Wombat - 2016

Simple tools for complex problems: making molehills out of mountains

Dr Zoe van Havre

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  - **making data analysis easier**

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3. boundless excitement.

Urgency?

Can we keep up?

- The exponential growth of computing has not slowed down.

to do: DIA-GRAM 1

to do: DIA-GRAM 2

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- New types of data and new challenges require new approaches
- in 10 years, expecting to see 1000 times growth

to do: DIA-GRAM 1

to do: DIA-GRAM 2

Hope...

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- Everyone is coming onboard! amazing advances

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    - This might mean going Bayesian, yes. Sorry.

Excitement!

Better tools make data analysis easier

Amazing things happen when data analysis combines clear research questions, appropriate data, and suitable, accessible tools.

- Accessibility: usability, and understanding what the tool does.

It doesnt have to be just "analysis", it can be exploration, discovery, and a little bit magical.

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- People can do more with less (ie. *bricks VS cement*)
- Simple models are less likely to be wrongly used

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A short story about Alzheimer's Disease| featuring... overfitted mixture models!

Key background

Alzheimer's Disease (AD) currently affects over 342,800 Australians, and this number is expected to rise to 900,000 by 2050.
Cognitive changes indicated something is amiss, but these occur late in the disease ($\geq$ 20 years).
During this time, AD causes irreversible damage to the brain:

- accumulation of **amyloid** β,

To better research and treat AD, we need to be able to treat it earlier.

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During this time, AD causes irreversible damage to the brain:

- accumulation of **amyloid** β,
- neurofibrillary tangles,
- overall atrophy.

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- disease development is very slow
- cognitive changes indetectable for $\geq$ 20 years
- Tests which assess physical change are $ $ $ and intrusive

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To better tackle AD, we need to be able to treat it earlier.

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To better tackle AD, we need to be able to treat it earlier.

- we know little about how AD behaves in its early stage
- could compare known cases to controls,
  - does not target early stage of AD
- **would like to identify individuals likely to be in early stage of AD**

How?

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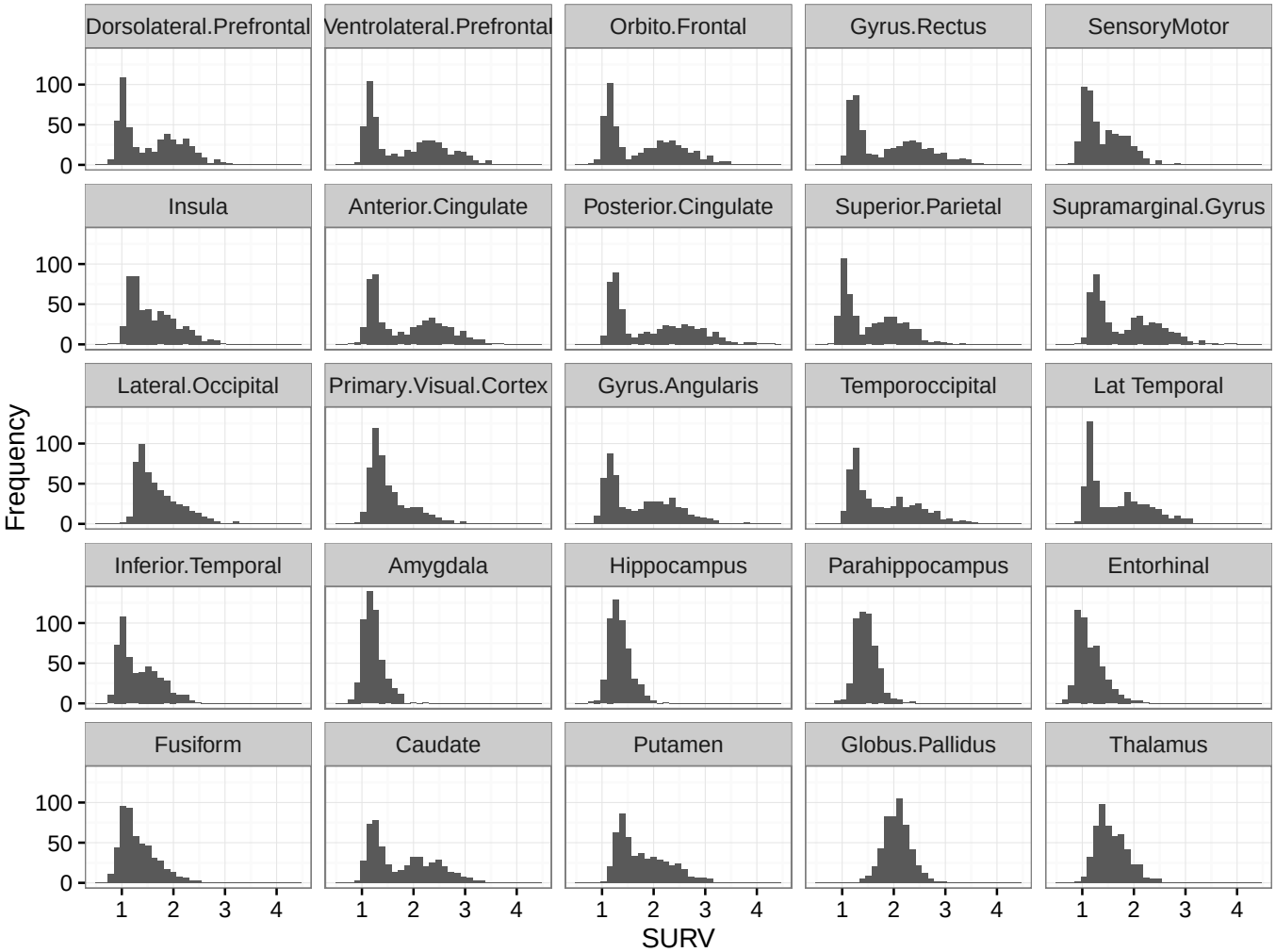
- What now...?

