

# Supplementary Material

## Cognitive Trajectories in Preclinical and Prodromal Alzheimer's Disease Related to Amyloid Status and Brain Atrophy: A Bayesian Approach

### Supplementary Table 1. Checklist of Bayesian Analysis Reporting Guidelines [1]

#### Preamble

*A. Why Bayesian. If the audience requires it, explain what benefits will be gleaned by a Bayesian analysis (as opposed to a frequentist analysis).*

The rationale for using a Bayesian approach is outlined in the second paragraph of the introduction.

*B. Goals of analysis. Explain the goals of the analysis. This prepares the audience for the type of models to expect and how the results will be described.*

The analysis goals are reported in the second to last and the last paragraph of the introduction.

#### Step 1. Explain the model

*A. Data variables. Explain the dependent (predicted) variables and independent (predictor) variables.*

Dependent and independent variables are explained in the methods section.

*B. Likelihood function and parameters. For every model, explain the likelihood function and all the parameters, distinguishing clearly between parameters of primary theoretical interest and ancillary parameters. If the model is multilevel, be sure that the hierarchical structure is clearly explained, along with any covariance structure if multivariate parameter distributions are used.*

In the statistics section, we describe the model construction, including parameters of primary interest (interaction effect of diagnosis by amyloid status or volumes with time), and the multilevel structure of the longitudinal models with random intercept and slope, nested within individuals.

*C. Prior distribution. For every model, explain and justify the prior distribution of the parameters in the model.*

For the **longitudinal mixed effect models with “brms”** we used uninformative flat priors and in a sensitivity analysis compared outcomes when using very weakly informed priors with a normal distribution of mean 0 and standard deviation of 10. For the **Bayesian random-effects meta-analysis** with “bayesmeta”, we used a weakly informed normally distributed prior with mean 0 and standard deviation of 0.5. The prior for the heterogeneity parameter  $\tau$  was chosen as a weakly informed half-normal distribution with a standard deviation of 0.5, consistent with a previous systematic review of heterogeneity estimates across a large range of meta-analyses from the Cochrane library [2]. In a sensitivity analysis, we compared effects when using an uninformative Jeffreys prior for heterogeneity.

*D. Formal specification. Include a formal specification (mathematical or computer code) of the likelihood and prior, located either in the main text or in a publicly and persistently accessible online supplementary material.*

For example, for the longitudinal outcome of ADNI memory and executive function scores the **likelihood**, i.e., the data generating process of the outcome, was defined as:

```
< library(brms)
```

```
< bf_MEM_amyl_lr = bf(ADNI_MEM ~ poly(Time, 3, raw= TRUE)*dia_by_amyloid + < Age  
+ Sex + (1 + Time|p|RID))
```

```

< bf_EXE_amyl_lr = bf(ADNI_EF ~poly( Time,3, raw = TEUE)*dia_by_amyloid + Age + Sex
+ (1 + Time|p|RID))
< bf_cog_Amyl_lr = brm(bf_MEM_amyl_lr + bf_EXE_amyl_lr, data= subvorlage, warmup =
2000, iter = 8000, chains = 4, cores = 12)
with a Gaussian distribution for cognitive scores, and flat priors for the fixed effect parameters.
For example for the Bayesian random effect meta-analysis for amyloid, the code was:
< library("bayesmeta")
< library("metafor")

#calculate the standard deviation and effect size (MD = mean difference) for m1 = memory in
#group 1 (amyloid negative) and m2 = memory in group 2 (amyloid positive); n = number of cases
per group, #slab = name of cohort
< meta.es <- escalc(measure = "MD", m1i = memory1, sd1i= sd_memory1, n1i =
n_memory1, m2i = memory0, sd2i= sd_memory0, n2i = n_memory0, slab = X, data =
meta_data)
#Meta—analysis for mean effect as calculated with the previous code, using a weakly #informed
half-normal distribution with a standard deviation of 0.5 as prior for the #heterogeneity parameter
τ.
< ma01 <- bayesmeta(y = meta.es[, "yi"], sigma = sqrt(meta.es[, "vi"]), labels = meta.es[,
"X"], mu.prior.mean = 0, mu.prior.sd = 1, tau.prior = function(t) dhalfnormal(t, scale = 0.5))

```

## Step 2. Report details of the computation

A. *Software.* Report the software used, including any specific added packages or plugins.

The software used and specific packages are reported in the statistics section.

