Supplementary Figures

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July 1, 2021

1 Forest Plots

Forest Plot of transcript of interest in a trait across all tissues (across all cohorts \(\dagger\)). The top plot shows predicted expression in all tissues/cohorts where a positive correlation (\(\beta\)) with the given trait is orange and purple when the correlation is negative. The second plot shows the GWAS trait association (\(\beta\)) for SNPs that appear in any of the PrediXcan models. The SNPs are all within 1 MB of the gene of interest but are not spaced by their physical separations. The PrediXcan and GTEx models display (\(\beta\)) of the same set of SNPs in the GWAS plot among all the tissues (single tissue for across cohorts) and are ordered the same so all SNPs are aligned.

1.1 Across Tissue Phom Results

Across Tissue
ENSG00000021488 (SLC7A9)
NIC ~ Across_Tissue

| Tissue                        | p-value |
|-------------------------------|---------|
| sHom                          | 1.16e−07|
| sHet                          | 1.85e−04|

Standard Association Model (beta values)

GWAS Model

PredXcan Model

GTE Model
| Tissue/Region                                | p-value       |
|---------------------------------------------|---------------|
| Putaminal_ganglia                           | 2.24e−03      |
| Nucleus_accumbens_basal_ganglia             | 4.75e−03      |
| Hypothalamus                                | 2.18e−04      |
| Hippocampus                                 | 1.27e−03      |
| Frontal_Cortex_BA9                         | 1.48e−02      |
| Cortex                                      | 1.34e−03      |
| Cerebellum                                  | 4.44e−02      |
| Cerebellar_Hemisphere                       | 5.42e−03      |
| Caudate_basal_ganglia                      | 4.81e−04      |
| Anterior_cingulate_cortex_BA24             | 2.28e−05      |

**Standard Association Model (beta values)**

**GWAS Model**

**PrediXcan Model**

**GTEx Model**
Family_Alcoholism ~ Across_Tissue

| Region                          | p-value     |
|--------------------------------|-------------|
| sHom                           | 3.37e−08    |
| sHet                           | 4.76e−05    |

- Putambasal_ganglia: 2.96e−03
- Nucleus_accumbens_basal_ganglia: 2.29e−02
- Hypothalamus: 1.35e−03
- Hippocampus: 1.45e−03
- Frontal_Cortex_BA9: 2.02e−02
- Cortex: 1.83e−03
- Cerebellum: 2.53e−03
- Cerebellar_Hemisphere: 2.74e−03
- Caudate_basal_ganglia: 5.03e−04
- Anterior_cingulate_cortex_BA24: 6.10e−03

Standard Association Model (beta values)
ENSG00000103245 (CIAO3)

Alc_Dep ~ Across_Tissue

\[ p\text{-value} \]

\begin{align*}
\text{sHom} & \quad 8.84\text{e}^{-08} \\
\text{sHet} & \quad 1.42\text{e}^{-04}
\end{align*}

-0.8 -0.6 -0.4 -0.2 0.0

\text{Standard Association Model (beta values)}

-1.5 -0.5 0.5 1.5

\text{GWAS Model}

\text{PrediXcan Model}

\text{GITE-Model}

-1.5 -0.5 0.5 1.5

Putam basal_ganglia 2.28e–03
Nucleus_accumbens_basal_ganglia 5.34e–03
Hypothalamus 8.37e–04
Hippocampus 2.30e–04
Frontal_Cortex_BA9 1.44e–02
Cortex 1.24e–02
Cerebellum 1.15e–03
Cerebellar_Hemisphere 3.09e–03
Caudate_basal_ganglia 4.72e–04
Anterior_cingulate_cortex_BA24 1.03e–03
| Tissue/Region                        | p-value |
|-------------------------------------|---------|
| Putambasal_ganglia                  | 1.77e−02|
| Nucleus_accumbens_basal_ganglia     | 8.78e−05|
| Hypothalamus                        | 7.59e−03|
| Hippocampus                         | 4.21e−03|
| Frontal_Cortex_BA9                  | 2.50e−03|
| Cortex                              | 1.49e−04|
| Cerebellum                          | 1.51e−03|
| Cerebellar_Hemisphere               | 9.11e−04|
| Caudate_basal_ganglia              | 1.50e−03|
| Anterior_cingulate_cortex_BA24      | 1.42e−02|

