

RBP4 and dementia

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Is Retinol Binding Protein 4 plasma concentration associated with cognitive performance and markers of AD in a normal older people?

Abstract

Retinol Binding protein has been linked to cognitive decline and Alzheimer's disease, both in humans, and in animal models of AD. Here we measured the plasma concentration of RBP4 in the participants of the Stratifying Depression Longitudinally (STRADL) cohort. We hypothesised that reduced RBP4 contrations in the plasma were associated with early signs of dementia.

Hypotheses

Hypothesis - RBP4 plasma concentration associated with cognitive decline and risk of developing Alzheimer's dementia

- Plasma analysis of RBP4 by Jason Clarke, under supervision of Prof Peter McCafferty.
- This analysis by Chris McNeil.
- 2021_02_24

Data Analysis

Import Packages

```
library(tidyverse)
library(readr)
library(readxl)
library(performance)
library(Hmisc) #correlations
library(corrplot) #plotting correlations
library(expss) # apply labels to variable names
library(knitr) #neat tables
library(kableExtra) #neater tables
library(viridis)
library(RColorBrewer)
library(modernrdiv) # linear regression
knitr::opts_chunk$set(echo=FALSE, message=FALSE, warning=FALSE, fig.align="left", fig.width = 5)
```

Data preparation

- import STRADL data
 - Confounding variables: demographics
 - Variables of interest: Brain MRI variables (volumes etc), cognitive variables

Rename variables

Merge dataframes

Calculate brain volumes as ml

Calculate brain volumes relative to skull size

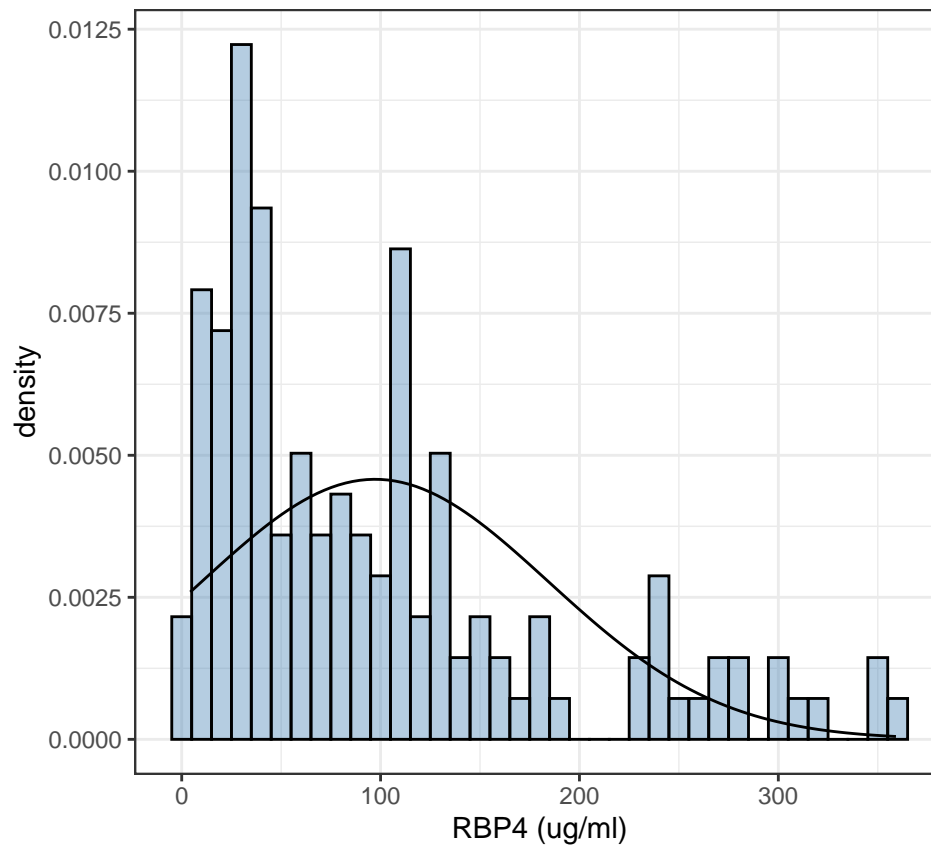
change sex character to numeric code (0=female, 1=male). dplyr because masking by expss

calculate BMI

label variables to make plots/tables easier to read:

