



**Karolinska  
Institutet**

# Brain Cell Type Enrichment

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# Introduction

Gene sets:

- Exome sequencing (cases vs controls)
- Transcriptome-wide association studies (TWAS)
- Co-localization analysis (GWAS, eQTL)
- Gene Set Enrichment Analysis (MAGMA)
- Differential expression (cases vs controls)

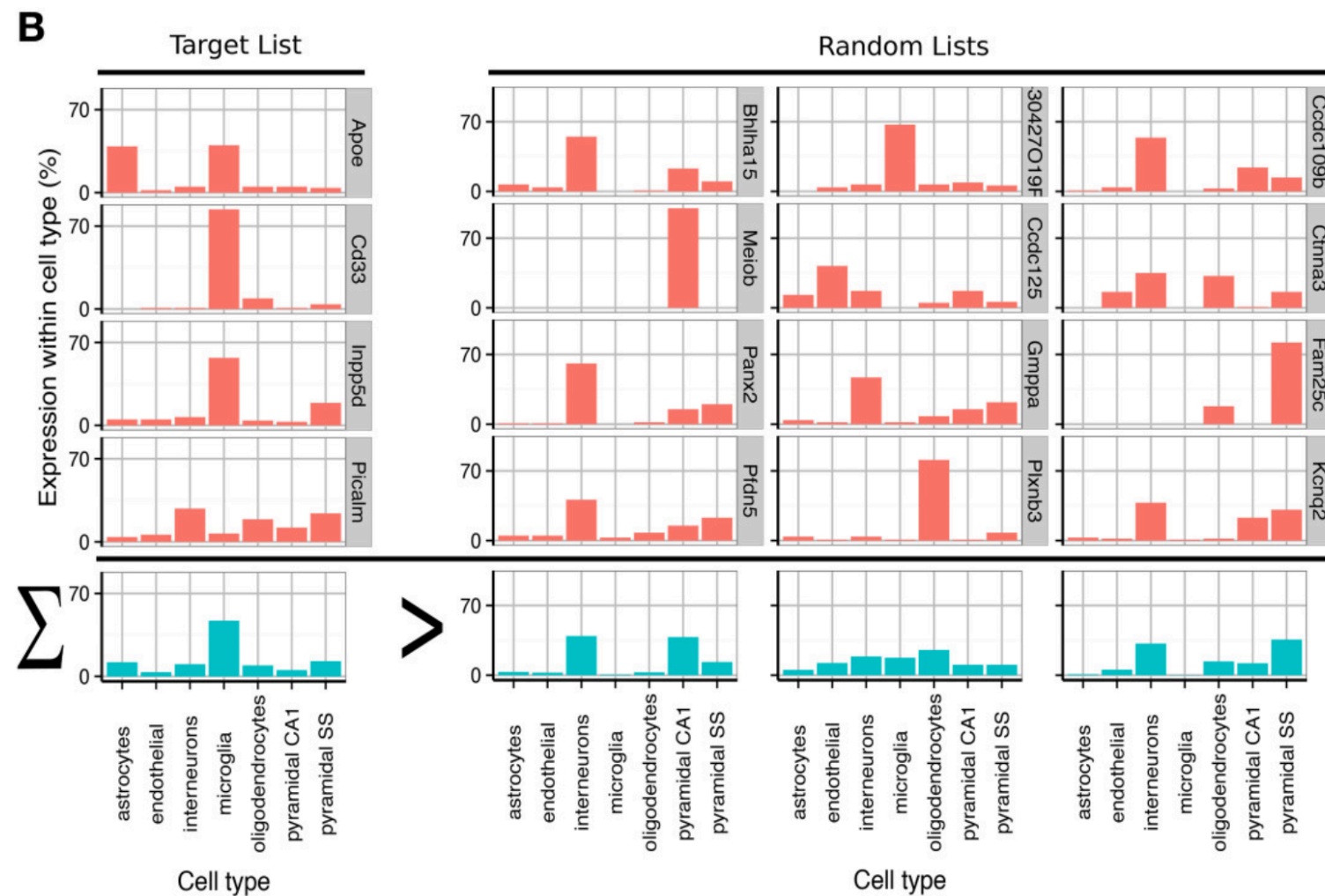
**Enrichment in specific brain cell types?**

# Expression Weighted Cell Type Enrichment

## Identification of Vulnerable Cell Types in Major Brain Disorders Using Single Cell Transcriptomes and Expression Weighted Cell Type Enrichment

Nathan G. Skene and Seth G. N. Grant \*

Frontiers in Neuroscience, 2016



**Good:** - Permutation based pvalue

**Drawbacks:** - Specific format required

- Slow

- Bounded pvalues

- Null distribution?