**Standard Association Model (beta values)**

**GWAS Model**

**PrediXcan Model**

**GTEx Model**
ENSG00000122085 (MTERF4)

Family_Alcoholism ~ Across_Tissue

| Tissue                                    | p-value   |
|-------------------------------------------|-----------|
| sHom                                      | 2.78e-07  |
| sHet                                      | 2.67e-04  |

- Putaminal_ganglia: 5.62e-03
- Nucleus_accumbens_basal_ganglia: 6.69e-02
- Hypothalamus: 1.40e-04
- Hippocampus: 1.07e-02
- Frontal_Cortex_BA9: 3.79e-03
- Cortex: 1.45e-02
- Cerebellum: 1.06e-02
- Cerebellar_Hemisphere: 2.70e-02
- Caudate_basal_ganglia: 4.46e-03
- Anterior_cingulate_cortex_BA24: 5.78e-04

Standard Association Model (beta values)
ENSG00000124713 (GNMT)

Family_Alcoholism ~ Across_Tissue

| Tissue                          | Beta Value   |
|---------------------------------|--------------|
| Putambasal_ganglia              | 8.23e-04     |
| Nucleus_accumbens_basal_ganglia | 1.97e-03     |
| Hypothalamus                    | 5.55e-03     |
| Hippocampus                     | 2.38e-03     |
| Frontal_Cortex_BA9              | 4.29e-03     |
| Cortex                          | 2.79e-03     |
| Cerebellum                      | 8.61e-02     |
| Cerebellar_Hemisphere           | 1.13e-02     |
| Caudate_basal_ganglia           | 3.26e-03     |
| Anterior_cingulate_cortex_BA24  | 3.34e-02     |

p-value

sHom: 4.09e-07
sHet: 3.53e-04

Standard Association Model (beta values)
ENSG00000131845 (ZNF304)
Marijuana_Strong_Desire ~ Across_Tissue

| Tissue                                    | p-value     |
|-------------------------------------------|-------------|
| sHom                                      | 6.55e–09    |
| sHet                                      | 8.44e–06    |

- Putambasal_ganglia: 1.96e–03
- Nucleus_accumbens_basal_ganglia: 2.52e–03
- Hypothalamus: 1.19e–03
- Hippocampus: 2.31e–03
- Frontal_Cortex_BA9: 6.77e–04
- Cortex: 5.61e–04
- Cerebellum: 2.17e–03
- Cerebellar_Hemisphere: 7.29e–04
- Caudate_basal_ganglia: 5.49e–04
- Anterior_cingulate_cortex_BA24: 5.04e–02

![Graph showing beta values for different tissues with p-values]
ENSG00000149089 (APIP)

Alc_Dep ~ Across_Tissue

| Tissue                                      | p-value     |
|---------------------------------------------|-------------|
| Putamensal_ganglia                          | 6.29e−03    |
| Nucleus_accumbens_basal_ganglia             | 4.78e−03    |
| Hypothalamus                                | 3.88e−03    |
| Hippocampus                                 | 1.89e−03    |
| Frontal_Cortex_BA9                          | 1.07e−03    |
| Cortex                                      | 4.65e−03    |
| Cerebellum                                  | 2.29e−03    |
| Cerebellar_Hemisphere                       | 2.23e−03    |
| Caudate_basal_ganglia                       | 3.40e−03    |
| Anterior_cingulate_cortex_BA24              | 1.24e−02    |

p−value 5.18e−07
sHom
sHet 8.85e−04
ENSG00000165502 (RPL36AL)

