Depression and HIV-Disease Duration Differentially Affect Subcortical Brain Regions in PWH

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BACKGROUND

- Many people living with HIV (PWH) are impacted by depression, around 40%
- Depression negatively impacts subcortical and limbic volumes in the general population, but the specific impact on subcortical volumes is relatively unknown in PWH
- The goal of this study was to investigate the impact of depression and HIV clinical factors on subcortical brain regions including:
  - Medial temporal lobe (MTL)
  - Basal ganglia (BG)
  - Diencephalon

METHODS

- All participants underwent a T1 weighted MRI on a Siemen's 3T scanner, then FreeSurfer (v8.0.0) was used for volumetric analyses of subcortical regions
- Subfields were segmented in FreeSurfer using histologically based atlases of the hippocampus, amygdala, thalamus, and hypothalamus
- The Beck Depression Inventory-II questionnaire was used to quantify depression symptoms within the last 2 weeks at the time of data collection, and binarized for analysis (≥14 indicating at least mild depression)
- Hierarchical linear regressions were run to examine the impact of depression on subcortical regions
- HIV clinical factors, demographic factors, and total intracranial volumes were included in all analyses
- Regression models were run on 3 separate trees comprising the MTL, BG, and diencephalon, with FDR correction at each level
- Subsequent levels of regression models were only performed when variables of interest were significant

Demographic Variables:						
	n	Age[1]	Education[1]	Sex[3] (Male)	Race[3] (Black)	Scanner Upgrade[3]
Total	100	56.2 (6.6)	14.3 (3.0)	74 (74)	64 (64)	41 (41)
BDI ≥ 14	14	55.6 (8.0)	*12.8 (2.5)	8 (57.1)	12 (85.7)	4 (28.6)
BDI < 14	86	56.3 (6.4)	*14.6 (3.0)	66 (76.7)	52 (60.5)	37 (43.0)
HIV Clinical Variables:						
	n	CD4 Nadir[2]	Disease Duration[1]	CD4 Count[2]	Log CD4[1]	Detectable Viral Load[3]
Total	100	199.5 [285.5]	25.1 (9.2)	711 [449.5]	6.5 (0.5)	17 (17)
BDI ≥ 14	14	150 [195.5]	25.3 (8.7)	653 [482]	6.5 (0.6)	5 (35.7)
BDI < 14	86	200 [287]	25.0 (9.4)	730.5 [439.3]	6.5 (0.5)	12 (14.0)

Table 1. Demographic (top) and clinical (bottom) variables included in regression models. Measures of central tendency are denoted as M(SD)[1] or Median[IQR][2], and measures of frequency are denoted as count(%)[3].
*significant (p<0.05) group difference, tested with t-test or chi-square

The medial temporal lobe (MTL) is heavily impacted by depression, whereas the basal ganglia is impacted by disease duration in people with HIV.

