

Amygdala and Hippocampal Volume Reductions as
Candidate Endophenotypes for Borderline Personality
Disorder: A Meta-Analysis of Magnetic Resonance
Imaging Studies

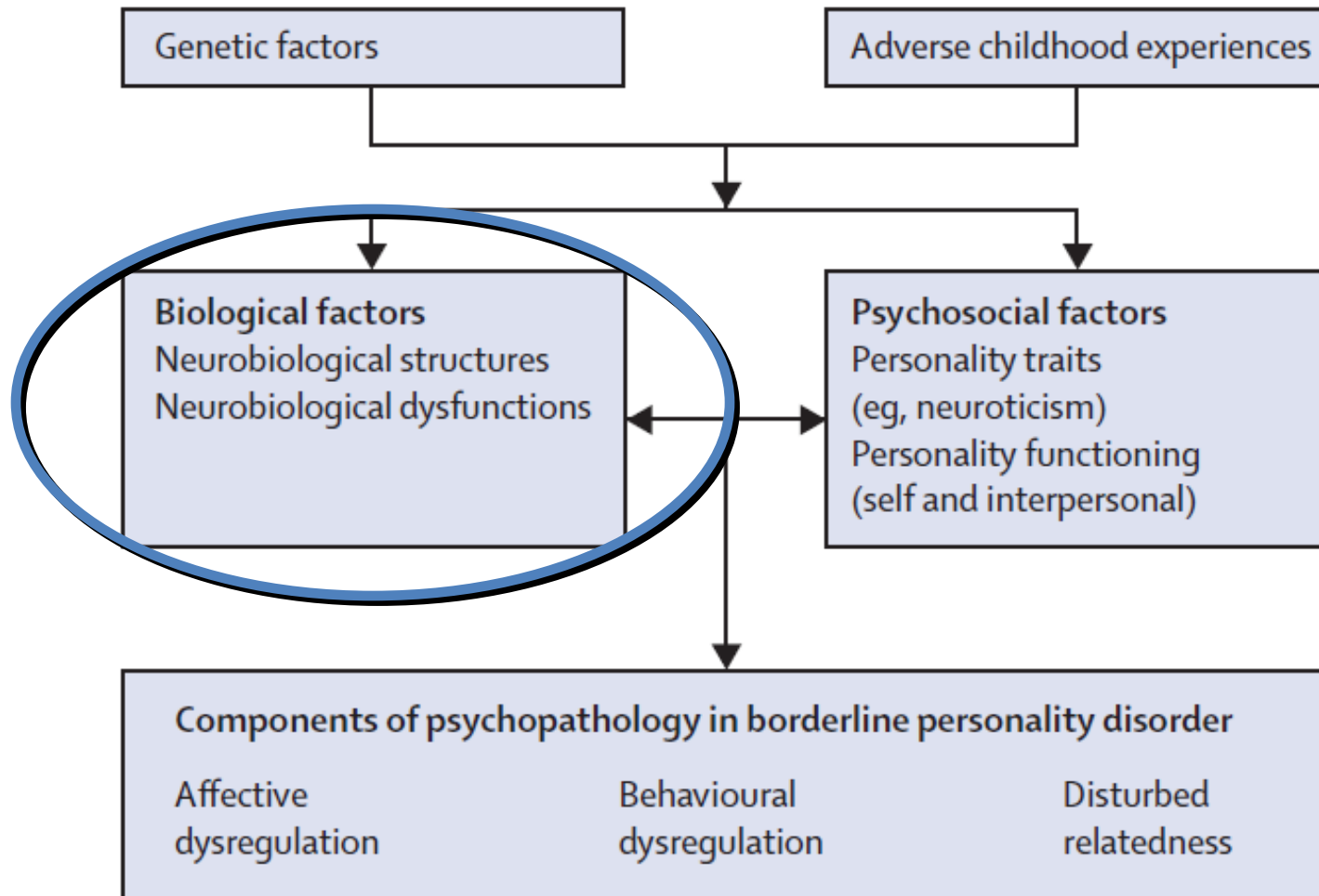
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What is Borderline Personality Disorder?