Alc_Dep ~ Across_Tissue

| Tissue                           | p-value   |
|----------------------------------|-----------|
| Putaminal_ganglia                | 9.07e-04  |
| Nucleus_accumbens_basal_ganglia | 1.29e-03  |
| Hypothalamus                     | 3.53e-04  |
| Hippocampus                      | 2.61e-04  |
| Frontal_Cortex_BA9               | 2.38e-02  |
| Cortex                           | 1.97e-02  |
| Cerebellum                       | 1.91e-03  |
| Cerebellar_Hemisphere            | 8.71e-04  |
| Caudate_basal_ganglia           | 2.71e-04  |
| Anterior_cingulate_cortex_BA24  | 1.14e-01  |

p-value

1.26e-07

2.68e-04

GWAS Model

PrediXcan Model

GTEx Model

Standard Association Model (beta values)
|                          | sHom   | sHet   |
|--------------------------|--------|--------|
| ENSG00000165502 (RPL36AL) | 1.26e−07 | 2.68e−04 |

**Family_Alcoholism ~ Across_Tissue**

- **Putaminal_ganglia**: 7.68e−03
- **Nucleus_accumbens_basal_ganglia**: 8.25e−04
- **Hypothalamus**: 6.85e−03
- **Hippocampus**: 1.94e−02
- **Frontal_Cortex_BA9**: 1.18e−02
- **Cortex**: 2.77e−03
- **Cerebellum**: 5.77e−03
- **Cerebellar_Hemisphere**: 1.12e−03
- **Caudate_basal_ganglia**: 7.32e−03
- **Anterior_cingulate_cortex_BA24**: 3.23e−03

**Standard Association Model (beta values)**

**GWAS Model**

**PredXcan Model**

**CITE Model**
ENSG00000168385 (SEPTIN2) Family_Alcoholism ~ Across_Tissue

| Location                                      | p-value     |
|-----------------------------------------------|-------------|
| Putambasal_ganglia                           | 5.02e-04    |
| Nucleus_accumbens_basal_ganglia              | 8.40e-04    |
| Hypothalamus                                  | 1.18e-02    |
| Hippocampus                                   | 5.16e-03    |
| Frontal_Cortex_BA9                           | 8.19e-03    |
| Cortex                                        | 2.59e-03    |
| Cerebellum                                    | 3.72e-03    |
| Cerebellar_Hemisphere                        | 4.67e-04    |
| Caudate_basal_ganglia                        | 1.14e-03    |
| Anterior_cingulate_cortex_BA24               | 3.63e-04    |

sHom: 5.51e-09  sHet: 1.36e-05
ENSG00000170802 (FOXN2)
Family_Alcoholism ~ Across_Tissue

| Tissue                              | p-value  |
|-------------------------------------|----------|
| sHom                                | 2.01e−07 |
| sHet                                | 2.90e−04 |

Standard Association Model (beta values)

- Putambasal_ganglia: 1.64e−03
- Nucleus_accumbens_basal_ganglia: 8.65e−03
- Hypothalamus: 3.29e−03
- Hippocampus: 1.72e−02
- Frontal_Cortex_BA9: 4.33e−03
- Cortex: 4.39e−02
- Cerebellum: 1.73e−03
- Cerebellar_Hemisphere: 2.70e−03
- Caudate_basal_ganglia: 3.63e−03
- Anterior_cingulate_cortex_BA24: 1.09e−02

PrediXcan Model

GWAS Model

GTEx Model
ENSG00000180376 (CCDC66)
Marijuana_Strong_Desire ~ Across_Tissue

**p-value**

- sHom: $2.03 \times 10^{-8}$
- sHet: $4.58 \times 10^{-5}$

**Beta Values**

- Putambasal_ganglia: $5.10 \times 10^{-3}$
- Nucleus_accumbens_basal_ganglia: $2.35 \times 10^{-4}$
- Hypothalamus: $4.01 \times 10^{-3}$
- Hippocampus: $2.82 \times 10^{-3}$
- Frontal_Cortex_BA9: $4.29 \times 10^{-3}$
- Cortex: $2.89 \times 10^{-3}$
- Cerebellum: $5.36 \times 10^{-3}$
- Cerebellar_Hemisphere: $3.11 \times 10^{-3}$
- Caudate_basal_ganglia: $1.16 \times 10^{-2}$
- Anterior_cingulate_cortex_BA24: $3.80 \times 10^{-4}$

**Standard Association Model (beta values)**

- GWAS Model
- PredXcan Model
- GTEx Model
ENSG00000186468 (RPS23)
NIC ~ Across_Tissues

