Circulating microRNAs as potential biomarkers of differential susceptibility to traumatic stress

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Introduction

Traumatic stressors are important and prevalent risk factors for mental health disorders, such as post-traumatic stress disorder (PTSD). People differ strikingly in their susceptibility to develop PTSD after traumatic stress, however the exact underlying biological mechanisms of differential susceptibility are unknown. The identification of biomarkers that distinguish between persons at high and low risk of developing PTSD following trauma exposure would enable more effective preventive strategies and early interventions. Epigenetic mechanisms have been proposed to underlie the relationship between exposure to traumatic stress and the susceptibility to develop PTSD. Recent evidences suggest that microRNAs (miRNAs) are key epigenetic players in mental health disorders. Furthermore, numerous studies demonstrated the high potential of miRNAs as promising non-invasive biomarkers for different health outcomes. We therefore aimed to identify miRNA candidates associated with differential susceptibility to develop PTSD after traumatic stress exposure in humans.

Methods

Prospective Stress-related Dutch Military Cohort (‘Prospec)ive Stress-related Dutch Military Cohort’). Pre-deployment baseline and post-deployment samples were collected from a group of combat-related trauma exposed people (4 months deployment to Afghanistan, 6 months post-deployment). Furthermore, data was collected from a control group (no traumatic stress exposure). To this end, we performed high throughput miRNA sequencing (Illumina HiSeq 2000). miRBase R Deseq2 package was used to calculate miRNA expression levels. Venn plots of fold changes (log2 values) and adjusted p-values (log10) for individual miRNAs differentially expressed between the different groups exclusively.

Results

Table 1. Total number of differentially expressed miRNAs

<table>
<thead>
<tr>
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<th>Susceptible vs Control</th>
<th>Resilient vs Control</th>
<th>Susceptible vs Resilient</th>
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<tbody>
<tr>
<td>Upregulated</td>
<td>115</td>
<td>96</td>
<td>30</td>
</tr>
<tr>
<td>Downregulated</td>
<td>92</td>
<td>84</td>
<td>24</td>
</tr>
<tr>
<td>Total</td>
<td>207</td>
<td>180</td>
<td>54</td>
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</tbody>
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Figure 1. Comparison of differentially expressed miRNAs between groups. Venn diagram showing the number and overlap of differentially expressed miRNAs between the different groups.

Figure 2. Differences in miRNAs expression between groups. Volcano plots of fold changes (log2 values) and adjusted p-values (log10) for individual miRNAs differentially expressed between the different groups exclusively. Dotted lines represent cut-off values of adjusted p-values <0.05 and Log2 fold change <0.5 or >0.5.

Conclusion

Although further experiments need to be performed with more subjects and with the inclusion of confounding parameters, the results of our pilot study suggest that profiles of circulating miRNAs in human serum might provide biomarker candidates and possibly mechanistic information relevant to PTSD. 

The authors declare no conflict of interest.