The Data

The study consists of 507 individuals, composed of Healthy Controls (HC), MCI, and AD patients.

```
##
##  AD MCI  HC
## 103 114 290
```


Dorsolateral.Prefrontal
Ventrolateral.Prefrontal
Orbito.Frontal
Gyrus.Rectus
SensoryMotor
Insula
Anterior.Cingulate
Posterior.Cingulate
Superior.Parietal
Supramarginal.Gyrus
Lateral.Occipital
Primary.Visual.Cortex
Gyrus.Angularis
Temporoccipital
Lat Temporal
Inferior.Temporal
Amygdala
Hippocampus
Parahippocampus
Entorhinal
Fusiform
Caudate
Putamen
Globus.Pallidus
Thalamus
Frequency
0
50
100
1
2
3
4
SURV

Overfitting with Zmix

Overfitted mixture models

We can model an unknown number of groups using **overfitted mixture models**, a Bayesian method found in the R package "Zmix".

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- data driven and fully parametric
- Bayesian, but straightforward
- Assumes only that up to K groups are normally distributed with an unknown mean and variance.

How it's done

Install the package

```
install_github('zoevanhavre/Zmix') # Thank you Hadley!
library(Zmix)
```

Run the model with $K = 5$ groups

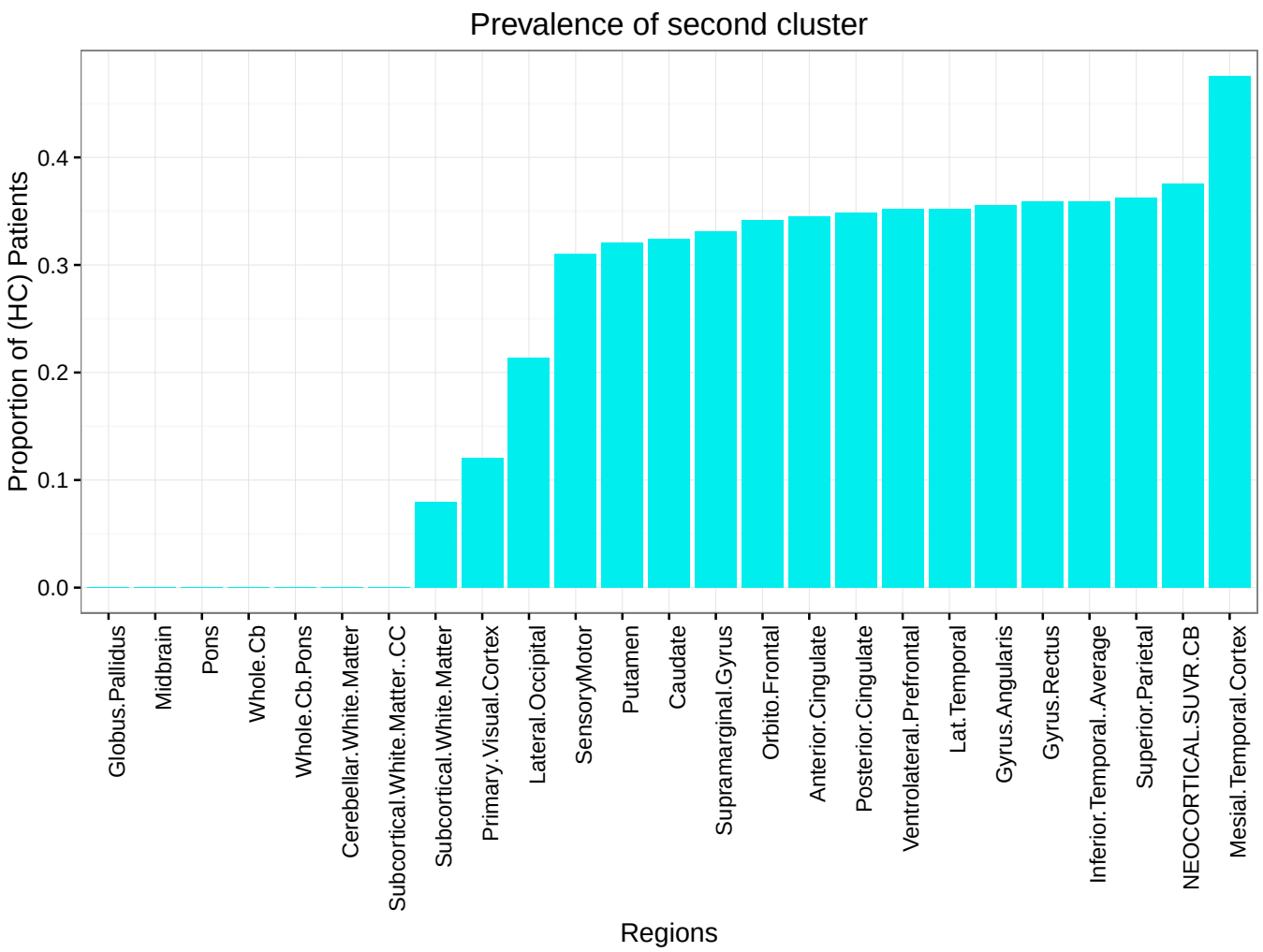
```
### <b>
Zmix.Y<-Zmix_univ_tempered (Y, iter=50000, k=5)
### </b>
```

Process the results

```
Proc.Zmix.Y<-Process_Output_Zmix(Zmix.Y, Burn=25000)
```

