main_transcripts

July 11, 2021

1 Tissue comparison for differential expression analysis

[1]:
```
import functools
import numpy as np
import pandas as pd
from plotnine import *
from scipy.stats import binom_test, fisher_exact, linregress

from warnings import filterwarnings
from matplotlib.cbook import mplDeprecation
filterwarnings('ignore', category=mplDeprecation)
filterwarnings('ignore', category=UserWarning, module='plotnine.*')
filterwarnings('ignore', category=DeprecationWarning, module='plotnine.*')
```

[2]:
```
config = {
    'caudate': '../../../caudate/_m/transcripts/diffExpr_maleVfemale_full.txt',
    'dlpfc': '../../../dlpfc/_m/transcripts/diffExpr_maleVfemale_full.txt',
    'hippo': '../../../hippocampus/_m/transcripts/diffExpr_maleVfemale_full.
 ↪txt',
}
```

[3]:
```
@functools.lru_cache()
def get_deg(filename):
    dft = pd.read_csv(filename, sep='\t', index_col=0)
    dft['Feature'] = dft.index
    dft['Dir'] = np.sign(dft['t'])
    if 'gene_id' in dft.columns:
        dft['ensemblID'] = dft.gene_id.str.replace('\\..*', '', regex=True)
    return dft[['Feature', 'ensemblID', 'adj.P.Val', 'logFC', 't', 'Dir']]

@functools.lru_cache()
def get_deg_sig(filename, fdr):
    dft = get_deg(filename)
    return dft[(dft['adj.P.Val'] < fdr)]


@functools.lru_cache()
```

```
def merge_dataframes(tissue1, tissue2):
    return get_deg(config[tissue1]).merge(get_deg(config[tissue2]),
                                          on='Feature', suffixes=['_%s' %␣
 ↪tissue1, '_%s' % tissue2])


@functools.lru_cache()
def merge_dataframes_sig(tissue1, tissue2):
    fdr1 = 0.05 if tissue1 != 'dlpfc' else 0.05
    fdr2 = 0.05 if tissue2 != 'dlpfc' else 0.05
    return get_deg_sig(config[tissue1], fdr1).
 ↪merge(get_deg_sig(config[tissue2], fdr2),
                                                  on='Feature',␣
 ↪suffixes=['_%s' % tissue1, '_%s' % tissue2])
```

[4]:
```
def enrichment_binom(tissue1, tissue2, merge_fnc):
    df = merge_fnc(tissue1, tissue2)
    df['agree'] = df['Dir_%s' % tissue1] * df['Dir_%s' % tissue2]
    dft = df.groupby('agree').size().reset_index()
    print(dft)
    return binom_test(dft[0].iloc[1], dft[0].sum()) if dft.shape[0] != 1 else␣
 ↪print("All directions agree!")


def cal_fishers(tissue1, tissue2):
    df = merge_dataframes(tissue1, tissue2)
    fdr1 = 0.05 if tissue1 != 'dlpfc' else 0.05
    fdr2 = 0.05 if tissue2 != 'dlpfc' else 0.05
    table = [[np.sum((df['adj.P.Val_%s' % tissue1]<fdr1) &
                     ((df['adj.P.Val_%s' % tissue2]<fdr2))),
              np.sum((df['adj.P.Val_%s' % tissue1]<fdr1) &
                     ((df['adj.P.Val_%s' % tissue2]>=fdr2)))],
             [np.sum((df['adj.P.Val_%s' % tissue1]>=fdr1) &
                     ((df['adj.P.Val_%s' % tissue2]<fdr2))),
              np.sum((df['adj.P.Val_%s' % tissue1]>=fdr1) &
                     ((df['adj.P.Val_%s' % tissue2]>=fdr2)))]]
    print(table)
    return fisher_exact(table)


def calculate_corr(xx, yy):
    '''This calculates R^2 correlation via linear regression:
         - used to calculate relationship between 2 arrays
         - the arrays are principal components 1 or 2 (PC1, PC2) AND gender
         - calculated on a scale of 0 to 1 (with 0 being no correlation)
        Inputs:
          x: array of Gender (converted to binary output)
```

```
            y: array of PC
        Outputs:
            1. r2
            2. p-value, two-sided test
              - whose null hypothesis is that two sets of data are uncorrelated
            3. slope (beta): directory of correlations
    '''
    slope, intercept, r_value, p_value, std_err = linregress(xx, yy)
    return r_value, p_value


def corr_annotation(tissue1, tissue2, merge_fnc):
    dft = merge_fnc(tissue1, tissue2)
    xx = dft['t_%s' % tissue1]
    yy = dft['t_%s' % tissue2]
    r_value1, p_value1 = calculate_corr(xx, yy)
    return 'R2: %.2f\nP-value: %.2e' % (r_value1**2, p_value1)


def tissue_annotation(tissue):
    return {'dlpfc': 'DLPFC', 'hippo': 'Hippocampus', 'caudate':␣
 ↪'Caudate'}[tissue]
```