B. *MCMC chain convergence.* Report evidence that the chains have converged, using a convergence statistic such as PSRF, for every parameter or derived value.

MCMC chain mixing was checked using trace plots in R (brms::plot), Rhat [3] was used for all parameters and models calculated, and was 1.0 for all reported models.

We used 4 chains with 8000 iterations each, including 2000 warm-up samplings.

C. *MCMC chain resolution.* Report evidence that the chains have high resolution, using the ESS, for every parameter or derived value.

The bulk and tail effective sample size (ESS) was higher than 8,000 for all parameters in the model, indicating low autocorrelation of the MCMC chains.

## Step 3. Describe the posterior distribution

A. *Posterior predictive check.* Provide a posterior predictive check to show that the model usefully mimics the data.

Posterior predictive checks are summarized in Figure 1.

B. *Summarize posterior of variables.* For continuous parameters, derived variables and predicted values, report the central tendency and limits of the credible interval. Explicitly state whether you are using density-based values (mode and HDI) or quantile-based values (median and ETI), and state the mass of the credible interval (for example, 95%).

Posterior variables are reported as mean and 95% credibility intervals, including the parameters of interest for the longitudinal models.

C. *BF and posterior model probabilities.* If conducting model comparison or hypothesis testing, report the BF and posterior probabilities of models for a range of prior model probabilities.

Bayes Factors comparing the index model with the base model are reported in the results section.

#### **Step 4. Report decisions (if any) and their criteria**

*A. Why decisions? Explain why the decisions are theoretically meaningful and which decision procedure is being used. Regardless of which decision procedure is used, if it addresses null values, it should be able to accept the null value not only reject it.*

Decisions were based on the 95% credibility intervals of the parameter estimates. Credibility intervals including the null values were considered to indicate some degree of evidence for the absence of an effect.

*B. BF, decision threshold and model probabilities. If using model comparison or hypothesis testing as the basis for a decision, state and justify the decision threshold for the posterior model probability, and the minimum prior model probability that would make the posterior model probability exceed the decision threshold.*

Bayes factors (BF) were calculated for the practice effect models. Here, we indicated that a  $BF > 3$  would be considered moderate evidence for the presence of an effect.

*C. Estimated values too. If deciding about null values, always also report the estimate of the parameter value (central tendency and credible interval).*

See point A.

#### **Step 5. Report sensitivity analysis**

*A. For default priors. If using a default prior, show the effect of varying its settings. Be sure that the range of default priors constitutes theoretically meaningful priors, and consider whether they mimic plausible empirically informed priors.*

For the **longitudinal mixed effect models with “brms”** in a sensitivity analysis we compared outcomes when using very weakly informed priors with a normal distribution of mean 0 and standard deviation of 10. For the **Bayesian random-effects meta-analysis** with “bayesmeta”, in a sensitivity analysis, we compared effects when using an uninformative Jeffreys prior for heterogeneity.

#### **Step 6. Make it reproducible**

*A. Software and installation. Explain all the software that is necessary and where to obtain it. If possible, use non-proprietary software.*

We used R and JASP as free to use software with specification of version and libraries used as detailed in the statistics section.

*B. Software version details. The posted script should include detailed information about the software version numbers.*

See point A.

#### **REFERENCES**

- [1] Kruschke JK (2021) Bayesian analysis reporting guidelines. *Nat Hum Behav* **5**, 1282-1291.
- [2] Rhodes KM, Turner RM, Higgins JPT (2015) Predictive distributions were developed for the extent of heterogeneity in meta-analyses of continuous outcome data. *J Clin Epidemiol* **68**, 52-60.
- [3] Gelman A, Rubin DB (1992) Inference from iterative simulation using multiple sequences (with discussion). *Stat Sci* **7**, 457–511.