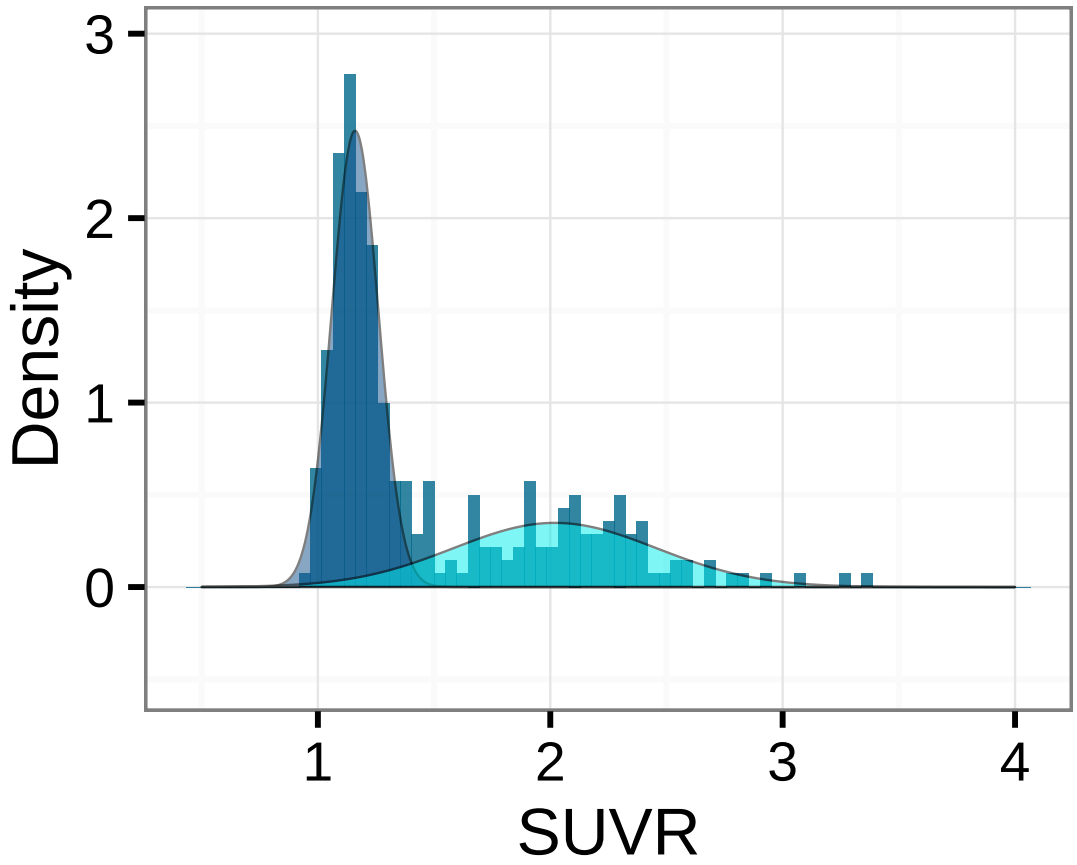
Check out the README for more examples

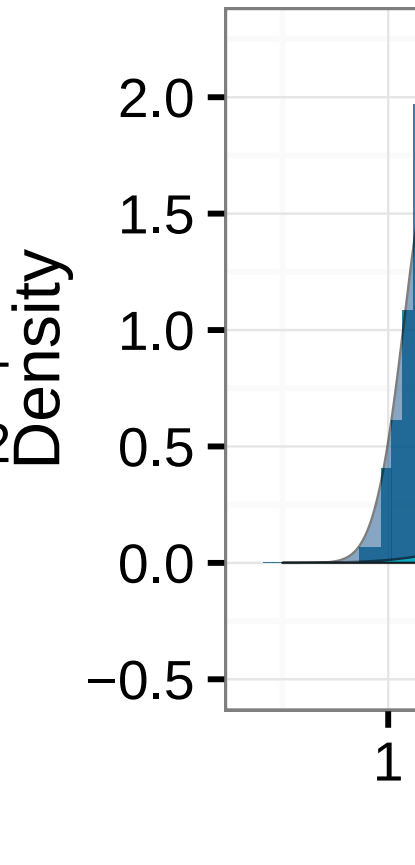
Results


Prevalence of second cluster
Proportion of (HC) Patients
0.0
0.1
0.2
0.3
0.4
Globus.Pallidus
Midbrain
Pons
Whole.Cb
Whole.Cb.Pons
Cerebellar.White.Matter
Subcortical.White.Matter..CC
Subcortical.White.Matter
Primary.Visual.Cortex
Lateral.Occipital
SensoryMotor
Putamen
Caudate
Supramarginal.Gyrus
Orbito.Frontal
Anterior.Cingulate
Posterior.Cingulate
Ventrolateral.Prefrontal
Lat.Temporal
Gyrus.Angularis
Gyrus.Rectus
Inferior.Temporal..Average
Superior.Parietal
NEOCORTICAL.SUVR.CB
Mesial.Temporal.Cortex
Regions

