

# Adverse Childhood Events (ACE) Studies

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# Why Should You Care About These Studies?

“The seeds of adult dysfunction and pathology are sown in early childhood stress and trauma.”

The most dramatic neurodevelopmental period in life is from conception to about 4 years of age. Hence traumas, stresses, and other neurological insults during this time period most easily alter brain development in its most crucial stage and pave the way for lifelong CNS structure and functioning.

Most of the ACE studies were actually done in adults who were asked to retrospectively recount the presence or absence of ACEs

So What Happens in Response to Chronic  
Stress and Trauma?

# Question 1

Which of the following CNS structures becomes smaller in response to chronic stress and trauma?

A) Cingulate Cortex

B) Prefrontal Cortex

C) Hypothalamus

D) Hippocampus

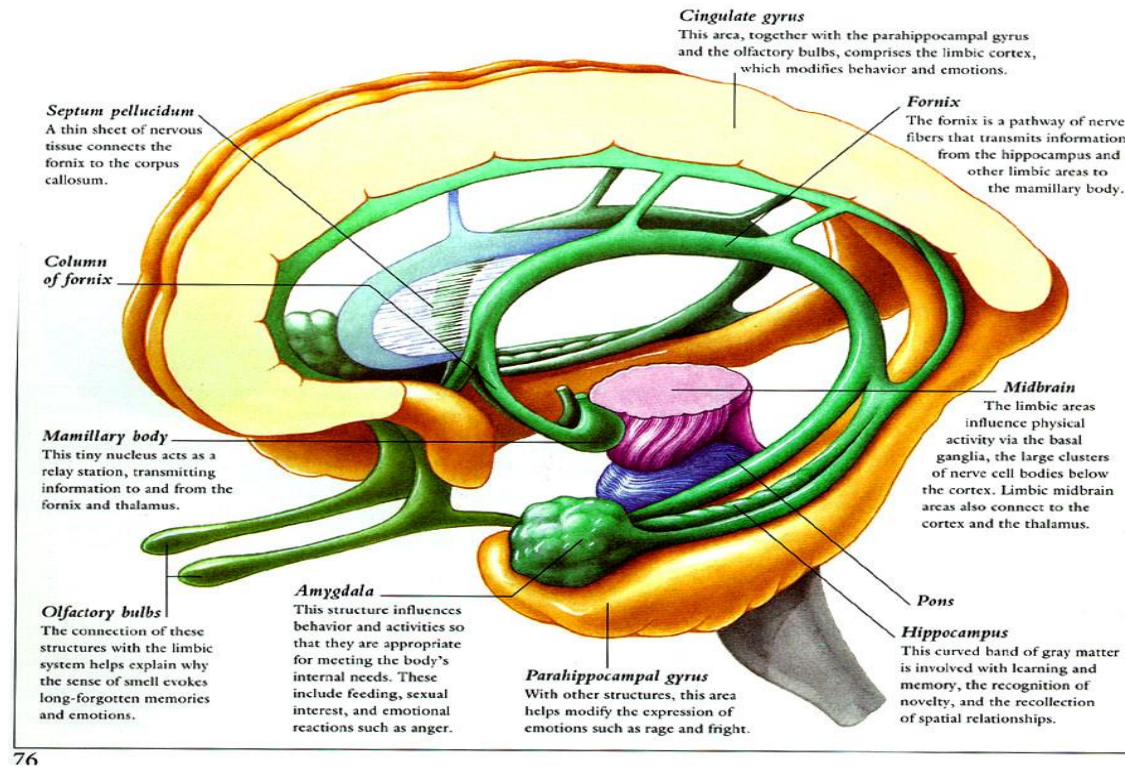
E) Pituitary Gland

# Answer

D (Hippocampus)

Prefrontal Cortex (executive functioning) and Cingulate Cortex (emotional processing and control) show decreased activation in stress but not reduced volume

# Limbic System/Cingulate Cortex



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# Limbic System/Cingulate Cortex

