Supplementary Tables


<table>
<thead>
<tr>
<th>Model 1 (Dependent variable: BDCAF score combined with predictor variable: fatigue score)</th>
<th>Unstandardized Coefficients</th>
<th>Standardized Coefficients</th>
<th>t</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>B</td>
<td>Std. Error</td>
<td>Beta</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fatigue score</td>
<td>.117</td>
<td>.019</td>
<td>.554</td>
<td>6.031</td>
</tr>
</tbody>
</table>
| R value= 0.554 | R ANOVA test; p= 0.001* | a. Dependent Variable: BDCAF score. b. Predictors: Fatigue score. c. Fatigue had significant impact to increase BDCAF score in BD cohort by percentage of 55%.

<table>
<thead>
<tr>
<th>Model 2 (Dependent variable: system. activity combined with predictor variable: fatigue score)</th>
<th>Unstandardized Coefficients</th>
<th>Standardized Coefficients</th>
<th>t</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>B</td>
<td>Std. Error</td>
<td>Beta</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fatigue score</td>
<td>.023</td>
<td>.005</td>
<td>.500</td>
<td>5.064</td>
</tr>
</tbody>
</table>
| R value= 0.500 | R ANOVA test; p= 0.001* | a. Dependent Variable: Systemic activity. b. Predictors: Fatigue score. c. Fatigue had significant impact to increase systemic activity in BD patients by percentage of 50%.

<table>
<thead>
<tr>
<th>Model 3 (Dependent variable: BDCAF scores combined with predictor variable: PSQI)</th>
<th>Unstandardized Coefficients</th>
<th>Standardized Coefficients</th>
<th>t</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>B</td>
<td>Std. Error</td>
<td>Beta</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Quality of sleep scores</td>
<td>.202</td>
<td>.058</td>
<td>.432</td>
<td>3.455</td>
</tr>
</tbody>
</table>
| R value= 0.43 | R ANOVA test; p= 0.001* | a. Dependent Variable: BDCAF scores. b. Predictors: PSQI. c. Quality of sleep had significant impact to increase BDCAF score in BD cohort by percentage of 43%.

<table>
<thead>
<tr>
<th>Model 4 (Dependent variable: system. activity combined with predictor variable: PSQI)</th>
<th>Unstandardized Coefficients</th>
<th>Standardized Coefficients</th>
<th>t</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>B</td>
<td>Std. Error</td>
<td>Beta</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Quality of sleep score</td>
<td>.037</td>
<td>.014</td>
<td>.176</td>
<td>2.656</td>
</tr>
</tbody>
</table>
| R value= 0.37 | R ANOVA test; p= 0.001* | a. Dependent Variable: Systemic activity. b. Predictors: PSQI. c. Quality of sleep had significant impact to increase systemic activity in BD cohort by percentage of 37%.

*p value is significant at level< 0.05.

Table S2. Regression analysis of fatigue score and quality of sleep questionnaire.

<table>
<thead>
<tr>
<th>Fatigue score</th>
<th>Unstandardized Coefficients</th>
<th>Standardized Coefficients</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>B</td>
<td>Std. Error</td>
<td>Beta</td>
<td></td>
</tr>
<tr>
<td>Sleep quality</td>
<td>4.086</td>
<td>2.146</td>
<td>.333</td>
</tr>
<tr>
<td>Sleep Latency</td>
<td>.632</td>
<td>.966</td>
<td>.073</td>
</tr>
<tr>
<td>Sleep duration</td>
<td>-.872</td>
<td>1.388</td>
<td>-.077</td>
</tr>
<tr>
<td>Habitual sleep efficiency</td>
<td>1.538</td>
<td>1.205</td>
<td>.158</td>
</tr>
<tr>
<td>Sleep disturbances</td>
<td>.767</td>
<td>1.628</td>
<td>.052</td>
</tr>
<tr>
<td>Use of sleeping medications</td>
<td>-.077</td>
<td>1.114</td>
<td>-.007</td>
</tr>
<tr>
<td>Daytime dysfunction</td>
<td>4.111</td>
<td>1.508</td>
<td>.355</td>
</tr>
</tbody>
</table>

Model (dependent outcome and independent variables integration)

R= 0.749
R²= 0.561
ANOVA: p=.001*

Dependent variable: Fatigue score. Predictor variables: sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleep medications, and daytime dysfunction.

*p values<0.05.

<table>
<thead>
<tr>
<th>Coefficients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Model 5 (Dependent variable: fatigue score combined with predictor variable: alpha-MSH)</td>
</tr>
<tr>
<td>alpha-MSH concentration (ng/ml)</td>
</tr>
<tr>
<td>R value:0.44</td>
</tr>
<tr>
<td>R Square value =0.193</td>
</tr>
<tr>
<td>ANOVA test; p=0.001*</td>
</tr>
<tr>
<td>Model 6 (Dependent variable: fatigue score combined with predictor variable: VIP)</td>
</tr>
<tr>
<td>VIP concentration (pg/ml)</td>
</tr>
<tr>
<td>R value:0.168</td>
</tr>
<tr>
<td>R Square value =0.028</td>
</tr>
<tr>
<td>ANOVA test; p=0.152</td>
</tr>
<tr>
<td>Model 7 (Dependent variable: PSQI combined with predictor variable: alpha-MSH)</td>
</tr>
<tr>
<td>alpha-MSH concentration(ng/ml)</td>
</tr>
<tr>
<td>R value:0.35</td>
</tr>
<tr>
<td>R Square value:0.121</td>
</tr>
<tr>
<td>ANOVA test; p=0.012*</td>
</tr>
<tr>
<td>Model 8 (Dependent variable: PSQI combined with predictor variable: VIP)</td>
</tr>
<tr>
<td>VIP concentration (pg/ml)</td>
</tr>
<tr>
<td>R value:0.343</td>
</tr>
<tr>
<td>R Square value:0.112</td>
</tr>
<tr>
<td>ANOVA test; p=0.018*</td>
</tr>
</tbody>
</table>

*p value is significant at level <0.05.

