Blood-bourne MicroRNA Biomarker Evaluation in Attention-Deficit/Hyperactivity Disorder of Han Chinese Individuals: An Exploratory Study

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Background:
Attention-deficit/hyperactivity disorder (ADHD) is a highly genetic neurodevelopmental disorder, and its dysregulation of gene expression involves microRNAs (miRNAs). The purpose of this study was to identify potential miRNAs biomarkers and then use these biomarkers to establish a diagnostic panel for ADHD.

Design and methods:
RNA samples from white blood cells of five ADHD patients and five healthy controls were combined to create one pooled patient library and one control library. We identified 20 candidate miRNAs with the next-generation sequencing (NGS) technique (Illumina). Blood samples were then collected from a Training Set (68 patients and 54 controls) and a Testing Set (20 patients and 20 controls) to identify the expression profiles of these miRNAs with real-time quantitative reverse transcription polymerase chain reaction (qRT-PCR). We used receiver operating characteristic (ROC) curves and the area under the curve (AUC) to evaluate both the specificity and sensitivity of the probability score yielded by the support vector machine (SVM) model.

Results:
We identified 13 miRNAs as potential ADHD biomarkers. The ΔCt values of these miRNAs in the Training Set were integrated to create a biomarker model using the SVM algorithm, which demonstrated good validity in differentiating ADHD patients from control subjects (sensitivity: 86.8%, specificity: 88.9%, AUC: 0.94, $p < 0.001$). The results of the blind testing showed that 85% of the subjects in the Testing Set were correctly classified using the SVM model alignment (AUC: 0.91, $p < 0.001$). The discriminative validity is not influenced by patients' age or gender, indicating both the robustness and the reliability of the SVM classification model.

Conclusion:
As measured in peripheral blood, miRNA-based biomarkers can aid in the differentiation of ADHD in clinical settings. Additional studies are needed in the future to clarify the ADHD-associated gene functions and biological mechanisms modulated by miRNAs.