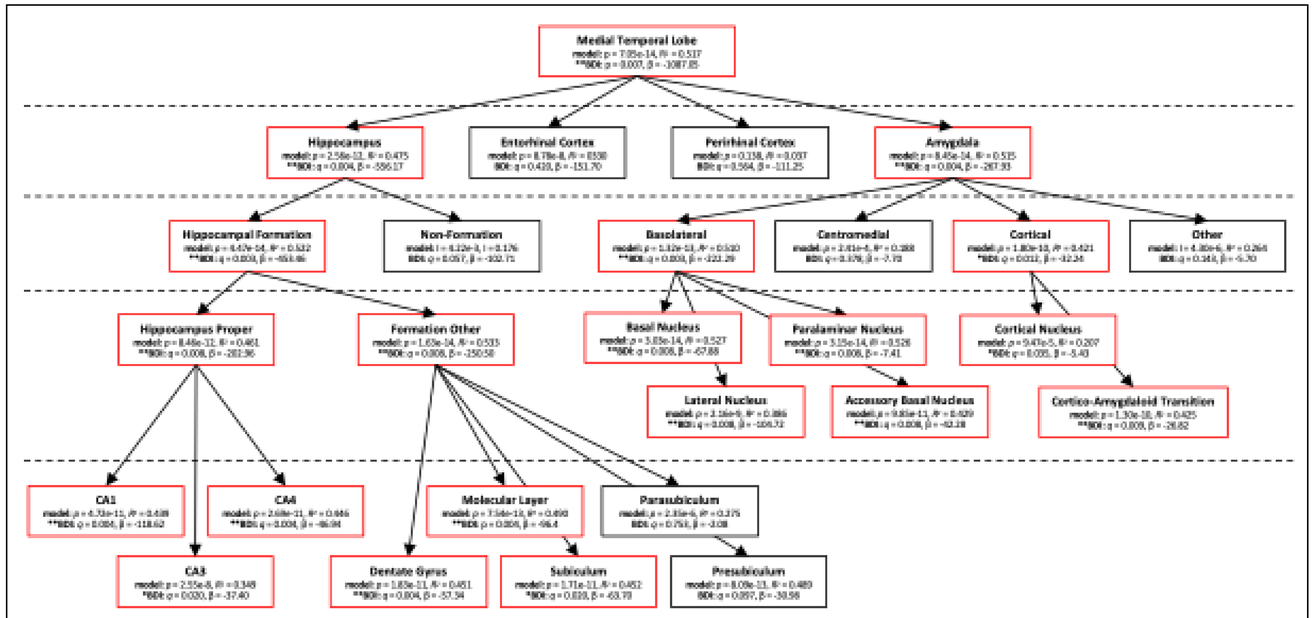


Figure 1. Hierarchical linear regression model predicting MTL volume. FDR correction for multiple comparisons was completed across each level (indicated by dashed lines), and models where depression is a significant variable are outlined in red. **q<0.01, *q<0.05



Figure 2. Significant (red) and non-significant (blue) regions associated with depression from each subcortical regression model. Dark red indicates q<0.01, light red indicates q<0.05, and blue indicates q>0.05. **a)** The entire MTL volume and many subregions of the hippocampus and amygdala were most significantly associated with depression (see Figure 1). **b)** The entire basal ganglia (pallidum, putamen, and accumbens) volume was significantly associated with depression, but individual subregions were not. Both HIV clinical and demographic factors were also associated with basal ganglia volume. **c)** The entire diencephalon (thalamus and hypothalamus) was not significantly associated with depression, but it was associated with various demographic factors.

RESULTS

Medial Temporal Lobe:

- Depression and age are significant predictors of total MTL volume (ps<0.01)
- Depression is a significant predictor of volume in all subfields of the hippocampus proper and many regions of the hippocampal formation
- Depression is a significant predictor of volume in all nuclei of the basolateral and cortical amygdala

Basal Ganglia:

- Depression, HIV disease duration, education, and race were significant predictors of total basal ganglia volume (ps<0.05)
- Disease duration was significant only before FDR correction for putamen volume (p=0.035, q=0.140)

Diencephalon:

- Age, and education were significant predictors of total diencephalon volume (ps<0.05)

CONCLUSIONS

- Similar to the general population, depression appears to impact the volume of the medial temporal lobe, particularly within the hippocampus and amygdala
- In contrast, other demographic and clinical factors appear to have a stronger association to volumes of other subcortical regions including the basal ganglia and diencephalon
- These findings suggest that depression may exert a neurotoxic effect on memory-related subcortical regions distinct from HIV-disease related factors

ADDITIONAL KEY INFORMATION

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Acknowledgements: We would like to thank all participants who have dedicated their time to this research project. Our work would not be possible without them!
Funding: This work is funded by the NIH under grants 1R01MH108466, 1R56NS124422, 1R01NS124422, R56AG089864, R01AG089864-01A1, and T32AG071745

Plain Language Summary:
The medial temporal lobe is impacted by depression in people living with HIV. A current depressive state is associated with decreased volume of various subfields of the hippocampus and nuclei of the amygdala.