Relationship Between Cortisol Levels and Depression

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Introduction

Depression

- Depression is the leading cause of disease worldwide with over 300 million people currently diagnosed
- To be diagnosed with depression, a patient needs to have just 5 of the 9 symptoms defined by the American Psychiatric Association DSM-5. This means there are 256 possible combinations of depressive symptoms that could be presented by an individual

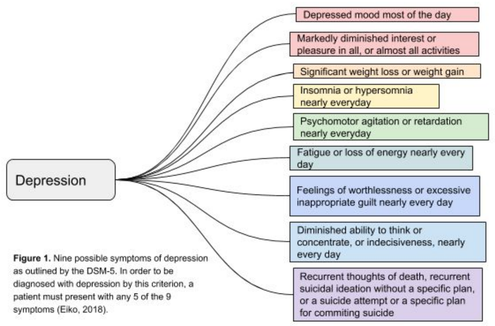


Figure 1. Nine possible symptoms of depression as outlined by the DSM-5. In order to be diagnosed with depression by this criterion, a patient must present with any 5 of the 9 symptoms (Eiko, 2018).

Single Nucleotide Polymorphisms

- Single nucleotide polymorphisms (SNPs) are changes in the sequence of the DNA in some genes; our lab is interested in the contribution to depression of SNPs in several genes including GR and MR receptors
- Previous work has demonstrated the list of SNPs below are the ones associated with depression

SNP	Association	Phenotype
rs41423247 (BCL1)	GR	Hypersensitivity
rs56149945 (N363S)	GR	Hypersensitivity
rs10052957 (Tth3)	GR	Resistance
rs12086634	11BHSD	Hypersensitivity
rs846910	11BHSD	Resistance
rs2070951	MR	Hypersensitivity
rs5522	MR	Resistance
rs1360780 (FK506)	FK506 binding protein 5	Hypersensitivity

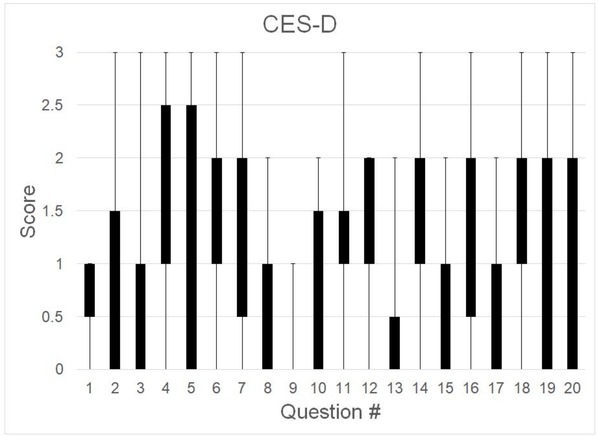
Hypothesis

There will be a positive correlation between the SNPs associated with increased cortisol responsiveness found within an individual's DNA sample and the likelihood that that individual will be more likely to suffer from depression

Experimental Approach

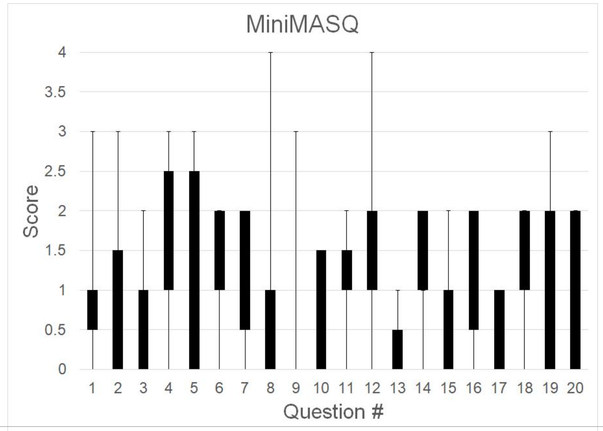
- Sample Collection
  - Process
    - Consent Form and Demographic Question
    - Collect DNA Sample by rotating the otate brush on the inside of cheek
    - Complete CES-D
    - Complete Mini MASQ
    - Debrief
- After Collection
  - Extract and isolate the DNA from each of the samples
  - By using allele specific PCR we can determine if an individual has any SNPs within their genes that may be related to GR and MR hypersensitivity or resistance
  - Perform an Agarose Gel Electrophoresis

