. Primary outcome (onset of depression; T4) was assessed with standardized (blinded) clinical interviews. Secondary (unblinded) outcome was risk of depression (at T2-T4) indicated by self- and parent-reported symptoms of internalizing, externalizing and depressive disorder. Potential mediators were emotion regulation, attributional style, knowledge of depression and parenting style. Potential moderators were parental depression severity and negative life events.

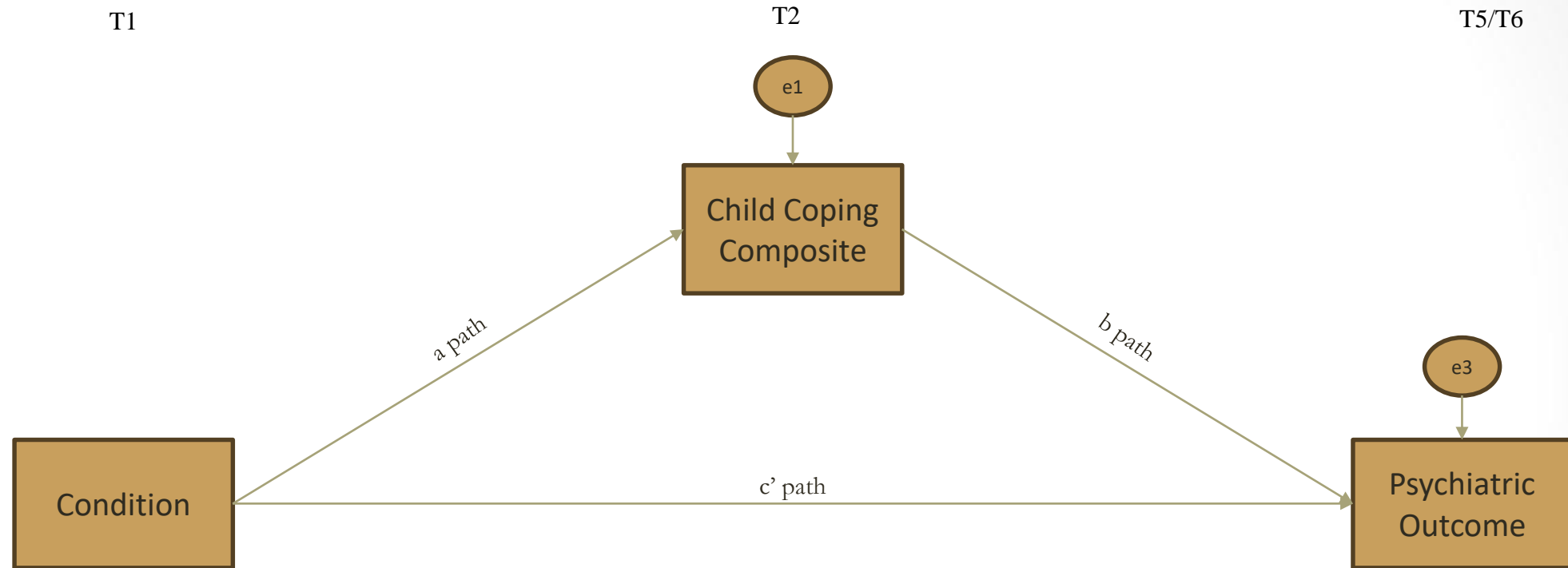
Part II: Mediators of Family Group Cognitive Behavioral Preventive Intervention

- **Criteria for testing mediation in interventions (Kazdin)**
 - Conduct sufficiently powered randomized clinical trials
 - Use valid and reliable measures for mediators that are sensitive to change
 - Apply a process design in which changes of the mediator temporally precede changes in therapeutic outcome and the mediator variable is measured repeatedly
 - Compare mediators that are theory-driven with non-specific mediators
 - Apply different dosages to prove that a stronger mediator-change leads to more therapeutic changes

Part II: Mediators of Family Group Cognitive Behavioral Preventive Intervention

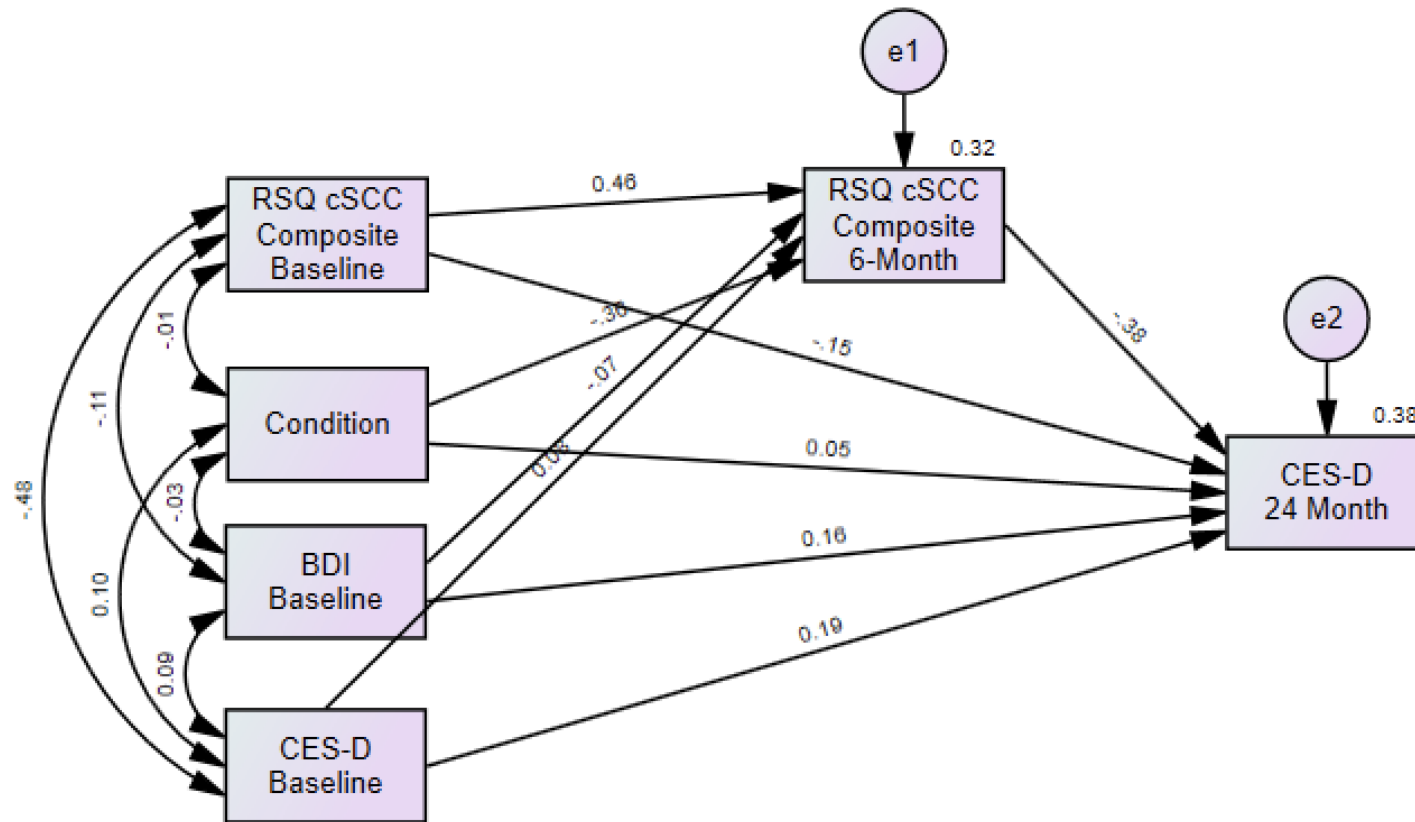
- Model 1: Single Mediator
 - Changes in adolescents' coping/ER
 - Changes in parenting
- Model 2: Dual Mediators
 - Changes in adolescents' coping/ER **and** parenting
- Model 3: Sequential Mediators
 - Changes in parenting **leading to** changes in adolescents' coping/ER

