

## Supplementary Figure 1:

- D) PCA plot of all samples and associated boxplot of the PC1 and PC2 values. The colors represent the discovery (red) and validation (blue) samples.
- D) Correlation heatmap who represent the Pearson correlation between the first 5 PC of the PCA plot and covariates of the PsyCourse Study. The values and color indicate the correlation. Stars indicate significance P-values (\*0.05; \*\* 0.01; \*\*\* 0.001.)
- D) Volcano plots of the comparisons between the control group and the affective (left) and psychotic (right) groups in the validation samples. The miRNA in red were those that were found differentially expressed in the validation samples. The black point represent miRNA that are not differentially expressed.
- D) Volcano plots of the comparisons between the psychotic and the affective group in the discovery (left) and validation (right) samples.

## Supplementary Figure 2:

- B) MDS plot representing the ancestry of the participants of the TWAS analysis.
- B) Scatter plot representing the heritability (left) and the heritability p-value (right) in the discovery and validation samples for miRNA in common to both analyses.

## Supplementary Figure 3:

- J) Flowchart of initial strategy for the use of Neural Network to validate miRNA link to the broad groups.
- J) Barplot representing the metrics of each models generated using our first strategy on the validation samples
- J) Confusion matrix resulting of the ML first strategy test on the validation samples for the model comparing PSY and CTL.
- J) Confusion matrix resulting of the ML first strategy test on the validation samples for the model comparing AFF and CTL.
- J) Barplots of metrics representing the performances of different classifications ML algorithms trained and tested on our data to differentiate the affective and control participants
- J) . Barplots of metrics representing the performances of different classifications ML algorithms trained and tested on our data to differentiate the psychotic and control participants
- J) Boxplot of residuals for the different classification algorithms trained to classify the affective and control participants
- J) of residuals for the different classification algorithms trained to classify the psychotic and control participants
- J) Graphes that represents the AUROC of the entire training and test sets for neural networks trained on fractions of the training sets (20 to 100%) to classify the affective (right) or psychotic (left) and the control participants

J) ROC plot of the first strategy ML models.

## Supplementary Figure 4:

- B) Description of the integration strategy
- B) Enrichment plot of the top miRNA of the affective GSEA analysis in the DLPC (left), ACC (center), and BLOOD (right). The GSEAs were realized using target genes ranked from a control versus psychotic (top) or affective (bottom) in the DLPC.

## Supplementary Tables:

- I. Summary of the DGE analysis results
- II. Table that resume the miRNAs identified in previous studies
- III. Table that indicate if the miRNA expressed in blood were identified in our DGE analysis and/or in previous studies of schizophrenia, bipolar disorders and major depressive disorder
- IV. Table that indicate the number of miRNA for which the TWAS models were computed and cis-heritability summary
- V. TWAS heritability of each miRNAs
- VI. Allelic proportions of the TWAS eQTL across the 3 broad groups
- VII. Table that resume the linkage disequilibrium ( $R^2$  and  $D'$ ) between the TWAS eQTL and the GWAS eQTL
- VIII. Results of our gene ontology analysis
- IX. Summary of the miRSNPs of the identified target genes
- X. Summary of the 10 genes that are targeted by the most miRNAs among those we identified