Data Supplement for Donovan et al., Longitudinal Association of Amyloid Beta and Anxious-Depressive Symptoms in Cognitively Normal Older Adults. Am J Psychiatry (doi: 10.1176/appi.ajp.2017.17040442)

CONTENTS

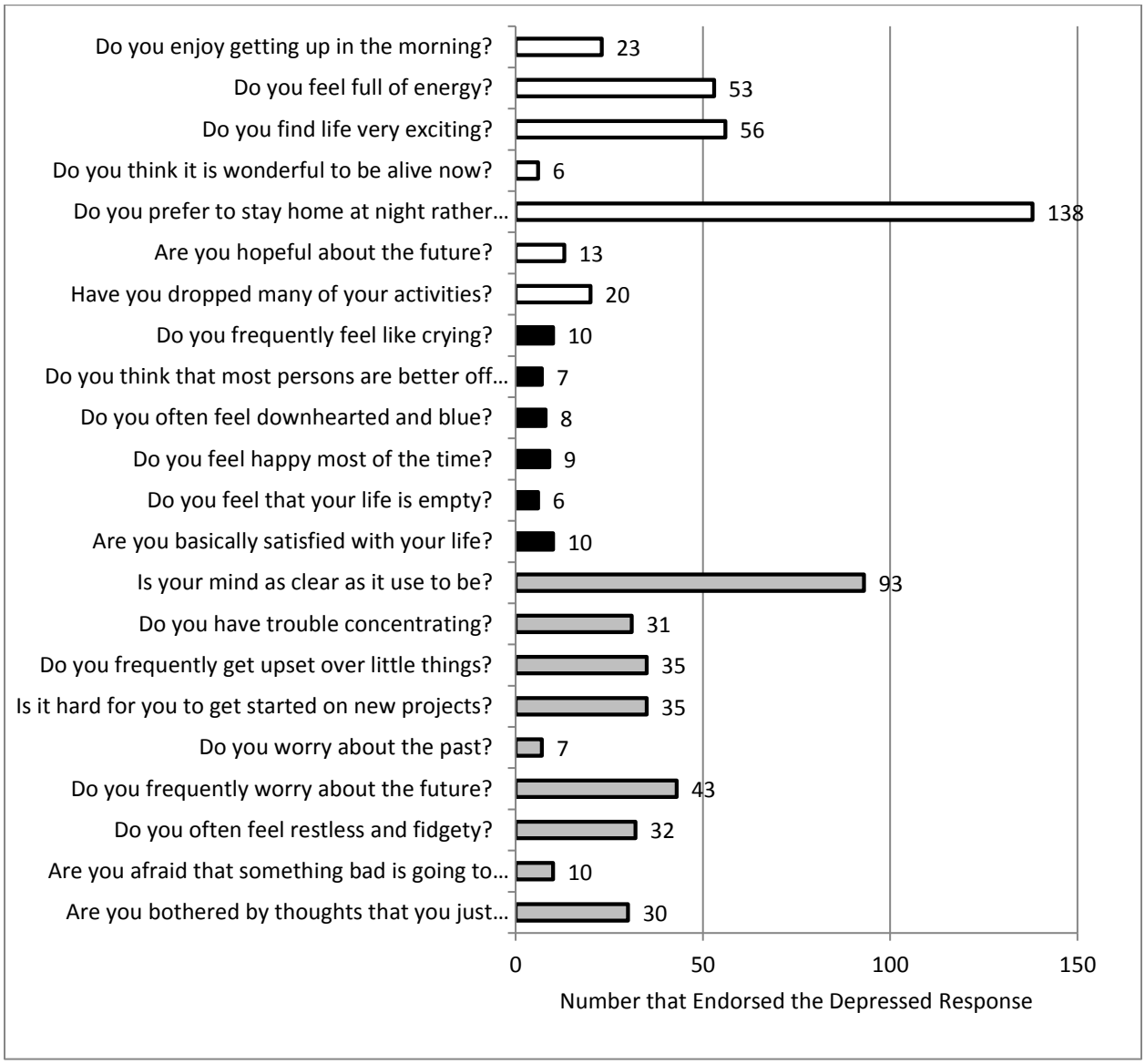
Supplementary Methods

We used Principal Component Analysis (PCA) of the Geriatric Depression Scale[1] (GDS) item scores from a baseline sample of 248 HABS participants to derive three factors defined as the Anxiety-Concentration Factor (component 1), the Dysphoria Factor (component 2) and the Dysphoria Factor (component 3) as previously described.[2] Briefly, a loading threshold of ≥ 0.3 and an oblimin rotation were employed, revealing a simple, three-factor structure. The Kaiser-Meyer-Okin value of 0.603 and Barlett's Test of Sphericity ($p<0.0001$) supported the factorability of the correlation matrix. The eigenvalues for components 1, 2, and 3 were 3.3, 2.1, and 2.0, respectively. There were low correlations between the resulting three factors (r=0.03 for Component 1 and 2, r=0.015 for Component 1 and 3, and r=0.04 for Component 2 and 3**).** Four of 30 GDS items were not included in the PCA because they were endorsed once or not at all (being in good spirits and feeling helpless, worthless and hopeless, GDS items 7, 10, 17 and 22, respectively). Of the remaining 26 items, the four GDS questions pertaining to social avoidance, boredom, decision-making and subjective memory symptoms (GDS items 28, 4, 29 and 14, respectively) did not load onto any of the 3 factors and were not included in analyses. Two GDS items pertaining to non-memory cognitive symptoms (GDS items 26 and 30) loaded onto the Anxiety-Concentration Factor. Details of this PCA and a method sensitivity test have been published elsewhere as Supplementary Material.[2]