Figure AB-16: Limbic System

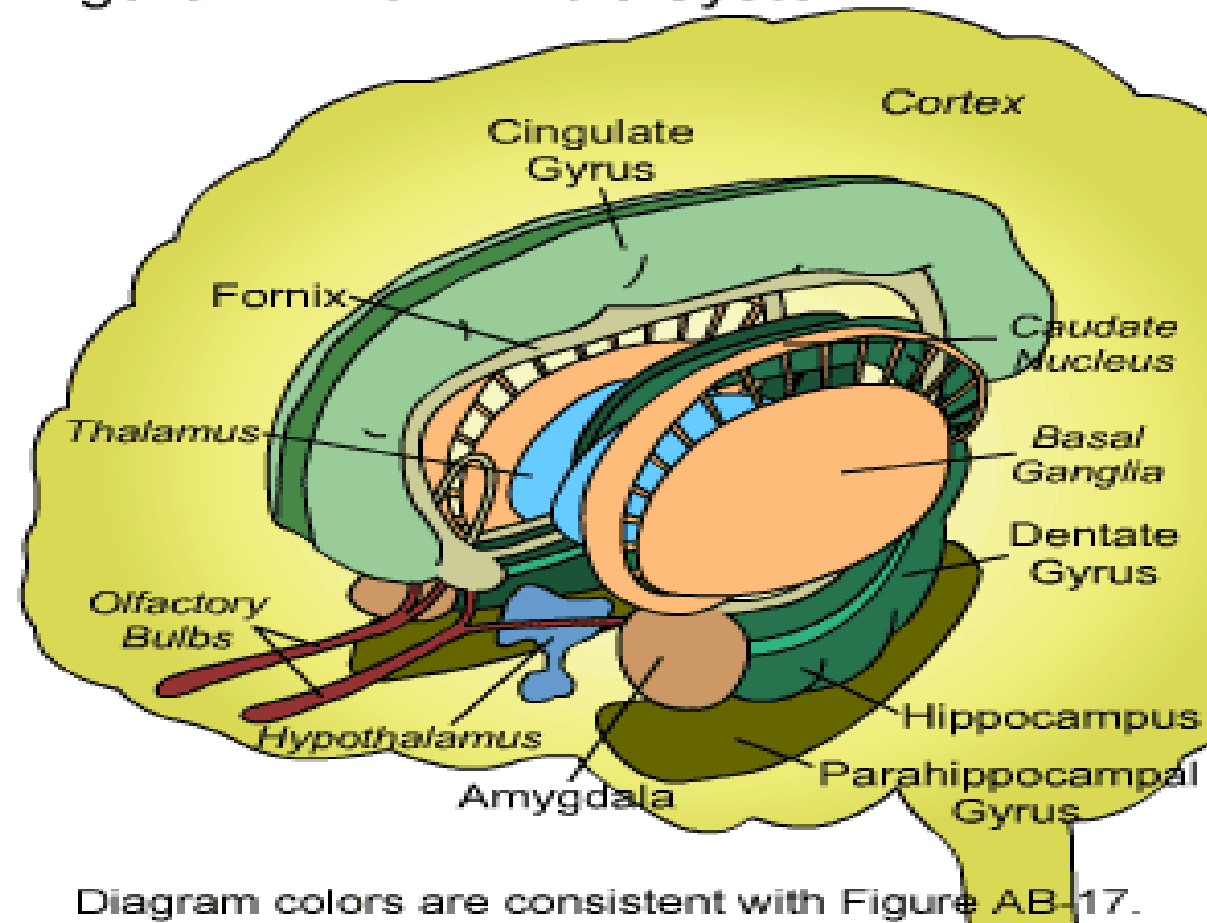


Diagram colors are consistent with Figure AB-17.

## Question 2

Which of the following compounds released in chronic stress and trauma is thought to be the cause of reduced hippocampal and amygdalar volumes?

- A) Adrenaline
- B) Serotonin
- C) Nor-Epinephrine
- D) Dopamine/Glutamate
- E) Cortisol



Answer

E (Cortisol)

What health problems are associated with chronically high levels of cortisol?

