Genomic Associations between Anxiety Disorders, Intelligence and Creativity

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Abstract: People with high levels of intelligence and creativity are able to understand complex topics, find and recognize patterns, picture vivid imagery in their heads and think more, unique thoughts at a fast pace. Since anxiety disorders such as generalized anxiety, obsessive compulsive disorder (OCD) and post traumatic stress disorder (PTSD) often involve the imagining of worse case scenarios and the ruminating of negative thoughts, it is natural to wonder if intelligence and or creativity might be associated with anxiety disorders. This paper investigates the genetic basis of anxiety disorders as well as the traits of intelligence and creativity. This is done using genome wide association studies (GWAS) that contain genes associated with each trait. The distribution of beta coefficients for the genes of each trait were used to find that the associations of PTSD, Intelligence and Creativity to genes was more narrow than OCD and anxiety, where their functionality seemed to be spread out across more genes. Manhattan plots for each chromosome showed that each trait/disorder was associated with genes in each chromosome implying that the expressions of these traits and disorders are complex and come from large systems and interaction of genes rather than any localized area. Finally, each trait was compared with each disorder. It was found that no genes are associated with creativity and any of the anxiety disorders. Genes for intelligence were not associated with OCD or general anxiety disorders. However there were 4 genes that were found to be highly associated with both PTSD and Intelligence. The large spread of genes associated with Intelligence and PTSD imply that these genes could just play some low level function that helps later downstream in the expression of both intelligence and PTSD.

I. Introduction

Anxiety disorders such as generalized anxiety, obsessive compulsive disorder (OCD) and post traumatic stress disorder (PTSD) have been shown to be somewhat associated with genes. Genome Wide Association Studies (GWAS) have been used to show different genetic variants that are highly associated with anxiety disorders and neuroticism [1]. GWAS were able to find a genetic basis for both OCD and OCS (obsessive-compulsive symptoms) and use this data to give credence to the idea that OCD is just an extreme case of OCS [2]. Similar methods have been used to show that there is a highly heritable component of PTSD [3]. These examples emphasize the fact that specific genes can be found to be highly associated with anxiety disorders lending to the idea that there is a genetic component to these disorders.

A similar connection between mental traits and genes can be found with the traits of intelligence and creativity. 24 genomic loci have been found to be linked to variation in intelligence, implying a genetic component for the trait [4]. GWASs have even been combined with machine learning techniques to not only find the connection between certain genes and creativity, but also the overlap between genes associated with creativity and genes associated with psychiatric disorders [5].

The topic of this last study motivates the purpose of this paper. Traits such as creativity and intelligence allow a person to create more advanced and vivid hypothetical thoughts and scenarios in their head. Ruminating on worst case scenario thoughts and situations is a common symptom of anxiety disorders. This idea motivates the hypothesis that higher intelligence and/or creativity in individuals increases the likelihood that one also has some sort of anxiety disorder, whether it is generalized anxiety, OCD or PTSD.

This paper starts to address this hypothesis from the genomic perspective by analyzing the genetic overlap between GWAS studies on generalized anxiety, OCD and PTSD with the traits of Intelligence and Creativity. If anxiety disorders are caused by higher levels of intelligence and/or creativity, and traits such as intelligence and creativity have a genetic component, then it would be reasonable to see that genes that are highly correlated with high intelligence and creativity would also be correlated with these anxiety disorders. For example, if a gene is found to be highly correlated with intelligence and PTSD, it might be possible that this gene increases the likelihood of intelligence which increases the likelihood of PTSD, hence explaining the association between the gene and PTSD. Of course, genetic overlap between the trait and the disorder is not enough to prove a statement like this. The point of this paper is to see if overlap exists to provide directions for further research on the connection between intelligence/creativity and anxiety disorders.

II. Methods

This paper utilizes GWAS datasets from the GWAS Catalog created by the National Human Genome Research Institute. On this website, one can access summary reports of studies that find genes associated with a specific trait, all at a low enough p-value to show significance. This paper uses 5 datasets under the following trait names: “creativity measurement,” “intelligence,” “anxiety disorder,” “post-traumatic stress disorder symptom measurement,” and “obsessive-compulsive disorder.” A list of each data set with the amount of data points can be seen in Table 1.

