WhiteRest manual

WhiteRest is a module of the Functionnectome software developed to help you explore the WhiteRest atlas and analyze the potential impact of a white matter lesion on RSNs.

For now, WhiteRest is only available through command line call, but we have plans to create a user interface and a web app to facilitate its use.

Disclaimers

No financial conflicts.

Not licensed for medical use.

The software and its codes are licenced under the GNU General Public License.

Installation

- A Python environment is needed to use WhiteRest. For detailed instructions, check the start of our video tutorial for the Functionnectome on YouTube.
- WhiteRest is installed along the Functionnectome, so following the instruction in the Functionnectome manual will install the software.
  The following commands in a terminal with a proper Python environment will install it:
  > pip install git+https://github.com/NotaCS/Functionnectome.git
  > *or*
  > python -m pip install git+https://github.com/NotaCS/Functionnectome.git

- Download and unzip the WhiteRest on our OSF page:
  https://www.doi.org/10.17605/OSF.IO/FB9UC
  - Note that the white matter atlas file is the same as the one downloadable from NeuroVault (https://neurovault.org/collections/11895/), so if you want to use the grey matter atlas, you can download it from there too (https://neurovault.org/collections/11937/).
- After the installation, to check if WhiteRest was properly installed, type "WhiteRest -h" (without the quotation marks) in the terminal and press Enter. The description and the help should be displayed.

Using WhiteRest

- WhiteRest can compute two types of scores: the **DiscROver** score, and the **Presence** score. The **DiscROver** score is the default option, it estimates the disruption of RSNs by a brain lesion, using Disconnectome maps (method available in the BCBtoolkit, www.bcblab.com, see Foulon et al. 2018). The **Presence** score measures locally, in a ROI, which and how much of each RSNs are present. For more detailed about the computation of the scores, refer to the ***Score computation*** section below.
- Prepare the lesion mask (or region of interest) file you wish to use. The file must be in NIfTI format (.nii or .nii.gz), in MNI space, and with 2mm^3 isotropic voxels. If you want

to compute the DiscROver score, you can also prepare the disconnectome of the lesion, or use the quickDisco algorithm embedded in WhiteRest (see the ***Score computation*** section below) by simply giving it the lesion mask (that's the default option).

- Open a terminal. If necessary, activate the Python environment where the Functionnectome is installed (if it is not the default one).
- Type "WhiteRest" followed by the paths to paths to the files and the chosen options and press Enter.
  The minimal inputs should be (in that order):
    - The path to the ROI file you wish to explore (as a nifti file in the MNI space)
    - The path to the white matter maps of the WhiteRest atlas
  For example:
  "WhiteRest /myhome/my_ROI.nii.gz /myhome/WhiteRestAtlas_WM.nii.gz /myhome/WhiteRest_labels.txt"

By default, WhiteRest will output a table with the computed score for each RSN. If no output file is given (with the "-ot" option), the table will be printed in the terminal. Otherwise, it can be saved as a text file (.txt or .csv), which can be imported to a spreadsheet software (such as Excel) for further processing.

If you are computing the DiscROver score and only giving the **lesion mask** (which is the default expected behavior), WhiteRest will need to compute the disconnectome of the lesion. It will do it using the quickDisco algorithms that employs white matter priors from the Functionnectome to estimate the disconnection pattern. For that, you will also need to download these white matter priors too (if it's not already the case). If you don't have them, an error message will pop-up explain how to do it, but essentially you need to launch the Functionnectome interface (command line: *FunctionnectomeGUI*), select the priors you want (in the "Choice of priors" drop-down menu), the V1.D.WB being the same as the one used to create the atlas. Then click on "Manual download" and follow the instructions.

Also, because computing a disconnectome can be a bit slow (though much faster with quickDisco than with the traditional method), ranging from a few second to a few minutes depending on the size of the lesion, **you can speed the process up** by parallelizing the task. Simply use the "**--multiproc**" (or just "-m") option, followed by a number, to specify the number of processes to launch in parallel. You can **save the generated disconnectome** for later use with the "**--out_disco**" (or "-od") option and giving a file-path to where to save the output file (in Nifti format).