Part II: Mediators of Family Group Cognitive Behavioral Preventive Intervention



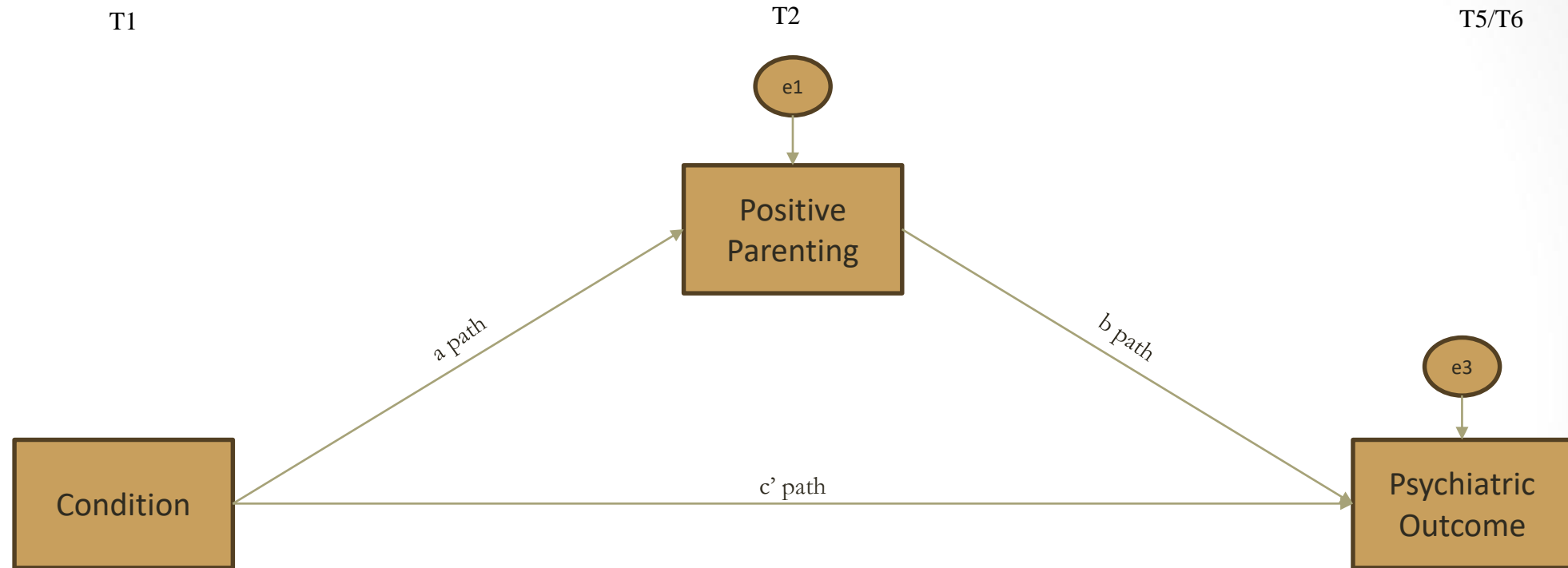
Note: Child coping composite, child psychiatric symptoms, and parental levels of depression at T1 are included as covariates (but not depicted).
T1 = baseline; T2 = 6-months post intervention; T5 = 18-months post intervention; T6 = 24-months post intervention

Part II: Mediators of Family Group Cognitive Behavioral Preventive Intervention



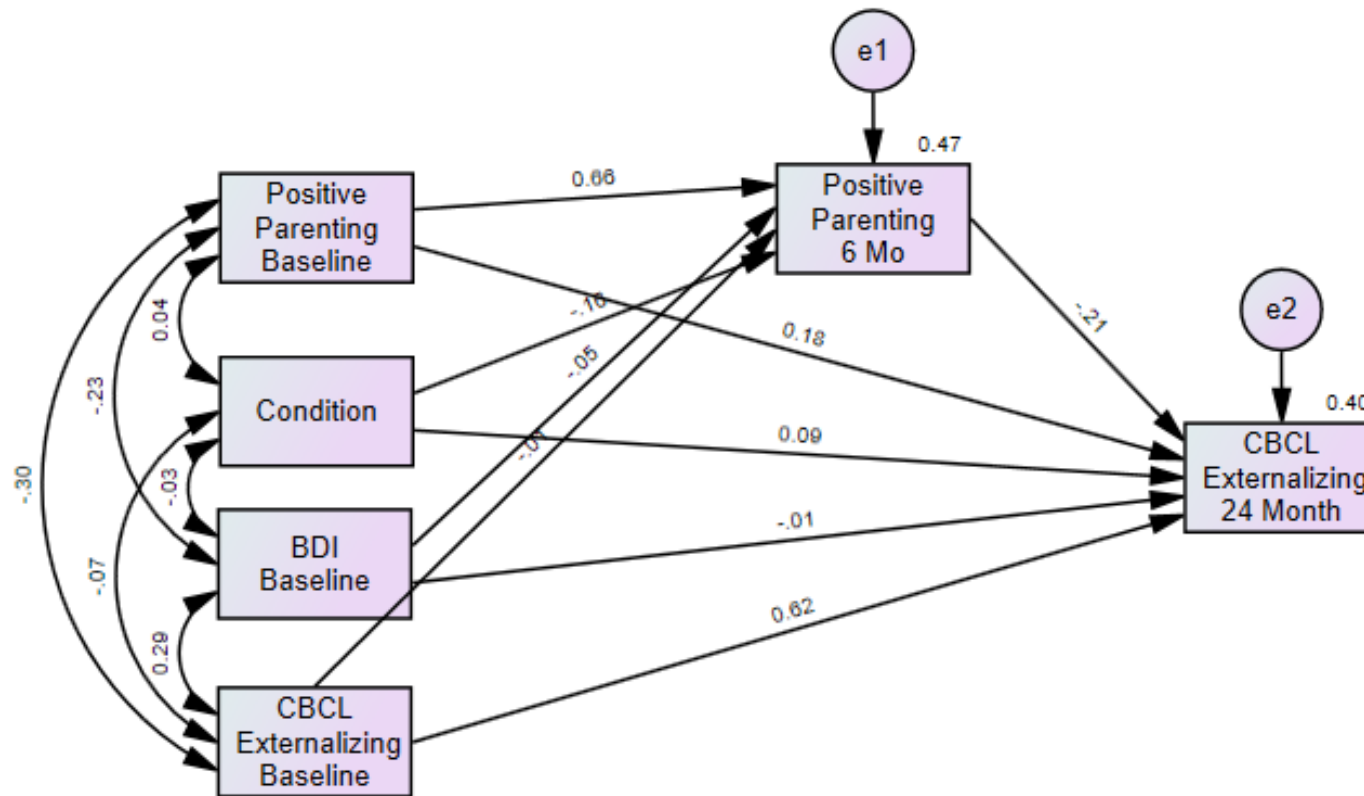
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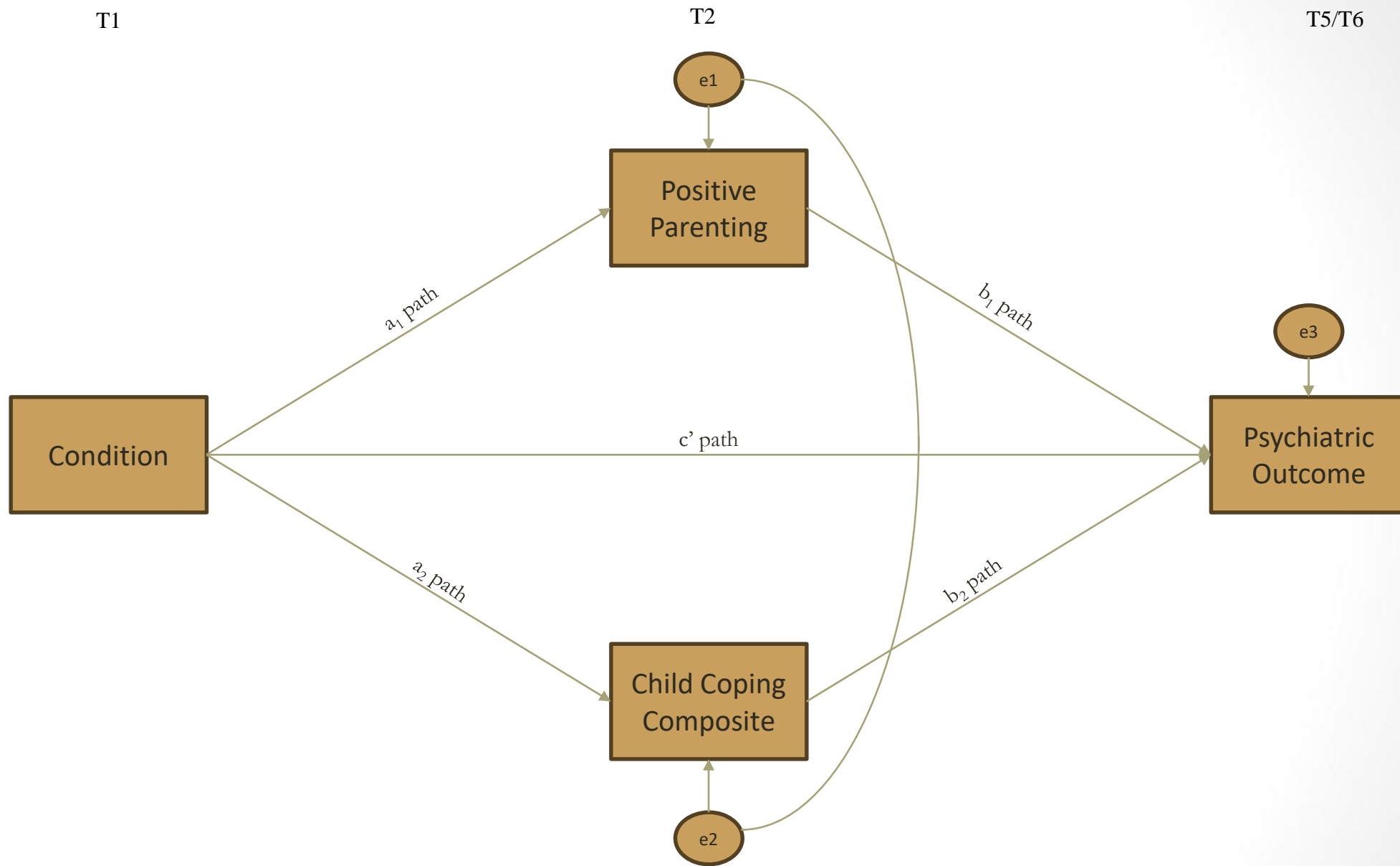


