

Adverse Childhood Experiences (ACEs) and the Cortisol Awakening Response (CAR) in Children

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Effects of Chronic Stress

Psychological

- Anxiety
- Depression
- Irritability
- Difficulty concentrating
- Impaired Memory

Musculoskeletal

- Tension headaches
- Back pain
- Neck Pain

Gastrointestinal

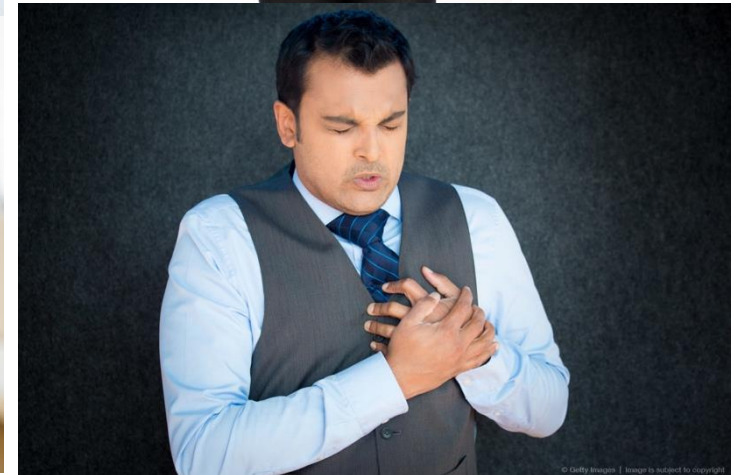
- Upset stomach
- Constipation

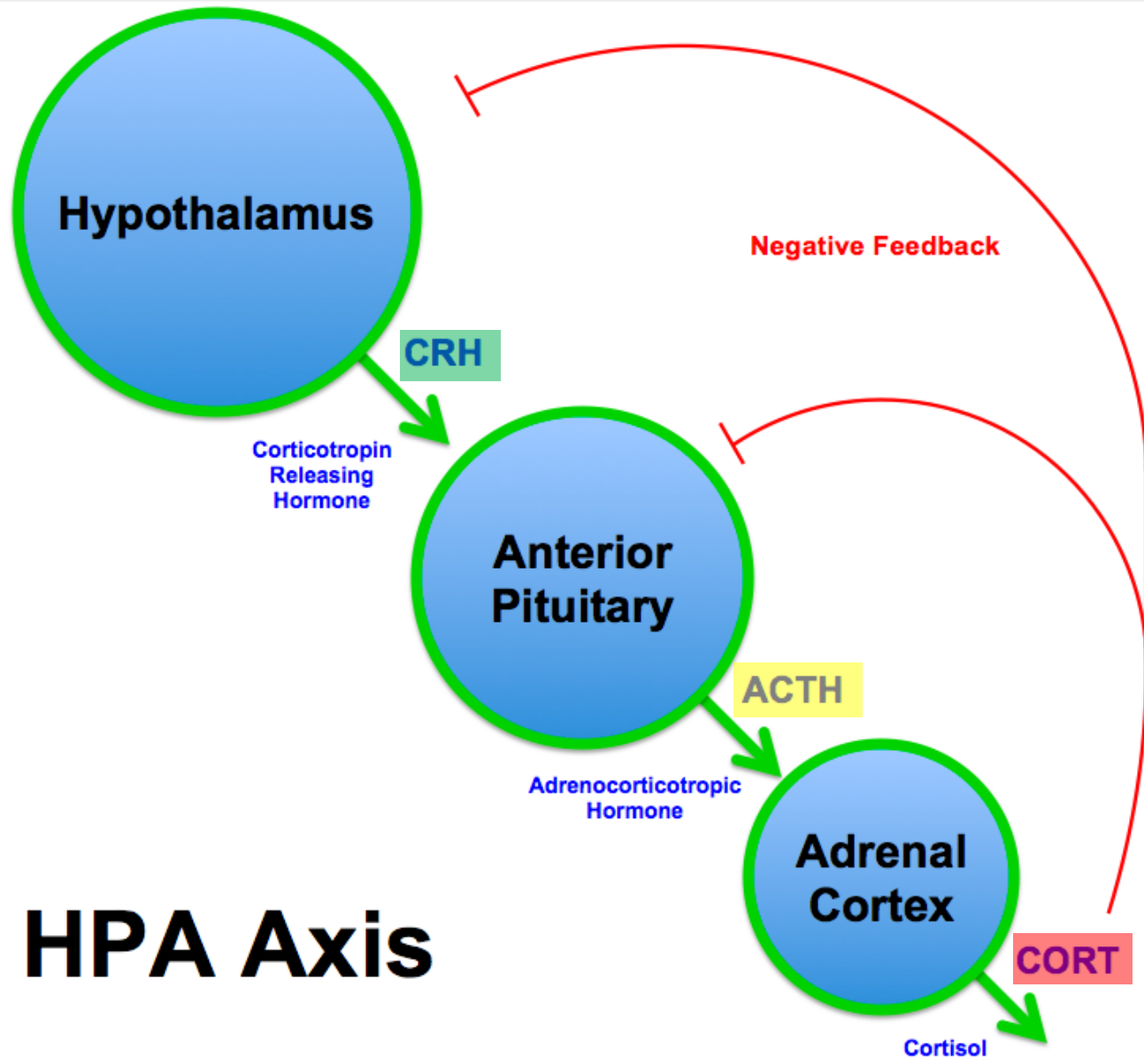
Immunological

- Immunosuppression

Cardiovascular

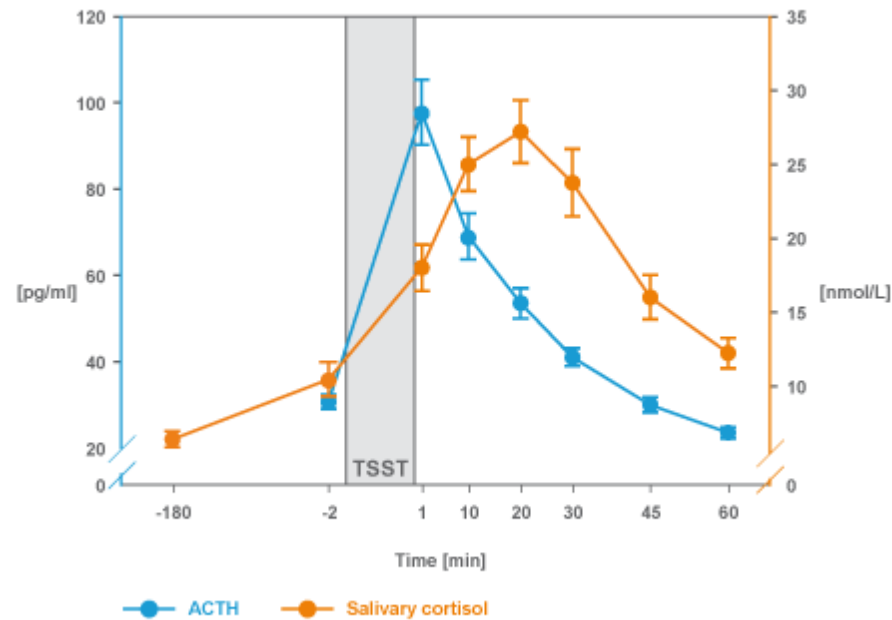
- Coronary Heart Disease (CHD)



