

1 **S1 Text**

2 **1. Relationship between hippocampal size and cross-sectional cognitive** 3 **performance**

4 We empirically tested which cognitive tests correlated with hippocampal size in
5 our sample. This was achieved by fitting regression models to check whether
6 hippocampal volume (independent variable) predicted cross-sectional
7 performance on a range of memory tests (dependent variable). Age, sex, FSIQ
8 and social class were included as covariates. Where the test score represented a
9 continuous variable, multiple linear regression was used. For count data, initially
10 Poisson regression was fitted and checked for over-dispersion. If this was found,
11 a negative binomial model was used. For the remainder of the tests, where the
12 upper score is bounded, regression models were initially fitted using binomial
13 distributions. In cases of over-dispersion a folded transformation was performed
14 and checked for approximate normality using Q-Q plots of residuals. The same
15 models were re-fitted with and without hippocampal size, and a hypothesis test
16 (likelihood ratio) was performed. Calculated p-values were used to test whether
17 hippocampal size made a significant difference to the model (**S5 Table**).

18 **2. Relationship between hippocampal size and future cognitive decline**

19 We used mixed effects models to test whether hippocampal atrophy, as defined
20 using the Scheltens scale, predicted future memory decline over approximately a
21 5-year period between Phases 11 and 12 of the Whitehall II study. Binomial
22 regression was used in view of count data (Whitehall II verbal memory test =
23 words recalled from a list of 20 (see Topiwala et al. 2017; **S6 Table**). In order to
24 test whether cognitive decline significantly differed between those with and

25 without hippocampal atrophy, interaction terms between time and Scheltens
26 category were added. Models were visually presented using graphs to predict
27 trends in cognitive test scores over the study for a “typical” participant – male, of
28 mean age (75 years), FSIQ (118 years) (**S7 Fig**).

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30 Topiwala A, Allan CL, Valkanova V, Zsoldos E, Filippini N, Sexton C, et al. Moderate alcohol
31 consumption as risk factor for adverse brain outcomes and cognitive decline: longitudinal
32 cohort study. *BMJ*. 2017; 357: j2353.