# Goals

- New method (BrainRich)
  - Fast
  - Flexible
  - Easy to use
- Re-implement EWCE
  - Easy to use

# BrainRich

## Differential Expression

- 9970 single cells in total (24 cell types)

	Pyramidal 1	Pyramidal ...	Pyramidal N	Microglia 1	Microglia ...	Microglia N	Astrocyte 1	Astrocyte ...	Astrocyte N	....
Gene 1	10	12	9	0	1	2	3	2	1	4
Gene 2	50	40	45	2	4	5	9	5	4	2
...	...	...	...	...	...	...	...	...	...	...
Gene N	0	1	2	40	50	34	4	4	2	1

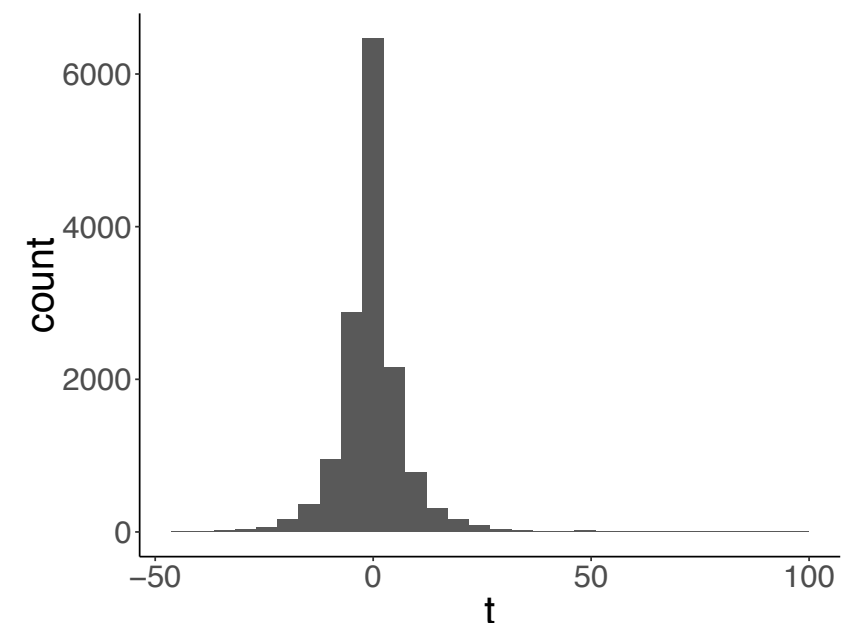
- Differential expression (BPSC)