[5]:
```
def plot_corr_impl(tissue1, tissue2, merge_fnc):
    dft = merge_fnc(tissue1, tissue2)
    title = '\n'.join([corr_annotation(tissue1, tissue2, merge_fnc)])
    xlab = 'T-statistic (%s)' % tissue_annotation(tissue1)
    ylab = 'T-statistic (%s)' % tissue_annotation(tissue2)
    pp = ggplot(dft, aes(x='t_%s'%tissue1, y='t_%s' % tissue2))\
    + geom_point(alpha=0.75, size=3)\
    + theme_matplotlib()\
    + theme(axis_text=element_text(size=18),
            axis_title=element_text(size=20, face='bold'),
            plot_title=element_text(size=22))
    pp += labs(x=xlab, y=ylab, title=title)
    return pp


def plot_corr(tissue1, tissue2, merge_fnc):
    return plot_corr_impl(tissue1, tissue2, merge_fnc)


def save_plot(p, fn, width=7, height=7):
    '''Save plot as svg, png, and pdf with specific label and dimension.'''
    for ext in ['.svg', '.png', '.pdf']:
        p.save(fn+ext, width=width, height=height)
```

1.1 Sample summary

[6]:
```
pheno_file = '/ceph/projects/v3_phase3_paper/inputs/phenotypes/merged/_m/
 ↪merged_phenotypes.csv'
pheno = pd.read_csv(pheno_file, index_col=0)
pheno = pheno[(pheno['Age'] > 17) & (pheno['Dx'].isin(['Schizo', 'Control']))]
pheno.head(2)
```

[6]:

	BrNum	RNum	Region	RIN	Age	Sex	Race	Dx
R12864	Br1303	R12864	Caudate	9.6	42.98	F	AA	Schizo
R12865	Br1320	R12865	Caudate	9.5	53.12	M	AA	Schizo

[7]:
```
pheno.groupby(['Region']).size()
```

[7]:
```
Region
Caudate    394
DLPFC      379
HIPPO      376
dtype: int64
```

[8]:
```
pheno.groupby(['Region', 'Sex']).size()
```

[8]:
```
Region   Sex
Caudate  F      121
         M      273
DLPFC    F      117
         M      262
HIPPO    F      121
         M      255
dtype: int64
```