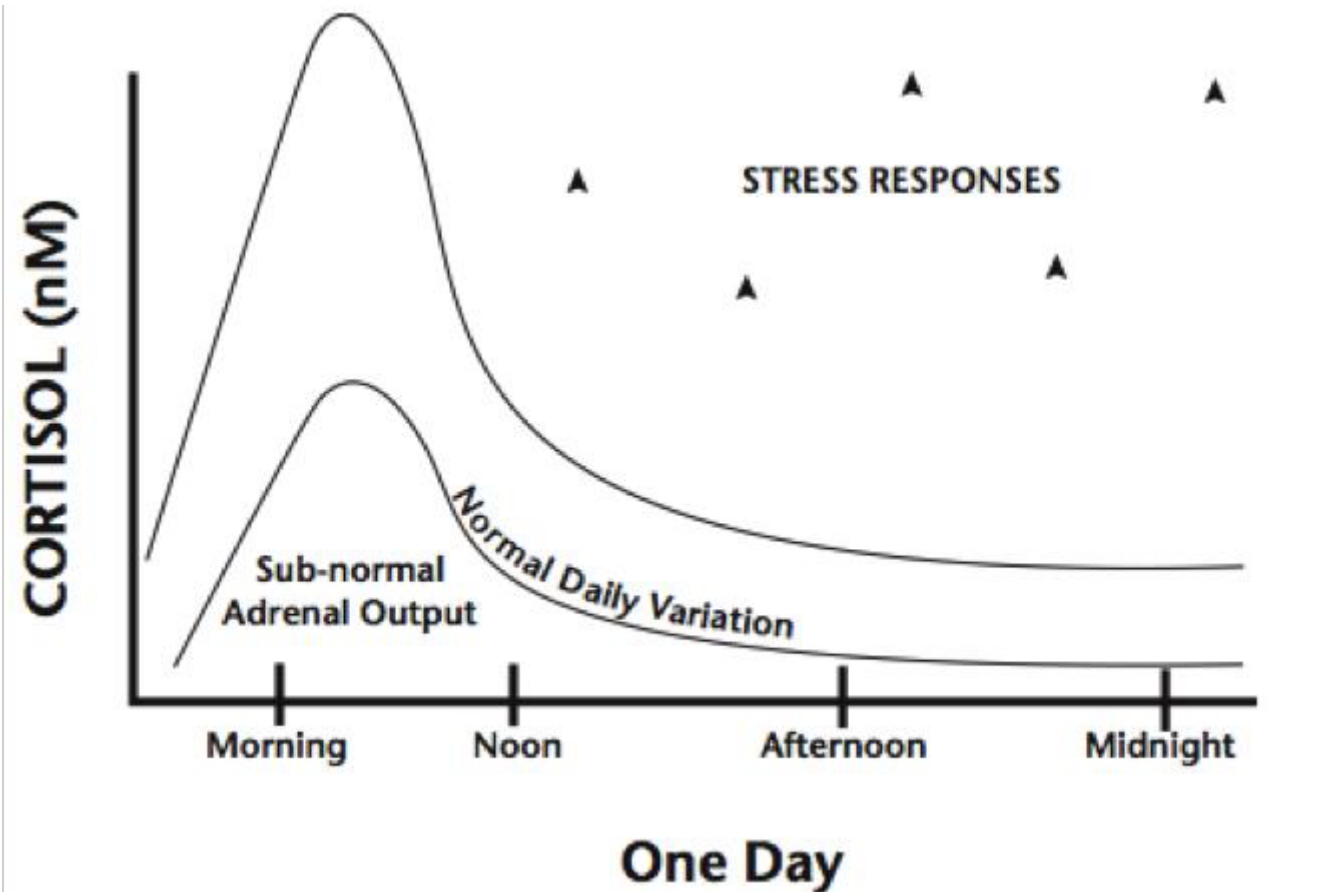


HPA Axis

Cortisol Stress Response

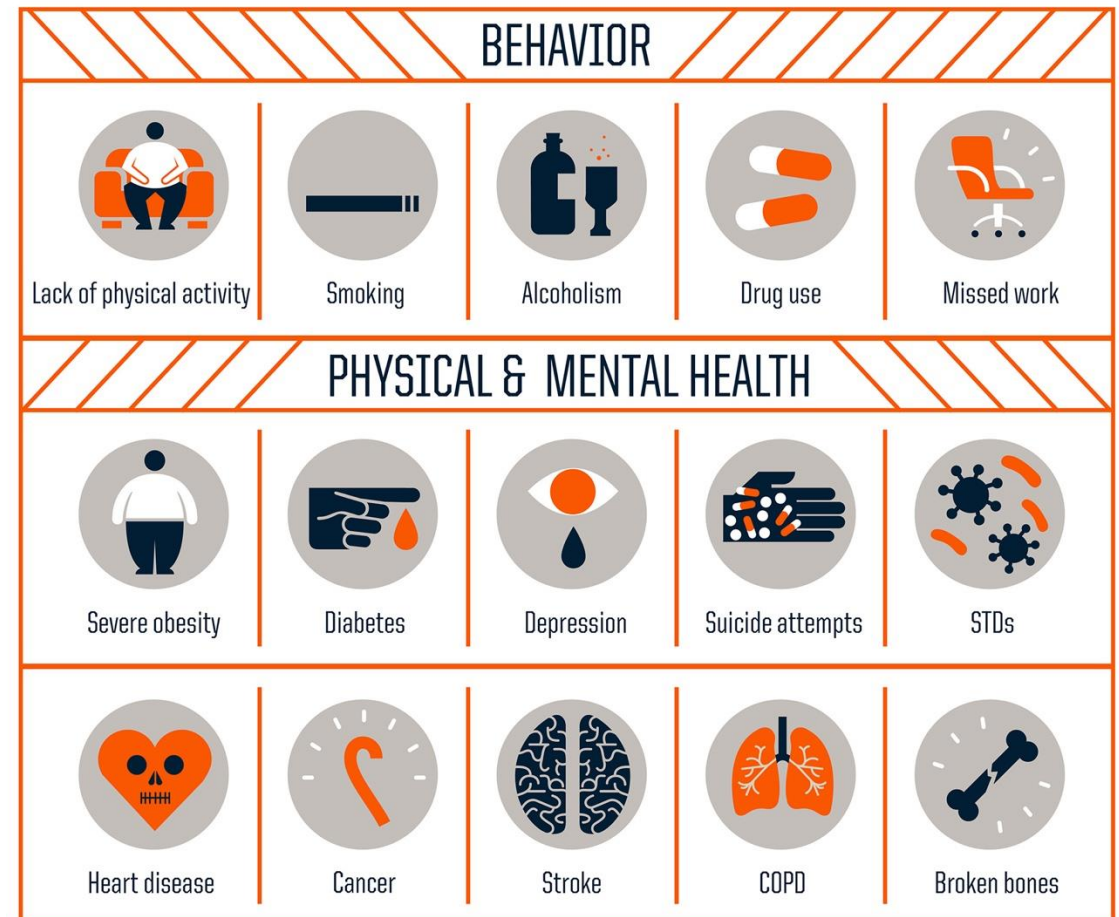


Diurnal Cortisol

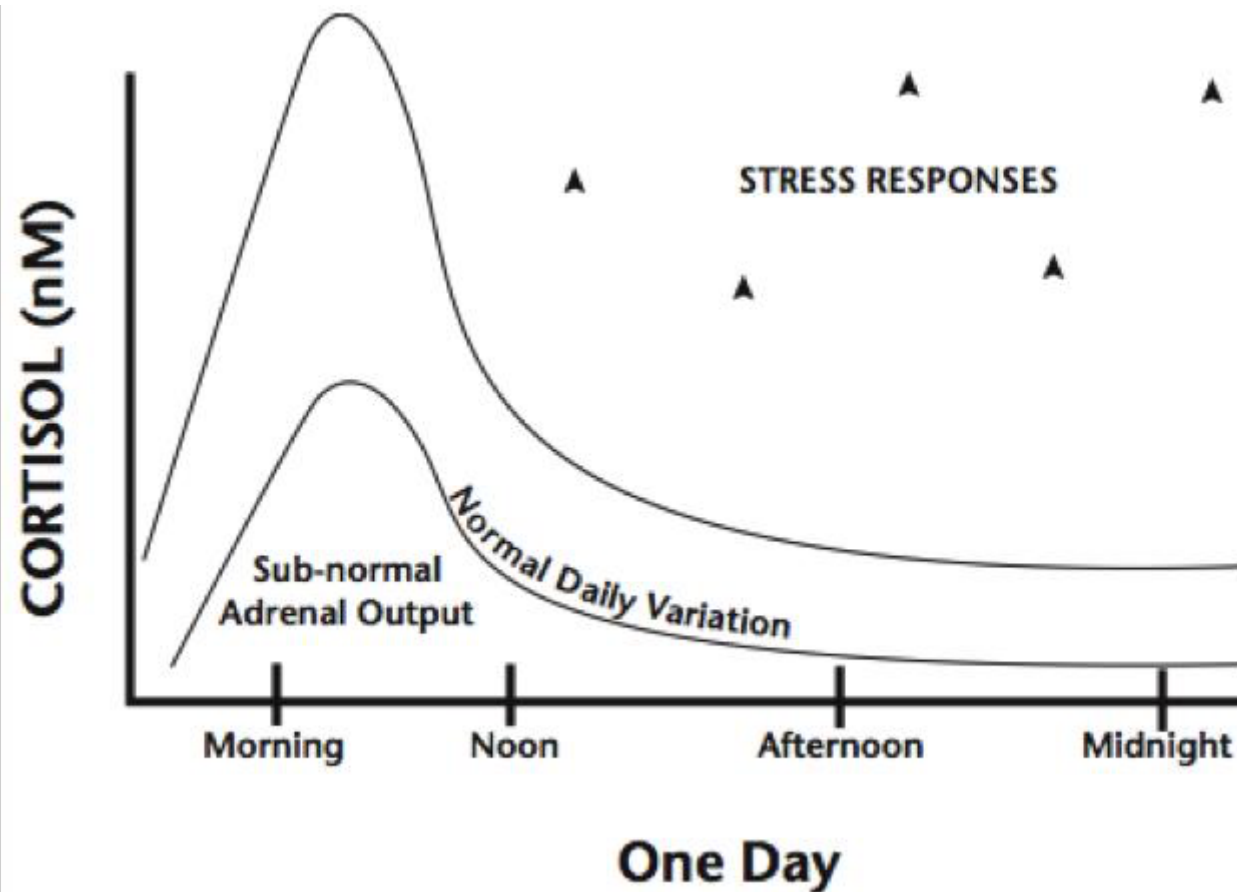


Adverse Childhood Experiences (ACEs)

Adverse Childhood Experiences (ACEs)



Diurnal Cortisol, Revisited



Cortisol Awakening Response (CAR)



One Day

Question:

How is the magnitude of the Cortisol Awakening Response (CAR) affected in children with Adverse Childhood Experiences (ACEs)?

Hypothesis:

Exposure to ACEs will increase the CAR in smaller children, but over time, chronic stress will give way to adrenal insufficiency, manifesting with a deceased CAR in older children.

Study

Examine and synthesize the relevant literature on the subject.