Table 1 *Dataset Name and Size*

Name	Number of Entries
Creativity Measurement	31
Intelligence	3846
Anxiety disorder	681
Post-traumatic stress disorder symptom measurement	190
Obsessive-compulsive disorder	276

Each dataset contained 38 columns where where then reduced to 5 of interests, chromosome number (CHR_ID), position of the gene on the chromosome (CHR_POS), p-value of associated (P), the Beta value (BETA), and the gene name (REPORTED GENE(S)). The distribution of beta coefficients for the three disorders were plotted to analyze the strength and consistency of the gene's effect on the trait (Figure 1). The distribution of beta coefficients was also then plotted for each trait against each disorder (Figure 2,3) for the same analysis.

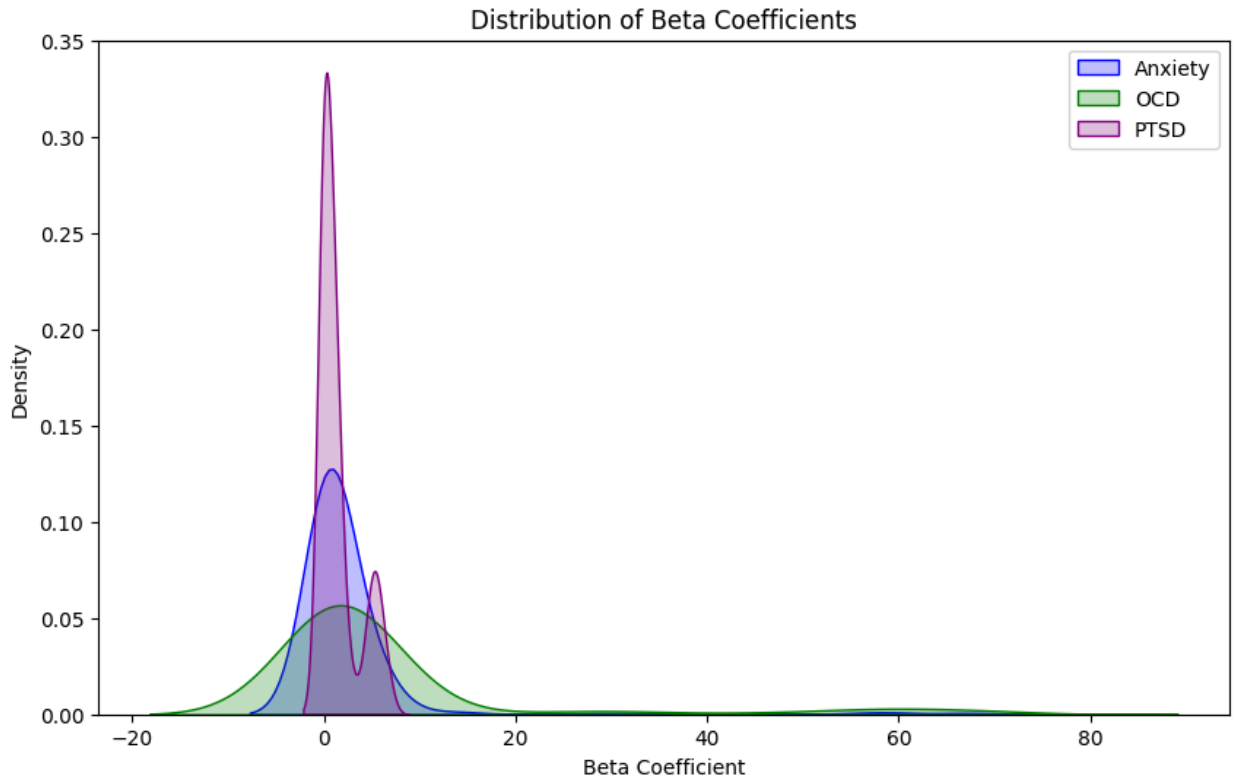


Figure 1 Distribution of Beta Coefficient for data points relating to Anxiety, OCD and PTSD