# Chronically High Levels of Cortisol

## Symptoms

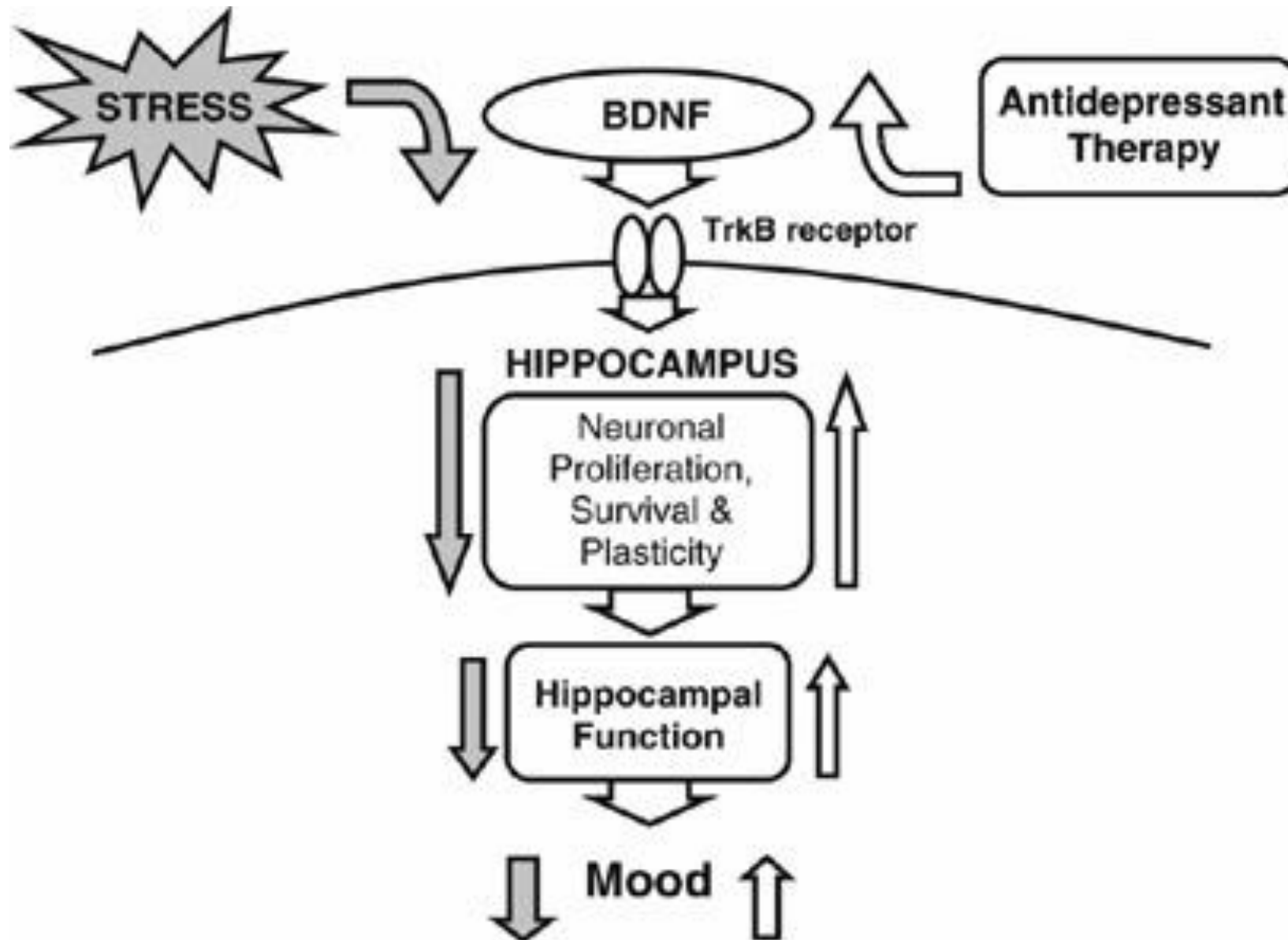
- Abdominal weight gain
- Red, round 'moon' face
- Thinning extremities
- 'Buffalo hump' →
- High blood pressure
- High blood sugar
- Muscle weakness
- Osteoporosis/ Fractures
- Infections
- Blood clots
- Visual field defects