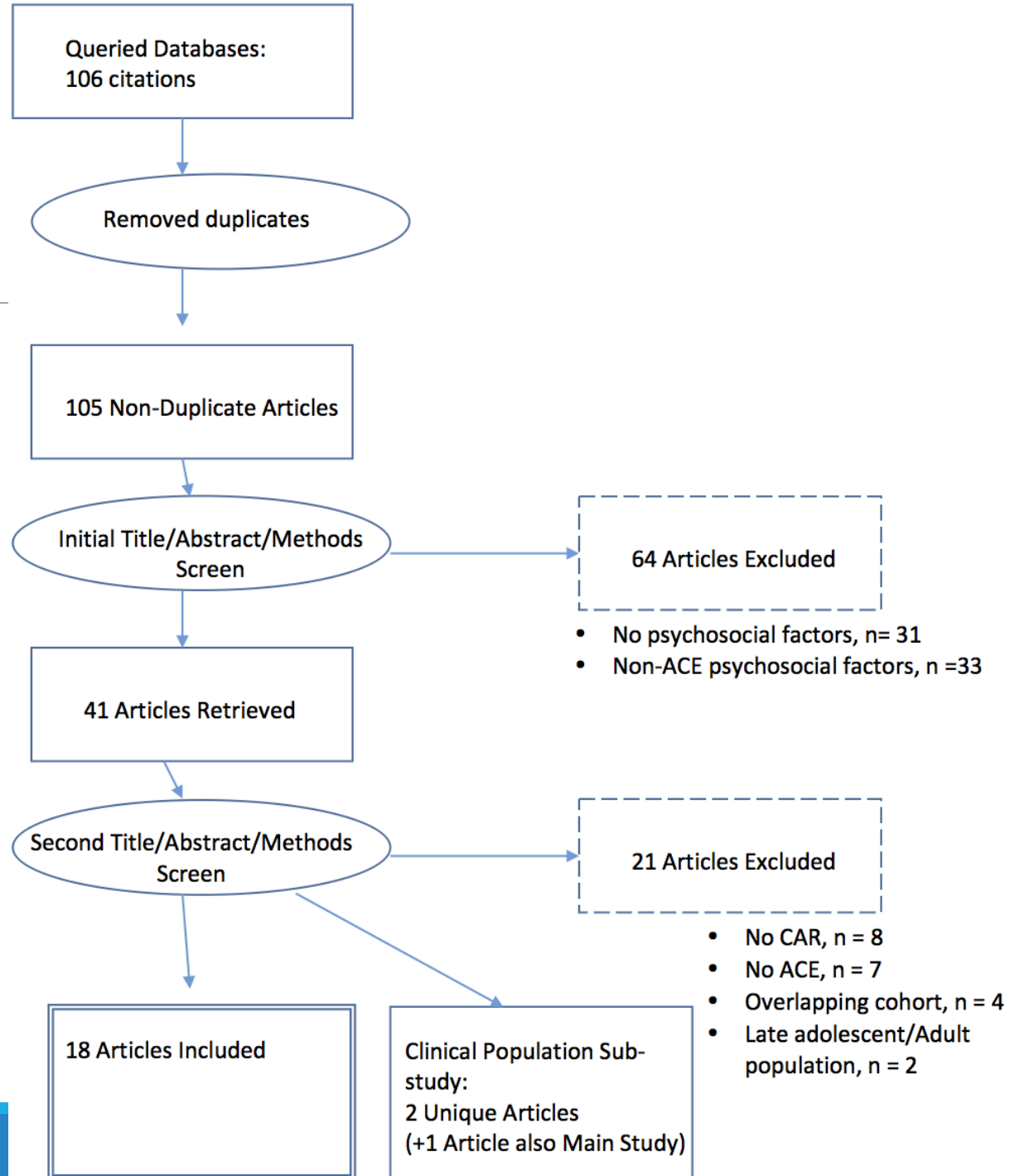
Steps

1. Query databases for potentially relevant articles
2. Eliminate irrelevant or uninterpretable articles
3. Compile, compare, and analyze final results of articles

Step 1: Query databases for potentially relevant articles

Database	Date	Search Terms	# of Records*
PubMed, PsycInfo	Aug 2013	Cortisol awakening response child(ren) Cortisol awakening response infant Cortisol awakening response adolescent	91
PubMed, PsycInfo	Apr 2015	Cortisol awakening response child(ren) Cortisol awakening response infant Cortisol awakening response adolescent	15
TOTAL			106

*62 additional articles were identified but eliminated during this first step, on the basis of the their titles.