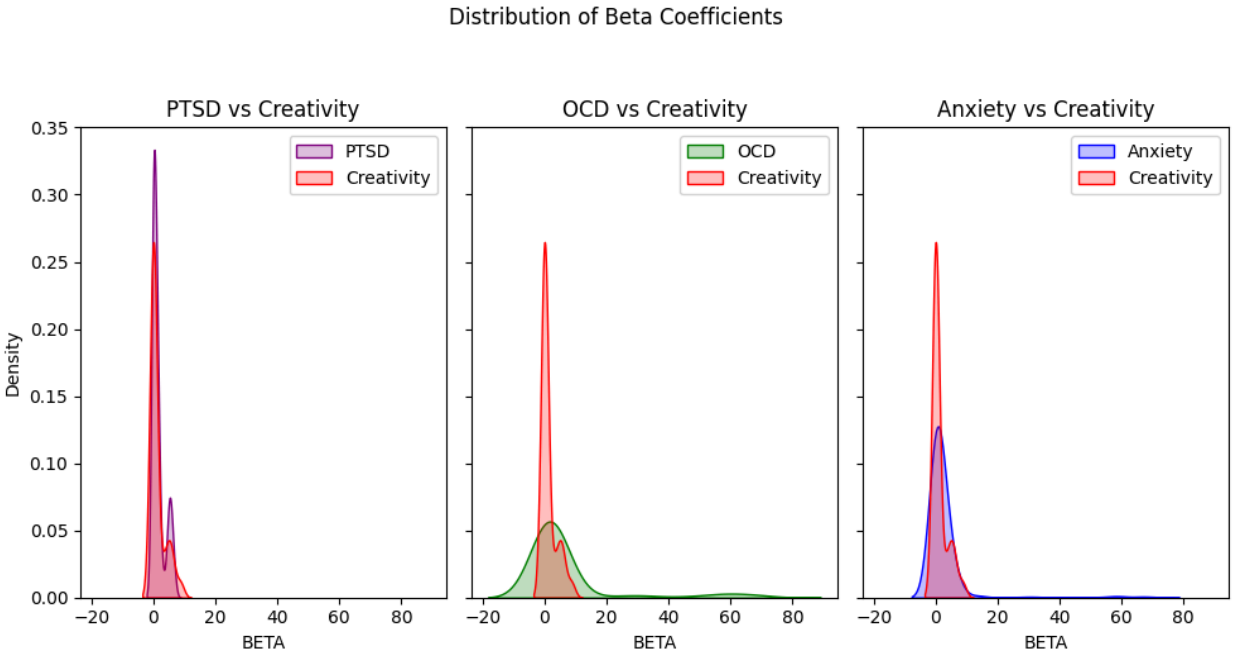


Figure 2 Distribution of Beta Coefficient for data points relating to Anxiety, OCD and PTSD vs creativity