**Supplementary Table 2.** Effect on individual-level practice effect estimates for memory**A) Effect of age, controlling for amyloid group and sex**

<b>Models</b>	<b>P(M)</b>	<b>P(M data)</b>	<b>BF<sub>M</sub></b>	<b>BF<sub>10</sub></b>	<b>error %</b>
Null model (incl. sex, amyloid group)	0.500	$5.826 \times 10^{-8}$	$5.826 \times 10^{-8}$	1.000	
age	0.500	1.000	$1.716 \times 10^{+7}$	$1.716 \times 10^{+7}$	2.090

**B) Effect of group, controlling for age and sex**

<b>Models</b>	<b>P(M)</b>	<b>P(M data)</b>	<b>BF<sub>M</sub></b>	<b>BF<sub>10</sub></b>	<b>error %</b>
Null model (incl. sex, age)	0.125	$3.948 \times 10^{-49}$	$2.764 \times 10^{-48}$	1.000	
diagnosis by amyloid + BF + Hip	0.125	0.621	11.452	$1.572 \times 10^{+48}$	2.267
diagnosis by amyloid + Hip	0.125	0.379	4.279	$9.609 \times 10^{+47}$	3.721
diagnosis by amyloid + BF	0.125	$3.091 \times 10^{-7}$	$2.164 \times 10^{-6}$	$7.830 \times 10^{+41}$	7.086
diagnosis by amyloid	0.125	$1.035 \times 10^{-9}$	$7.245 \times 10^{-9}$	$2.622 \times 10^{+39}$	1.874
diagnosis by BF + Hip	0.125	$2.233 \times 10^{-11}$	$1.563 \times 10^{-10}$	$5.656 \times 10^{+37}$	4.355
diagnosis by Hip	0.125	$3.457 \times 10^{-12}$	$2.420 \times 10^{-11}$	$8.757 \times 10^{+36}$	1.871
diagnosis by BF	0.125	$2.685 \times 10^{-20}$	$1.880 \times 10^{-19}$	$6.801 \times 10^{+28}$	2.443

BF<sub>10</sub>, Bayes factor in favor of the model in this row against the null model on top; BF<sub>M</sub>, degree of change from prior to posterior model odds; error%, numerical stability of the result; P(M), assumed prior model probability; P(M|data), posterior model probability after having analyzed the data.

**Supplementary Table 3.** Effect on individual-level practice effect estimates for executive function**A) Effect of age controlling for amyloid group and sex**