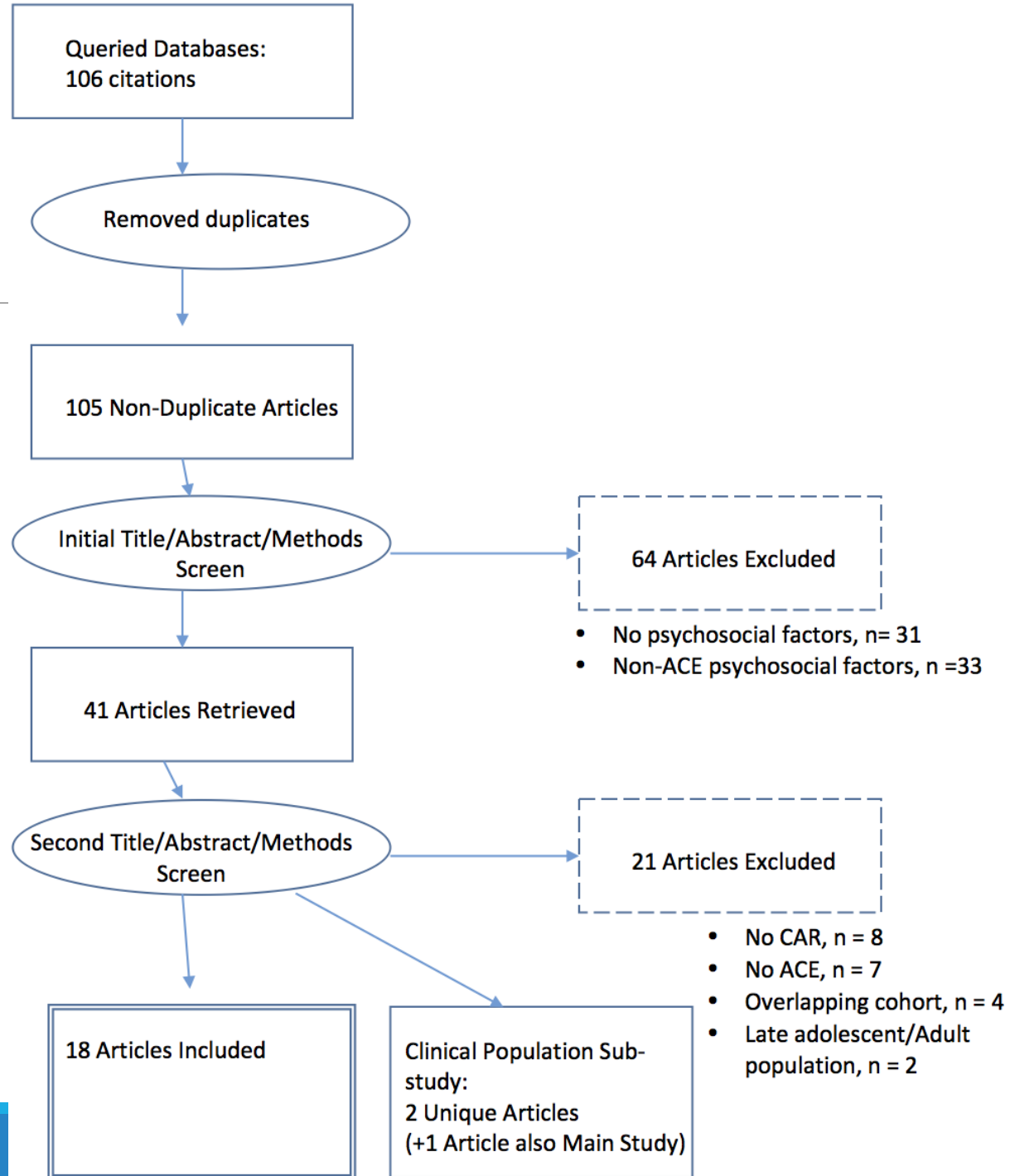


Step 2: Eliminate irrelevant or uninterpretable articles

Achieved through two rounds of independent Title/Abstract/Methods screens between the researchers, until consensus was achieved.