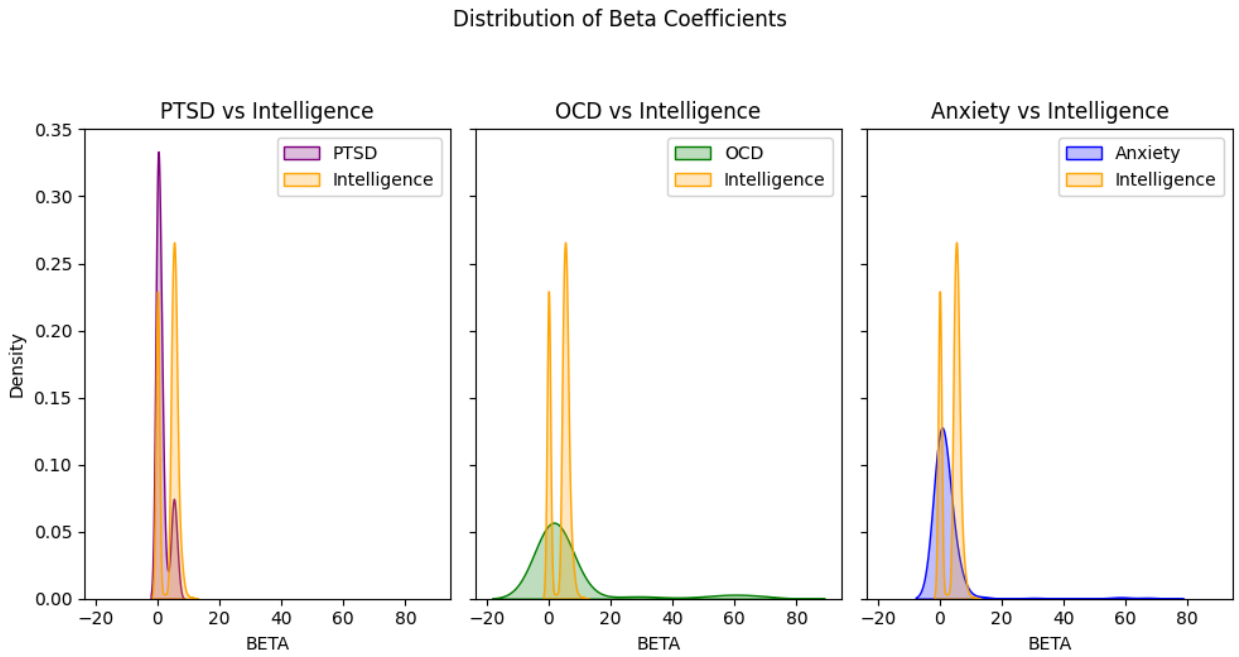
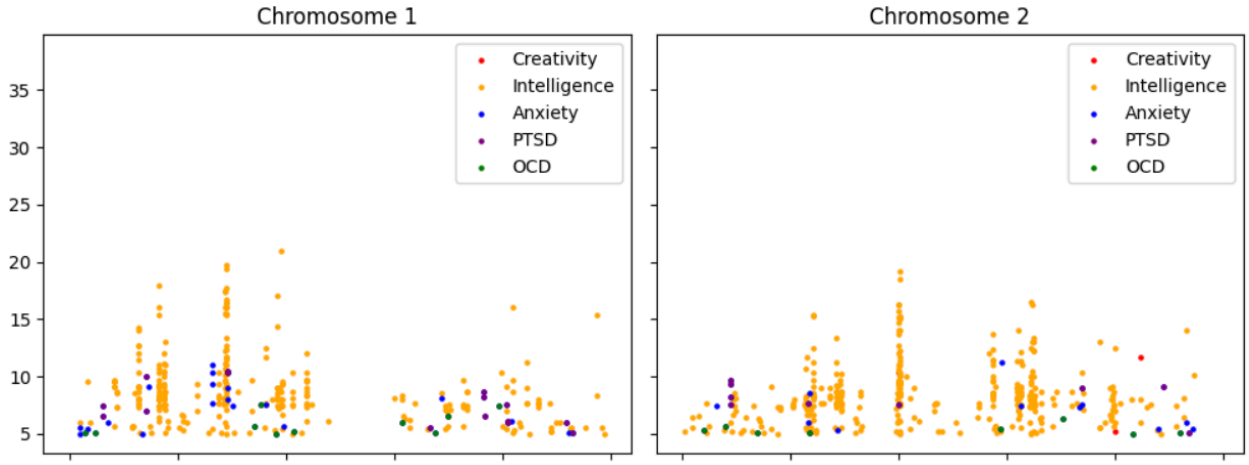


Figure 3 Distribution of Beta Coefficient for data points relating to Anxiety, OCD and PTSD vs intelligence

After this, Manhattan plots were created to analyze the spread of these traits throughout the human genome and to find any local clusters of genes responsible for certain traits. The plots were also used to see if any local clusters of genes seemed to correlate to more than one trait. A few select graphs are shown in figure 4.



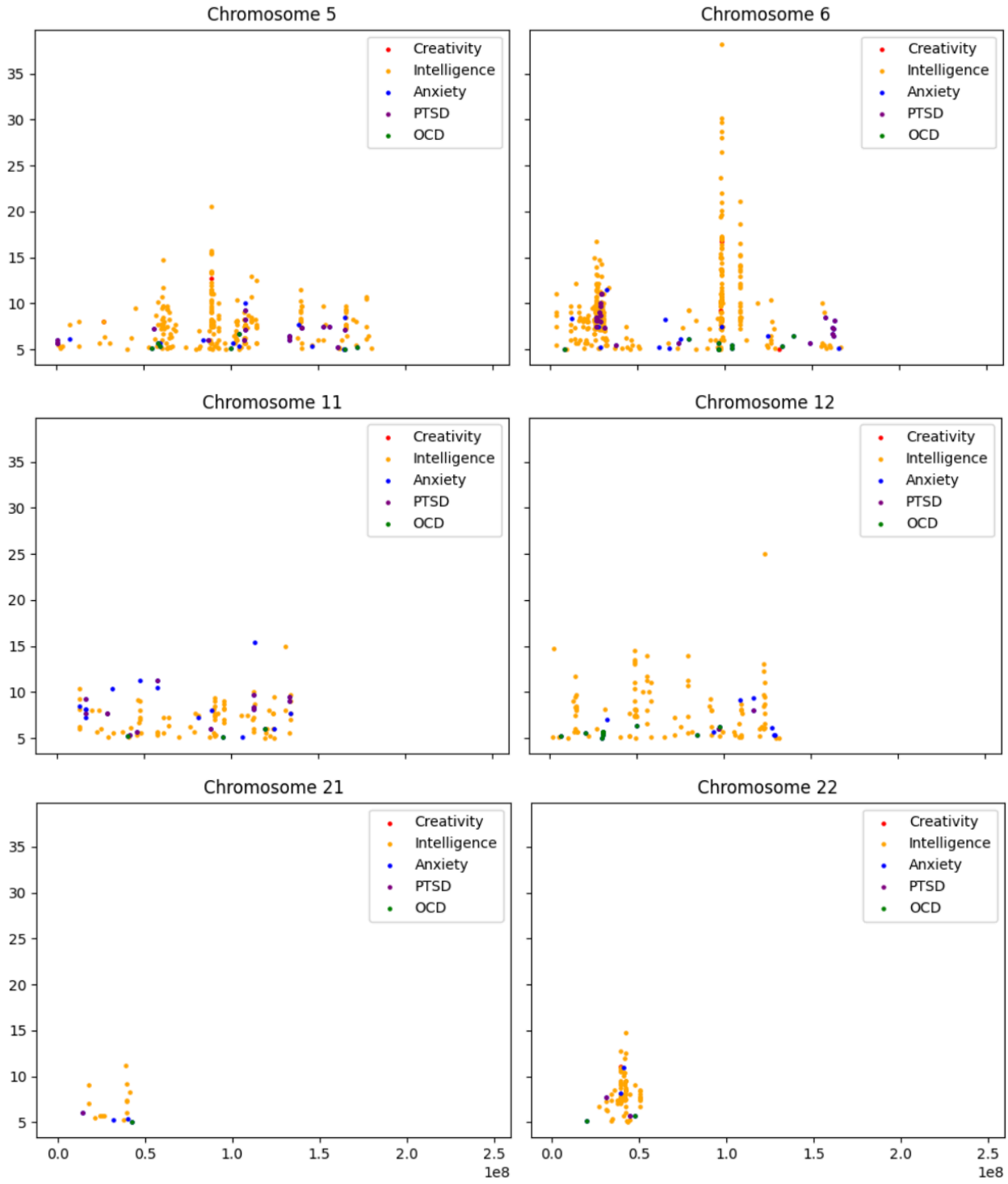


Figure 4 Manhattan plots for chromosome 1, 2, 5, 6, 11, 12, 21, and 22.

Finally, the dataset for each trait was merged with the dataset for each anxiety condition in order to find overlapping genes for the corresponding trait and anxiety disorder. The resulting overlaps for each combination can be seen in Table 2.

Table 2 *Number of Overlapping Genes between Trait and Anxiety Disorder*

	Anxiety	OCD	PTSD
Creativity	0	0	0
Intelligence	9	0	9

III. Results and Discussion

The results from figure 1 show that the strength and consistency of the effects of the associated genes to PTSD seem to be higher than that of the genes associating to OCD and anxiety. It makes sense that genes for anxiety would be the weakest because the dataset includes a lot of different types of anxiety ranging from neuroticism to generalized anxiety. The dataset also includes the data from PTSD and OCD which adds the the variability of the dataset and heterogeneity of the trait "anxiety." PTSD is a more well defined disorder with a narrower scope so it makes sense that the genes correlating to it would seem to have a stronger effect. A similar thing might be expected for OCD under the same logic yet the data shows that the effect strength of the genes is even weaker than anxiety. One possibility for this could be the way in which the data is collected. OCD often goes under diagnosed or misdiagnosed as anxiety so it's possible that there is some underlying variable for those that self proclaim to have ocd in the surveys such as the ability to accurately tell what you are feeling or the access to proper mental health education to properly diagnose oneself.

Figure 2 and 3 show that the strength of the genes' effect on intelligence and creativity is much higher than the strength of the genes' effects on anxiety and OCD. However, for PTSD, the strength of the genes affecting PTSD seems to be on par with or stronger than that of intelligence and creativity. This again could be the case due to the fact that PTSD is a more concrete, easily defined concept compared to something more abstract such as intelligence or creativity.

The Manhattan plots do a good job representing the dispersion of the genes related to each trait and disorder along the human genome. Every trait and disorder had at least one gene located on each of the 22 chromosomes graphed, except for creativity which was absent on chromosome 11, 12, 14, 15, 16, 20, and 21. This was likely due to lack of data for creativity relative to the other datasets as it had significantly less data points than the other traits and disorders.

This dispersion lends to the idea that although these traits and disorders have a genetic basis, it is a complex basis that arises from many different genes and locations on the genome. The lack of a noticeable clustering of associated genes for a trait around one area shows that these characteristics are multifaceted at the genomic level receiving an influence from all over the genome. As for the hypothesis of the paper, despite the spread of the data, there are some local clusters that can be found where traits overlap heavily such as with intelligence and PTSD

which can be seen on chromosome 5 and 6. While this overlap could potentially lend credence towards the association between Intelligence and PTSD, much more data points for PTSD would be needed to fill out these plots more.

Finally, the genetic overlapping of the traits and disorders were tested to find genes that were associated with both traits and disorders. From table 2 it is seen that the total amount of overlapping genes was sparse, with only 9 data points overlapping by chromosome number and position for the trait intelligence and the disorders anxiety and PTSD. However, the 9 data points in the anxiety dataset are identical to that of the PTSD dataset implying that the only true overlaps are between intelligence and PTSD.

From the merged dataset between intelligence and PTSD, 4 individual genes were found to correlate highly with both PTSD and Intelligence. “ANAPC4,” “SLC39A8,” “RPSAP2,” and “BTN2A1.” The beta coefficients for the corresponding genes and characteristics can be seen in Table 3.

Table 3 *Values of the Beta Coefficient for Overlapping Genes between Intelligence and PTSD*

Intelligence Beta	PTSD Beta	Gene Name
0.023439	0.013091	ANAPC4
5.797000	0.013091	ANAPC4
0.050441	0.022836	SLC39A8
8.327000	0.022836	SLC39A8
6.899000	0.017133	RPSAP2
5.572000	0.014036	BTN2A1

The beta coefficients for intelligence are significantly higher than that of PTSD implying that the strength of the effect these genes have on intelligence are much stronger than they are on PTSD. This gives credence to the idea that intelligence could increase the likelihood of PTSD as these genes might be more directly related to intelligence yet they still show up often with patients with PTSD as well. Of course further research on this would need to be done.

IV. Conclusions

While the traits of intelligence and creativity were shown to not be correlated genetically with anxiety disorders such as OCD and anxiety, it is worth doing more research on this topic with larger datasets, especially for the trait of creativity to better test the hypothesis or rule it out.

The results of this paper leave the reader with 4 different genes that are shown to be highly correlated to both intelligence and PTSD. This gives a good starting of point for genes to

investigate in order to learn more about the potential connection between PTSD and intelligence at the genetic level.

V. References

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