Vu et al., Bioinformatics, 2016

- Size factors

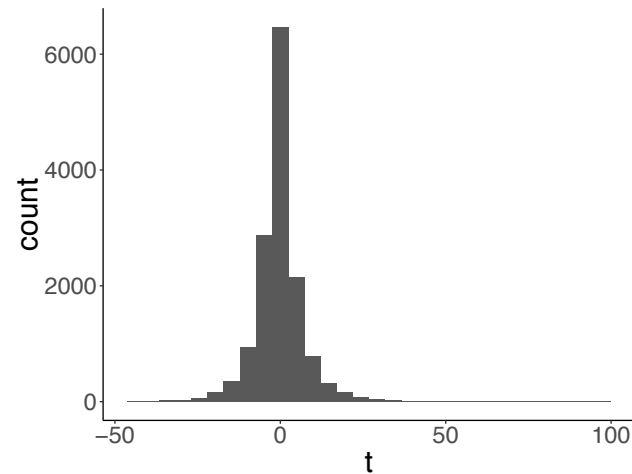
Lun et al., Genome Biology, 2016

## Pyramidal CA1 vs all

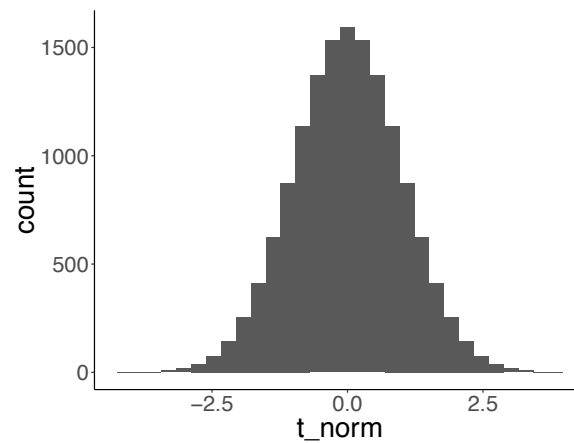


# BrainRich

## Differential Expression (Pyramidal CA1 vs all)

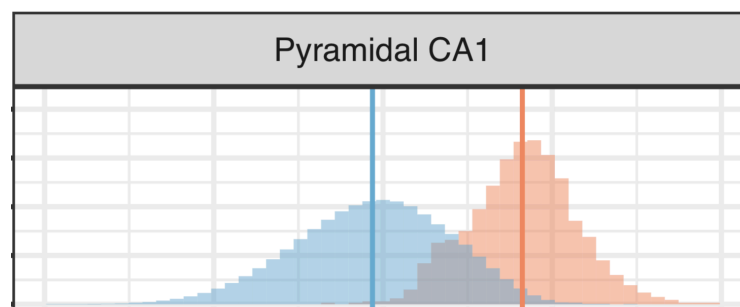


## Standard Normalisation



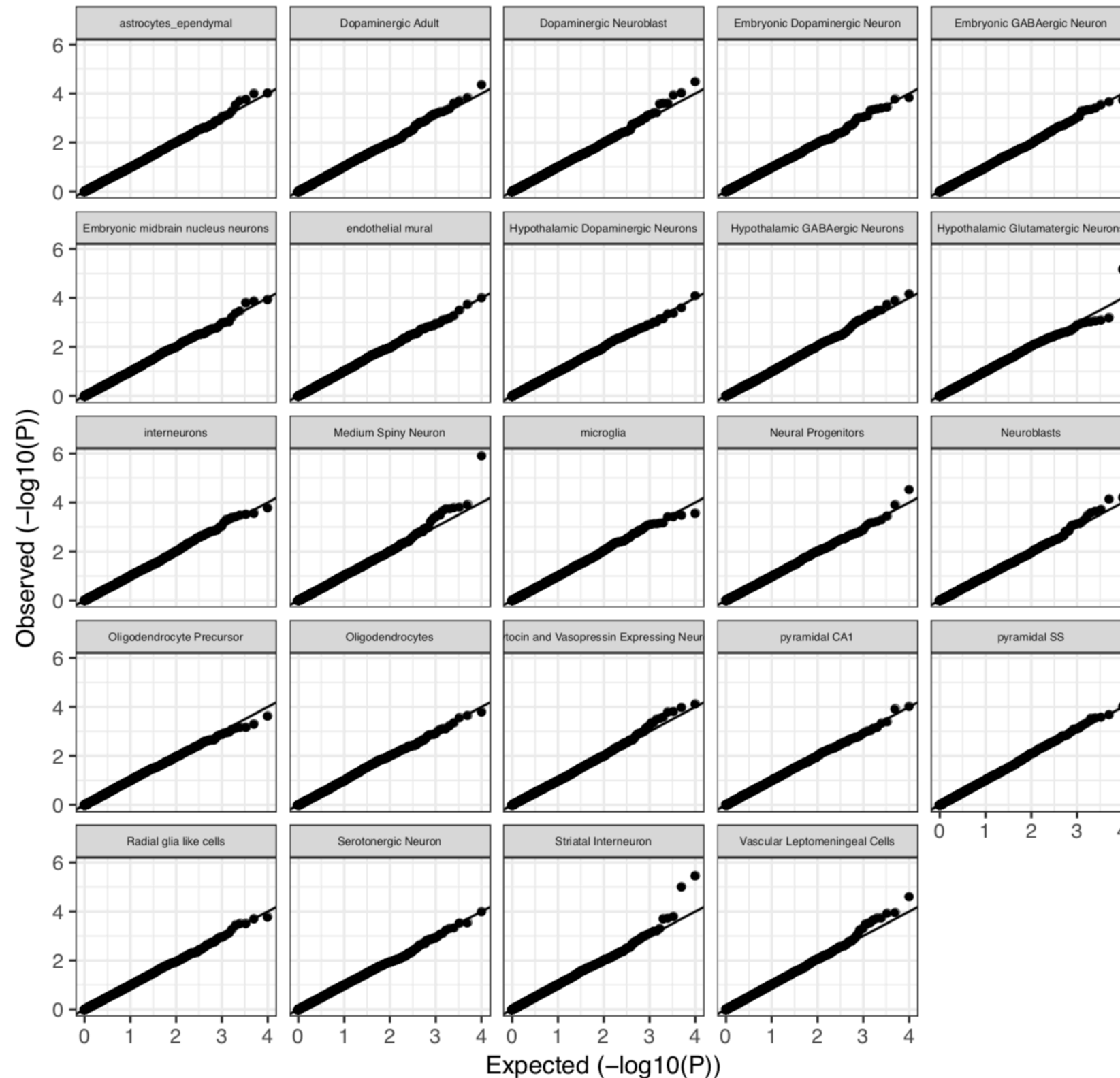
## Linear Regression

$t\_norm \sim \text{gene\_set}(0/1)$



# BrainRich - Simulations

- 1000 random gene sets of different size  
(50, 100, 200, 300, 400, 500, 1000, 2000, 3000, 5000)