	A	B	C	D	E	F	G	H	I	J	K	L	M	N	O
1	Article	Year	1st Author	2nd Author	3rd Author	4th Author	5th Author	Title	Journal	Study	Psychosocial factor	ACE? (Y/N)	Psychosocial factor	Outcome Measure	Outcome measure
2	1	2006	Adam, EK					Transactions am	Psychoneuroendocrinology		1	0	Child trait, momentary emotion		
3	2	2013	Azak, S	Murison, J	Wentzel, L	Smith, L	Gunnar, M	Maternal Depression	Developmental Psychobiology		1	1	Maternal Depression		
4	3	2013	Ayer, L	Greaves, L	Althoff, F	Hudziak, G	Dieleman, J	Blunted HPA axis	Biological Psychology		1	0	Child behavior disorder	AUCg, AUCi	
5	4	2012	Bright, M	Granger, C	Frick, JE			Do Infants Show	Developmental Psychobiology		0	0			µg/dL
6	5	2003	Buske-K	Von Aue, J	Krieger, J	Weis, S	Rauh, W	Blunted Cortisol	Psychosomatic Medicine		0	0			
7	6	2003	Bartels, I	Van den, H	Sluyter, F	Boomsma, D	de Geus, E	Heritability of cortisol	Psychoneuroendocrinology		0	0			
8	7														
9	8	2012	Dietrich, J	Ormel, J	Buitelaar, J	Verhulst, F	Hoekstra, R	Cortisol in the morning	Psychoneuroendocrinology	TRAILS study	1	0	Child depressive and externalizing psychopathology		
10	9														
11	10	2013	Dykens, E	Lambert, W				Trajectories of Disruptive Behavior	Journal of Autism and Developmental Disorders		0	0			
12	11	2009	Freita, C	Hanig, S	Palmaso, J	Meyer, J	Wust, S	Cortisol awakening response	Psychoneuroendocrinology		1	1	Child ADHD, Adverse Parenting conditions, family conflict		
13	12	2004	Feder, A	Coplan, J	Goetz, R	Mathew, S	Pine, DS	Twenty-Four-Hour Cortisol Secretion	Biological Psychiatry		1	0	Child Anxiety, Depression		
14	13	2013	Gabriels, R	Agnew, J	Pan, Z	Holt, KD	Reynolds, CR	Elevated repetitive and restricted interests	Biological Psychology		1	0	Child Autism Spectrum Disorder		
15	14	2007	Greaves, L	Ferdinand, R	Oldehinkel, T	Sonkeijck, H	Ormel, J	Higher cortisol awakening response	Acta Psychiatrica Scandinavica		1	0			
16	15	2012	Gribbin, J	Atamura, K	Cairns, A	Harsh, J	LeBourgeois, M	The Cortisol Awakening Response	Developmental Psychobiology		0	0			
17	16	2013	Isaksson, A	Nilsson, L	Lindblad, F			Early psychosocial stress	European Child & Adolescent Psychiatry		1	0	Child ADHD, Fetal Adversity, Childhood Adversity		
18	17	2006	Jones, A	Godfrey, K	Wood, P	Osmond, C	Goulden, S	Fetal Growth and Cortisol	Journal of Clinical Endocrinology & Metabolism		0	0			
19	18	2013	Kaplow, N	Shapiro, N	Wardeck, J	Howell, E	Abelson, J	Psychological and physiological stress	Journal of Traumatic Stress		1	1	Child psychological distress, Parental bereavement		
20	19	2003	Kudielka, B	Kirschbaum, C				Awakening cortisol response	Psychoneuroendocrinology		1	0	"Health"		
21	20	2013	Kočovská, M	Wilson, F	Young, L	Wallace, J	Gorski, C	Cortisol secretion	Psychiatry Research		1	1	Child Reactive Attachment Disorder, Child Maltreatment		
22	21	2012	Michels, N	Sioen, I	De Vries, J	Huybrechts, E	Vanaelst, S	Children's Morning Cortisol	Hormone Research in Paediatrics		0	0			
23	22	2013	Martikair, K	Pesonen, L	Lahti, J	Heinonen, K	Feldt, K	Higher Levels of Cortisol	Journal of Clinical Endocrinology & Metabolism		0	0			
24	23	2009	Oskis, A	Loveday, J	Hucklebridge, L	Thorn, L	Clow, A	Diurnal patterns of cortisol	Psychoneuroendocrinology		1	0	Adolescent Trait Anxiety		
25	24	2013	O'Donoghue, K	Glover, V	Jenkins, S	Browne, S	Ben-Shlomo, Y	Prenatal maternal stress	Psychoneuroendocrinology	ALSPAC	1	1	Adolescent CAR change risk, Maternal prenatal mood		
26	25	2012	Oskis, A	Loveday, J	Hucklebridge, L	Wood, D	Clow, A	Recovery from Acute Stress	Case Reports in Psychiatry - Hindawi Publishing Corporation		1	0	Adolescent Anorexia Nervosa Recovery		
27	26	1997	Pruessner, M	Wolf, OT	Hellhammer, D	Buske-Kronenberg, H	von Auer, J	Free Cortisol Levels	Life Sciences	Meta-analysis	0	0			
28	27	2013	Platje, E	Jansen, L	Raines, J	Branje, S	Doreleijers, F	Longitudinal associations	Biological Psychology		1	0	Persistent aggressive/rule-breaking behavior		
29	28	2012	Pesonen, L	Kajantie, M	Heinonen, K	Pyhälä, I	Lahti, J	Sex-specific associations	Psychoneuroendocrinology		0	0			
30	29	2011	Quevedo, J	Johnson, J	Loman, J	LaFavor, L	Gunnar, M	The confluence of stressors	International Journal of Behavioral Development		1	1	Child neglect/deprivation		