Data Distribution

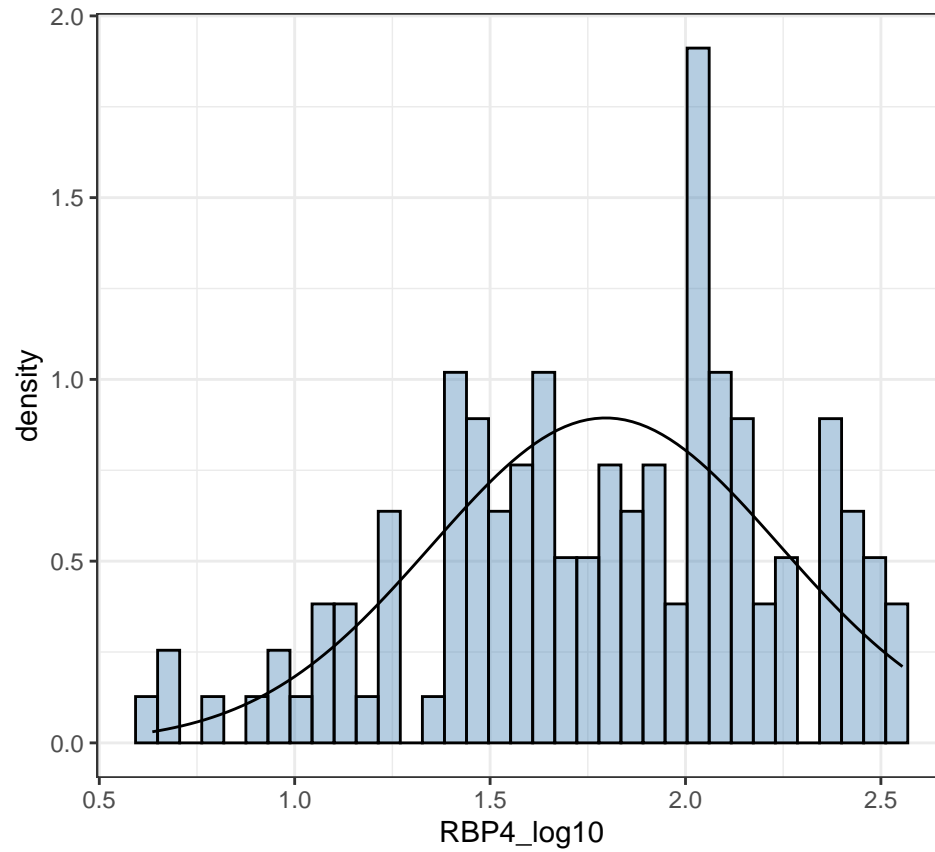
- Check the distribution of RBP4 concentrations



RBP4 distribution is non-normal. Log Transform the data. **Transform the RBP4 data using log10**

Check distribution

Sex	mean	median	sd	not.na
0	101.57	68.26	95.43	82
1	94.07	81.31	74.75	54
NA	35.15	30.84	20.21	3



Data summary

RBP4 concentration by sex Table 1. [RBP4]^{ug.ml⁻¹} by sex. 0 = Female, 1= Male ##### RBP4 and BMI

