

Package ‘RVIpkg’

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Title Regional Vulnerability Index

Version 0.3.4

Description The Regional Vulnerability Index (RVI), a statistical measure of brain structural abnormality, quantifies an individual's similarity to the expected pattern (effect size) of deficits in schizophrenia (Kochunov P, Fan F, Ryan MC, et al. (2020) <[doi:10.1002/hbm.25045](https://doi.org/10.1002/hbm.25045)>).

License GPL (>= 2)

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Imports stats

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Ave_func	<i>Optimizing data from UK Biobank</i>
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Description

The Ave_func() can optimize data from UK Biobank(UKB). It will rename field IDs of regional neuroimaging traits to abbreviation names, and then average data of left and right hemispheres of the same field.

Usage

```
Ave_func(resp.range, type = "all", data)
```

Arguments

resp.range	a numeric vector specifying column range of regional neuroimaging traits.
type	a character string specifying data types of regional neuroimaging traits(i.e. All traits(type='all'), White matter(type='WM'),Gray matter(type='GM') or Subcortical(type='Subcortical'))
data	a data frame contains regional neuroimaging traits with field IDs from UKBB. Default(type='all')

Value

a dataframe of regional neuroimaging traits with abbreviated field names.

Note

The RVI_func() function is developed at the the University of Texas Health Science Center at Houston, Department of Psychiatry and Behavioral Sciences, McGovern Medical School. This project is supported by NIH R01 EB015611 grant. Please cite our funding if you use this software.

References

Kochunov P, Fan F, Ryan MC, et al. Translating ENIGMA schizophrenia findings using the regional vulnerability index: Association with cognition, symptoms, and disease trajectory (2020). Hum Brain Mapp. 2020;10.1002/hbm.25045. doi:10.1002/hbm.25045

R Core Team (2020). R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. URL <https://www.R-project.org/>.

data

Simulated volumes of subcortical structures

Description

Simulated volumes of subcortical structures of Schizophrenia spectrum disorder are used as an example for this function. You can calculate RVI for this dataset

Usage

data

Format

A data frame with 196 rows and 12 variables:

ID subjects' ID

DX indicators of control group

Age subjects' age

Sex subjects' gender

Site subjects' scanning site

Lateral.Ventricle simulated volumes of lateral Ventricle

Thalamus simulated volumes of Thalamus

Caudate simulated volumes of Caudate

Putamen simulated volumes of Putamen

Pallidum simulated volumes of Pallidum

Hippocampus simulated volumes of Hippocampus

Amygdala simulated volumes of Amygdala

Left.Accumbens.area simulated volumes of left Accumbens

Source

The 'data' dataset is from Maryland Psychiatric Research Center, Department of Psychiatry, University of Maryland School of Medicine.

EP.GM

*Expected patterns of gray matter***Description**

the expected patterns of gray matter in schizophrenia derived from large-scale meta-analyses by the ENIGMA.

Usage

EP.GM

Format

A data frame with 33 rows and 13 variables:

GM grey matter thickness

SSD the expected pattern of Schizophrenia Spectrum Disorder ([doi:10.1016/j.biopsych.2018.04.023](https://doi.org/10.1016/j.biopsych.2018.04.023) table S4a)

MDD the expected pattern of Major Depressive Disorder ([doi:10.1038/mp.2016.60](https://doi.org/10.1038/mp.2016.60) table 1)

AD_ADNI the expected pattern of Alzheimer's Disease ([doi:10.1016/j.nicl.2021.102574](https://doi.org/10.1016/j.nicl.2021.102574) table S1)

AD_ADNIOSYRIX the expected pattern of Alzheimer's Disease Neuroimaging Initiative + OSIRIX

BD the expected pattern of Bipolar Disorder ([doi:10.1038/mp.2017.73](https://doi.org/10.1038/mp.2017.73) table 1)