Hom
Het
p-value
4.09e−07
7.21e−04

Standard Association Model (beta values)

GWAS Model

PrediXcan Model

CITE Model

Putaminal_ganglia 1.19e−02
Nucleus_accumbens_ganglia 3.54e−03
Hypothalamus 1.50e−02
Hippocampus 1.52e−03
Frontal_Cortex_BA9 2.21e−02
Cerebellum 2.97e−03
Cerebellar_Hemisphere 2.33e−02
Caudate_ganglia 4.36e−03
Anterior_cingulate_cortex_BA24 1.42e−02

GWAS Model

PrediXcan Model

CITE Model
**ENSG00000189306 (RRP7A)**

**MJ ~ Across_Tissue**

- **sHom**: p-value 1.04e−07
- **sHet**: p-value 1.73e−04

**Standard Association Model (beta values)**

| Tissue                                      | Beta Value |
|---------------------------------------------|------------|
| Putam basal ganglia                         | 2.50e−02   |
| Nucleus accumbens basal ganglia             | 8.71e−03   |
| Hypothalamus                                | 1.41e−03   |
| Hippocampus                                 | 2.88e−03   |
| Frontal Cortex BA9                          | 2.82e−03   |
| Cortex                                      | 8.74e−04   |
| Cerebellum                                  | 3.15e−03   |
| Cerebellar Hemisphere                       | 1.05e−02   |
| Caudate basal ganglia                       | 3.29e−03   |
| Anterior cingular cortex BA24               | 2.52e−03   |

**GWAS Model**

**PredXcan Model**

**CITE-Model**
ENSG00000197558 (SSPO) NIC ~ Across_Tissue

| Location                          | p−value       |
|----------------------------------|---------------|
| sHom                             | 1.08e−08      |
| sHet                             | 3.11e−05      |

-0.15 -0.10 -0.05 0.00

Standard Association Model (beta values)

| Location                          | Value  |
|----------------------------------|--------|
| Putambasal_ganglia               | 2.39e−03|
| Nucleus_accumbens_basal_ganglia  | 2.30e−03|
| Hypothalamus                     | 5.89e−03|
| Hippocampus                      | 3.25e−03|
| Frontal_Cortex_BA9               | 2.53e−03|
| Cortex                           | 3.50e−03|
| Cerebellum                       | 2.12e−03|
| Cerebellar_Hemisphere            | 2.20e−03|
| Caudate_basal_ganglia           | 2.68e−03|
| Anterior_cingulate_cortex_BA24   | 1.93e−03|

GWAS Model

PrediXcan Model

GTEx Model
The page contains statistical data related to the association of ERV3−1 with Family_Alcoholism across different tissues. The table shows the p-values for homogeneity (sHom) and heterogeneity (sHet). The tissues listed include: Putambasal_ganglia, Nucleus_accumbens_basal_ganglia, Hypothalamus, Hippocampus, Frontal_Cortex_BA9, Cortex, Cerebellum, Cerebellar_Hemisphere, Caudate_basal_ganglia, and Anterior_cingulate_cortex_BA24.

The p-values are as follows:

- sHom: 4.51e−07
- sHet: 6.96e−04

The diagram shows the standard association model (beta values) and the associations of different models (GWAS, PredXcan, and GTEx) across various tissues.
ENSG00000237765 (FAM200B)
MJ ~ Across_Tissue

| Tissue                                    | p-value     |
|-------------------------------------------|-------------|
| Putambasal_ganglia                        | 6.55e−04    |
| Nucleus_accumbens_basal_ganglia           | 4.88e−03    |
| Hypothalamus                              | 1.78e−02    |
| Hippocampus                               | 2.00e−03    |
| Frontal_Cortex_BA9                        | 1.38e−03    |
| Cortex                                    | 1.47e−02    |
| Cerebellum                                | 3.23e−02    |
| Cerebellar_Hemisphere                     | 2.82e−02    |
| Caudate_basal_ganglia                    | 1.64e−02    |
| Anterior_cingulate_cortex_BA24            | 1.83e−03    |

p-value
- sHom 6.87e−07
- sHet 1.12e−03

Standard Association Model (beta values)
1.2 Across Tissue Phet Results
ENSG00000054219 (LY75)
MJ ~ Across_Tissue

| Tissue                        | p-value  |
|-------------------------------|----------|
| sHom                          | 1.10e−08 |
| sHet                          | 1.22e−05 |