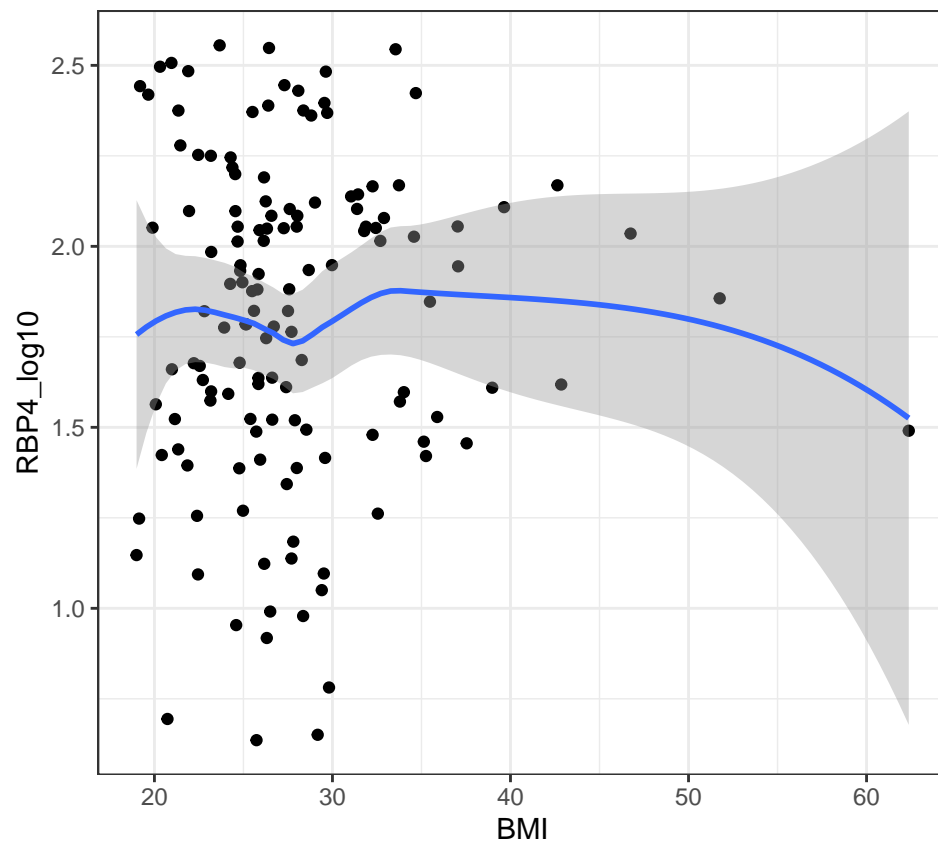


Figure 1. $[\text{RBP4}]^{\text{ug.ml}^{-1}}$ and BMI #### RBP4 against hippocampal volume

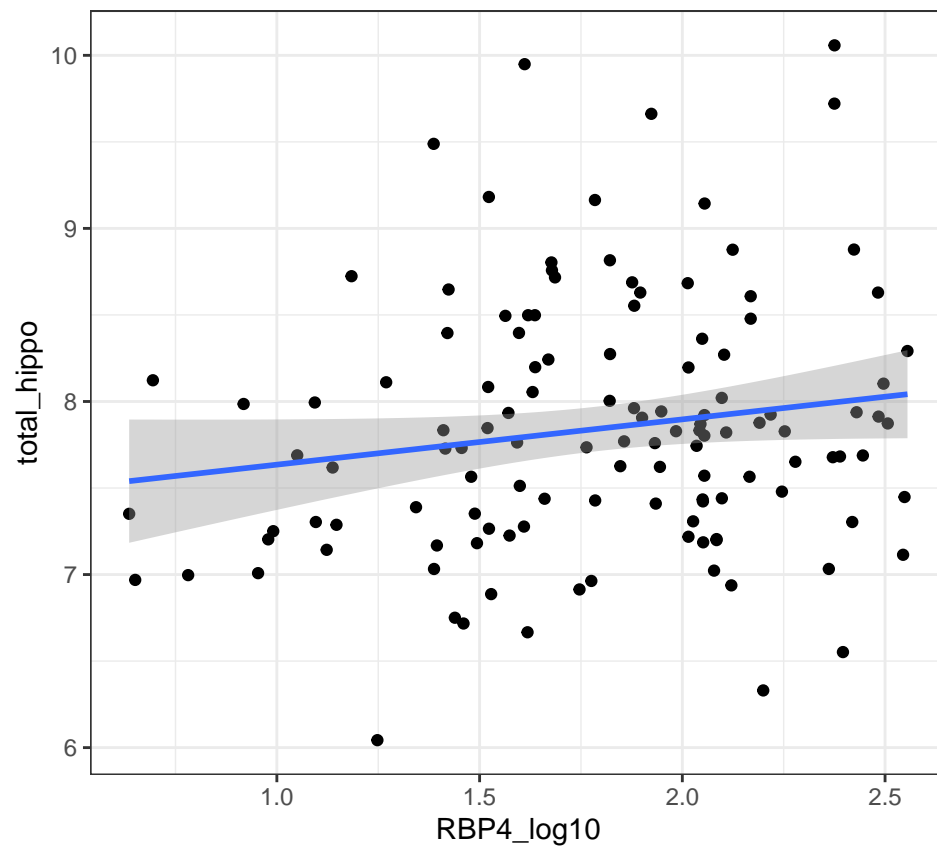


Figure 2 $[\text{RBP4}]^{\text{ug.ml}^{-1}}$ and Total Hippocampal Volume ml^{-1}