Table S4. The differences of cytokines concentrations between fatigue groups and PSQI groups in BD.

<table>
<thead>
<tr>
<th></th>
<th>BD. Fatigue groups</th>
<th>Mean ± SD</th>
<th>Mean Rank</th>
<th>p value</th>
<th>BD. PSQI groups</th>
<th>Mean ± SD</th>
<th>Mean Rank</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>IL-1β</td>
<td>Low fatigue</td>
<td>1.26 ± 2.17</td>
<td>13.00</td>
<td>0.639</td>
<td>PSQI &lt;5</td>
<td>0.39 ± 0.64</td>
<td>7.00</td>
<td>0.684</td>
</tr>
<tr>
<td></td>
<td>High fatigue</td>
<td>0.58 ± 0.68</td>
<td>11.56</td>
<td></td>
<td>PSQI &gt;5</td>
<td>-0.14 ± 0.18</td>
<td>6.14</td>
<td></td>
</tr>
<tr>
<td>IL-6</td>
<td>Low fatigue</td>
<td>3.02 ± 2.19</td>
<td>33.93</td>
<td><strong>0.007</strong>*</td>
<td>PSQI &lt;5</td>
<td>1.71 ± 1.04</td>
<td>17.43</td>
<td>0.184</td>
</tr>
<tr>
<td></td>
<td>High fatigue</td>
<td>1.32 ± 1.34</td>
<td>20.62</td>
<td></td>
<td>PSQI &gt;5</td>
<td>2.08 ± 0.303</td>
<td>12.80</td>
<td></td>
</tr>
<tr>
<td>IL-10</td>
<td>Low fatigue</td>
<td>3.65 ± 3.07</td>
<td>17.06</td>
<td>0.255</td>
<td>PSQI &lt;5</td>
<td>-3.45 ± 1.95</td>
<td>9.67</td>
<td>0.58</td>
</tr>
<tr>
<td></td>
<td>High fatigue</td>
<td>5.06 ± 5.30</td>
<td>22.54</td>
<td></td>
<td>PSQI &gt;5</td>
<td>10.98 ± 1.03</td>
<td>11.79</td>
<td></td>
</tr>
<tr>
<td>TNF-α</td>
<td>Low fatigue</td>
<td>2.09 ± 1.79</td>
<td>9.58</td>
<td><strong>0.074</strong>*</td>
<td>PSQI &lt;5</td>
<td>1.25 ± 0.68</td>
<td>6.67</td>
<td>0.08</td>
</tr>
<tr>
<td></td>
<td>High fatigue</td>
<td>13.47 ± 22.96</td>
<td>14.64</td>
<td></td>
<td>PSQI &gt;5</td>
<td>1.24 ± 1.83</td>
<td>10.86</td>
<td></td>
</tr>
</tbody>
</table>

*p value is significant at level <0.05.
Table S5. The association of cytokines concentrations with α-MSH and VIP.

<table>
<thead>
<tr>
<th>Spearman's Correlation Coefficient</th>
<th>IL-1 β</th>
<th>IL-6</th>
<th>IL-10</th>
<th>TNF-α</th>
<th>α-MSH</th>
<th>VIP</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>R</td>
<td>p value</td>
<td>N</td>
<td>R</td>
<td>p value</td>
<td>N</td>
</tr>
<tr>
<td>IL-1 β</td>
<td></td>
<td></td>
<td>1.00</td>
<td></td>
<td></td>
<td>23</td>
</tr>
<tr>
<td>IL-6</td>
<td>.232</td>
<td>.299</td>
<td>1.00</td>
<td></td>
<td></td>
<td>22</td>
</tr>
<tr>
<td>IL-10</td>
<td>.259</td>
<td>.300</td>
<td>.174</td>
<td></td>
<td></td>
<td>18</td>
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<tr>
<td>TNF-α</td>
<td>.007</td>
<td>.980</td>
<td>.760</td>
<td>.700</td>
<td></td>
<td>15</td>
</tr>
<tr>
<td>α-MSH</td>
<td>-.357</td>
<td>.146</td>
<td>-.368</td>
<td>-.079</td>
<td>.495</td>
<td>18</td>
</tr>
<tr>
<td>VIP</td>
<td>-.366</td>
<td>.164</td>
<td>.169</td>
<td>-.028</td>
<td>-.008</td>
<td>18</td>
</tr>
</tbody>
</table>

Statistical analysis of the associations between detectable cytokine levels in serum with α-MSH and VIP. *p value is significant at level <0.05.

Supplementary figures

Fig. S1. Receiver operating characteristic (ROC) curve of α-MSH concentration for predicting high fatigue in BD patients. Accuracy is measured by the area under the ROC curve (AUC). An area of 1.0 represents a perfect test; an area of 0.5 represents a worthless test. AUC, in this cohort= 0.774.

Fig. S2. Receiver operating characteristic (ROC) curve of IL-6 concentration for predicting low fatigue in BD patients. Accuracy is measured by the area under the ROC curve (AUC). An area of 1.0 represents a perfect test; an area of 0.5 represents a worthless test. AUC in this cohort= 0.777.