For the slightly larger sample used in these longitudinal analyses (n=270), we assigned each non-excluded GDS item accordingly, to one of the 3 clusters (Anxiety-Concentration, Dysphoria, Apathy-Anhedonia) as previously defined. For each participant at each time point we calculated an average cluster score corresponding to the GDS items assigned to each cluster. Since each item was binary, scored 0 or 1, the latter indicating endorsement, the score for each cluster for

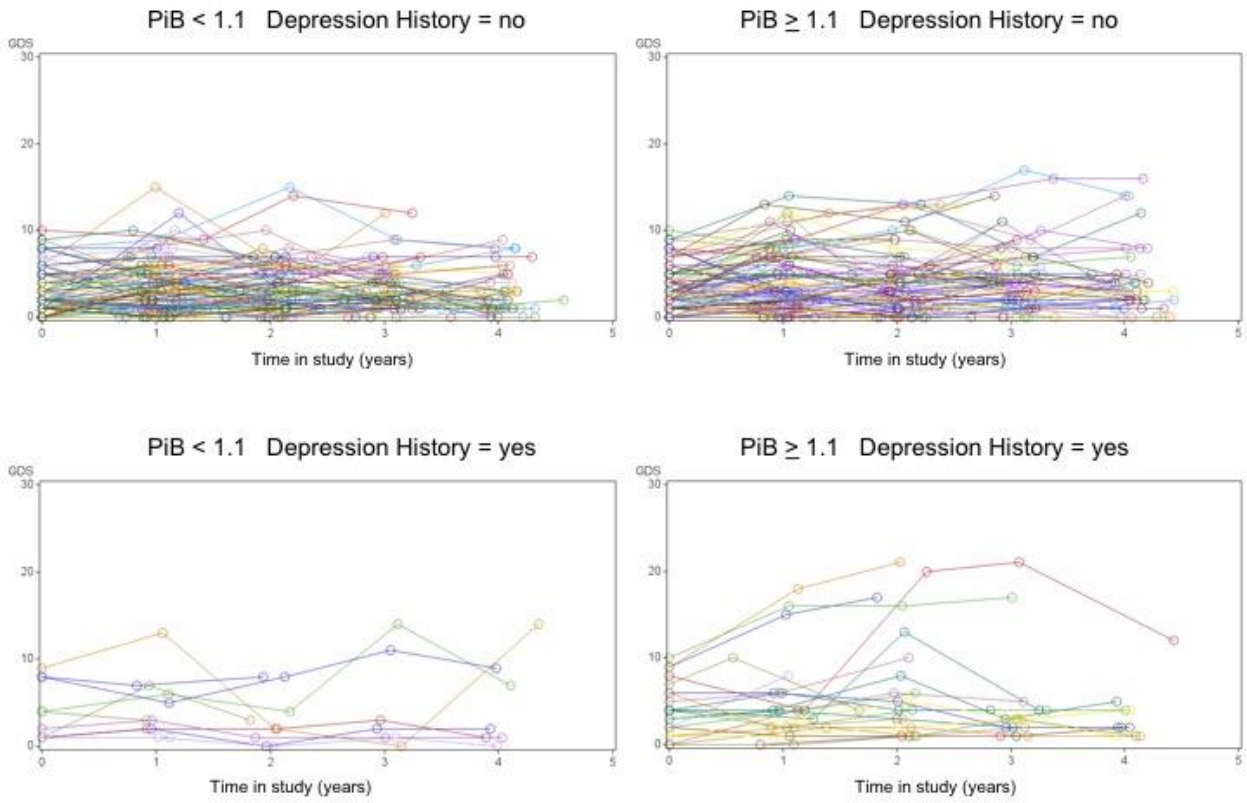
each person-time point was equivalent to the proportion of the items corresponding to that cluster that the participant endorsed at that time. Across the 1078 study visits that included 32,340 GDS item scores there were a total of 41 missing values (16, 5 and 20 missing values for the Anxiety-Concentration, Dysphoria and Apathy-Anhedonia clusters, respectively). Thirty-one of these values were a single missing GDS item value for a given time point for 29 different participants. The remaining missing values corresponded to four different participants who had either 2 or 3 simultaneous missing GDS item values at a single time point. For person-time point data with missing values, the average of the non-missing values for each cluster were used. These GDS cluster scores were used as outcome measures in separate mixed effects models as reported in the current manuscript. Figure S1 shows how many participants endorsed each of the GDS items included in the cluster scores, at baseline.

FIGURE S1. Endorsement of GDS items at baseline by Apathy-Anhedonia, Dysphoria, and Anxiety-Concentration clusters (n=270)



Numbers of study participants endorsing GDS items corresponding to the Apathy-Anhedonia cluster (top/unfilled bars), Dysphoria cluster (middle/solid bars) and Anxiety-Concentration cluster (lower/grey bars) are shown. Abbreviation: GDS (Geriatric Depression Scale- 30 item version).

FIGURE S2. Spaghetti plots of raw data showing individual participant trajectories for GDS divided by median split for PiB and depression history categories



Study participants are classified into one of four panels according to depression history (yes/no) and PiB distribution volume ratio (DVR) value above or below the median split.

References

1. Yesavage JA, Brink TL, Rose TL, et al. Development and validation of a geriatric depression screening scale: a preliminary report. *J Psychiatr Res.* 1982;17(1):37-49.
2. Donovan NJ, Hsu DC, Dagley AS, et al. Depressive Symptoms and Biomarkers of Alzheimer's Disease in Cognitively Normal Older Adults. *J Alzheimers Dis.* 2015;46(1):63-73.