1.2 BrainSeq Tissue Comparison

[9]:
```
caudate = get_deg(config['caudate'])
caudate.groupby('Dir').size()
```

[9]:
```
Dir
-1.0    51647
 1.0    55569
dtype: int64
```

[10]:
```
caudate[(caudate['adj.P.Val'] < 0.05)].shape
```

[10]:
```
(462, 6)
```

[11]:
```
dlpfc = get_deg(config['dlpfc'])
dlpfc.groupby('Dir').size()
```

[11]:
```
Dir
-1.0    38553
 1.0    43774
dtype: int64
```

[12]:
```
dlpfc[(dlpfc['adj.P.Val'] < 0.05)].shape
```

[12]:
```
(422, 6)
```

[13]:
```
hippo = get_deg(config['hippo'])
hippo.groupby('Dir').size()
```

[13]:
```
Dir
-1.0    42370
 1.0    39061
dtype: int64
```

[14]:
```
hippo[(hippo['adj.P.Val'] < 0.05)].shape
```

[14]:
```
(252, 6)
```

1.2.1 Enrichment of DEG

[15]:
```
cal_fishers('caudate', 'dlpfc')
```

```
[[184, 158], [216, 78168]]
```

[15]:
```
(421.44022503516175, 0.0)
```

[16]:
```
cal_fishers('caudate', 'hippo')
```

```
[[183, 160], [60, 77793]]
```

[16]:
```
(1482.9290625, 0.0)
```

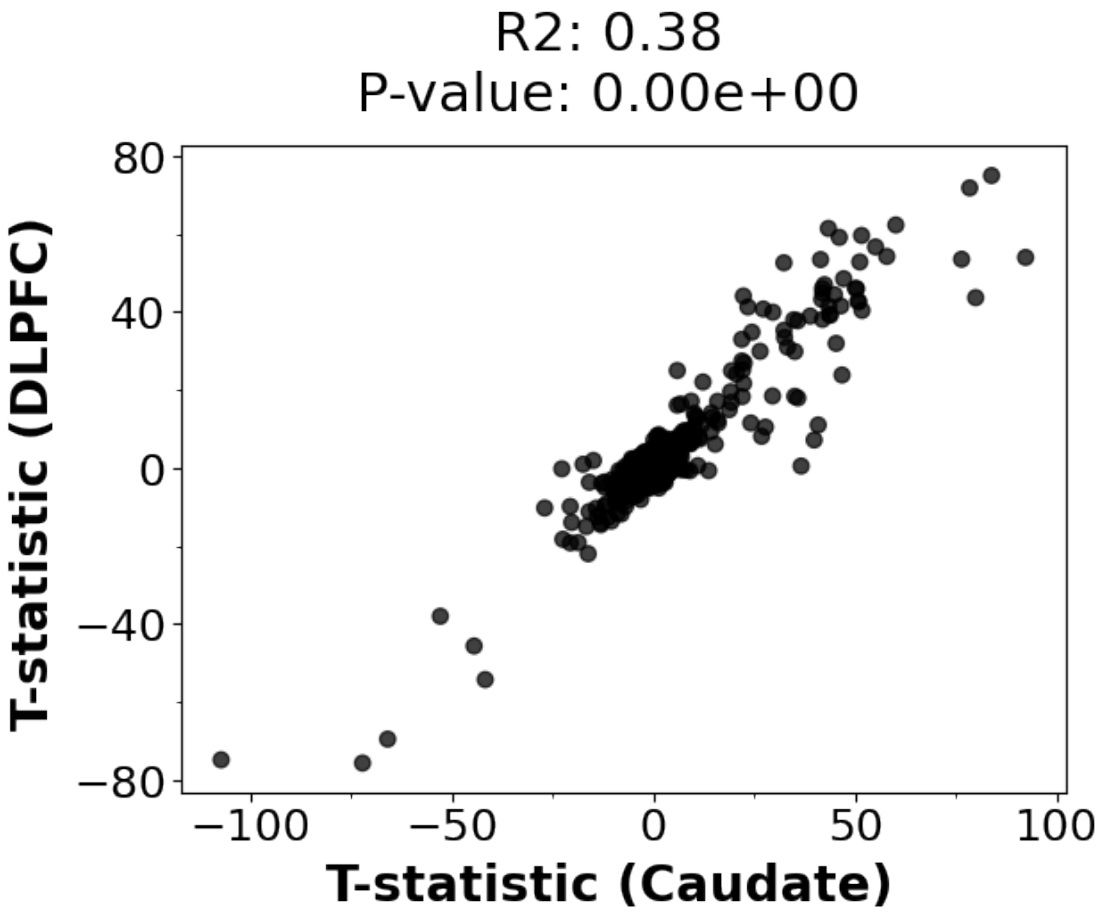
[17]:
```
cal_fishers('dlpfc', 'hippo')
```

```
[[179, 224], [54, 77583]]
```