Results



CES-D Questions

1. I was bothered by things that usually don't bother me.	11. My sleep was restless.
2. I did not feel like eating; my appetite was poor.	12. I was happy.
3. I felt that I could not shake off the blues even with help from my family or friends.	13. I talked less than usual.
4. I felt I was just as good as other people.	14. I felt lonely.
5. I had trouble keeping my mind on what I was doing	15. People were unfriendly.
6. I felt depressed.	16. I enjoyed life.
7. I felt that everything I did was an effort.	17. I had crying spells.
8. I felt hopeful about the future.	18. I felt sad.
9. I thought my life had been a failure.	19. I felt that people disliked me.
10. I felt fearful.	20. I could not get "going."



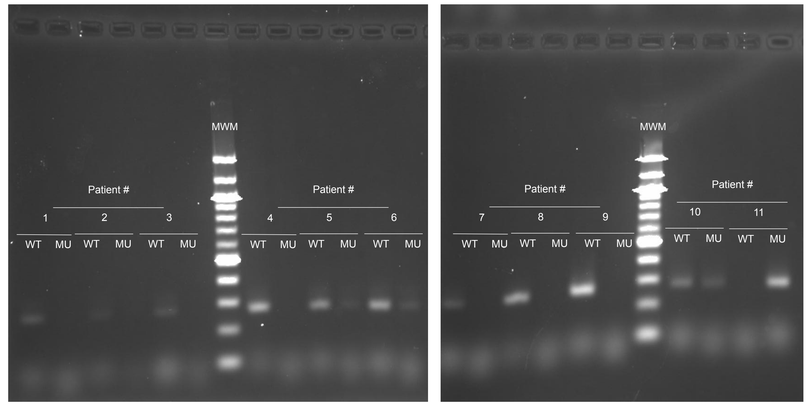
Mini-MASQ Questions

1. Felt really happy	14. Had trouble swallowing
2. Felt tense or "high strung"	15. Felt like I had a lot of interesting things to do
3. Felt depressed	16. Had hot or cold spells
4. Was short of breath	17. Felt like a failure
5. Felt withdrawn from other people	18. Felt like I was choking
6. Felt dizzy or lightheaded	19. Felt really lively, "up"
7. Felt hopeless	20. Felt uneasy
8. Hands were cold or sweaty	21. Felt discouraged
9. Felt like I had a lot to look forward to	22. Muscles twitched or trembled
10. Hands were shaky	23. Felt like I had a lot of energy
11. Felt like nothing was very enjoyable	24. Was trembling or shaking
12. Felt keyed up, "on edge"	25. Felt like I was having a lot of fun
13. Felt worthless	26. Had a very dry mouth

The Box and Whisker Plots above show the range of responses for each question within the CES-D and Mini MASQ surveys

Other Experiments from the Cohen Lab

Allele Specific PCR for Rs846910



Example of allele specific PCR for detecting single nucleotide polymorphisms. In this example DNA samples were analyzed to detect the rs846910 SNP of the 11 beta-hydroxysteroid dehydrogenase enzyme. Two separate reactions are performed- one to detect the presence of the wild type allele and the other to detect the mutant allele.

Conclusions

- From the Work So Far
  - We have been able to identify some "spike questions" that will serve as a basis for us trying to identify certain alleles that are connected to the expression of depression (CES-D)
  - We are also able to see how certain individuals are expression depression and what degree of depression they fall into (Mini MASQ)
- Overall Goal
  - The long term goal of this research is to create the ability to predict risk for depression so that clinicians can provide early intervention for at-risk patients, improving treatment and patient outcomes
- Future Work
  - Continuing allele specific PCR so we can determine if an individual has any SNPs within their genes that may be related to GR and MR hypersensitivity or resistance
  - Create a multiplex assay where both alleles of a particular SNP can be detected in a single reaction, specifically adapt our current allele specific PCR to the simpler, 1-step multiplex assay

References and Acknowledgements

- Chen, N., Chen, J., Wang, Z., Zhang, S., & Zuo, W. (2016). Does mineralocorticoid receptor play a vital role in the development of depressive disorder? *Life Sciences, 152*, 76-81.

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