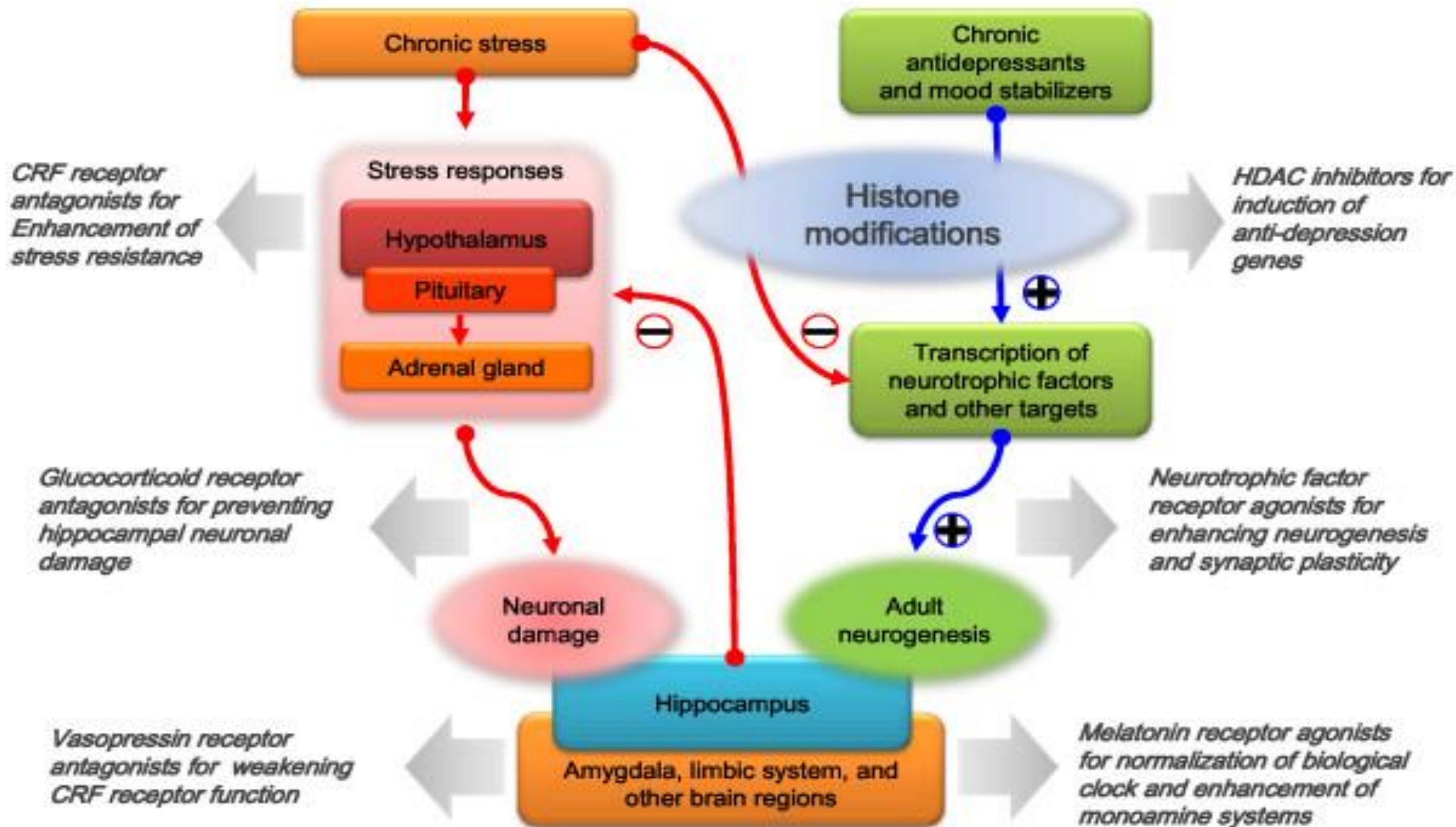


- Easy bruising
- Thinning skin
- Poor wound healing
- Acne
- Purple striae
- Hirsutism
- Female balding
- Menstrual irregularity
- Sleep disorders
- Excessive hunger
- Excessive thirst
- Frequent urination
- Sweating
- Anxiety
- Confusion
- Concentration loss
- Memory loss
- Depression
- Suicidal thoughts
- Panic attacks

# Effects of Hypercortisolemia (Issa 2010, Gray 2013)

- Chronic elevated levels of cortisol in the cerebral vasculature and CSF
- Reduced level of Brain-Derived Neurotrophic Factor (BDNF)
- Decreased volume of hippocampus/amygdala