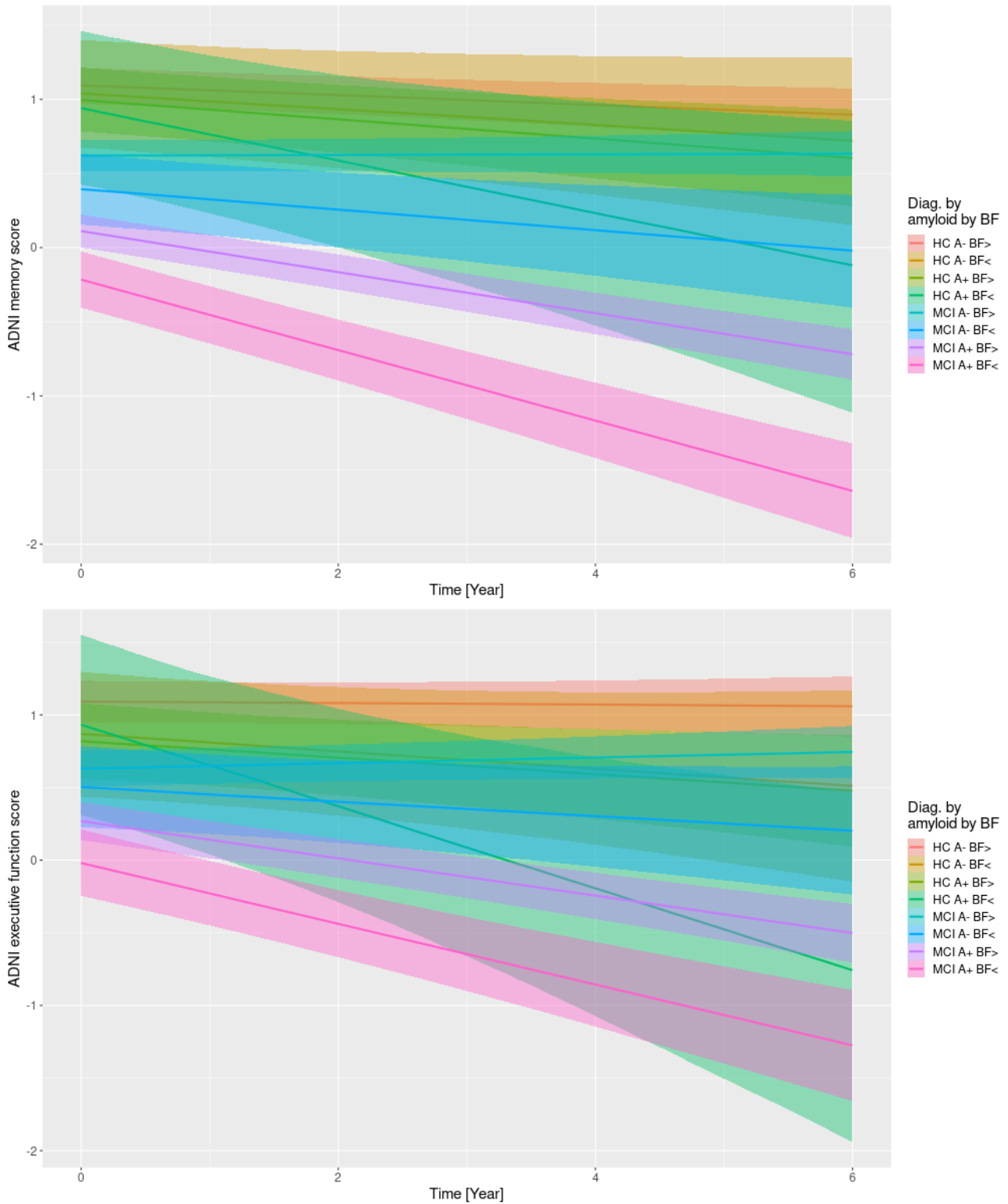
<b>Models</b>	<b>P(M)</b>	<b>P(M data)</b>	<b>BF<sub>M</sub></b>	<b>BF<sub>10</sub></b>	<b>error %</b>
Null model (incl. sex, amyloid group)	0.500	$6.525 \times 10^{-6}$	$6.525 \times 10^{-6}$	1.000	
age	0.500	1.000	153253.404	153253.404	2.776

**B) Effect of group, controlling for age and sex**

<b>Models</b>	<b>P(M)</b>	<b>P(M data)</b>	<b>BF<sub>M</sub></b>	<b>BF<sub>10</sub></b>	<b>error %</b>
Null model (incl. sex, age)	0.125	$7.707 \times 10^{-29}$	$5.395 \times 10^{-28}$	1.000	5.099
diagnosis by amyloid + BF + Hip	0.125	0.706	16.802	$9.159 \times 10^{+27}$	3.471
diagnosis by amyloid + BF	0.125	0.262	2.488	$3.402 \times 10^{+27}$	3.318
diagnosis by amyloid + Hip	0.125	0.031	0.226	$4.062 \times 10^{+26}$	3.088
diagnosis by amyloid	0.125	$5.707 \times 10^{-4}$	0.004	$7.404 \times 10^{+24}$	5.099
diagnosis by BF + Hip	0.125	$1.862 \times 10^{-16}$	$1.303 \times 10^{-15}$	$2.416 \times 10^{+12}$	3.319
diagnosis by Hip	0.125	$2.054 \times 10^{-18}$	$1.438 \times 10^{-17}$	$2.665 \times 10^{+10}$	2.936
diagnosis by BF	0.125	$1.685 \times 10^{-18}$	$1.179 \times 10^{-17}$	$2.186 \times 10^{+10}$	25.198