- Characterized by a pervasive pattern of instability of interpersonal relationships, self-image, and affects, and marked impulsivity (American Psychiatric Association, 2000)
- Affects approximately 1% of the general population (Lenzenweger et al., 2007)
- BPD is substantially influenced by genetic factors with concordance rates of 45% and 21% among monozygotic and dizygotic twin pairs, respectively (Distel et al., 2009)



Endophenotype Approach

- The endophenotype concept in psychiatry has its roots in evolution and insect biology, where it was used to describe biological markers which lie between the gene and the disease process (Gottesman & Gould, 2003)

Decreased complexity
of both phenotype
and genetic analysis

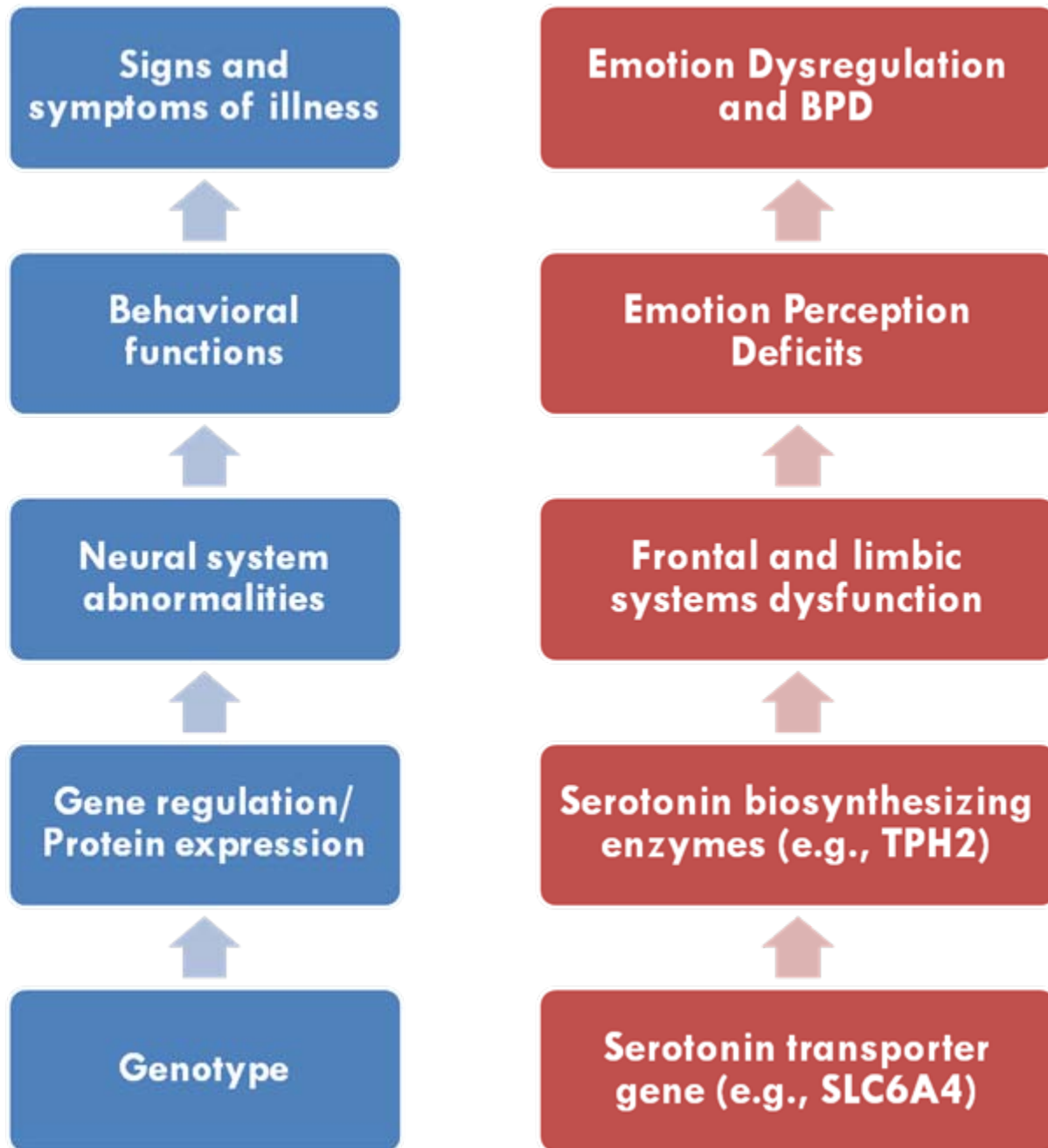


Less

More

Number of Genes

Increased complexity
of both phenotype
and genetic analysis



Endophenotypes in Psychiatry

Are associated
with illness in
the population

Are heritable

Are state
independent

Co-segregate
with illness in
families

Are found in
unaffected
family members
at a higher rate
than in the
general
population