PD the expected pattern of Parkinson's disease

Diabetes the expected pattern of Diabetes

HighBP the expected pattern of Hypertension

HighLipids the expected pattern of Hyperlipidemia

MET the expected pattern of Metabolic diseases (Diabetes, Hypertension and Hyperlipidemia)

DS_22q the expected pattern of 22q11.2 deletion syndrome ([doi:10.1038/s4138001800785](https://doi.org/10.1038/s4138001800785) table S10a)

Suicide the expected pattern of suicidal ideation ([doi:10.1101/2021.09.27.21264068](https://doi.org/10.1101/2021.09.27.21264068) table S8)

OCD_pediatic the expected pattern of Obsessive-compulsive disorder in pediatric subjects ([doi:10.1176/appi.ajp.2017.17050485](https://doi.org/10.1176/appi.ajp.2017.17050485) table S6)

OCD_adult the expected pattern of Obsessive-compulsive disorder in adults ([doi:10.1176/appi.ajp.2017.17050485](https://doi.org/10.1176/appi.ajp.2017.17050485) table S4)

AN the expected pattern of Anorexia Nervosa

ASD the expected pattern of Autism Spectrum Disorder ([doi:10.1176/appi.ajp.2017.17010100](https://doi.org/10.1176/appi.ajp.2017.17010100) table 2)

ADHD the expected pattern of Attention-Deficit/Hyperactivity Disorder

EP.Subcortical	<i>Expected patterns of subcortical</i>
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Description

the expected patterns of subcortical in schizophrenia derived from large-scale meta-analyses by the ENIGMA.

Usage

EP.Subcortical

Format

A data frame with 8 rows and 13 variables:

Subcortical subcortical grey matter volume

SSD the expected pattern of Schizophrenia Spectrum Disorder ([doi:10.1038/mp.2015.63](https://doi.org/10.1038/mp.2015.63) table 1)

MDD the expected pattern of Major Depressive Disorder ([doi:10.1038/mp.2015.69](https://doi.org/10.1038/mp.2015.69) table 1)

AD_ADNI the expected pattern of Alzheimer's Disease ([doi:10.1016/j.nicl.2021.102574](https://doi.org/10.1016/j.nicl.2021.102574) table S1)

AD_ADNIOSYRIX the expected pattern of Alzheimer's Disease Neuroimaging Initiative + OSIRIX

BD the expected pattern of Bipolar Disorder ([doi:10.1038/mp.2015.227](https://doi.org/10.1038/mp.2015.227) table 1)

PD the expected pattern of Parkinson's disease

Diabetes the expected pattern of Diabetes

HighBP the expected pattern of Hypertension)

HighLipids the expected pattern of Hyperlipidemia

MET the expected pattern of Metabolic diseases (Diabetes, Hypertension and Hyperlipidemia)

DS_22q the expected pattern of 22q11.2 deletion syndrome ([doi:10.1176/appi.ajp.2019.19060583](https://doi.org/10.1176/appi.ajp.2019.19060583) table S14a)

Suicide the expected pattern of suicidal ideation ([doi:10.1101/2021.09.27.21264068](https://doi.org/10.1101/2021.09.27.21264068) table S8)

OCD_pediatric the expected pattern of Obsessive-compulsive disorder in pediatric subjects ([doi:10.1176/appi.ajp.2016.16020201](https://doi.org/10.1176/appi.ajp.2016.16020201) table S2)

OCD_adult the expected pattern of Obsessive-compulsive disorder in adults ([doi:10.1176/appi.ajp.2016.16020201](https://doi.org/10.1176/appi.ajp.2016.16020201) table 3)

AN the expected pattern of Anorexia Nervosa

ASD the expected pattern of Autism Spectrum Disorder ([doi:10.1176/appi.ajp.2017.17010100](https://doi.org/10.1176/appi.ajp.2017.17010100) table 2)

ADHD the expected pattern of Attention-Deficit/Hyperactivity Disorder

EP.WM

*Expected patterns of white matter***Description**

the expected patterns of white matter in schizophrenia derived from large-scale meta-analyses by the ENIGMA.