Note: Positive parenting, child psychiatric symptoms, and parental levels of depression at T1 are included as covariates (but not depicted).
T1 = baseline; T2 = 6-months post intervention; T5 = 18-months post intervention; T6 = 24-months post intervention

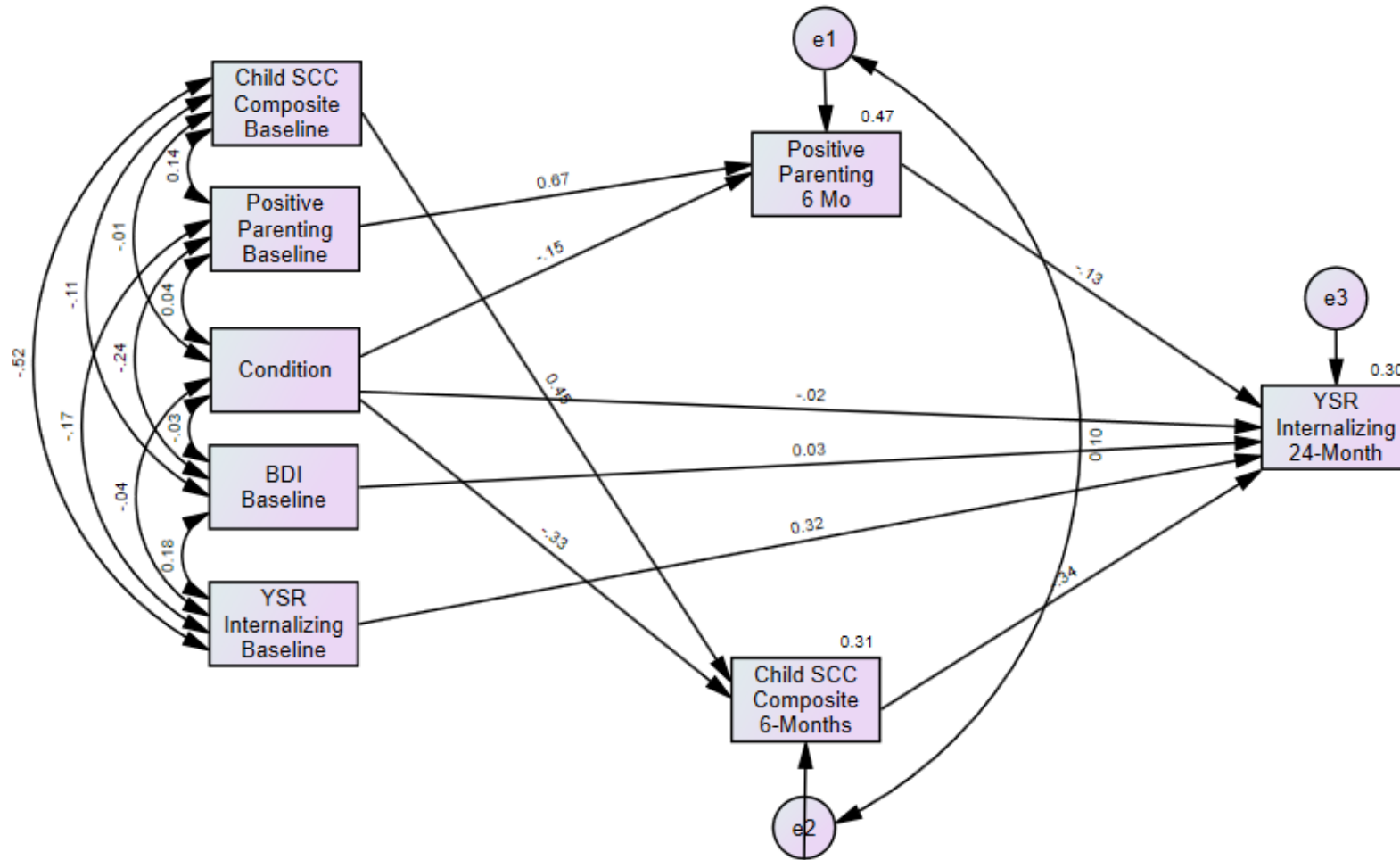
Part II: Mediators of Family Group Cognitive Behavioral Preventive Intervention