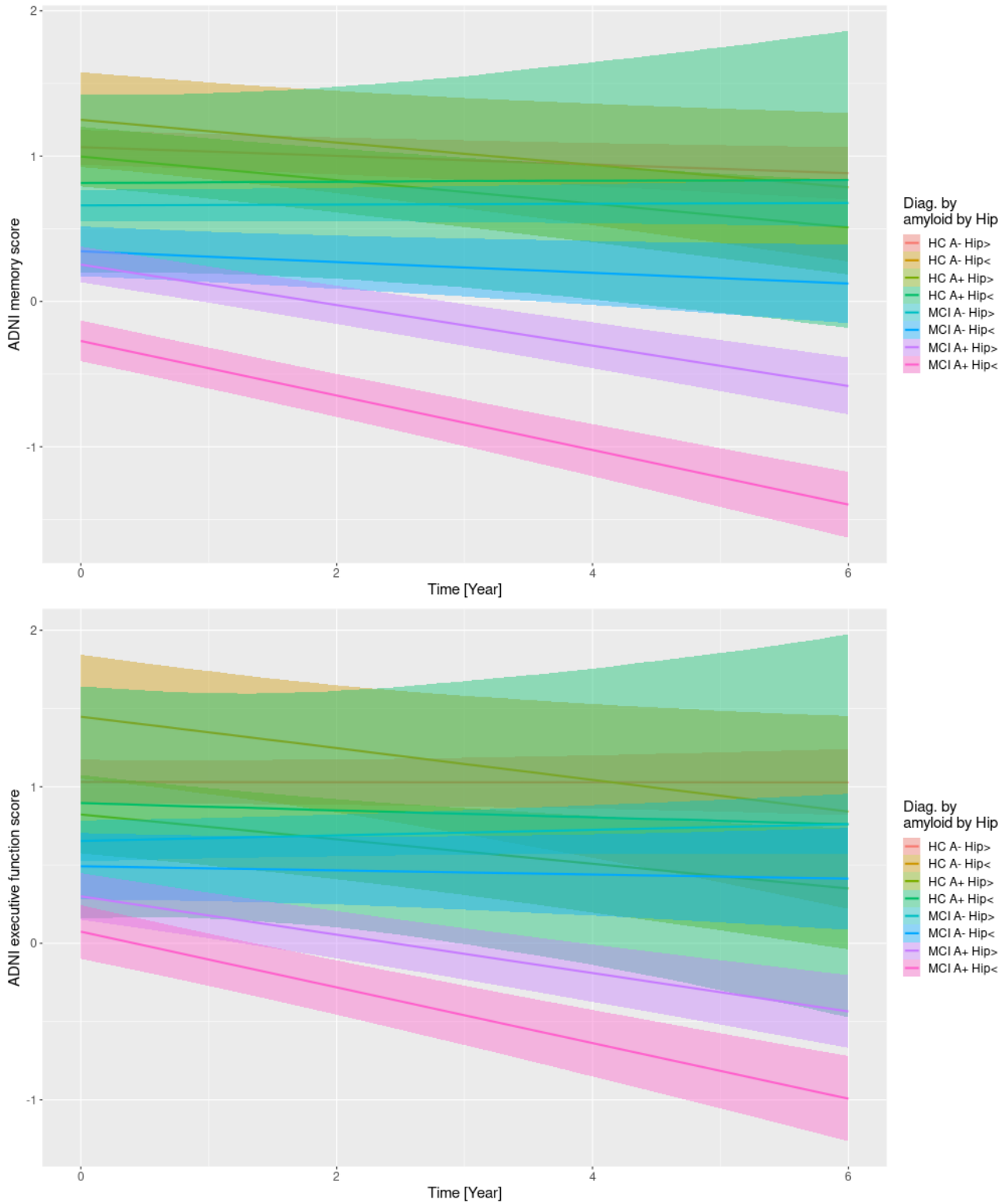
BF<sub>10</sub>, Bayes factor in favor of the model in this row against the null model on top; BF<sub>M</sub>, degree of change from prior to posterior model odds; error%, numerical stability of the result; P(M), assumed prior model probability; P(M|data), posterior model probability after having analyzed the data.