-0.8 -0.6 -0.4 -0.2 0.0

Standard Association Model (beta values)

GWAS Model

-1.5 -0.5 0.5 1.5

PredXcan Model

-0.20 0.05

GTEx Model

-1.5 -0.5 0.5 1.5

Anterior_cingulate_cortex_BA24 2.28e−05
Cerebellar_Hemisphere 5.42e−03
Caudate_basal_ganglia 4.81e−04
Cortex 1.34e−03
Cerebellum 4.44e−02
Frontal_Cortex_BA9 1.48e−02
Hippocampus 1.27e−03
Hypothalamus 2.18e−04
Nucleus_accumbens_basal_ganglia 4.75e−03
Putambasal_ganglia 2.24e−03
ENSG00000084072 (PPIE)
Family_Alcoholism ~ Across_Tissue

| Tissue                                | p-value    |
|---------------------------------------|------------|
| Putambasal_ganglia                    | 2.96e−03   |
| Nucleus_accumbens_basal_ganglia       | 2.29e−02   |
| Hypothalamus                          | 1.35e−03   |
| Hippocampus                           | 1.45e−03   |
| Frontal_Cortex_BA9                    | 2.02e−02   |
| Cortex                                | 1.83e−03   |
| Cerebellum                            | 2.53e−03   |
| Cerebellar_Hemisphere                 | 2.74e−03   |
| Caudate_basal_ganglia                 | 5.03e−04   |
| Anterior_cingulate_cortex_BA24        | 6.10e−03   |

GWAS Model

PrediXcan Model

GTEx Model
| Tissue                        | p-value  |
|-------------------------------|----------|
| sHom                         | 8.84e−08 |
| sHet                         | 1.42e−04 |

- **Standard Association Model (beta values)**
  - **Anterior_cingulate_cortex_BA24**
  - **Caudate_basal_ganglia**
  - **Cerebellar_Hemisphere**
  - **Cerebellum**
  - **Cortex**
  - **Frontal_Cortex_BA9**
  - **Hippocampus**
  - **Hypothalamus**
  - **Nucleus_accumbens_basal_ganglia**
  - **Putambasal_ganglia**

- **GWAS Model**
  - -1.5
  - -0.5
  - 0.5
  - 1.5

- **PrediXcan Model**
  - -1.5
  - 0.0
  - 1.0

- **GITE-Model**
  - -1.5
  - -0.5
  - 0.5
  - 1.5

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**ENSG00000103245 (CIAO3)**

- **Alc_Dep ~ Across_Tissue**

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**GWAS Model**

**PrediXcan Model**

**GITE-Model**
ENSG00000112031 (MTRF1L)
MJ ~ Across_Tissue

| Region                      | p-value    |
|-----------------------------|------------|
| Putamiasl_ganglia           | 1.77e−02   |
| Nucleus_accumbens_basal_ganglia | 8.78e−05  |
| Hypothalamus                | 7.59e−03   |
| Hippocampus                 | 4.21e−03   |
| Frontal_Cortex_BA9          | 2.50e−03   |
| Cortex                      | 1.49e−04   |
| Cerebellum                  | 1.51e−03   |
| Cerebellar_Hemisphere       | 9.11e−04   |
| Caudate_basal_ganglia       | 1.50e−03   |
| Anterior_cingulate_cortex_BA24 | 1.42e−02   |

GWAS Model

PrediXcan Model

GTEx Model
ENSG00000131845 (ZNF304)
Marijuana_Strong_Desire ~ Across_Tissue

| Structure                          | p-value  |
|------------------------------------|----------|
| Putambasal_ganglia                 | 1.96e−03 |
| Nucleus_accumbens_basal_ganglia    | 2.52e−03 |
| Hypothalamus                       | 1.19e−03 |
| Hippocampus                        | 2.31e−03 |
| Frontal_Cortex_BA9                 | 6.77e−04 |
| Cortex                             | 5.61e−04 |
| Cerebellum                         | 2.17e−03 |
| Cerebellar_Hemisphere              | 7.29e−04 |
| Caudate_basal_ganglia             | 5.49e−04 |
| Anterior_cingulate_cortex_BA24     | 5.04e−02 |