# BrainRich - Shiny App

## Brain Cell Type Enrichment

**Separator**

☐ Tab

☒ Space

☐ Comma

☐ xls

☐ xlsx

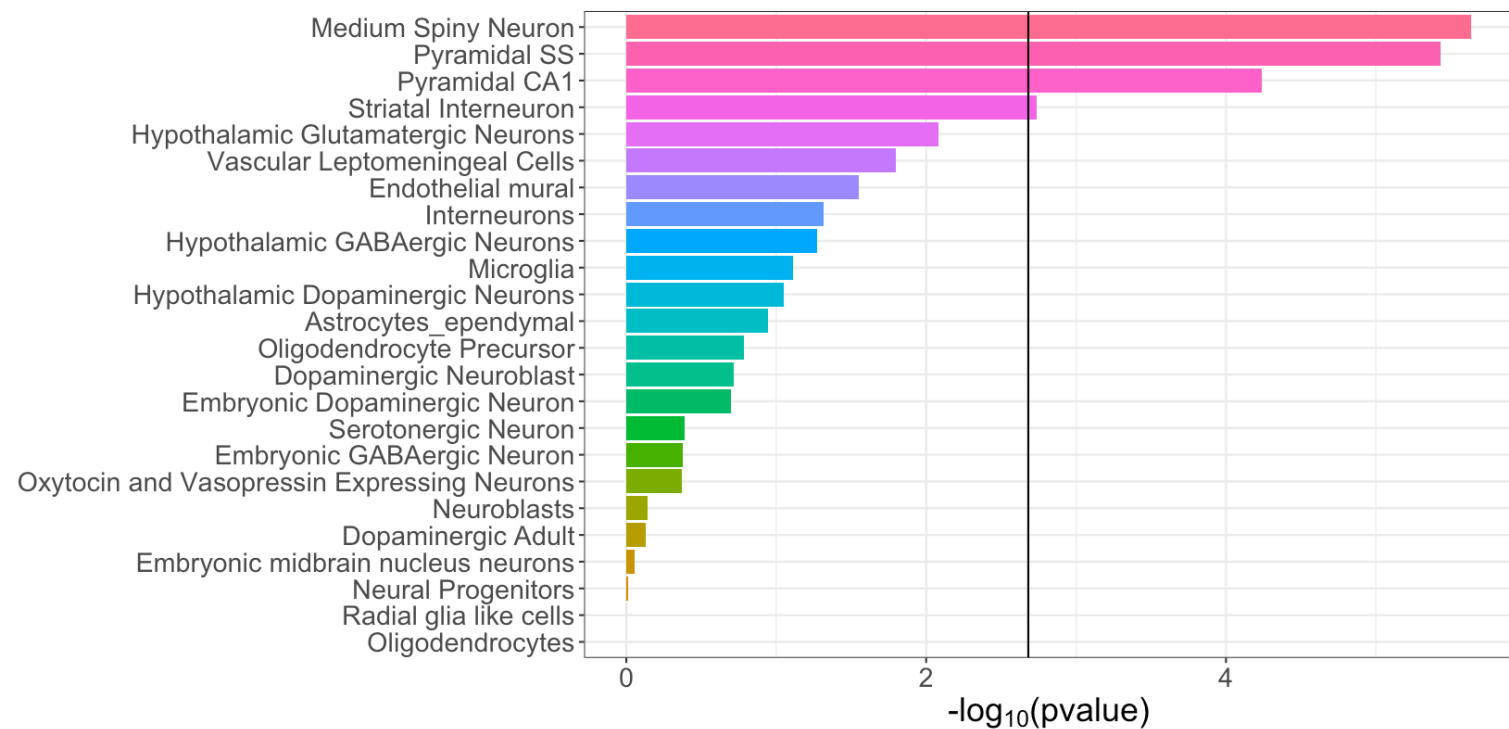
☐ Header

**Input File**

Browse... antipsychotic.txt

Upload complete

Category	Number_genes
Input	104
Matched	82
Selected	82
Not selected	0



- Easy to use
- Fast
- Any type of genes (ENTREZ, Ensembl, Symbol) (**1st column**)
- Possibility to filter on numerical columns
- If multiple columns and > 4000 genes, corrects for genes tested



# Demo

**<https://jbryois.shinyapps.io/BrainRich/>**