Amygdala and Hippocampus Volumes in BPD

- These structures may be affected by experiences of emotional and physical trauma (Bremner et al., 1995; Bremner et al., 1997), which are often considered etiologic in the development of BPD (Herman et al., 1989)
- One of the earliest volumetric MRI studies of BPD showed a nearly 16% reduction in the size of the hippocampus and 8% reduction in the size of the amygdala bilaterally compared to healthy controls (Driessen et al., 2000)

Hypotheses

1. Volumetric decreases of the amygdala and hippocampus will be present in BPD
2. Volumetric decreases of the amygdala and hippocampus will not be associated with treatment status or comorbid psychopathology

Current Meta-Analysis

- Results from 11 studies comprising 205 BPD patients and 222 healthy controls
- Mean age = 30.4 years
- Nearly all BPD patients were female (93.9%)
- Most were currently on medications for acute symptom reduction (70.7%) and had a history of abuse (61.6%)

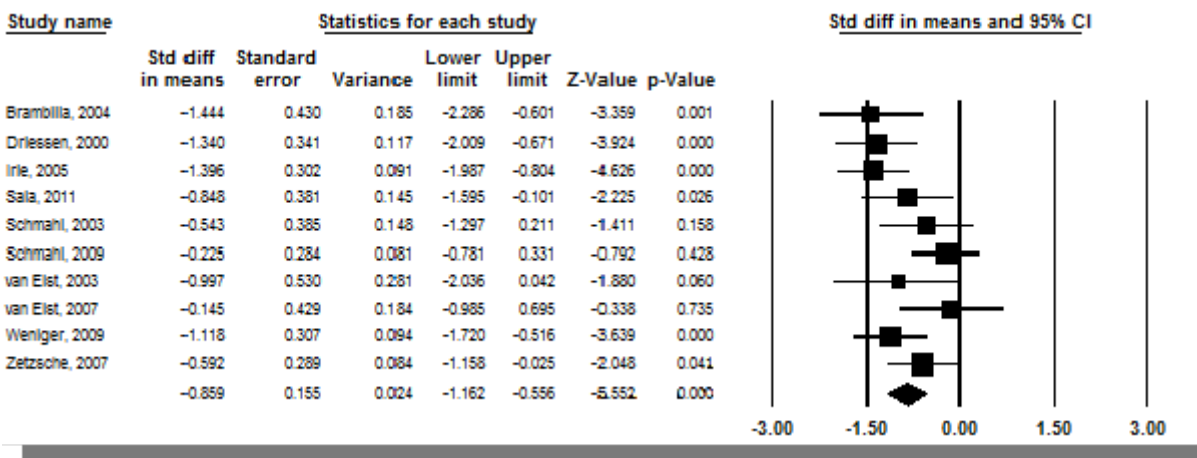
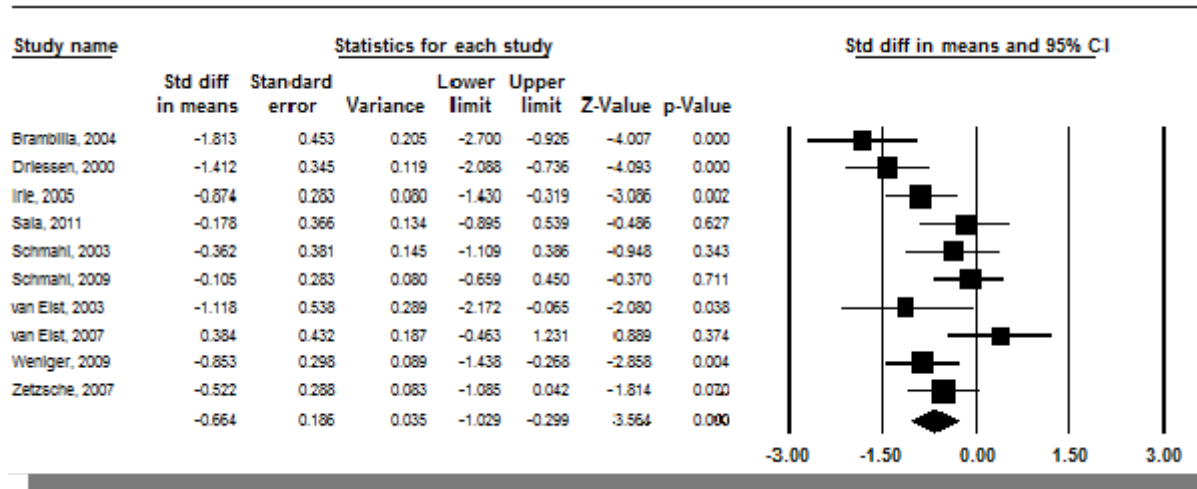
Primary Findings

