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)
Leichsenring et al. (2011)
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

Increased complexity of both phenotype and genetic analysis

Number of Genes
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%)

Ruocco, Amirthavasagam, & Zakzanis (in press)
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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