RBP4 concentration and Digit Symbol

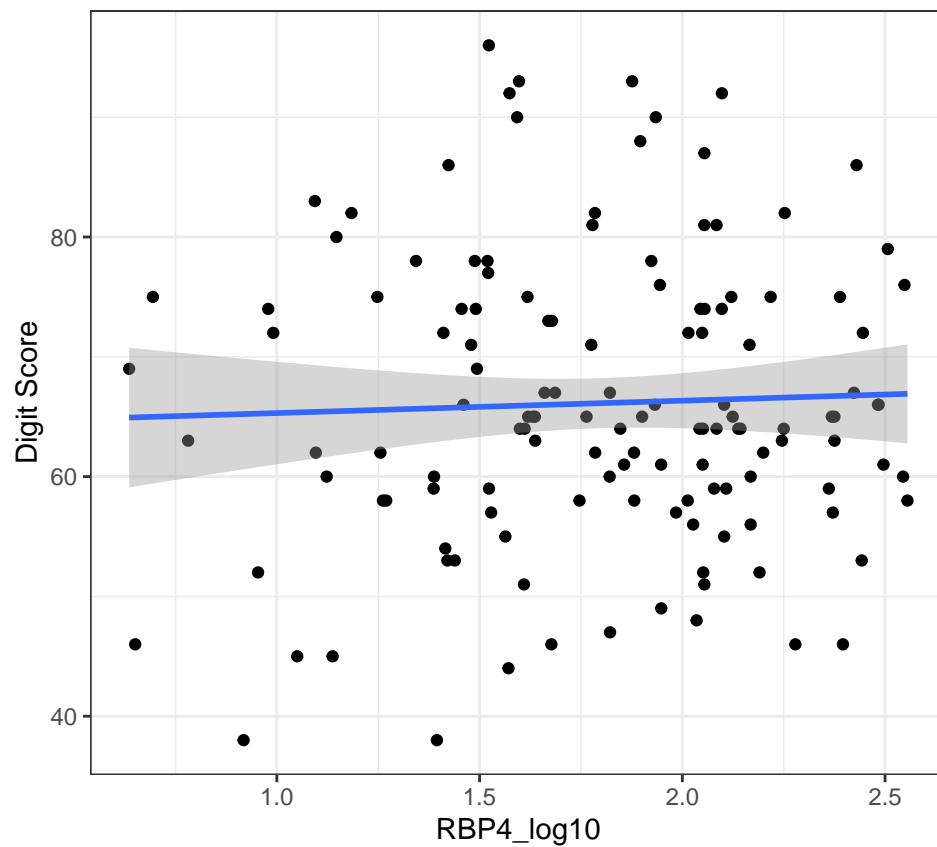


Figure 3 $[\text{RBP4}]^{\text{ug}\cdot\text{ml}^{-1}}$ and Digit Symbol Score
 #### RBP4 concentration against age