GWAS Model

PrediXcan Model

GTEx Model
**ENSG00000168385 (SEPTIN2)**

**Family_Alcoholism ~ Across_Tissue**

| Tissue                        | p-value   |
|-------------------------------|-----------|
| sHom                          | 5.51e−09  |
| sHet                          | 1.36e−05  |

- Putambasal_ganglia 5.02e−04
- Nucleus_accumbens_basal_ganglia 8.40e−04
- Hypothalamus 1.18e−02
- Hippocampus 5.16e−03
- Frontal_Cortex_BA9 8.19e−03
- Cortex 2.59e−03
- Cerebellum 3.72e−03
- Cerebellar_Hemisphere 4.67e−04
- Caudate_basal_ganglia 1.14e−03
- Anterior_cingulate_cortex_BA24 3.63e−04

**Standard Association Model (beta values)**

**GWAS Model**

**PrediXcan Model**

**GTEx Model**
ENSG00000180376 (CCDC66)
Marijuana_Strong_Desire ~ Across_Tissue

| Tissue                          | p-value   |
|---------------------------------|-----------|
| sHom                            | 2.03e−08  |
| sHet                            | 4.58e−05  |

- Standard Association Model (beta values)
- GWAS Model
- PrediXcan Model
- GTEx Model

- Putambasal_ganglia: 5.10e−03
- Nucleus_accumbens_basal_ganglia: 2.35e−04
- Hypothalamus: 4.01e−03
- Hippocampus: 2.82e−03
- Frontal_Cortex_BA9: 4.29e−03
- Cortex: 2.89e−03
- Cerebellum: 5.36e−03
- Cerebellar_Hemisphere: 3.11e−03
- Caudate_basal_ganglia: 1.16e−02
- Anterior_cingulate_cortex_BA24: 3.80e−04
ENSG00000189306 (RRP7A)
MJ ~ Across_Tissue

| Tissue                        | p-value  |
|-------------------------------|----------|
| sHom                          | 1.04e-07 |
| sHet                          | 1.73e-04 |

Standard Association Model (beta values)

- Putambasal_ganglia: 2.50e-02
- Nucleus_accumbens_basal_ganglia: 8.71e-03
- Hypothalamus: 1.41e-03
- Hippocampus: 2.88e-03
- Frontal_Cortex_BA9: 2.82e-03
- Cortex: 8.74e-04
- Cerebellum: 3.15e-03
- Cerebellar_Hemisphere: 1.05e-02
- Caudate_basal_ganglia: 3.29e-03
- Anterior_cingulate_cortex_BA24: 2.52e-03

GWAS Model

PrediXcan Model

CITE-Model

30
ENSG00000197558 (SSPO)

NIC ~ Across_Tissue

|                      | sHom   | sHet   |
|----------------------|--------|--------|
|                      | 1.08e−08 | 3.11e−05 |

- Anterior_cingulate_cortex_BA24
- Caudate_basal_ganglia
- Cerebellar_Hemisphere
- Cerebellum
- Cortex
- Frontal_Cortex_BA9
- Hypothalamus
- Nucleus_accumbens_basal_ganglia
- Putambasal_ganglia
- PrediXcan Model
- GTEx Model
- PrediXcan Model
- GWAS Model
- Standard Association Model (beta values)
1.3 Across Cohort Phom Results †
ENSG00000005206 (SPPL2B)
Across_Cohort ~ Hippocampus

- Hom: p-value 2.87e−05
- Het: p-value 1.80e−05

**Standard Association Model (beta values)**

- NIC: 3.51e−01
- MJ: 3.96e−02
- Marijuana_Strong_Desire: 1.13e−01
- Family_Alcoholism: 1.42e−02
- Alc_Dep: 3.90e−08