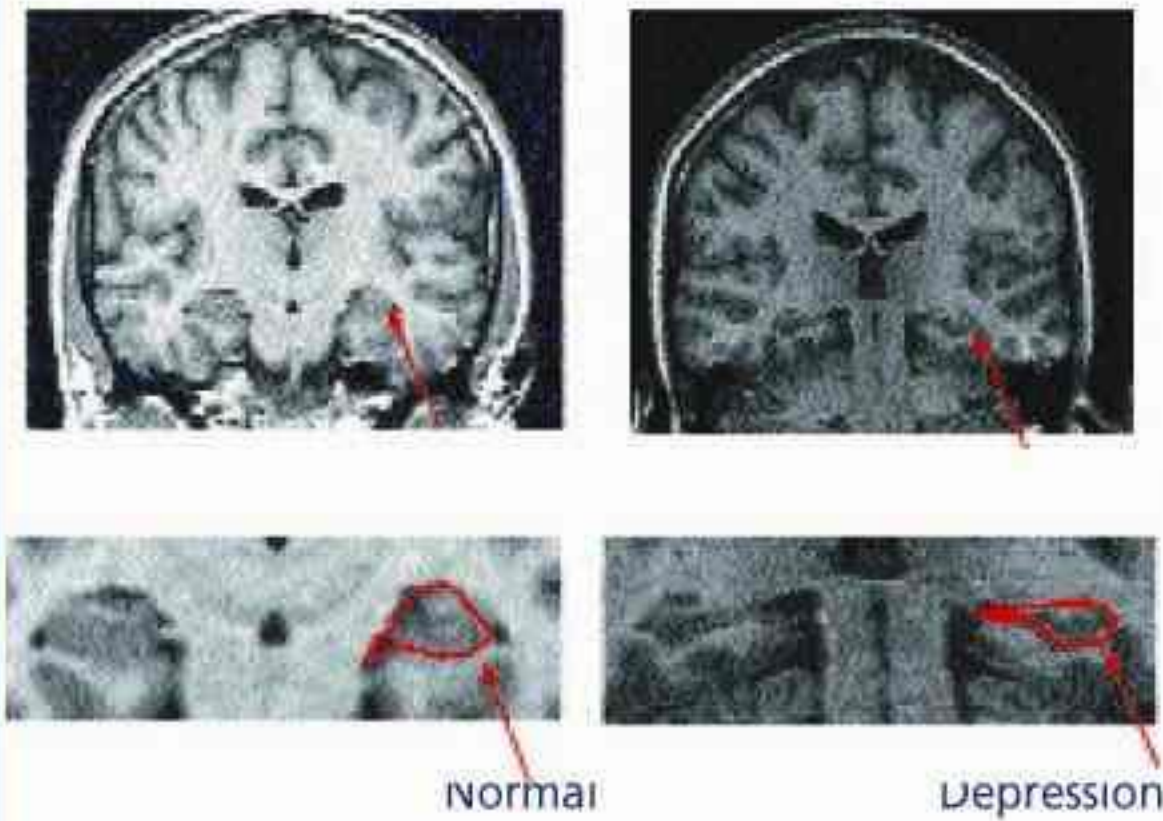



FIGURE 1. Atrophy of the hippocampus in depression.

Bremner JD. *CNS Spectrums*. Vol 7, No 2. 2002.

# Chronic Stress Effects on CNS Structures

Structure	Effect of Stress	Source
Prefrontal Cortex	Decreased OFC activity	Dedovic 2009
Cingulate Cortex	Decreased ACC volume	Meng 2014 Baldacara 2014
Amygdala	Decreased volume	Hanson 2014, Stratmann 2014
Hippocampus	Decreased volume (GM) Deactivity	Issa 2010, Gray 2013, Dedovic 2009
Temporo-Parietal Junction Insula	Decreased volume	Stratmann 2014, Meng 2014



“Activation” refers to increased blood flow and/or increased metabolism



# Summary of ACE Studies

61 so far

Initially a Joint Effort Between Kaiser Permanente  
and the U.S. Centers for Disease Control (CDC)

## Question 3

Which of the following would be considered an Adverse Childhood Event:

- A) Incarceration of a Household Member
- B) Parental Separation
- C) Household Members Using Substances
- D) Household Members with a Mental Illness
- E) Emotional Neglect