[17]:
```
(1148.094990079365, 0.0)
```

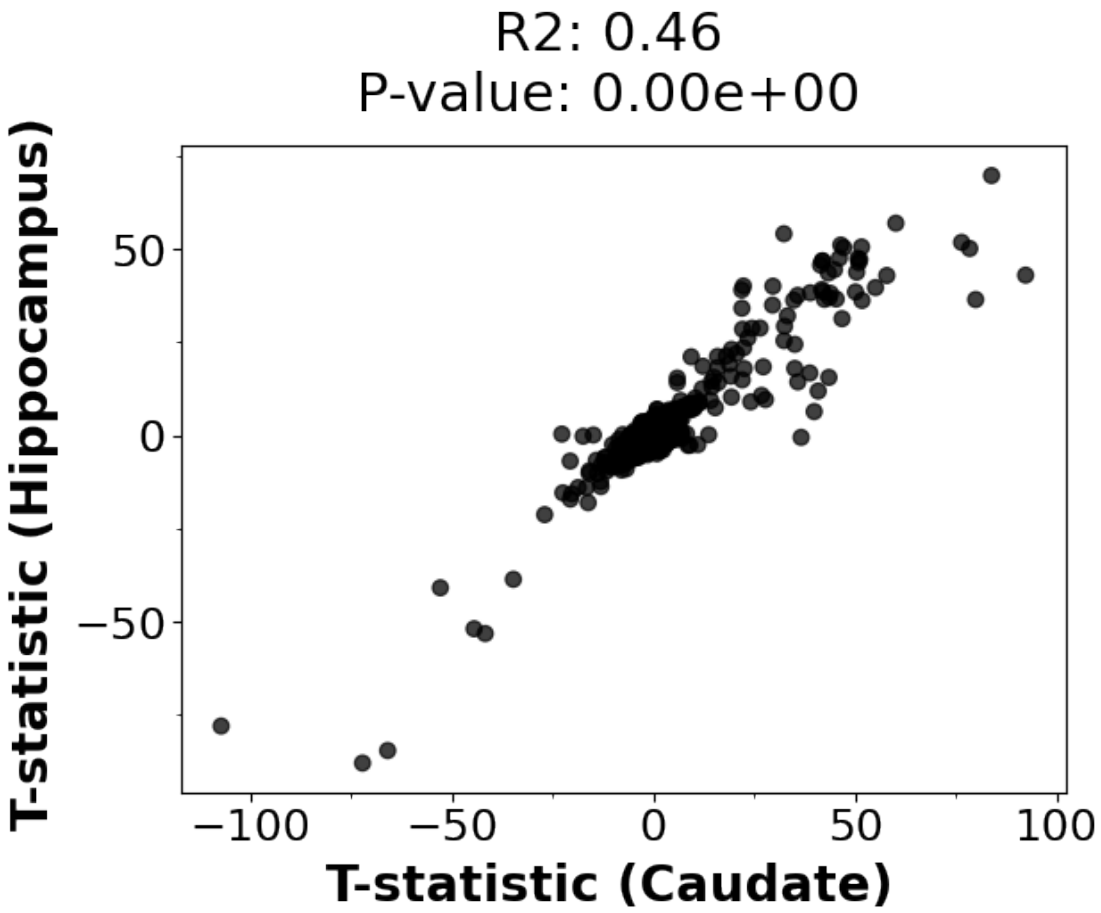
1.2.2 Correlation

[18]:
```
pp = plot_corr('caudate', 'dlpfc', merge_dataframes)