If you are computing the DiscROver score and **already have the disconnectome** on hand, you can skip the process and replace the input ROI by the disconnectome. You just need to specify it simply by adding the "**--disco**" (or "-d") option in command line.

If you are computing the Presence score, you will need to specify it in the "--score" (or "-s") option, by adding either "presence" (if you only want the Presence sore) or "both" (if you want Presence and DiscROver scores) after the option.

All WhiteRest options and arguments:

```
positional arguments:
  in_ROI          Path of the ROI file (.nii, .nii.gz).
  atlas_maps      Path of the RSN atlas (.nii, nii.gz).

optional arguments:

  -h, --help
            show this help message and exit

  -s SCORE, --score SCORE
            The score(s) to be computed. Can be "discrover",
            "presence", or "both" (default is "discrover")

  -ot OUT_TABLE, --out_table OUT_TABLE
            Path to save the score results (.txt or .csv).

  -od OUT_DISCO, --out_disco OUT_DISCO
            Path to save the lesion's disconnectome (.nii or
            .nii.gz), if computed.

  -z Z_THRESH, --Z_thresh Z_THRESH
            Threshold to apply to the atlas z-maps (default z>7).

  -b, --binarize
            Binarize the maps after thresholding.

  -p OUT_PIE, --out_pie OUT_PIE
             Path to save a pie-chart figure of the results (.png).

  -pt THR_LOW_PIE, --thr_low_pie THR_LOW_PIE
            DiscROver % under which the RSNs are grouped on the
            pie-chart (default <5%).

  -d, --disco
            To be specified when the "in_ROI" input given is not
            the lesion but the disconncetome of the lesion.
            Incompatible with Presence score computation.

  -m MULTIPROC, --multiproc MULTIPROC
            Number of processes to run in parallel (default = 1).

  -l ATLAS_LABELS, --atlas_labels ATLAS_LABELS (optional)
          Path to the atlas labels identifying the RSNs, when using
          custom labels).
```

Example of command lines:

- Computation of DiscROver score from a lesion:

WhiteRest /myhome/myProject/my_lesion.nii.gz /myhome/WhiteRestAtlas_WM.nii.gz /myhome/WhiteRest_labels.txt -ot /myhome/myProject/table_results.txt -m 4 -od /myhome/myProject/my_lesion_disco.nii.gz

- Computation of DiscROver score from a disconnectome (not the "-d" at the end):

WhiteRest /myhome/myProject/my_lesion_disco.nii.gz /myhome/WhiteRestAtlas_WM.nii.gz /myhome/WhiteRest_labels.txt -ot /myhome/myProject/table_results.txt -d

- Computation of the Presence score:

WhiteRest /myhome/myProject/my_ROI.nii.gz /myhome/WhiteRestAtlas_WM.nii.gz /myhome/WhiteRest_labels.txt -s presence -ot /myhome/myProject/table_results.txt

