Relationship between BDNF genotype, hippocampus volume, and anxiety

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Background
• Anxiety is one of the most prevalent mood disturbances in the U.S. and can be present in subclinical forms. (NIMH, 2012)
• Anxiety may be associated with alterations in hippocampus volume (Rusch et al., 2001)
• Smaller hippocampus volume is typically more associated with higher anxiety
• Anxiety may be associated with genetic variations of the Brain Derived Neurotrophic Factor gene (BDNF) (Hashimoto, 2007)
  • The BDNF gene has a Met and Val allele.
  • The Met allele is more typically associated with higher anxiety
  • The Met allele is also typically associated with smaller hippocampus volume (Hajek et al., 2012)
• The goal of this project is to investigate the underlying neurobiological components of anxiety.

Research Hypotheses
1. Met+ carriers will have smaller hippocampus volumes than Val/Val
2. Individuals with smaller hippocampus volumes will have higher anxiety
3. Met+ carriers will have higher anxiety than Val/Val

Methods
Participants:
• 62 total participants
  • Val/Val: 41 (22 males, 19 females; mean age: 20.3)
  • Met+: 21 (11 males, 10 females; mean age: 19.4)

Procedure:
• Phase 1
  • Genotyping
  • Completion of State-Trait anxiety inventory (STAI)
• Phase 2:
  • MRI scan
  • Voxel based morphometry analysis (VBM)
  • Completion of the state scale of the STAI

STAI:
• Self-report measure of anxiety consisting of two scales (Spielberger, 1970)
• State: A measure of anxiety at the time of testing
• Trait: A measure of more general and long-standing anxiety
• Both scales have 20 questions each and scores range from 1-4 on each question, so total scores can range from 20-80. A higher score corresponds to higher anxiety

Voxel Based Morphometry (VBM)
• Technique of analyzing a structural MRI brain scan to gain a measure of volume

Hypothesis 1: Met+ carriers will have smaller hippocampus volumes than Val/Val
1. Total hippocampus volume was not significantly different between BDNF genotype groups (p=0.147)
2. However, in a voxel-wise analysis, the Met+ group showed smaller grey matter volume in two areas of bilateral hippocampus than the Val/Val group

Hypothesis 2: Individuals with smaller hippocampus volumes will have higher anxiety
• There was no significant correlation between hippocampus volume and anxiety (p=0.353)

Hypothesis 3: Met+ carriers will have higher anxiety than Val/Val
• Met+ carriers show trend of lower anxiety than Val/Val
• This finding was only significant in measures of state anxiety at the time of fMRI scanning (p=0.017)
• Right posterior hippocampus (p=0.013)
• Left anterior hippocampus (p=0.036)

Results

Interactions
The relationship between hippocampus volume and anxiety did not differ between Val/Val and Met+:
1. The BDNF and hippocampus interaction does not significantly predict anxiety (p=0.784)
2. Hippocampus volume was categorized into high or low. The interaction between hippocampus volume and BDNF group did not significantly predict anxiety (p=0.139)

Conclusions
• Aside from the voxel-wise analysis, the three main hypotheses were not well supported by the data
• Possible reasons include:
  • Perhaps the study was studying a too limited subset of anxiety
  • Limited population size
  • Between BDNF groups, there may be other underlying differences
  • What does grey matter size really tell us?
  • Clinical vs. Subclinical anxiety trends

Future Directions
• How BDNF genotype may have different effects depending on anxiety level (clinical vs. subclinical)
• How grey matter volume may affect anxiety (is bigger better or worse)
• How anxiety may affect hippocampus volume and therefore cloud the expected relationship between BDNF genotype and anxiety level
• Other unmeasured factors might impact anxiety

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