pp
```



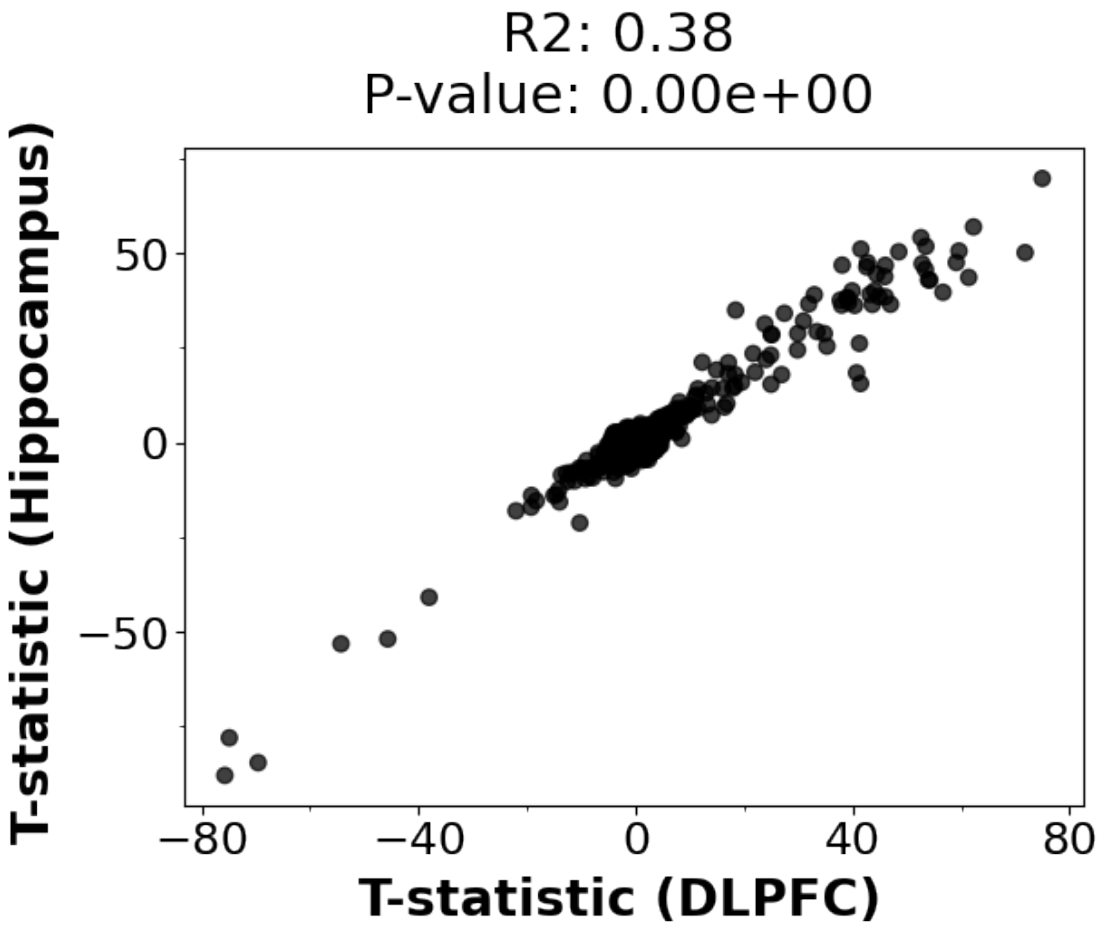
[18]:
```
<ggplot: (8767858987382)>
```

[19]:
```
qq = plot_corr('caudate', 'hippo', merge_dataframes)
