Psychiatric symptoms are common in acute HIV and correlate with disease biomarkers

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Background
To assess the trajectory of anxiety and depression in acute HIV infection over six months following diagnosis, and assess correlations between affective symptoms and blood and cerebrospinal fluid (CSF) disease biomarkers prior to treatment.

Methods
A total of 123 participants were enrolled during acute HIV infection (Fiebig I) through the SEARCH010/RV254 cohort in Bangkok, Thailand. Participants completed the Hospital Anxiety and Depression Scale (HADS) and the Patient Health Questionnaire (PHQ-9) at baseline prior to combination antiretroviral therapy (cART) and again at weeks 4, 12, and 24 following diagnosis. Depression was defined as a score ≥ 8/21 on HADS-D or ≥10/27 on PHQ-9, with anxiety defined as a score ≥8/21 on HADS-A. Disease biomarkers of plasma and CSF HIV RNA levels, CD4 count, and plasma and CSF neopterin were obtained at entry, as was magnetic resonance spectroscopy (MRS).

Results
At diagnosis, 46% of subjects met the clinical cutoff for depression on the PHQ-9 and 41% on the HADS-D, with 66% meeting the threshold for anxiety on the HADS-A. Affective symptoms significantly decreased over time with mixed model analyses, and at week 24 8% had depression on HADS-D, 18% on PHQ-9, and 17% with anxiety on HADS-A. At baseline, higher average log₂ plasma HIV RNA was observed in participants experiencing depression on the PHQ-9 (6.0 vs. 5.6; p=0.03) compared to those not experiencing significant depression. Similarly, lower CD4 counts were observed in those with baseline depression on either HADS-D (322 vs. 413 cells/mm³; p=0.01) or PHQ-9 (331 vs. 414 cells/mm³; p=0.01). Plasma neopterin was higher in those with PHQ-9 depression (2945 vs. 1835 pg/mL; p=0.02) and CSF neopterin was higher in those with HADS-D depression (3401 vs. 1140 pg/mL; p=0.03). Plasma neopterin levels positively correlated with total PHQ-9 depression scores (r=0.29, p=0.04). MRS indices did not associate.

Conclusions
In acute HIV infection, depression, but not anxiety, consistently linked to markers of HIV infection, and plasma and intrathecal immune activation. We also confirm high rates of anxiety and depression in acute HIV that decrease with time in the setting of early cART.

Summary of results
• Depression and anxiety are frequent in acute HIV infection, and decrease with time
• Baseline plasma viral loads are higher in acute HIV participants with initial depression on the PHQ-9
• Baseline CD4 counts are lower in acute HIV participants with initial depression on the PHQ-9 or HADS-D
• Baseline plasma neopterin, a marker of macrophage activation, is higher in those with depression at diagnosis by PHQ-9
• Baseline CSF neopterin, a marker of intrathecal macrophage activation, is higher in those with initial depression on the HADS-D
• At baseline, plasma neopterin correlates with total score on the PHQ-9 depression scale

Conclusions
• Markers of HIV infection and immune activation are consistently worse in those with initial depression in acute HIV infection
• It is possible that disease related factors contribute to depression in acute HIV

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1. Demographics of acute HIV participants
2. Plasma viral load in depression, week 0
3. CD4 counts in depression, week 0
4. Plasma neopterin and depression, week 0
5. CSF neopterin and depression, week 0
6. Correlation between total PHQ-9 depression scores and plasma neopterin in acute HIV

Table 1. Demographics of acute HIV participants

<table>
<thead>
<tr>
<th>Participant demographics</th>
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<tbody>
<tr>
<td>Number of participants</td>
</tr>
<tr>
<td>Age, years (mean)</td>
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<tr>
<td>Infection duration, weeks (mean)</td>
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<tr>
<td>% Male participants</td>
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<tr>
<td>% in Fiebig stage II</td>
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<tr>
<td>% in Fiebig stage III</td>
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<tr>
<td>% with drug use</td>
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<tr>
<td>% on antiretroviral therapy</td>
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<tr>
<td>CD4 cell count, cells/mm³ (mean)</td>
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<tr>
<td>Plasma HIV RNA (mean)</td>
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<td>CSF log₂ HIV RNA (mean)</td>
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Figure 1. Plasma viral load in depressed (PHQ-9) and psychiatrically normal participants with acute HIV

Figure 2. Plasma viral load in depressed (PHQ-9) and psychiatrically normal participants with acute HIV

Figure 3. CD4 counts in depressed (HADS-D and PHQ-9) and psychiatrically normal participants with acute HIV

Figure 4. Plasma neopterin in depression (PHQ-9) and psychiatrically normal participants with acute HIV

Figure 5. CSF neopterin in depressed (HADS-D) and psychiatrically normal participants with acute HIV

Figure 6. Correlation between total PHQ-9 depression scores and plasma neopterin in acute HIV

Figure 7. Plasma viral load in depression, week 0

Figure 8. Plasma neopterin and depression, week 0

Figure 9. CSF neopterin and depression, week 0

Figure 10. Plasma neopterin and depression, week 0

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Figure 51. CSF neopterin and depression, week 0

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Figure 53. Summary of results