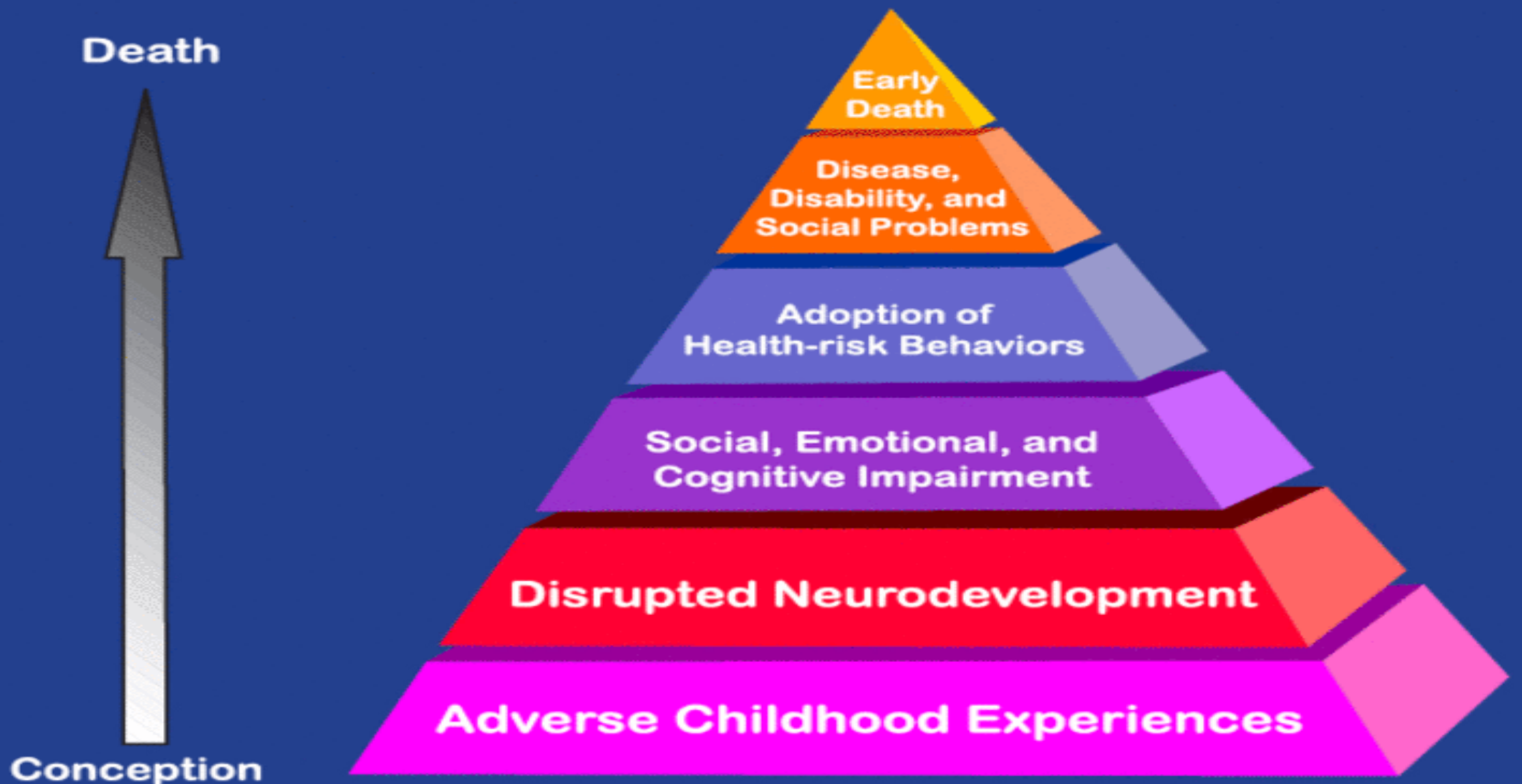
# DEFINITION of ACE

- Physical abuse
- Sexual abuse
- Emotional abuse
- Physical neglect
- Emotional neglect
- Mother treated violently
- Household substance abuse
- Household mental illness
- Parental separation or divorce
- Incarcerated household member

## Question 4

According to the Adverse Childhood Events Studies, which of the following processes is most proximal to the adverse event itself and ends up contributing to poor health outcomes?

- A) Disrupted Neurodevelopment
- B) Social, Emotional, and Cognitive Impairment
- C) Adoption of Health-Risk Behaviors
- D) Disease, Disability, and Social Problems
- E) Early Death



**Mechanisms by Which Adverse Childhood Experiences Influence Health and Well-being Throughout the Lifespan**

Association Does Not Necessarily Imply  
Causation

## *Relationship of childhood abuse and household dysfunction to many of the leading causes of death in adults (1998)*

Persons who had experienced four or more categories of childhood exposure, compared to those who had experienced none, had 4- to 12-fold increased health risks for **alcoholism, drug abuse, depression, and suicide attempt**; a 2- to 4-fold increase in **smoking, poor self-rated health, > or = 50 sexual intercourse partners, and sexually transmitted disease**; and 1.4- to 1.6-fold increase in **physical inactivity and severe obesity**.

The number of categories of adverse childhood exposures showed a graded relationship to the presence of adult diseases including **ischemic heart disease, cancer, chronic lung disease, skeletal fractures, and liver disease**.

## *Unintended pregnancy among adult women exposed to abuse or household dysfunction during their childhood (1999)*

After adjustment for confounders (marital status at first pregnancy and age at first pregnancy), the strongest associations between childhood experiences and unintended first pregnancy included frequent psychological abuse (risk ratio [RR], 1.4; 95% confidence interval [CI], 1.2-1.6), frequent physical abuse of the mother by her partner (RR, 1.4; 95% CI, 1.1-1.7), and frequent physical abuse (RR, 1.5; 95% CI, 1.2-1.8).

Women who experienced 4 or more types of abuse during their childhood were **1.5 times (95% CI, 1.2-1.8) more likely to have an unintended first pregnancy during adulthood than women who did not experience any abuse.**



## *Adverse childhood experiences and smoking during adolescence and adulthood (1999)*

Compared with those reporting no adverse childhood experiences, persons reporting 5 or more categories had **substantially higher risks of early smoking initiation** (odds ratio [OR], 5.4; 95% confidence interval [CI], 4.1-7.1), **ever smoking** (OR, 3.1; 95% CI, 2.6-3.8), **current smoking** (OR, 2.1; 95% CI, 1.6-2.7), and **heavy smoking** (OR, 2.8; 95% CI, 1.9-4.2). Each relationship between smoking behavior and the number of adverse childhood experiences was strong and graded (**P<.001**). For any given number of adverse childhood experiences, recent problems with depressed affect were more common among smokers than among nonsmokers.

*Adverse childhood experiences and sexually transmitted diseases in men and women: a retrospective study (2000)*

**Among those with 0, 1, 2, 3, 4 to 5, and 6 to 7 ACEs, the proportion with STDs was 4.1%, 6.9%, 8.0%, 11.6%, 13.5%, and 20.7% for women and 7.3%, 10.9%, 12.9%, 17.1%, 17.1%, and 39.1% for men.**

After adjustment for age and race, all odds ratios for reporting an STD had confidence intervals that excluded 1. Among those with 1, 2, 3, 4 to 5, and 6 to 7 ACEs, the odds ratios were 1.45, 1.54, 2.22, 2.48, and 3.40 for women and 1.46, 1.67, 2.16, 2.07, and 5.3 for men.