qq
```



[19]: <ggplot: (8767858379578)>

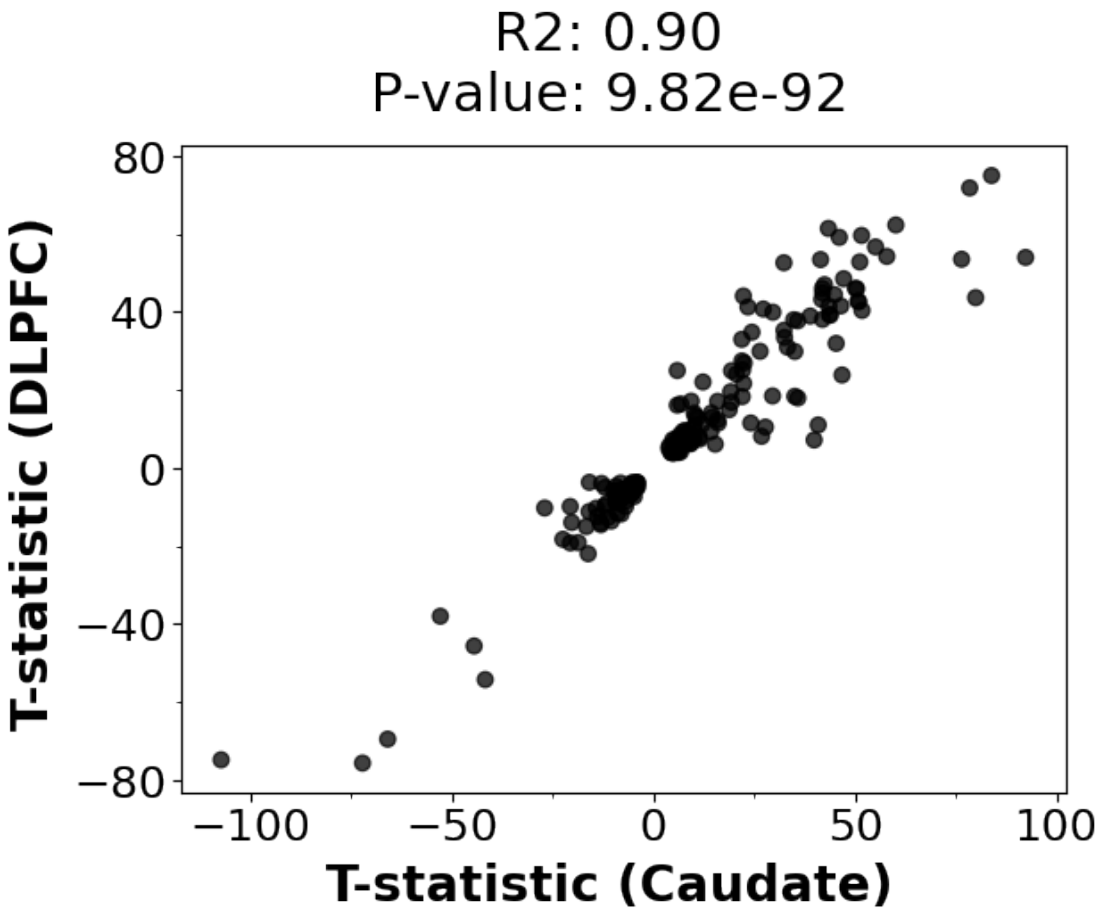
[20]:
```
ww = plot_corr('dlpfc', 'hippo', merge_dataframes)
ww
```