- Patients showed an average 11% and 13% decrease in the size of the hippocampus and amygdala, respectively

Primary Findings

- Hippocampus:
 - ▣ Left side $d = -0.66$ ($p < 0.001$)
 - ▣ Right side $d = -0.86$ ($p < 0.001$)

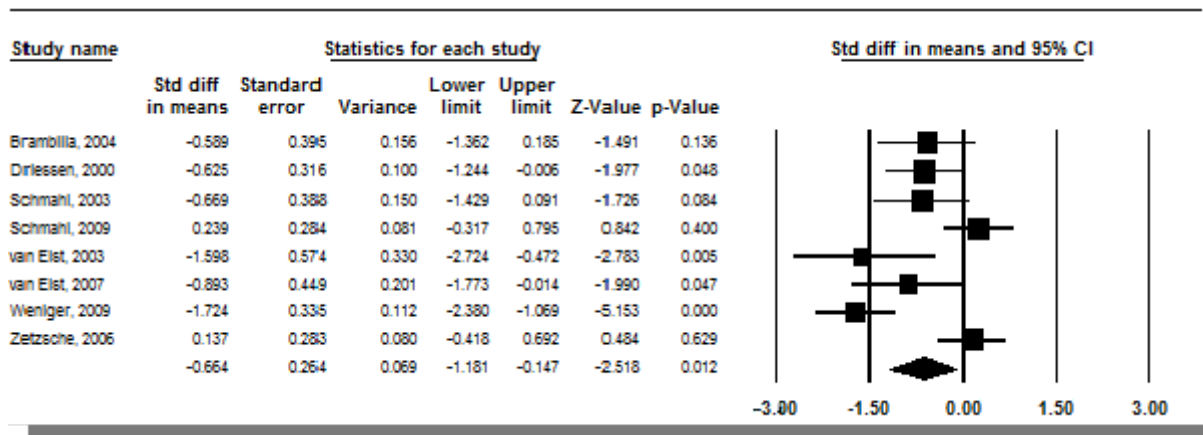
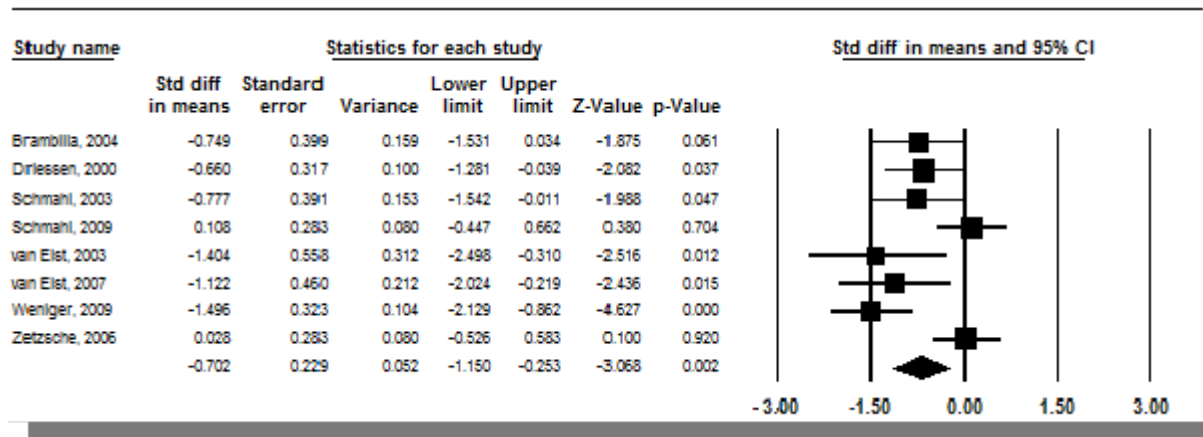
Left and Right Hippocampus



Primary Findings

- Amygdala:
 - ▣ Left side $d = -0.70$ ($p = 0.002$)
 - ▣ Right side $d = -0.66$ ($p = 0.012$)