**GWAS Model**

**PredXcan Model**

**GTEx Model**
ENSG00000141127 (PRPSAP2)
Across_Cohort ~ Hypothalamus

| Trait              | p-value  |
|--------------------|----------|
| sHom               | 6.52e−06 |
| sHet               | 6.95e−05 |

| Trait              | p-value  |
|--------------------|----------|
| NIC                | 1.98e−04 |
| MJ                 | 8.71e−04 |
| Marijuana_Strong_Desire | 5.95e−02 |
| Family_Alcoholism  | 3.46e−01 |
| Alc_Dep            | 1.53e−02 |

Standard Association Model (beta values)
ENSG00000198160 (MIER1)
Across_Cohort ~ Cortex

| Trait                        | p-value       |
|------------------------------|---------------|
| sHom                         | 2.99e−05      |
| sHet                         | 8.21e−04      |

- NIC: 2.27e−04
- MJ: 8.86e−02
- Marijuana_Strong_Desire: 9.70e−01
- Family_Alcoholism: 1.02e−02
- Alc_Dep: 1.66e−02

Standard Association Model (beta values)

GWAS Model

PrediXcan Model

GTEx Model
1.4 Across Cohort Phet Results †
**ENSG00000005206 (SPPL2B)**
Across_Cohort ~ Hippocampus

| Trait              | p-value  |
|--------------------|----------|
| sHom               | 2.87e−05 |
| sHet               | 1.80e−05 |

- NIC: 3.51e−01
- MJ: 3.96e−02
- Marijuana_Strong_Desire: 1.13e−01
- Family_Alcoholism: 1.42e−02
- Alc_Dep: 3.90e−08

**Standard Association Model (beta values)**

**GWAS Model**

**PrediXcan Model**

**GTEx Model**
ENSG00000141127 (PRPSAP2)
Across_Cohort ~ Hypothalamus

| Trait                      | p-value  |
|----------------------------|----------|
| sHom                       | 6.52e−06 |
| sHet                       | 6.95e−05 |

| Trait                      | p-value  |
|----------------------------|----------|
| NIC                        | 1.98e−04 |
| MJ                         | 8.71e−04 |
| Marijuana_Strong_Desire    | 5.95e−02 |
| Family_Alcoholism          | 3.46e−01 |
| Alc_Dep                    | 1.53e−02 |

Standard Association Model (beta values)
ENSG00000173705 (SUSD5)
Across_Cohort ~ Frontal_Cortex_BA9

- sHom: 5.10e−02
- sHet: 6.39e−05

| Trait                      | p-value  |
|----------------------------|----------|
| NIC                        | 2.60e−02 |
| MJ                         | 8.62e−05 |
| Marijuana_Strong_Desire    | 5.33e−01 |
| Family_Alcoholism          | 1.61e−02 |
| Alc_Dep                    | 4.68e−01 |

GWAS Model

PredXcan Model

GTEx Model

Standard Association Model (beta values)
ENSG00000206344 (HCG27)
Across_Cohort ~ Hypothalamus

| Trait                  | p-value   |
|------------------------|-----------|
| sHom                   | 3.75e-04  |
| sHet                   | 2.40e-06  |

- NIC: 9.30e-02
- MJ: 7.81e-01
- Marijuana_Strong_Desire: 4.91e-01
- Family_Alcoholism: 1.28e-01
- Alc_Dep: 3.80e-09

![Image of genetic association analysis](image-url)
2 Manhattan Plots

Manhattan Plots of the ‘phenotype across tissues’/‘tissue across all phenotypes’ analysis. Displays distribution of implicated genes across genome. Genes annotated are most significant and/or most implicated† genes within a chromosome.