[20]: <ggplot: (8767856901834)>

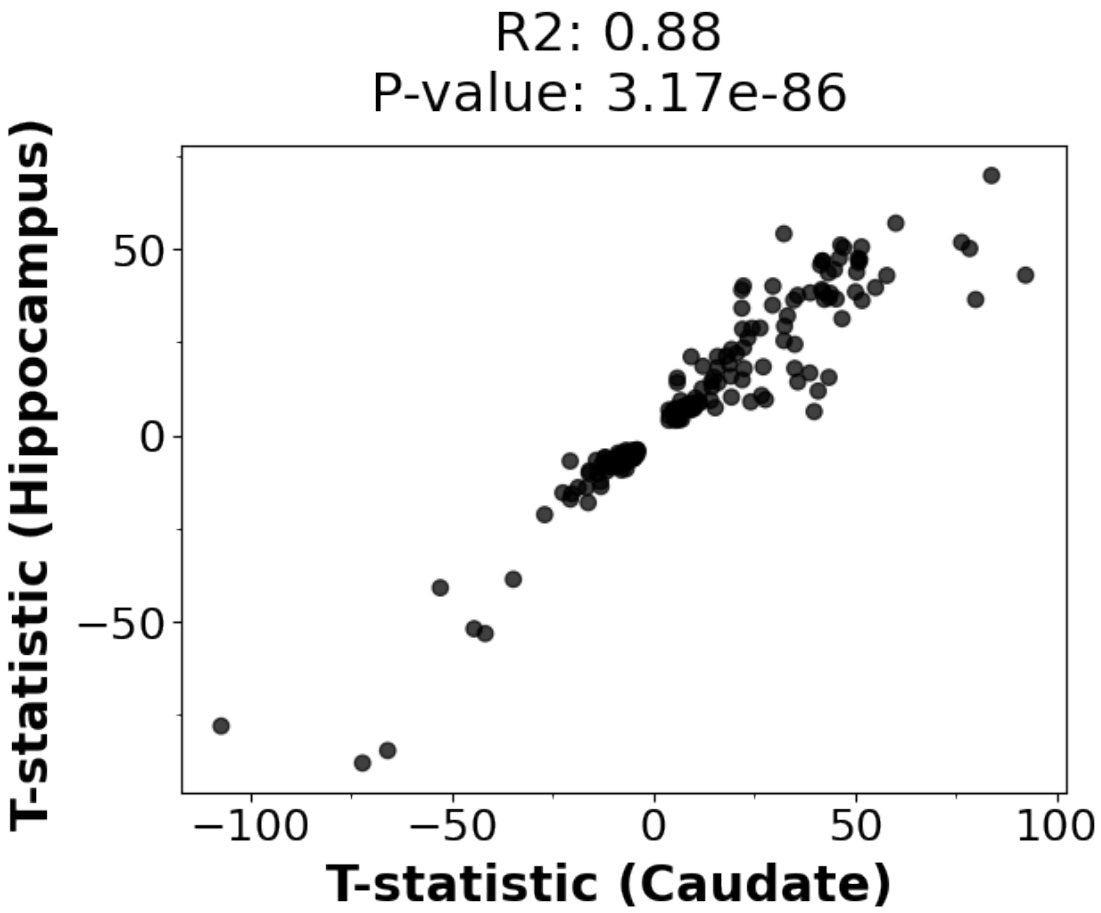
1.2.3 Significant correlation, FDR < 0.05