Usage

EP.WM

Format

A data frame with 24 rows and 14 variables:

WM white matter fractional anisotropy

SSD the expected pattern of Schizophrenia Spectrum Disorder ([doi:10.1038/mp.2017.170](https://doi.org/10.1038/mp.2017.170) table 1; [doi:10.1002/hbm.24998](https://doi.org/10.1002/hbm.24998) table 2)

MDD the expected pattern of Major Depressive Disorder ([doi:10.1038/s4138001904772](https://doi.org/10.1038/s4138001904772) Table S4; [doi:10.1002/hbm.24998](https://doi.org/10.1002/hbm.24998) table 2)

AD_ADNI the expected pattern of Alzheimer's Disease ([doi:10.1016/j.nicl.2021.102574](https://doi.org/10.1016/j.nicl.2021.102574) table S1)

AD_ADNIOYRIX the expected pattern of Alzheimer's Disease Neuroimaging Initiative + OSIRIX

BD the expected pattern of Bipolar Disorder ([doi:10.1002/hbm.24998](https://doi.org/10.1002/hbm.24998) table 2)

Diabetes the expected pattern of Diabetes

HighBP the expected pattern of Hypertension

HighLipids the expected pattern of Hyperlipidemia

MET the expected pattern of Metabolic diseases (diabetes, hypertension and hyperlipidemia)

DS_22q the expected pattern of 22q11.2 deletion syndrome ([doi:10.1002/hbm.24998](https://doi.org/10.1002/hbm.24998) table 2; [doi:10.1038/s4138001904500](https://doi.org/10.1038/s4138001904500) table S6)

PTSD the expected pattern of Post-traumatic stress disorder ([doi:10.1002/hbm.24998](https://doi.org/10.1002/hbm.24998) table 2)

TBI the expected pattern of Traumatic brain injury ([doi:10.1002/hbm.24998](https://doi.org/10.1002/hbm.24998) table 2)

OCD_pediatic the expected pattern of Obsessive-compulsive disorder in pediatric subjects ([doi:10.1038/s4139802101276z](https://doi.org/10.1038/s4139802101276z) table 4)

OCD_adult the expected pattern of Obsessive-compulsive disorder in adults ([doi:10.1038/s41398-02101276z](https://doi.org/10.1038/s41398-02101276z) table 3)

SADHC the expected pattern of Social Anxiety Disorder

ASD the expected pattern of of Autism Spectrum Disorder ([doi:10.1038/s4138001905537](https://doi.org/10.1038/s4138001905537) table S26)

RVI_batch_func *Regional Vulnerability Index by Multi-site*

Description

The Regional Vulnerability Index (RVI), a statistical measure of brain structural abnormality, quantifies an individual's similarity to the expected pattern (effect size) of deficits seen in schizophrenia derived from large-scale meta-analyses by the ENIGMA consortium. This version of RVI function will specifically calculate RVI for data collected from different scanners/sites. The function outputs the inverse-normal transformed (INT) residuals, z-normalized INT residuals, RVI and Alignment Vulnerability Index (AVI).

Usage

```
RVI_batch_func(
  ID,
  DXcontrol,
  covariates = NULL,
  batch,
  resp.range,
  EP,
  sign = FALSE,
  fisherZ = FALSE,
  data
)
```

Arguments

ID	a column name of subject IDs in data.
DXcontrol	a character string specifying control subset(i.e. DXcontrol='DX==0' or DXcontrol='DX=="CN"'). Mean and standard deviation of z-normalization should be calculated in healthy controls.
covariates	a character vector specifying column names of covariates (i.e. Age, Sex). If covariates=NULL (the default), residuals will not be adjusted for any covariate. If covariates are specified (i.e. covariates=c('Age','Sex')), residuals will be adjusted for covariates.
batch	a character string of a column name indicating the scanning site or scanner or etc.
resp.range	a numeric vector specifying column indices of regional neuroimaging traits.
EP	a numeric vector specifying an expected pattern of regional neuroimaging traits. The expected patterns(EP.WM, EP.GM and EP.Subcortical) for white matter fractional anisotropy (FA), cortical matter thickness and subcortical volume are included in the package (Note: If you use an expected pattern, you need to make sure the order of regional neuroimaging traits in your data match up the corresponding order of the expected pattern). The patterns can be extract in the package (i.e. RVIpkg::EP.WM\$SSD, RVIpkg::EP.WM\$MDD, RVIpkg::EP.WM\$AD,