Ventrolateral.Prefrontal

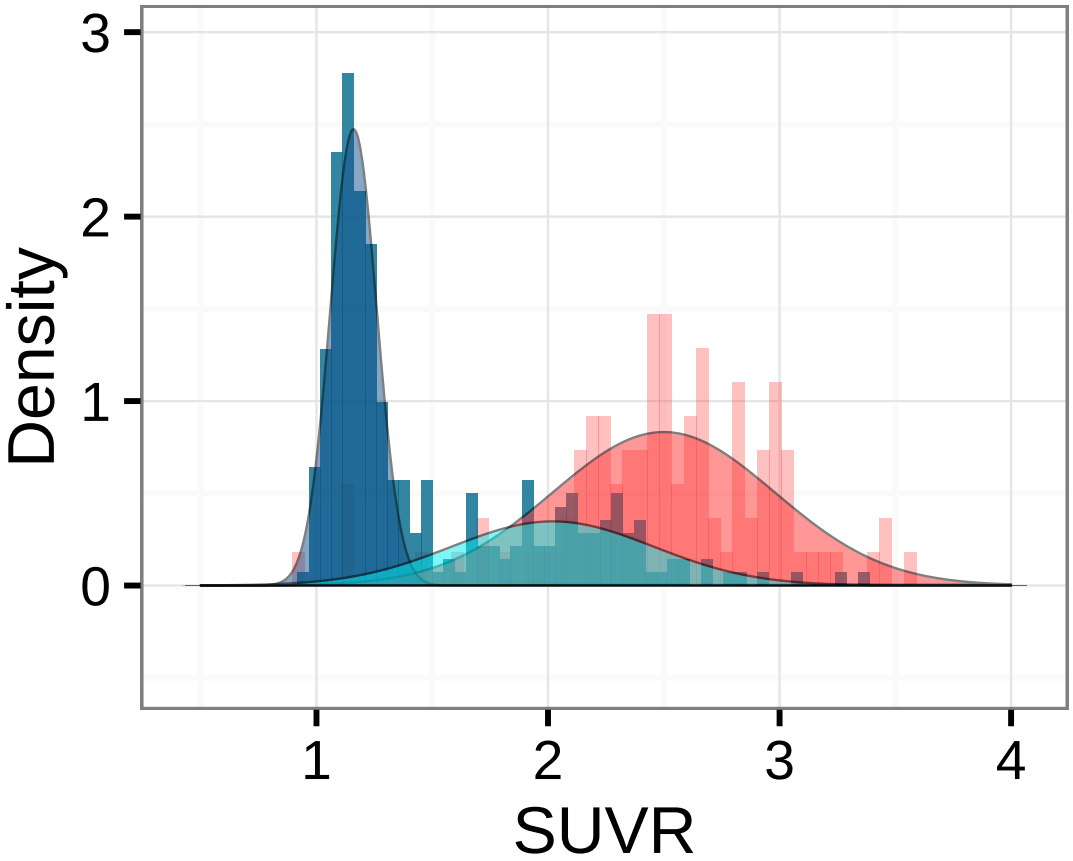
HC (Blue)

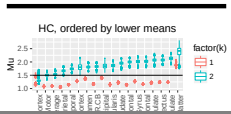


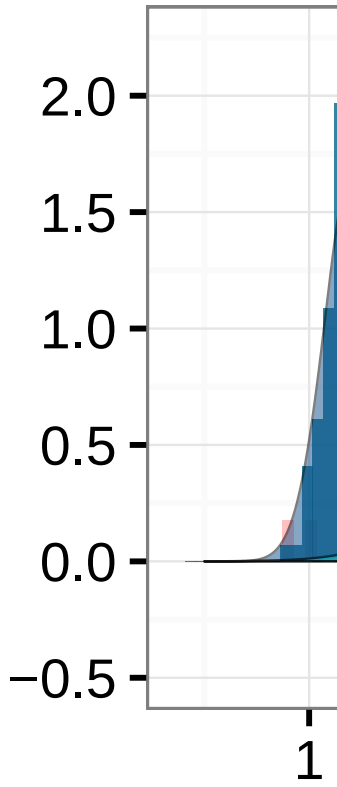


Ventrolateral.Prefrontal

HC (Blue) & AD (Red)