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4	3	2013	Ayer, L	Greaves, R	Althoff, F	Hudziak, G	Dieleman, J	Blunted HPA axis	Biological Psychology		1	1	maltreatment	AUC	
5	4	2012	Bright, M	Granger, C	Frick, JE			Do Infants Show	Developmental Psychobiology		0	0	N	CAR	ug/dL
6	5	2003	Buske-K	Von Aue, J	Krieger, T	Weis, S	Rauh, W	Blunted Cortisol	Psychosomatic Medicine		0	0	N	CAR	nmol/L
7	6	2003	Bartels, S	Van den Bergh, L	Sluyter, I	Boomsma, D	de Geus, E	Heritability of cor	Psychoneuroendocrinology		0	0		REVIEW ARTICLE	
8	7														
9	8	2012	Dietrich, J	Ormel, J	Buitelaar, J	Verhulst, F	Hoekstra, R	Cortisol in the m	Psychoneuroenc	TRAILS study	0	0	-	CAR	
10	9														
11	10	2013	Dykens, E	Lambert, W				Trajectories of D	Journal of Autism and Developmental Psychology		0	0	-	adult participants	-
12	11	2009	Freita, C	Hanig, S	Palmasco, J	Meyer, J	Wust, S	Cortisol awakeni	Psychoneuroendocrinology		0	0	-		
13	12	2004	Feder, A	Coplan, J	Goetz, F	Mathew, S	Pine, DS	Twenty-Four-Hou	Biological Psychiatry		0	0	-		
14	13	2013	Gabriels, R	Agnew, J	Pan, Z	Holt, KD	Reynolds, C	Elevated repetiti	Biological Psychology		0	0			
15	14	2007	Greaves, R	Ferdinand, R	Oldehinkel, H	Sondejck, J	Ormel, J	Higher cortisol a	Acta Psychiatrica	TRAILS study	0	0	-	CAR	
16	15	2012	Gribbin, J	Atamura, K	Cairns, A	Harsh, J	LeBourgeois, M	The Cortisol Aw	Developmental Psychobiology		0	0	-	CAR	
17	16	2013	Isaksson, A	Nilsson, L	Lindblad, F			Early psychosoc	European Child & Adolescent Psychology		1	1	divorce, sub abu	CAR	
18	17	2006	Jones, A	Godfrey, P	Wood, P	Osmond, C	Goulden, S	Fetal Growth and	Journal of Clinical Endocrinology & Metabolism		0	0	-		
19	18	2013	Kaplow, N	Shapiro, G	Wardecki, J	Howell, I	Abelson, J	Psychological ar	Journal of Traumatic Stress		1	1	parental death	CAR	
20	19	2003	Kudielka, K	Kirschbaum, C				Awakening cortis	Psychoneuroendocrinology		0	0			
21	20	2013	Kočovská, M	Wilson, F	Young, L	Wallace, J	Gorski, C	Cortisol secretio	Psychiatry Research						
22	21	2012	Michels, N	Sioen, I	De Vries, J	Huybrechts, E	Vanaelst, S	Children's Mornin	Hormone Research in Paediatrics		0	0			
23	22	2013	Martikainen, M	Pesonen, J	Lahti, J	Heinonen, K	Feldt, K	Higher Levels of	Journal of Clinical Endocrinology and Metabolism		0	0			
24	23	2009	Oskis, A	Loveday, J	Huckleberry, B	Thorn, L	Clow, A	Diurnal patterns	Psychoneuroendocrinology		0	0			
25	24	2013	O'Donoghue, K	Glover, V	Jenkins, R	Browne, G	Ben-Shlomo, Y	Prenatal matern	Psychoneuroenc	ALSPAC	1	1	caregiver mental	CAR	
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27	26	1997	Pruessner, J	Wolf, OT	Hellhammer, D	Buske-Kemper, G	von Auer, J	Free Cortisol Lev	Life Sciences	Meta-analysis					
28	27	2013	Platje, E	Jansen, R	Raines, J	Branje, S	Doreleijers, F	Longitudinal ass	Biological Psychology		0	0			
29	28	2012	Pesonen, J	Kajantie, M	Heinonen, K	Pyhälä, I	Lahti, J	Sex-specific ass	Psychoneuroendocrinology		0	0			
30	29	2011	Quevedo, J	Johnson, J	Loman, C	LaFavor, L	Gunnar, M	The confluence of	International Journal of Behavioral Development		1	1	abuse/neglect	CAR	



Step 3: Compile, compare, and analyze final results of articles

This step presented unforeseen challenges...

The Challenge... Measuring CAR



One Day

The compromise... “Big Picture” Effect

Arrange the studies by cohort age, and compare the Results Sections' descriptions of the final effect (if not effect size), by “Increase” “Decrease” or “No significant effect”



Results



Mean Age (SD)	Effect on CAR	ACE	Study
1.167	ns	Early Childhood adversity	Saridjan et al., 2010
4.021 (1.729)	ns	Parent stress	Baumler et al., 2013
8.41	ns	Recent Life Events (CLES)	Michels et al., 2012
9.13 (1.41)	ns	Maternal anxiety	Williams et al., 2013
9.2 (0.9)	ns	Negative family life events	Donoho et al., 2011
9.6 (2.04)	↓	Child posttraumatic stress, parent maladaptive grief symptoms	Kaplow et al., 2013
10.5 (2.122)	↑	Maltreatment, urban violence, family functioning	Mello et al., 2015
11.08 (0.54)	ns	Perceived parental Emotional Warmth	Marsman et al., 2012
11.14 (1.28)	↓ (in girls, ns in boys)	Witnessing violence	Kliewer, 2006
12.23 (1.09)	↓	Bullying victimization	Knack et al., 2011
12.5 (2.0)	ns	Cumulative risk exposure	Willner, et al., 2014
12.8 (1.68)	↻	Accumulated adversity (Negative life events, Traumatic events, SES)	Gustafsson et al., 2010
12.93 (0.70)	↓	Adverse Early Care (AEC)	Quevedo et al., 2010
15.0 (1.5)	ns	Sexual abuse	Keeshin et al., 2013
15.3 (0)	↓	Prenatal anxiety	O'Donnell et al., 2013
15.3 (0.5)	↑	Perceived discrimination	Zeiders et al., 2012
17.06 (0.39)	ns	Baseline episodic stress, Baseline chronic stress	Vrshek-Schallhorn et al., 2013
19.48 (3.38)	↑	Parental Bipolar Disorder + Interpersonal Stress	Ostiguy et al., 2011



Future Directions

Compare effect sizes, standardized coefficients (F values, β values) in meta-analysis

Special Thanks

Jonathan Shuster, PhD