	RVIpkg::EP.WM\$BD ,RVIpkg::EP.WM\$PD .etc.). They were developed using neuroimaging data of UK Biobank (UKBB).
sign	a logical value indicating whether the AVI use signs from RVI.
fisherZ	a logical value indicating whether the result should generate fisher-z transformed RVI.
data	a data frame contains a column of subject IDs, a column of controls, columns of covariates, columns of responses.

Details

The RVI is developed as a simple measure of agreement between an individual's pattern of regional neuroimaging traits and the expected pattern of schizophrenia. First, all observations of each regional neuroimaging trait are regressed out optional covariates using linear regression, and then residuals are extracted from the model after removing effects of the optional covariates. The optional covariates could be age, sex, intracranial brain volume and/or .etc within each site and then the residuals are inverse-normal transformed (INT) based on residuals' ranks. All INT residuals data from all sites are combined and z-normalized/standardized using mean and standard deviation from the healthy controls to get z-normalized residuals. For each subject, the RVI is then calculated as a Pearson correlation coefficient between the z-normalized INT residuals of the traits and corresponding expected pattern of the traits and the AVI is the dot product of the z-normalized INT residuals of the traits and corresponding expected pattern of the traits. These expected patterns include cortical thickness, subcortical volume, and white matter FA for mental illnesses and metabolic diseases.

Value

A list with the following elements:

i.norm.resid	inverse-normal transformed residuals
z.norm.resid	z-normalized INT residuals
RVI	RVI: the Pearson correlation coefficient between the z-normalized INT residuals and corresponding expected pattern; AVI: the dot product of the z-normalized INT residuals and corresponding expected pattern; RVI.fisherz: Fisher z-transformed RVI

Note

The RVI_func() function is developed at the the University of Texas Health Science Center at Houston, Department of Psychiatry and Behavioral Sciences, McGovern Medical School. This project is supported by NIH R01 EB015611 grant. Please cite our funding if you use this software.

References

- Kochunov P, Fan F, Ryan MC, et al. Translating ENIGMA schizophrenia findings using the regional vulnerability index: Association with cognition, symptoms, and disease trajectory (2020). *Hum Brain Mapp.* 2020;10.1002/hbm.25045. doi:10.1002/hbm.25045
- R Core Team (2020). R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. URL <https://www.R-project.org/>.

Examples

```
EP1 <- c(-0.37,0.31,-0.02,-0.08,-0.21,0.46,0.31,0.25)
RVI1 <- RVI_batch_func(ID='ID', DXcontrol='DX==0',batch='Site', covariates=c('Age','Sex'),
  resp.range=c(6:13), EP=EP1, data=RVIpkg::data)
```

RVI_func

*Regional Vulnerability Index***Description**

The Regional Vulnerability Index (RVI), a statistical measure of brain structural abnormality, quantifies an individual's similarity to the expected pattern (effect size) of deficits seen in schizophrenia derived from large-scale meta-analyses by the ENIGMA consortium. The function outputs the inverse-normal transformed (INT) residuals, z-normalized INT residuals, RVI and Alignment Vulnerability Index (AVI).