## *Body weight and obesity in adults and self-reported abuse in childhood (2002)*

Compared with no physical abuse (55%), being '**often hit and injured**' (2.5%) had a **4.0 kg** (95% confidence interval: 2.4-5.6 kg) **higher weight** and a **1.4** (1.2-1.6) **relative risk (RR) of body mass index (BMI) > or = 30.**

Compared with no verbal abuse (53%), being '**often verbally abused**' (9.5%) had an **RR of 1.9** (1.3-2.7) **for BMI > or = 40.**

The abuse associations were not mutually independent, however, because the abuse types strongly co-occurred.

## *Adverse childhood experiences and personal alcohol abuse as an adult (2002)*

Each of the eight individual ACEs was associated with a higher risk alcohol abuse as an adult.

Compared to persons with no ACEs, **the risk of heavy drinking, self-reported alcoholism, and marrying an alcoholic were increased twofold to fourfold** by the presence of multiple ACEs, regardless of parental alcoholism.

*Childhood abuse, neglect, and household dysfunction and the risk of illicit drug use: the adverse childhood experiences study (2003)*

Compared with people with 0 ACEs, people with  $\geq 5$  ACEs **were 7- to 10-fold more likely to report illicit drug use problems, addiction to illicit drugs, and parenteral drug use.**

The attributable risk fractions as a result of ACEs for each of these illicit drug use problems were 56%, 64%, and 67%, respectively. For each of the 4 birth cohorts examined, the ACE score also had a strong graded relationship to lifetime drug use.

## *Adverse childhood experiences and self-reported liver disease: new insights into the causal pathway (2003)*

Each of 10 ACEs increased the risk of liver disease 1.2 to 1.6 times ( $P < .001$ ). The number of ACEs (ACE score) had a graded relationship to liver disease ( $P < .001$ ).

Compared with persons with no ACEs, the **adjusted odds ratio of ever having liver disease among persons with 6 or more ACEs was 2.6 ( $P < .001$ )**. The ACE score also had a strong graded relationship to risk behaviors for liver disease. The strength of the ACEs-liver disease association was reduced 38% to 50% by adjustment for these risk behaviors, suggesting they are mediators of this relationship.

## *The association between adverse childhood experiences and adolescent pregnancy, long-term psychosocial consequences, and fetal death (2004)*

Teen pregnancy occurred in 16%, 21%, 26%, 29%, 32%, 40%, 43%, and 53% of those with 0, 1, 2, 3, 4, 5, 6, and 7 to 8 ACEs. As the ACE score rose from zero to 1 to 2, 3 to 4, and  $\geq 5$ , odds ratios for each adult consequence increased (**family problems**: 1.0, 1.5, 2.2, 3.3; **financial problems**: 1.0, 1.6, 2.3, 2.4; **job problems**: 1.0, 1.4, 2.3, 2.9; **high stress**: 1.0, 1.4, 1.9, 2.2; and **uncontrollable anger**: 1.0, 1.6, 2.8, 4.5, respectively).

The ACE score was associated with **increased fetal death after first pregnancy** (odds ratios for 0, 1-2, 3-4, and 5-8 ACEs: 1.0, 1.2, 1.4, and 1.8, respectively); teen pregnancy was not related to fetal death.

## *Insights into causal pathways for ischemic heart disease: adverse childhood experiences study (2004)*

Nine of 10 categories of **ACEs significantly increased the risk of IHD by 1.3- to 1.7-fold** versus persons with no ACEs.

The ACE-IHD relation was mediated more strongly by individual psychological risk factors commonly associated with ACEs than by traditional IHD risk factors.

We observed **significant association** between increased likelihood of reported **IHD** (adjusted ORs) and **depressed affect** (2.1, 1.9 to 2.4) and **anger** (2.5, 2.1 to 3.0) as well as traditional risk factors (smoking, physical inactivity, obesity, diabetes and hypertension), with ORs ranging from 1.2 to 2.7.



# *Adverse childhood experiences and the risk of depressive disorders in adulthood (2004)*

**Childhood emotional abuse increased risk for lifetime depressive disorders**, with adjusted odds ratios (ORs) of 2.7 [95% confidence interval (CI), 2.3-3.2] in women and 2.5 (95% CI, 1.9-3.2) in men.

Strong, dose-response relationship between the ACE score and the probability of lifetime and recent depressive disorders (P<0.0001). This relationship was attenuated slightly when a history of growing up with a mentally ill household member was included in the model, but remained significant (P<0.001).

## *Long-term consequences of childhood sexual abuse by gender of victim (2005)*

Compared to reporting no sexual abuse, a history of suicide attempt was more than twice as likely among both men and women who experienced CSA ( $p < 0.05$ ).

Compared with those who did not report CSA, men and women exposed to CSA were at a **40% increased risk of marrying an alcoholic, and a 40% to 50% increased risk of reporting current problems with their marriage** ( $p < 0.05$ ).