2.1 Across Tissue Phom Results
2.2 Across Tissue Phet Results
2.3 Across Cohort Phom Results
2.4 Across Cohort Phet Results †
3 QQ-Plots

All quantile-quantile plots produced after GEMMA association is performed. Each tissue-phenotype combination is shown.
Alc_Dep by Anterior_cingulate_cortex_BA24
Expected − log_{10}(p)

Observed − log_{10}(p)

Alc_Dep by Cerebellar_Hemisphere
Alc_Dep by Cortex

Expected $-\log_{10}(p)$

Observed $-\log_{10}(p)$
Alc_Dep by Hippocampus
Alc_Dep by Nucleus_accumbens_basal_ganglia
Alc_Dep by Caudate_basal_ganglia
Alc_Dep by Cerebellum

Expected $\log_{10}(p)$

Observed $\log_{10}(p)$
Alc_Dep by Hypothalamus
Alc_Dep by Putamen_basal_ganglia

Observed − log_{10}(p)

Expected − log_{10}(p)
Family_Alcoholism by Anterior_cingulate_cortex_BA24
Family_Alcoholism by Cerebellar_Hemisphere
Family_Alcoholism by Nucleus_accumbens_basal_ganglia
Family_Alcoholism by Caudate_basal_ganglia
Family_Alcoholism by Cerebellum
Family_Alcoholism by Frontal_Cortex_BA9

Expected − log_{10}(p)

Observed − log_{10}(p)
Family_Alcoholism by Hypothalamus
Family_Alcoholism by Putamen_basal_ganglia
MarijuanaStrDsr by Cortex
MarijuanaStrDsr by Nucleus_accumbens_basal_ganglia
MarijuanaStrDsr by Caudate_basal_ganglia
MarijuanaStrDsr by Putamen_basal_ganglia
MJ by Anterior_cingulate_cortex_BA24
MJ by Cerebellar_Hemisphere

Observed − log_{10}(p)

Expected − log_{10}(p)
Observed \(-\log_{10}(p)\) vs. Expected \(-\log_{10}(p)\)

MJ by Cortex
MJ by Hippocampus

![Graph showing Observed - \log_{10}(p) vs. Expected - \log_{10}(p) with data points and a trend line. The graph illustrates the expected and observed values for MJ by Hippocampus.]

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MJ by Caudate_basal_ganglia
MJ by Cerebellum

Expected $-\log_{10}(p)$ vs. Observed $-\log_{10}(p)$
Expected $-\log_{10}(p)$

Observed $-\log_{10}(p)$

MJ by Frontal_Cortex_BA9
Observed − log₁₀(p)
Expected − log₁₀(p)

MJ by Putamen_basal_ganglia
NIC by Anterior_cingulate_cortex_BA24
NIC by Cerebellar_Hemisphere
NIC by Cortex
NIC by Hippocampus

Expected $-\log_{10}(p)$

Observed $-\log_{10}(p)$
NIC by Nucleus_accumbens_basal_ganglia

![Graph showing NIC by Nucleus_accumbens_basal_ganglia with observed and expected values on a log10 scale.](image-url)
NIC by Caudate_basal_ganglia
NIC by Cerebellum
4 Single Marker Association QQ-plots

Below are quantile-quantile plots of our EPACTS single marker association results stratified by minor allele frequency (MAF). Lambda was calculated on markers with allele frequencies between 0.05 and 0.5.

\[
\text{lambda} = 0.9759519
\]

Alcohol Dependence
lambda = 1.019263

Family Alcoholism

lambda = 1.018789

Cannabis Craving
lambda = 0.9916276

Cannabis Dependence

lambda = 0.9962726

Nicotine Dependence
5 Correlation Matrices

5.1 Tissue by Tissue correlation

This correlation matrix shows the correlation between all tissues based on predicted gene expression for all samples.
5.2 Trait by Trait Correlation

The following correlation matrix displays the correlation between traits based on their disease status across all samples.
| Tissue                                      | Samples in GTEx (with genotype) |
|---------------------------------------------|--------------------------------|
| Anterior Cingulate Cortex                   | 147                            |
| Caudate Basal Ganglia                       | 194                            |
| Cerebellar Hemisphere                       | 175                            |
| Cerebellum                                  | 209                            |
| Cortex                                      | 205                            |
| Frontal Cortex BA9                          | 175                            |
| Hippocampus                                 | 165                            |
| Hypothalamus                                | 170                            |
| Nucleus Accumbens Basal Ganglia            | 202                            |
| Putamen Basal Ganglia                       | 170                            |

Table 4. Samples per tissue in GTEx data upon which Predixcan weights are Estimated.