The Effect of Genes on the Stress Response

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Project Purpose
To better understand the role that corticotropin releasing hormone genes play in the stress response.

Project Importance
In response to stress, the brain initiates a cascade of chemical reactions that prepares the body to deal with the stressful situation. This cascade begins in the hypothalamus with the production of corticotropin releasing hormone (CRH), a chemical messenger that leads to the release of adrenocorticotropin hormone (ACTH) from the pituitary and subsequently the release of cortisol. Although these chemical reactions prepare the body to deal with potentially dangerous situations in an adaptive way, chronic or high exposure to these biochemicals can have maladaptive physiological and behavioral effects. For example, chronic stress can disrupt the normal function of the immune system. A study with rhesus macaques found that highly nervous animals expressed a disrupted anti-inflammatory response to cortisol levels, suggesting that chronic exposure to cortisol had made these animals glucocorticoid resistant (Capitanio et al., 2011; Higley et al., 1992). Such a disruption can lead to inflammatory diseases.

While environmental factors are certainly related to stress, evidence suggests that high HPA Axis activity following stress shows an individual trait-like consistency (Capitanio et al., 1998). Such consistency hints at a possible genetic source for variability in the stress response system. One study with rhesus macaques showed that a single nucleotide polymorphism (SNP), CRH-248 C/T, up-regulates the production of CRH, inhibits the down-regulation of CRH expression in the presence of glucocorticoids, and is related to stress-induced alcohol consumption (Barr, 2009). Other studies have shown that genetic variants CRH-2232 C/G and NPY-1002 T/G also affect the stress response system (Barr, 2011). This project involves genotyping rhesus macaques that took part in a biobehavioral assessment (BBA) at the California National Primate Research Center. By determining the genotype of these animals, we will be able to look at the effects of genotype on behavioral and physiological measures that have already been taken and thus come to better understand the way genetics influence the stress response system.

Project Profile Body
This project seeks to better understand the role of genetic variation in the stress response. The animals involved in the study will be approximately three hundred subjects that all took part in the CNPRC's BBA program in 2010. These animals live in open field cages in groups of approximately 100-150 animals. When they are between three and four months of age, infants are removed from the field cage, separated from their mothers and run through a battery of behavioral tests that lasts for 25 hours. Over the course of testing four blood plasma samples are taken and a number of analyses are performed on the samples, including checking for cortisol concentration and white blood cell levels.

For this project, I will use blood plasma samples collected from rhesus macaques at the California National Primate Research Center (CNPRC) to determine the animals' genotype at several genetic loci. Classification of these animals' genotypes, specifically at CRH-248, CRH-2232, and NPY-1002, will allow us to compare behavioral variation to genetic variation and to see the way genes, behavior, and the immune system interact. This information can be added to the data already gained from these animals to facilitate future research.

Anticipated Academic Outcome
Using the data I gather from this project, I hope to find a significant relationship between genotypes and physiological measures taken during BBA testing. I plan on using this research to prepare a poster I can submit to present at the Utah Conference of Undergraduate Research (UCUR), the Mary Lou Fulton Undergraduate Research Conference, and the American Society of Primatology Conference in 2015. I also plan to write an article that can be submitted to a scientific journal for publication.

This project will also help me better understand the research process and the way genes affect physiology and behavior. I am majoring in neuroscience and plan to pursue a career in medical research.

Working on this project will give me a glimpse of what it's like managing my own research project and broaden my understanding of genetics.

Qualifications

This summer I participated in an internship at the CNPRC. I gained experience working with coppery titi monkeys and rhesus macaques. I worked directly with Dr. Erin Kinnally, who studies genetics and neurobehavioral development. I learned to isolate DNA from rhesus macaque blood and umbilical cords. I currently work in Dr. J. Dee Higley's lab here at Brigham Young University. Using information from databases from the National Institutes of Health, my research team is currently analyzing the effects of CRH and NPY genotypes in a small number of subjects for their effect on physiological and behavioral measures of anxiety and fear. I have submitted an abstract on this research and plan to present a poster at the UCUR and to ultimately author a scientific journal article.

For this project I will continue working with Dr. Higley. Dr. Higley has worked with nonhuman primates for over 25 years and done extensive research on the interaction of genes and environment across developmental time points. Dr. Higley acted as the head of the primate research lab at the National Institute of Alcohol Abuse and Alcoholism and the National Institutes of Health (NIH) for 20 years. Over the last eight years he has been a mentor for a number of ORCA grant recipients as they have completed their projects.

Project Timetable

The projected timeline for this project is:

- By mid-March 2014, have finalized list of animal subjects for whom to pull blood samples for genotyping
- By mid-April 2014 coordinate the transfer of blood samples from the CNRPC to the NIH for genotyping
- During the summer 2014 analyze data from the BBA with new genotype data and finalize data analyses by August 2014
- By mid-October 2014 prepare and submit a poster for the UCUR
- During the months of September-November work on an article to submit for publication to a scientific journal.
- By January 2015, submit an abstract to present a poster at the American Society of Primatology in 2015.

Scholarly Sources

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