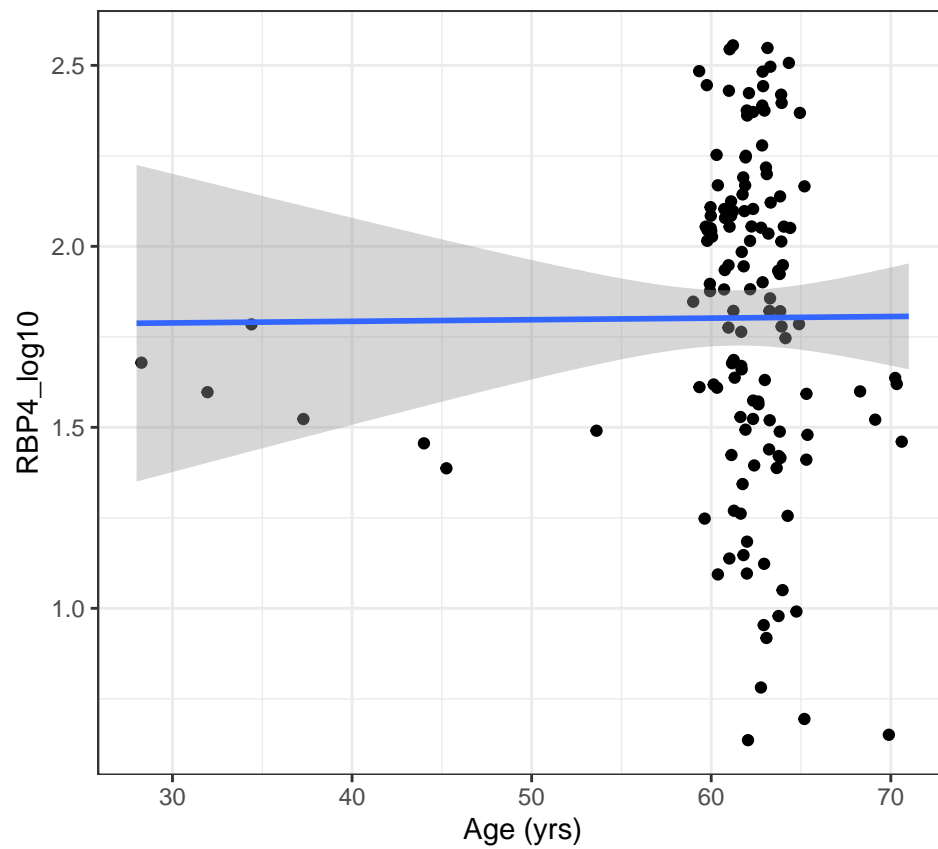
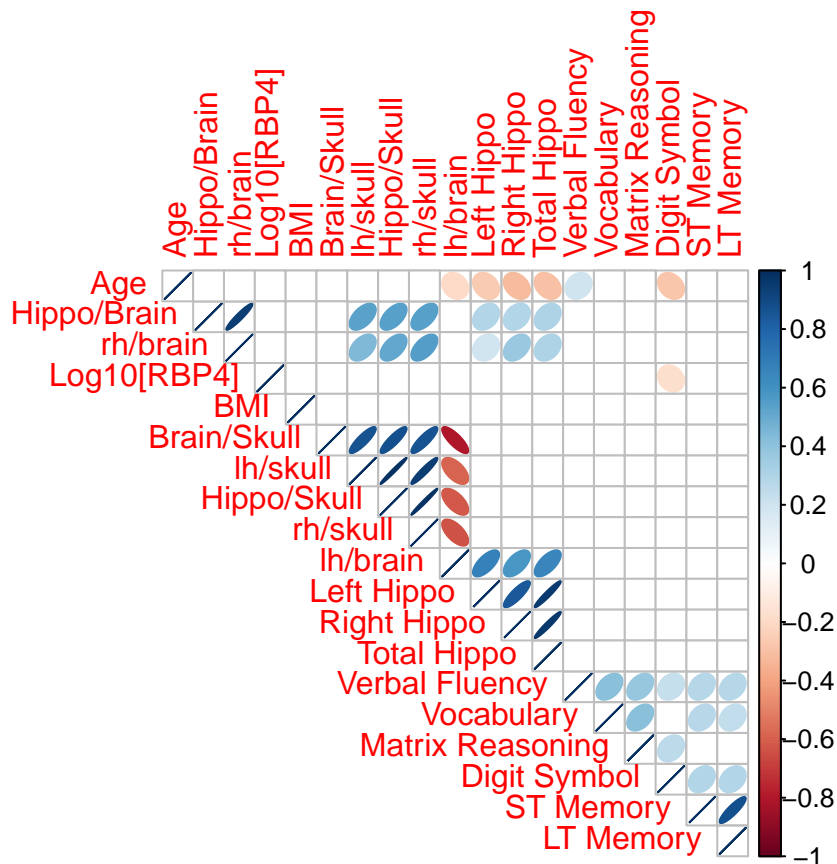


Figure 4. Age and $[\text{RBP4}]^{\text{ug.ml}^{-1}}$.
 ### Correlation Matrix of RBP4 against key variables



There is no correlation between RBP4 concentrations and brain/cognition variables. (uncorrected)

Regression Analysis [RBP4] and it's risk factors or consequences

RBP4 and the brain

RBP4 and hippocampal volume

```
##
## Call:
## lm(formula = RBP4_log10 ~ `L Hippo (ml) total_hippo`)
##
## Residuals:
##      Min       1Q   Median       3Q      Max
## -1.12473 -0.27226  0.02744  0.31466  0.82471
##
## Coefficients:
##              Estimate Std. Error t value Pr(>|t|)
## (Intercept)    1.01955     0.42990   2.372   0.0193 *
## `L Hippo (ml) total_hippo`  0.09842     0.05458   1.803   0.0738 .
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Residual standard error: 0.4459 on 123 degrees of freedom
## (14 observations deleted due to missingness)
## Multiple R-squared:  0.02575,    Adjusted R-squared:  0.01783
```



```
## F-statistic: 3.252 on 1 and 123 DF, p-value: 0.07381
```

RBP4 abd hippocampal volume (corrected)

```
##
## Call:
## lm(formula = RBP4_log10 ~ `TH/IVC` + Sex + BMI)
##
## Residuals:
##      Min       1Q   Median       3Q      Max
## -1.11184 -0.28993  0.07078  0.27085  0.85833
##
## Coefficients:
##              Estimate Std. Error t value Pr(>|t|)
## (Intercept)  1.104e+00  3.510e-01   3.144  0.0021 **
## `TH/IVC`      8.547e+04  4.608e+04   1.855  0.0661 .
## Sex          1.064e-01  8.710e-02   1.221  0.2243
## BMI          4.900e-03  7.155e-03   0.685  0.4948
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Residual standard error: 0.4476 on 121 degrees of freedom
## (14 observations deleted due to missingness)
## Multiple R-squared:  0.03441, Adjusted R-squared:  0.01047
## F-statistic: 1.437 on 3 and 121 DF, p-value: 0.2353
```

RBP4 and Digit symbol score (cognition - processing speed)

```
##
## Call:
## lm(formula = RBP4_log10 ~ `Digit Score`)
##
## Residuals:
##      Min       1Q   Median       3Q      Max
## -1.16430 -0.31266  0.05313  0.31122  0.77052
##
## Coefficients:
##              Estimate Std. Error t value Pr(>|t|)
## (Intercept)  1.704100   0.214656   7.939 7.79e-13 ***
## `Digit Score` 0.001390   0.003193   0.436   0.664
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Residual standard error: 0.449 on 132 degrees of freedom
## (5 observations deleted due to missingness)
## Multiple R-squared:  0.001435, Adjusted R-squared: -0.00613
## F-statistic: 0.1897 on 1 and 132 DF, p-value: 0.6639
```

RBP4 and mema (cognition -short term memory)

```
##
## Call:
## lm(formula = RBP4_log10 ~ `Memory (immediate)`)
##
## Residuals:
```

```
##      Min      1Q   Median      3Q      Max
## -1.17101 -0.29138  0.06037  0.30185  0.75618
##
## Coefficients:
##              Estimate Std. Error t value Pr(>|t|)
## (Intercept)      1.824653   0.175228  10.413 <2e-16 ***
## `Memory (immediate)` -0.001491   0.011373  -0.131   0.896
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Residual standard error: 0.4495 on 134 degrees of freedom
## (3 observations deleted due to missingness)
## Multiple R-squared:  0.0001283, Adjusted R-squared:  -0.007333
## F-statistic: 0.01719 on 1 and 134 DF, p-value: 0.8959
```

RBP4 and memdela (cognition -medium term memory)

```
##
## Call:
## lm(formula = RBP4_log10 ~ `Memory (delayed)`)
##
## Residuals:
##      Min      1Q   Median      3Q      Max
## -1.18468 -0.29669  0.03332  0.29492  0.77845
##
## Coefficients:
##              Estimate Std. Error t value Pr(>|t|)
## (Intercept)      1.894439   0.145083  13.058 <2e-16 ***
## `Memory (delayed)` -0.006572   0.009971  -0.659   0.511
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Residual standard error: 0.4488 on 134 degrees of freedom
## (3 observations deleted due to missingness)
## Multiple R-squared:  0.003231, Adjusted R-squared:  -0.004207
## F-statistic: 0.4344 on 1 and 134 DF, p-value: 0.511
```

Results and Discussion

- RBP4 concentrations were in the range expected in human plasma
- RBP4 was not associated with age, BMI or sex.
- RBP4 was not correlated with cognitive test performance that is sensitive to the symptoms of early dementia
- There was no significant association of RBP4 with hippocampal volumes, however the effect seen approached significance.