## *Adverse childhood experiences and hallucinations (2005)*

Compared to persons with 0 ACEs, those with 7 or more ACEs had a **five-fold increase in the risk of reporting hallucinations.**

# *Adverse childhood experiences and the association with ever using alcohol and initiating alcohol use during adolescence (2006)*

Initiating alcohol use **by age 14 years was increased two- to threefold by individual ACEs** ( $p < .05$ ).

ACEs also accounted for a **20% to 70% increased likelihood of alcohol use initiated during mid adolescence.**

The total number of ACEs (ACE score) had a very strong graded relationship to initiating alcohol use during early adolescence and a robust but somewhat less strong relationship to initiation during mid adolescence

## *Adverse childhood experiences and prescribed psychotropic medications in adults (2007)*

Compared with persons with an ACE Score of 0, persons with a score of equal to or more than 5 had a nearly **threefold increase in rates of psychotropic prescriptions.**

Graded relationships were observed between the score and prescription rates for antidepressant, anxiolytic, antipsychotic, and mood-stabilizing/bipolar medications; rates for persons with a score of equal to or more than 5 for these classes of drugs increased 3-, 2-, 10-, and 17-fold, respectively.

# *Health-related quality of life among adults who experienced maltreatment during childhood (2008)*

Health-related quality-of-life data (or "utilities") were imputed from the Medical Outcomes Study 36-Item Short Form Health Survey using the Short Form-6D preference-based scoring algorithm.

Persons who experienced childhood maltreatment had **significant and sustained losses in health-related quality of life in adulthood** relative to persons who did not experience maltreatment

## *Adverse childhood experiences and chronic obstructive pulmonary disease in adults (2008)*

Compared to people with an ACE Score of 0, those with an ACE Score of  $\geq 5$  had **2.6 times the risk of prevalent COPD, 2.0 times the risk of incident hospitalizations, and 1.6 times the rates of prescriptions** ( $p < 0.01$  for all comparisons).

**These associations were only modestly reduced by adjustment for smoking.** The mean age at hospitalization decreased as the ACE Score increased ( $p < 0.01$ ).

## *The relationship of adverse childhood experiences to a history of premature death of family members (2009)*

**Family members** of respondents who experienced any type of ACEs were **more likely to have elevated prevalence for premature death** relative to those of respondents without such experience ( $p < 0.01$ ).

The highest risk occurred among those who reported having been physically neglected and living with substance abusing or criminal family members during childhood.

Powerful graded relationship between the number of ACEs and premature mortality in the family was observed for all age group, and comparison between groups reporting 0 ACE and  $\geq 4$  ACEs yielded an OR of 1.8 (95%CI, 1.6-2.0).



# *Adverse childhood experiences are associated with the risk of lung cancer: a prospective cohort study (2010)*

The ACE score also showed a **graded relationship to the incidence of lung cancer**.

Risk of lung cancer for those with  $\geq 6$  ACEs **was increased approximately 3-fold** (hospital records: RR = 3.18, 95%CI = 0.71-14.15; mortality records: RR = 3.55, 95%CI = 1.25-10.09; hospital or mortality records: RR = 2.70, 95%CI = 0.94-7.72).

After a priori consideration of a causal pathway (i.e., ACEs  $\rightarrow$  smoking  $\rightarrow$  lung cancer), risk ratios were attenuated toward the null, although not completely. Persons with  $\geq 6$  ACEs were roughly **13 years younger on average at presentation** than those without ACEs.

# *Adverse childhood experiences and frequent headaches in adults (2010)*

Each of the ACEs was associated with an increased prevalence and risk of frequent headaches.

As the ACE score increased the prevalence and risk of frequent headaches increased in a "dose-response" fashion.

**The risk of frequent headaches increased more than 2-fold** (odds ratio 2.1, 95% confidence interval 1.8-2.4) in persons with an ACE score  $\geq 5$ , compared to persons with and ACE score of 0

# Summary

Adverse Childhood Events have been linked to:

- Alcoholism (early)
- Smoking (early)
- Drug Abuse
- Depression
- Psychosis
- Psychotropic Meds
- Suicide Attempts
- Decreased Quality of Life
- Increased Sexual Partners and STDs
- Decreased Physical Activity
- Unintended First Pregnancy
- Increased Fetal Death
- Severe Obesity
- Chronic Heart, Lung, Liver, Skeletal, and Autoimmune Disease
- Headaches
- Cancer
- Family/Financial/Job/Marital Problems
- Premature Death of Family Members
- Subsequent Stress
- Uncontrollable Anger
- Overall Health-Related Quality of Life

What Do You Take Away From This  
Information?

# Take Home Message

Bi-Directional Screening

Referring for Appropriate Treatment

Prevention

Public Policy Efforts