Left and Right Amygdala

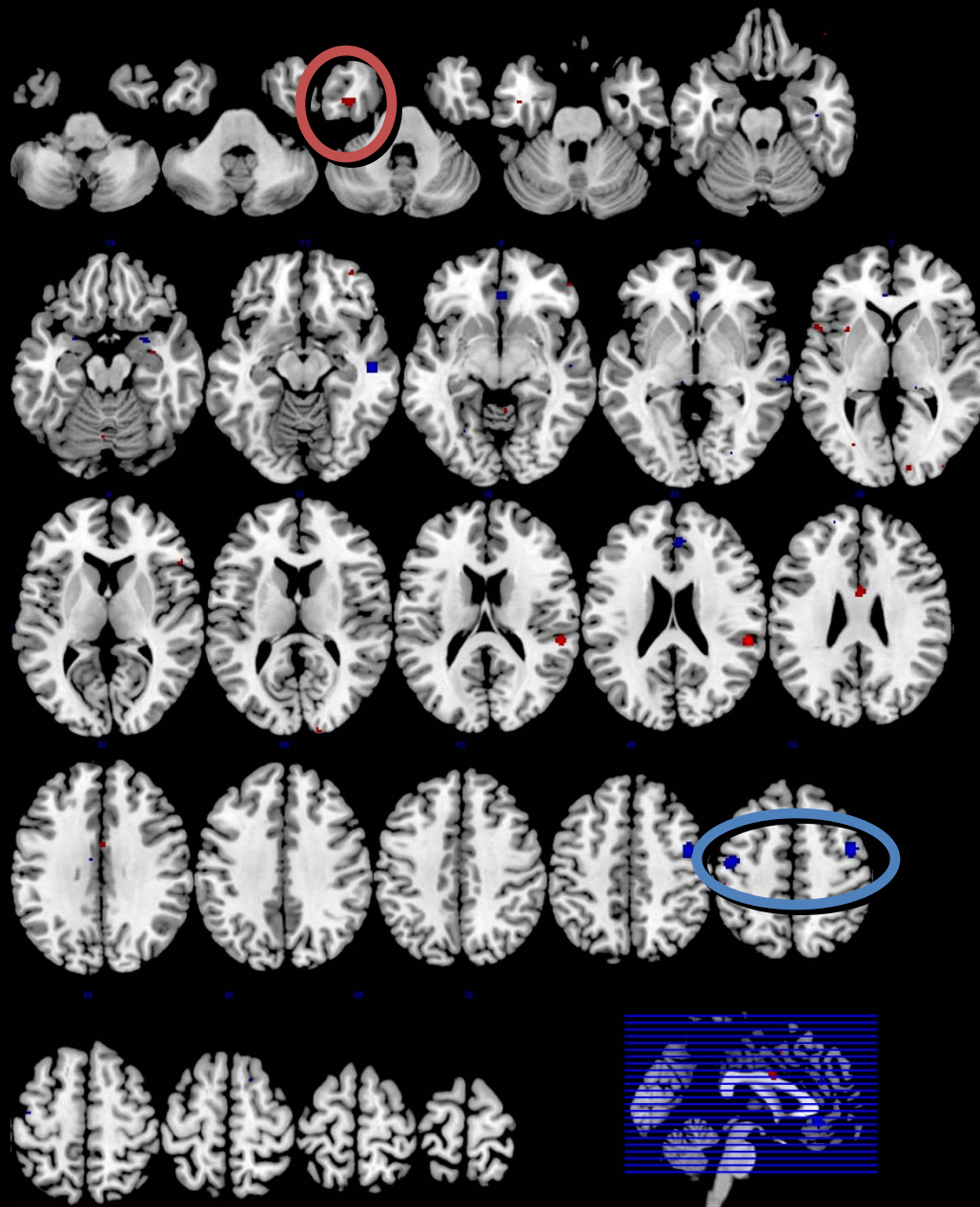


Secondary Analyses

□ State-of-Illness

■ Amygdala and hippocampal volume differences were not correlated with either:

1. Medication/Treatment Status (all p 's $> .05$)
2. Comorbid Psychiatric Disorder (all p 's $> .05$)
 - Major Depression
 - Post-Traumatic Stress Disorder
 - Substance Use Disorders



Conclusions

- There are dramatic volume reductions of the hippocampus and amygdala in BPD
 - ▣ Perhaps more severe reductions than are found in schizophrenia, depression and bipolar disorder
 - ▣ Not related to state of illness or comorbid psychiatric disorders
- Volume reductions in these structures show significant promise as candidate endophenotypes for BPD

Implications

- Incorporation of these measures may improve genetic linkage analyses to identify specific susceptibility genes for BPD
- Open doors for early identification and prevention of illness in at-risk individuals

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