[21]:
```
pp = plot_corr('caudate', 'dlpfc', merge_dataframes_sig)
pp
```



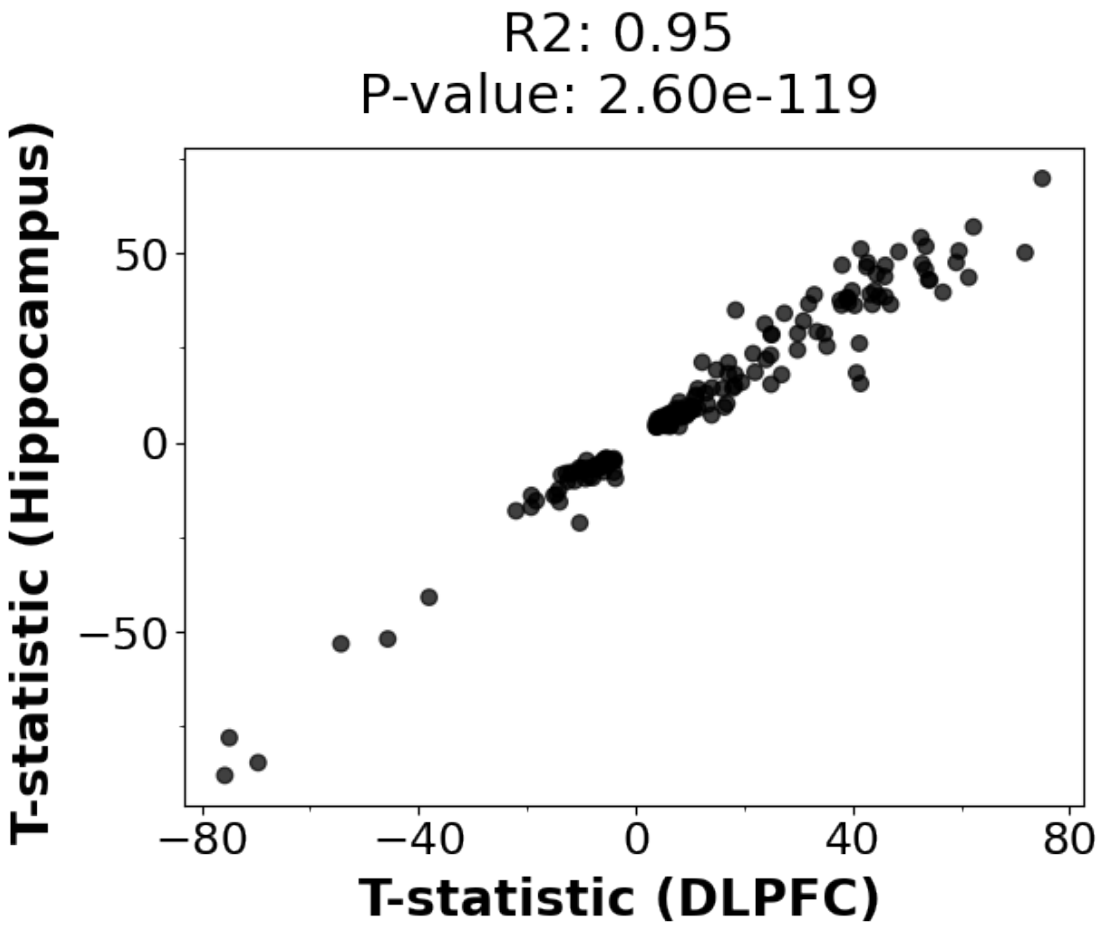
[21]:
```
<ggplot: (8767854509135)>
```

[22]:
```
qq = plot_corr('caudate', 'hippo', merge_dataframes_sig)
qq
```



[22]:
```
<ggplot: (8767855385941)>
```

[23]:
```
ww = plot_corr('dlpfc', 'hippo', merge_dataframes_sig)
ww
```



[23]: <ggplot: (8767856058257)>

1.2.4 Directionality test

All genes

[24]:
```
enrichment_binom('caudate', 'dlpfc', merge_dataframes)
```

	agree	0
0	-1.0	35065
1	1.0	43661

[24]: 1.755313978693651e-206

[25]:
```
enrichment_binom('caudate', 'hippo', merge_dataframes)
```

	agree	0
0	-1.0	32347
1	1.0	45849

[25]: 1e-323

[26]:
```
enrichment_binom('dlpfc', 'hippo', merge_dataframes)
```

```
   agree      0
0   -1.0  35300
1    1.0  42740
```

[26]: 1.8250523208853138e-156

Significant DEG (FDR < 0.05)

[27]:
```
enrichment_binom('caudate', 'dlpfc', merge_dataframes_sig)
```

```
   agree    0
0    1.0  184
All directions agree!
```

[28]:
```
enrichment_binom('caudate', 'hippo', merge_dataframes_sig)
```

```
   agree    0
0    1.0  183
All directions agree!
```

[29]:
```
enrichment_binom('dlpfc', 'hippo', merge_dataframes_sig)
```

```
   agree    0
0    1.0  179
All directions agree!
```

[ ]: