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The Effect of Exercise Training on Myotonic Dystrophy Type 1 Patients Level of Gene Expression

Acknowledgments:

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Introduction:

Myotonic dystrophy type 1 (DM1) is caused by a CTG-repeat expansion in the 3′-untranslated region of the dystrophia myotonica protein kinase (DMPK) gene (Brook et.al, 1992). DM1 is the most common form of adult-onset muscular dystrophy, and the worldwide prevalence of DM1 is believed to be 1 in 8,000. However, a recent study reveals the prevalence is higher in New York State with it being 1 in 2,100 (Johnson et. al, 2021).

DM1 is a multisystemic disorder characterized by a wide range of symptoms such as muscle weakness and wasting, heart issues, cognitive impairment, gastrointestinal issues, and cataracts, among many health challenges (Davey et. al., 2023).

A lesser-studied aspect of DM1 is differential gene expression (DGE). Dysregulation of gene expression has been identified across multiple tissues in DM1 patients (Wang et. al, 2018).

Not only are there no current therapies for DM1, but patients can also go often years before receiving a proper diagnosis even after visiting multiple doctors. Due to the symptoms of muscle wasting and weakness of DM1, exercise training is being used to relieve these symptoms. This study looks into and compares 2 methods of training: aerobic and strength.

It is important to note that both training programs had already been done prior. Davey et. al completed the strength training while Mikhail et. all completed the aerobic training. Both programs were 12 weeks long, one involving strength training and the other being cycling. The strength experiment was made up of 9 male samples while the aerobic experiment was made up

of 9 male samples. Biopsies were collected before and after the program to evaluate transcriptomic changes (Davery et. al, 2023)(Mikhail et. al., 2022).

This study looks into both methods of exercise training and compares the two for transcriptomic results.

Materials and Methods:

Data from strength training experiments was provided by my institution while data from the aerobic experiment was available publicly(5).

The data was first copied and transferred into my folder. FASTQ files were generated, aligned, and mapped with STAR using the UAlbany HPCC. Then using Terminal, all RNA-Seq libraries were sequenced. DESeq2 was used to complete the differential gene expression analysis while RStudio was used for figure generation. Volcano and Normalized Counts plots were generated to show patterns and variance within data. Each part described in the paragraph above was done independently for each exercise.

Taking all the csv files, I gathered all the Ensemble Is of significant genes. Sorting them by p-value and only taking those which are significant (less than 0.05), I was able to create 2 data sets and compare them. Using the figures generated, I was then able to compare gene expression levels between methods of exercise.

Results:

Volcano plots were first generated for each method of exercise which show gene expression changes after training. They show a general trend of upregulation.

Next, both data sets were cross-checked to find any pairs. The number of significant genes found after strength training was 138 while the number of significant genes found after Aerobic training was 52. The number of significant pairs found was 15.

Normalized counts plots were generated from each of the most significant genes for each method of exercise. The plots were then compared to the other method of exercise with the corresponding gene. Overall, a similar trend in upregulation was found between the 2 exercises.

Discussions and Conclusions:

Overall, it was found that transcriptomic changes were present in gene expression after both 12-week training programs. Both strength and aerobic training showed similar levels of changes to one another. Collectively, this study suggests that exercise is a promising therapeutic for DM1 individuals.

One huge setback of this experiment is not comparing the results to the control group. Without doing this, we are unable to know how much the exercises generated improvements or not.

The current study only looked at male DM1 patients. A future study can look at female DM1 patients and look at their level of gene expression.

Gene ontology could also be done on the genes found in common between the 2 data sets and see if there is anything significant to DM1.

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