Usage

```
RVI_func(
  ID,
  DXcontrol,
  covariates = NULL,
  resp.range,
  EP,
  sign = FALSE,
  fisherZ = FALSE,
  data
)
```

Arguments

ID	a column name of subject IDs in data.
DXcontrol	a character string specifying control subset(i.e. DXcontrol='DX==0' or DXcontrol='DX=="CN"'). Mean and standard deviation of z-normalization should be calculated in healthy controls.
covariates	a character vector specifying column names of covariates (i.e. Age, Sex). If covariates=NULL (the default), residuals will not be adjusted for any covariate. If covariates are specified (i.e. covariates=c('Age','Sex')), residuals will be adjusted for covariates.
resp.range	a numeric vector specifying column indices of regional neuroimaging traits.
EP	a numeric vector specifying an expected pattern of regional neuroimaging traits. The expected patterns(EP.WM, EP.GM and EP.Subcortical) for white matter fractional anisotropy (FA), cortical matter thickness and subcortical volume are included in the package (Note: If you use an expected pattern, you need to make

sure the order of regional neuroimaging traits in your data match up the corresponding order of the expected pattern). The patterns can be extract in the package (i.e. RVIpkg::EP.WM\$SSD, RVIpkg::EP.WM\$MDD, RVIpkg::EP.WM\$AD, RVIpkg::EP.WM\$BD ,RVIpkg::EP.WM\$PD .etc.). They were developed using neuroimaging data of UK Biobank (UKBB).

sign	a logical value indicating whether the AVI use signs from RVI.
fisherZ	a logical value indicating whether the result should generate fisher-z transformed RVI.
data	a data frame contains a column of subject IDs, a column of controls, columns of covariates, columns of responses.

Details

The RVI is developed as a simple measure of agreement between an individual's pattern of regional neuroimaging traits and the expected pattern of schizophrenia. First, all observations of each regional neuroimaging trait are regressed out optional covariates using linear regression, and then residuals are extracted from the model after removing effects of the optional covariates. The optional covariates could be age, sex, intracranial brain volume and/or .etc and the residuals are inverse-normal transformed (INT) based on residuals' ranks. The INT residuals are then z-normalized/standardized using mean and standard deviation from the healthy controls to get z-normalized residuals. For each subject, the RVI is then calculated as a Pearson correlation coefficient between the z-normalized INT residuals of the traits and corresponding expected pattern of the traits and the AVI is the dot product of the z-normalized INT residuals of the traits and corresponding expected pattern of the traits. These expected patterns include cortical thickness, subcortical volume, and white matter FA for mental illnesses and metabolic diseases.

Value

A list with the following elements:

i.norm.resid	inverse-normal transformed residuals
z.norm.resid	z-normalized INT residuals
RVI	RVI: the Pearson correlation coefficient between the z-normalized INT residuals and corresponding expected pattern; AVI: the dot product of the z-normalized INT residuals and corresponding expected pattern; RVI.fisherz: Fisher z-transformed RVI

Note

The RVI_func() function is developed at the the University of Texas Health Science Center at Houston, Department of Psychiatry and Behavioral Sciences, McGovern Medical School. This project is supported by NIH R01 EB015611 grant. Please cite our funding if you use this software.

References

Kochunov P, Fan F, Ryan MC, et al. Translating ENIGMA schizophrenia findings using the regional vulnerability index: Association with cognition, symptoms, and disease trajectory (2020). Hum Brain Mapp. 2020;10.1002/hbm.25045. doi:10.1002/hbm.25045

R Core Team (2020). R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. URL <https://www.R-project.org/>.

Examples

```
EP1 <- c(-0.37, 0.31, -0.02, -0.08, -0.21, 0.46, 0.31, 0.25)
RVI1 <- RVI_func(ID='ID', DXcontrol='DX==0', covariates=c('Age', 'Sex'), resp.range=c(6:13),
EP=EP1, data=RVIpkg::data)
RVI2 <- RVI_func(ID='ID', DXcontrol='DX==0', covariates=NULL, resp.range=c(6:13),
EP=EP1, data=RVIpkg::data)
EP2 <- RVIpkg::EP.Subcortical$SSD
RVI3 <- RVI_func(ID='ID', DXcontrol='DX==0', covariates=c('Age', 'Sex'), resp.range=c(6:13),
EP=EP2, data=RVIpkg::data)
```

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