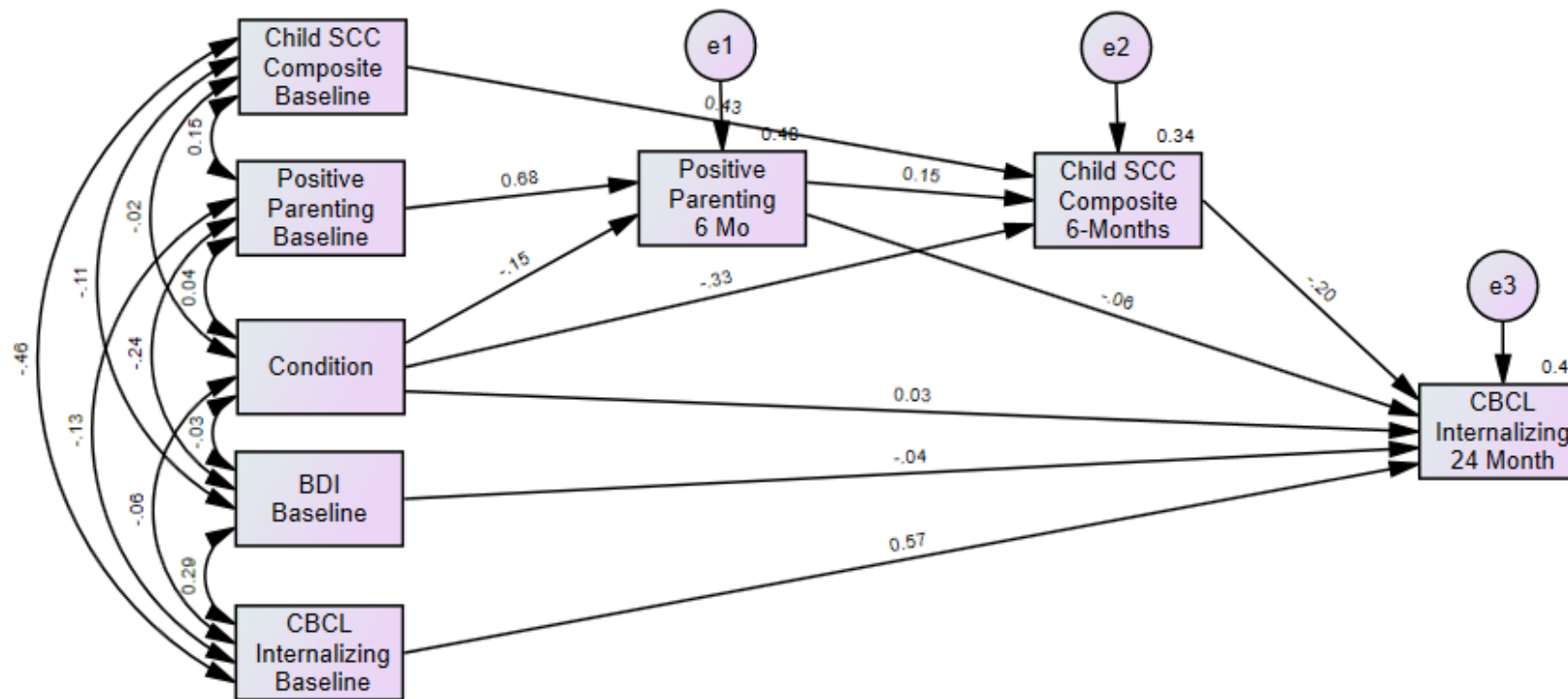
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Part III: Where to Look: MDD and Medical Comorbidities

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- Research on parental depression has been carried out in Silos

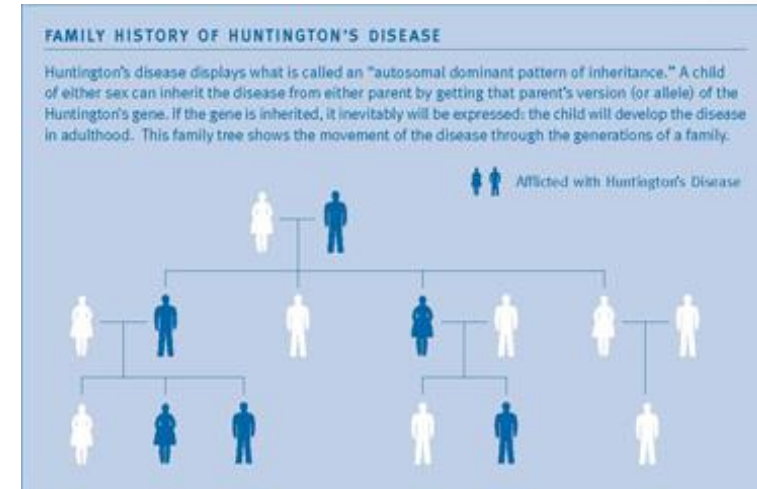


Part III: Where to Look: MDD and Medical Comorbidities

- Diseases and Medical Conditions and MDD
 - Cancer:
 - Breast cancer: 21%
 - Diabetes: Type 2: 20%
 - Cardiovascular Disease
 - Adults with a depressive disorder or symptoms have a 64 percent greater risk of developing coronary artery disease (CAD)
 - Depressed CAD patients are 59 percent more likely to have a future adverse cardiovascular event, such as a heart attack or cardiac death.
 - Example: Huntington's Disease

Huntington's Disease

- Neurodegenerative genetic disease
- Expanded cytosine-adenine-guanine (CAG) repeats on HD/HTT gene (4p16.3)
- Autosomal dominant
- 100% penetrant
- Affects multiple areas of functioning:
 - Motor (chorea)
 - Cognitive (impaired EF)
 - Emotional (depression, anger, anxiety)
 - Behavioral (loss of impulse control)
- Diagnosis based on emergence motor symptoms, typically in 30s or 40s
- Currently no cure
- Challenge for offspring:
 - Experiencing the progression of the disease and decline in function in parent
 - Knowing they have a 50-50 chance they are observing their own future



Huntington's Disease

- **In the words of offspring of parents with HD:**
- “It has changed the way we have to do things but it has brought us closer as a family.”
- “We still struggle deeply as a family and I don't think I'll ever be able to say I had a happy childhood. Despite this, we are coming through together as my mom's sickness begins to come to a close. I am grateful for the healing I am beginning to find.”

Huntington's Disease

- **In the words of offspring of parents with HD:**
- “Currently one of my biggest challenges is my mental health. I honestly don't know what to do about it. I cannot afford a therapist and I don't have anyone to talk to about all my stress and anxiety. My family is not someone I can openly share my feelings with.”
- “The biggest challenge I face with HD is thinking about my future. I find myself going weeks in denial and blacking it out and then weeks where it consumes me to where I cannot get out of bed. I envy just about anything and everyone that does not have this illness consuming their life.”