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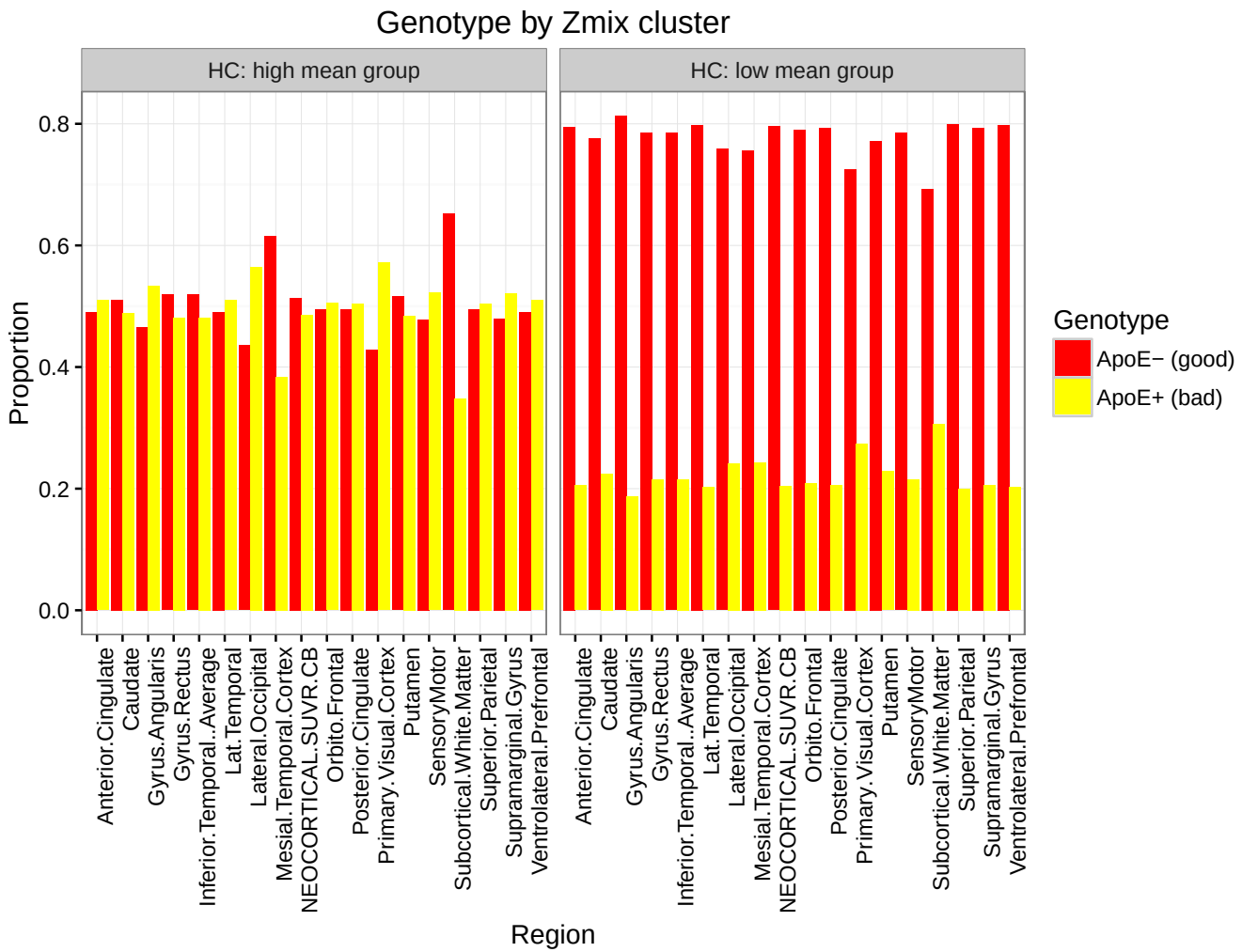
- Allocations to 2nd group highly correlated (across individuals)
- The HC clusters with larger means resemble the distribution of SUVR in AD, shifted to a lower mean, (as would be expected in early stages of the disease).
- They also follow a similar pattern across regions to AD


Genotype by Zmix cluster
HC: high mean group
HC: low mean group
Proportion
0.0
0.2
0.4
0.6
0.8
Anterior.Cingulate
Caudate
Gyrus.Angularis
Gyrus.Rectus
Inferior.Temporal..Average
Lat.Temporal
Lateral.Occipital
Mesial.Temporal.Cortex
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Subcortical.White.Matter
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Ventrolateral.Prefrontal
Region
Genotype
ApoE− (good)
ApoE+ (bad)


Memory Status by Zmix cluster
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