**Supplementary Figure 1.** Cognitive change by diagnosis, amyloid status, and basal forebrain volume. Marginal interaction effects of time with amyloid status, basal forebrain volume, and diagnosis for ADNI memory and executive function in the ADNI cohort as dependent variables in generalized mixed effect models predicting cognitive scores by diagnosis, amyloid status, and basal forebrain volume and their interaction with time with random slope and intercept terms, nested within individuals.



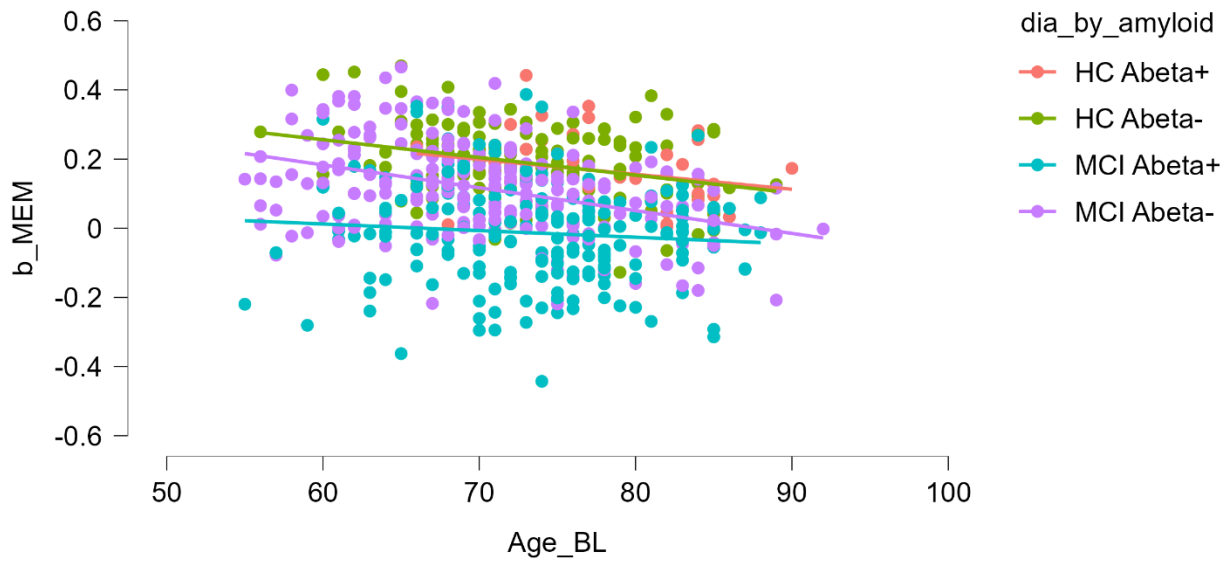
HC/MCI A- BF>, amyloid negative healthy controls/MCI cases with larger basal forebrain volume  
 HC/MCI A+ BF>, amyloid positive healthy controls/MCI cases with smaller basal forebrain volume

**Supplementary Figure 2.** Cognitive change by diagnosis, amyloid status, and hippocampus volume. Marginal interaction effects of time with amyloid status, hippocampus volume, and diagnosis for ADNI memory and executive function in the ADNI cohort as dependent variables in generalized mixed effect models predicting cognitive scores by diagnosis, amyloid status, and hippocampus volume and their interaction with time with random slope and intercept terms, nested within individuals.



HC/MCI/SCD A- Hip>, amyloid negative healthy controls/MCI cases with larger hippocampus volume  
 HC/MCI/SCD A+ Hip>, amyloid positive healthy controls/MCI cases with smaller hippocampus volume

**Supplementary Figure 3.** Association of the practice effect estimate for memory with age and diagnosis by amyloid groups.  $b\_MEM$  (the estimated practice effect from the third degree polynomial function) regressed on age, stratified according to diagnosis.





**Supplementary Figure 4.** Practice effect estimate for memory versus diagnosis by amyloid groups.  $b\_MEM$  (the estimated practice effect from the third degree polynomial function) according to diagnosis by amyloid status, with 95% credibility intervals.