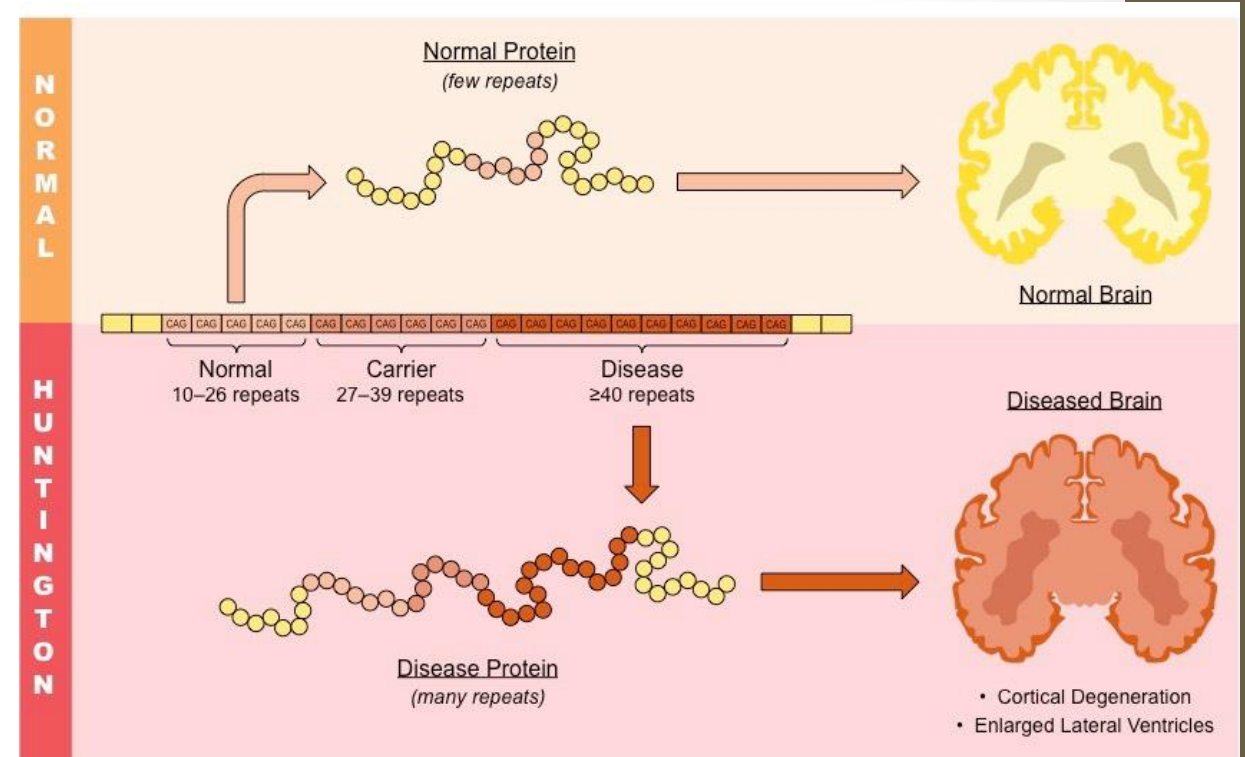
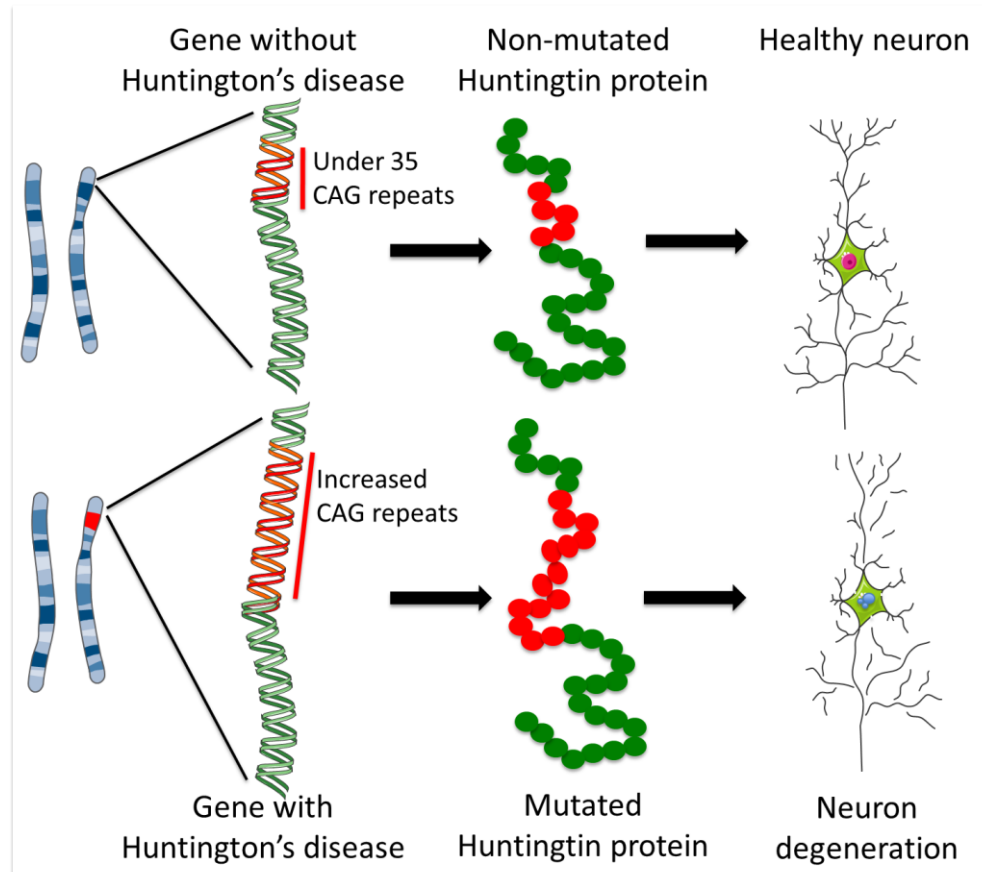
Huntington's Disease

- **In the words of offspring of parents with HD:**
- “I am nothing but terrified of HD.... I live in fear that HD made me less than human to the rest of the world...I didn't want to have dreams or continue with the things I'm passionate about. I was so hopeless that by the time I was 15, I wanted to commit suicide.”

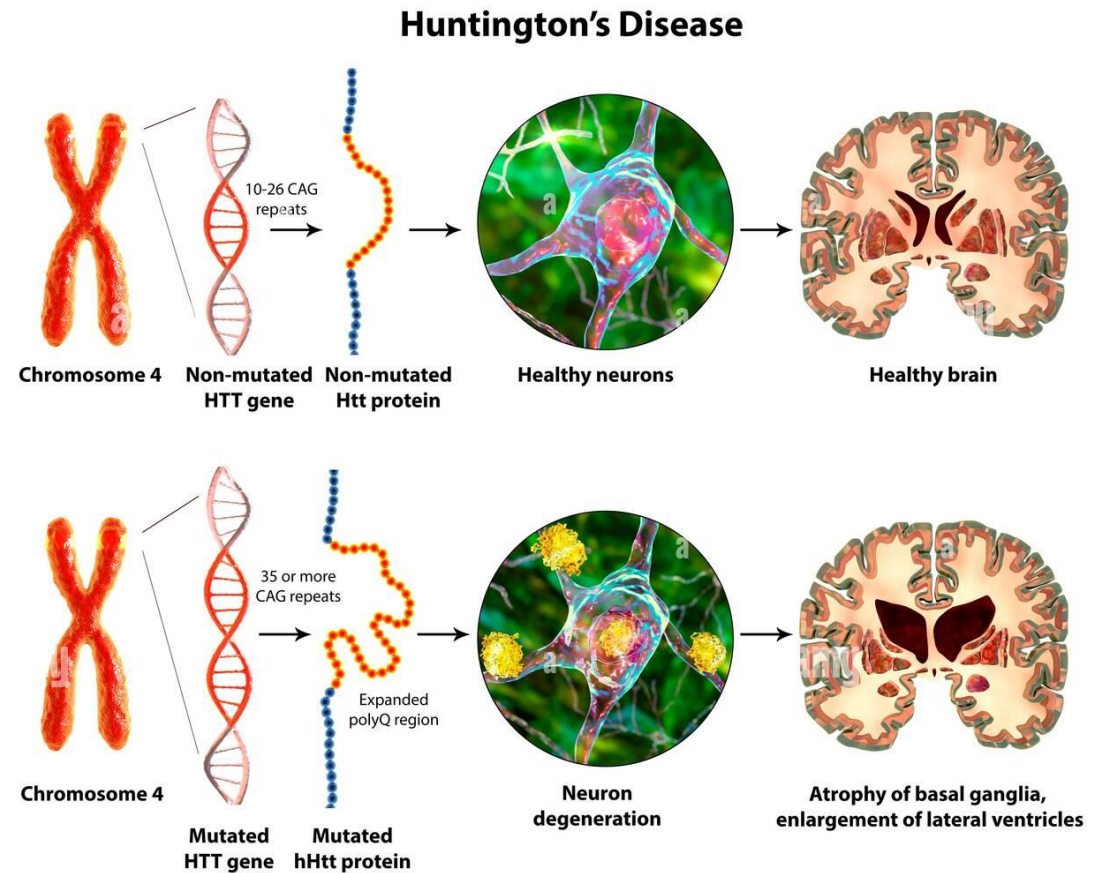
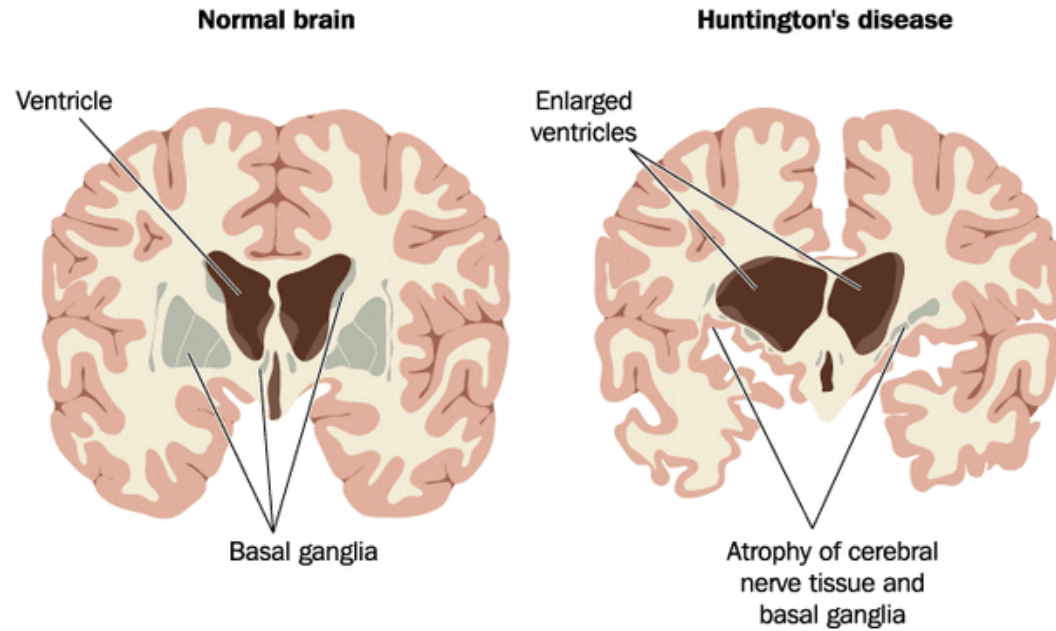
Huntington's Disease

- Rates of major depressive disorder in Huntington's disease:
 - Meta-analysis (Clark et al., 2023, *Neuroscience and Biobehavioral Reviews*)
 - Depression frequency in the lifetime in adults affected by or at-risk for HD was 38%.
 - The robustness of the findings improved when limiting the analysis to gene-positive individuals only depression was 43% respectively.

Huntington's Disease

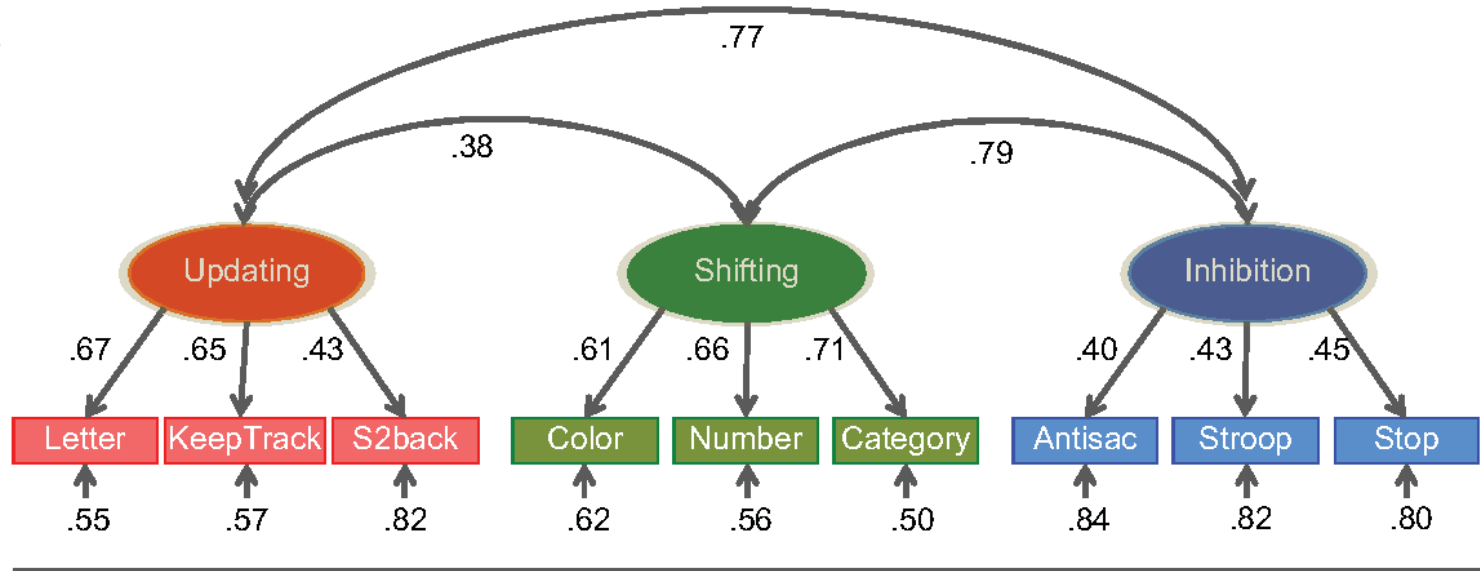


Huntington's Disease

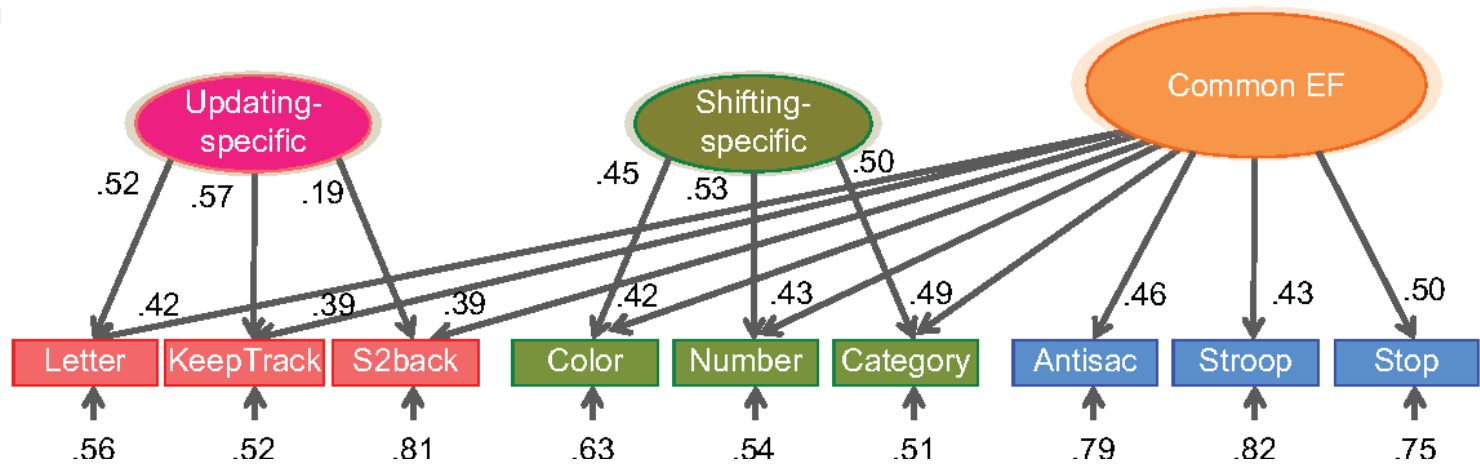


Miyake & Friedman Model of Executive Function

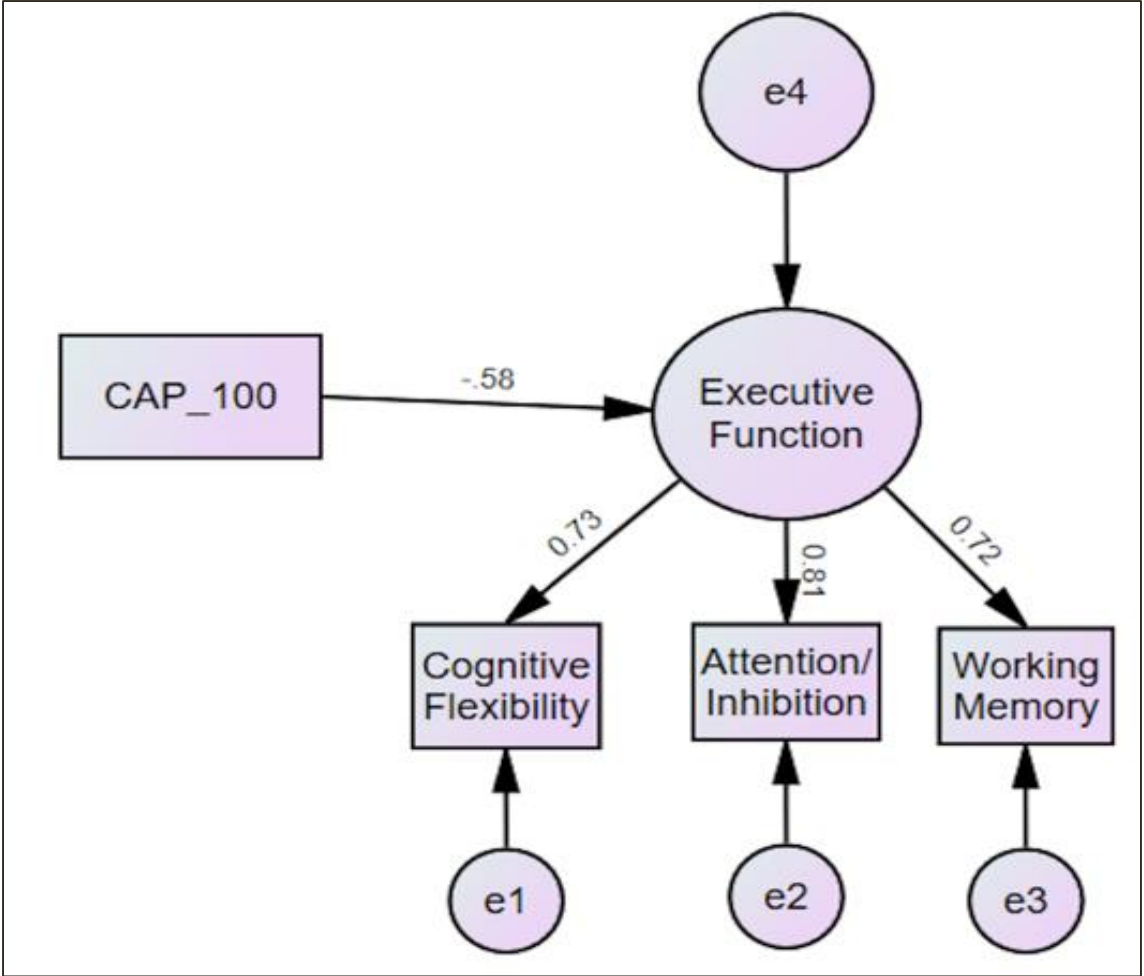
a



b



Latent Variable Model of Executive Function in HD Patients



Ciriegio et al. (2023)

Figure 2

Huntington's Disease

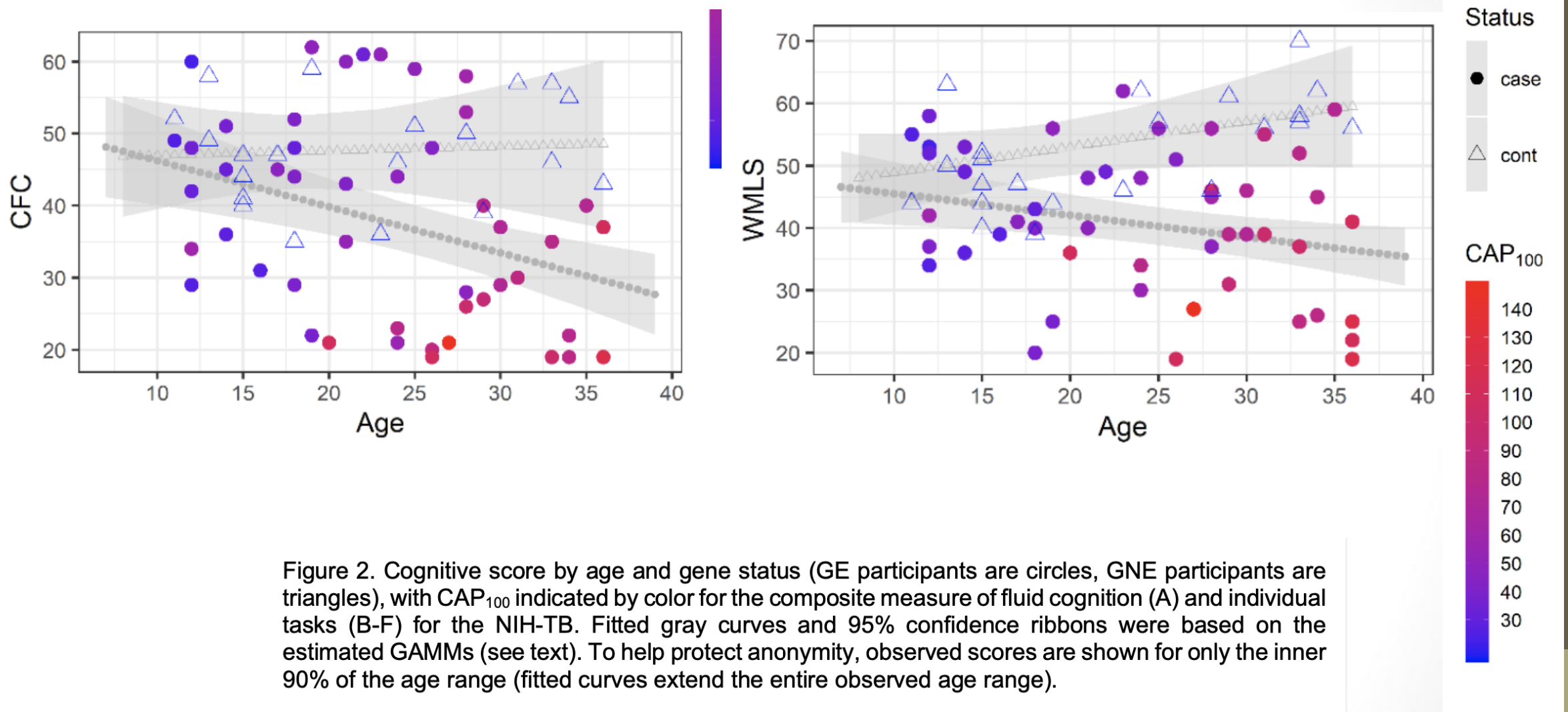
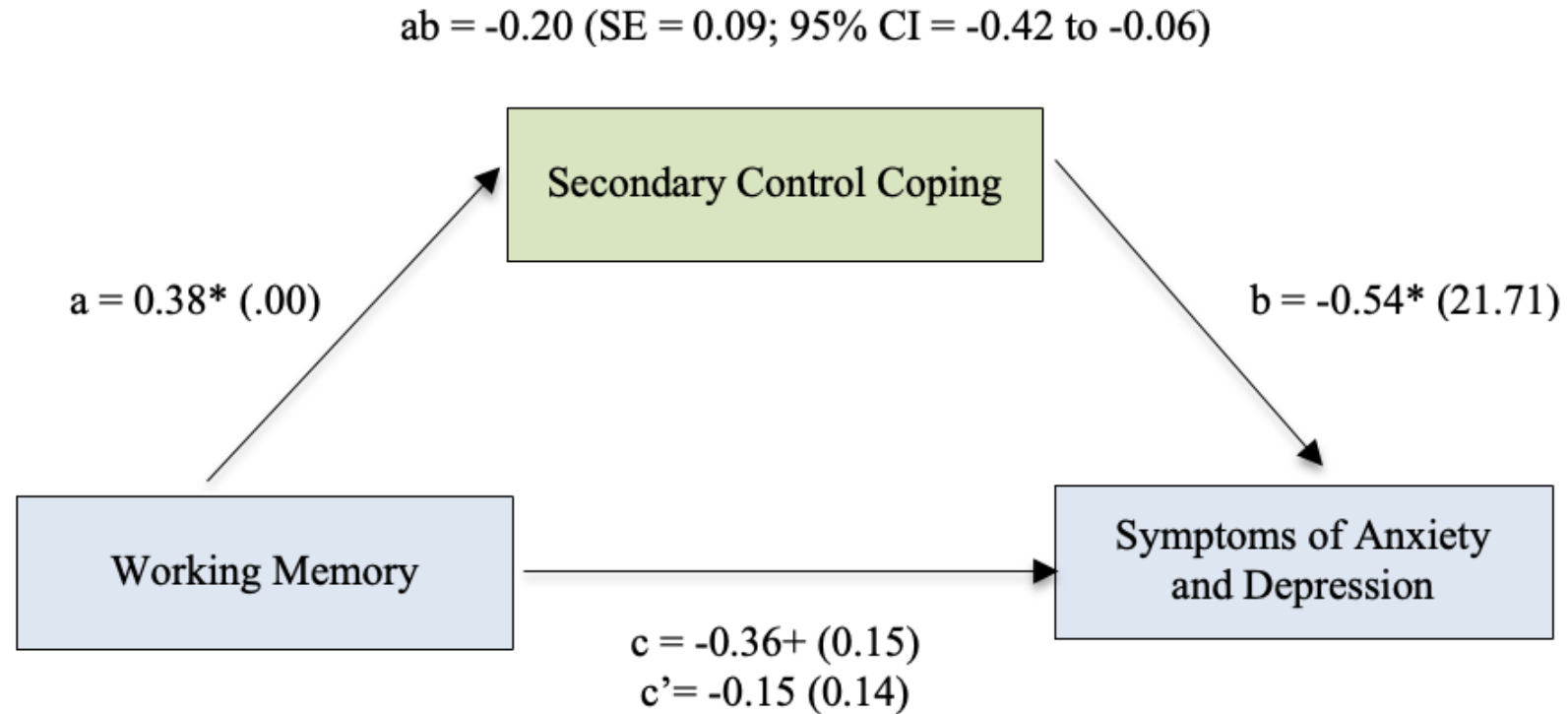


Figure 2. Cognitive score by age and gene status (GE participants are circles, GNE participants are triangles), with CAP₁₀₀ indicated by color for the composite measure of fluid cognition (A) and individual tasks (B-F) for the NIH-TB. Fitted gray curves and 95% confidence ribbons were based on the estimated GAMMs (see text). To help protect anonymity, observed scores are shown for only the inner 90% of the age range (fitted curves extend the entire observed age range).

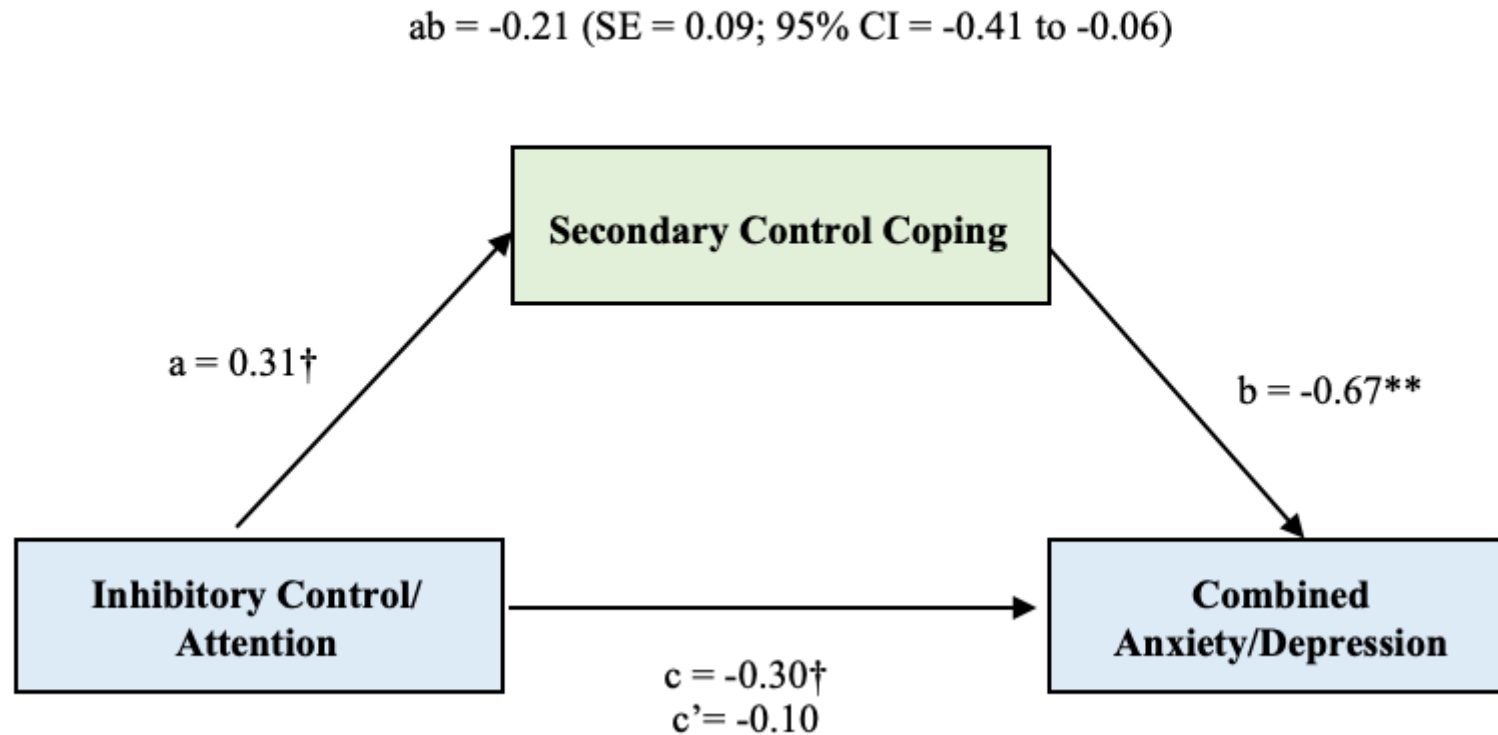
Huntington's Disease



N = 33 individuals at-risk for HD

Ciriegio et al. 2020 *Neuropsychology*

Huntington's Disease



N = 32 HD patients

Ciriegio et al. 2022 *Neuropsychology*

Huntington's Disease

- **Current Research**
- 5-year descriptive longitudinal study (NICHD; Compas & Claassen)
 - 200 HD families and 200 control families
 - Model progression of disease and psychiatric symptoms in HD patients and offspring
- Biomarkers of stress in HD and executive function and ER (Ciriegio; NINDS)
 - Pro- and anti-inflammatory cytokines in response to stress in HD patients and at-risk family members
- Glymphatic system markers of disease (Claassen; NINDS)
- Intervention development (CHDI Foundation; Compas & Claassen; CHDI)
 - Pilot tested program to build resilience in HD patients and families
 - Modeled after FGCB Prevention of Depression
 - Delivered virtually (Zoom and Teams) to groups

Summary

- Emotion regulation and coping are closely related constructs
- Emotion regulation and coping are critical mediators of preventive interventions for offspring of depressed parents
- Depression is comorbid with many medical conditions
- HD is prototypic example
- The exception (rare condition) can help us understand the rule (parental depression)