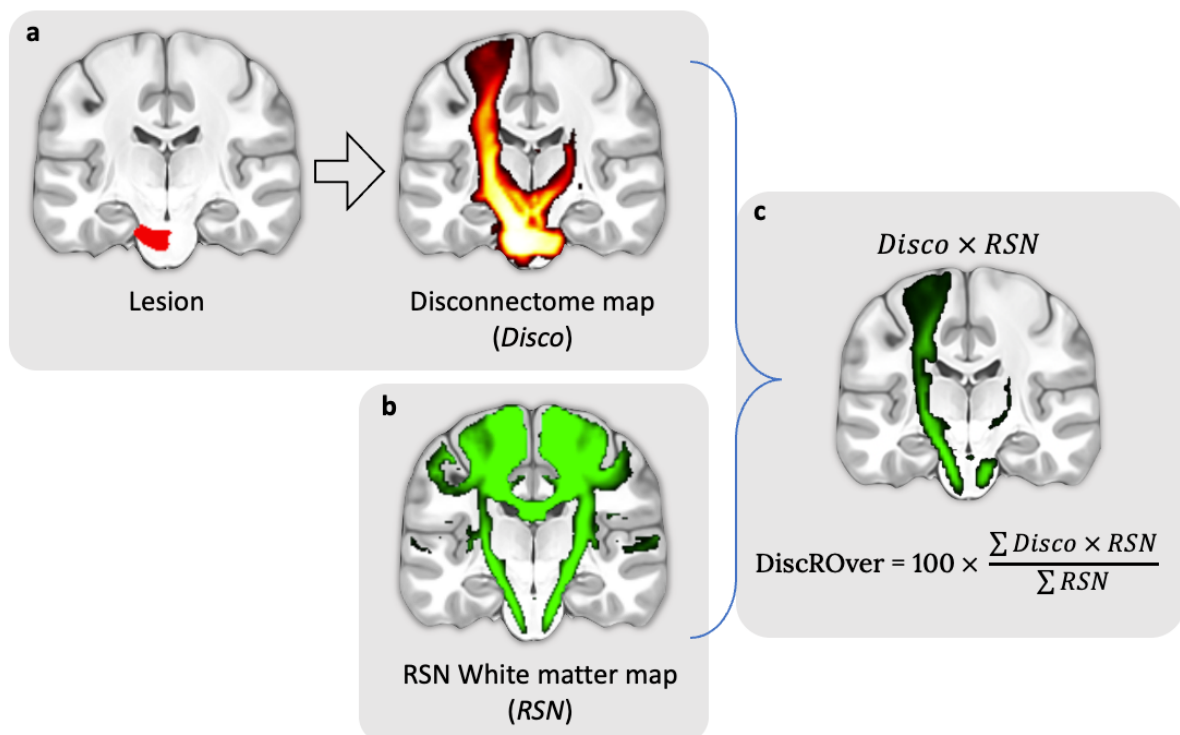## Score computation

DiscROver score

Figure: Steps for the computation of the DiscROver score. **a** - Lesion mask (left) and associated disconnectome (right). **b** - RSN map used for the DiscROver score computation. **c** - Visual representation of the weighted overlap, and computation of the DiscROver score. Disco: Disconnectome map; RSN: Resting-state network map.

DiscROver stands for "Disconnectome RSN Overlap". For a given RSN and a given lesion, the DiscROver score is computed as follows: First, the extent of white matter fibres disconnected by the lesion is estimated using the Disconnectome method. This method yields a disconnectome map displaying the probability of structural connectivity between the lesion

and each voxel of the brain (Fig. a). Hence, the higher the value on the disconnectome map, the more likely the disruption of connectivity in the voxel due to the lesion. Then, the weighted overlap of the RSN (Fig. b) with the disconnectome is computed by voxel-wise multiplication of the RSN map and the disconnectome map (Fig. c). The DiscROver score is computed as the sum of the values of this weighted overlap map, normalised by the sum of the values in the RSN, and multiplied by 100. With this score, 0 means that the lesion does not impact any white matter voxel part of the RSN, 100 means that it impacts the whole RSN.

The complete computation of the DiscROver score is summarised here:

$$DiscROver(RSN, Disco) = 100 * \frac{\sum_{v \in RSN} Z_{RSN}(v) \times P_{Disco}(v)}{\sum_{v \in RSN} Z_{RSN}(v)}$$

With "*RSN*" the atlas white matter Z-map of a given RSN, with its voxel values annotated as "$Z_{RSN}(v)$", and "*Disco*" the disconnectome map of a given lesion, with its voxel values annotated as "$P_{Disco}(v)$".

In the output from WhiteRest, the DiscROver score is in the column "DiscROver (%)", while the "DiscROver (raw)" column results from the non-normalised score computed with $\sum_{v \in RSN} Z_{RSN}(v) \times P_{Disco}(v)$ in the above equation.

QuickDisco

To compute ease the computation of the disconnectome required to compute the DiscRover score, we introduced the **quickDisco algorithm**. It is used by the WhiteRest program but can also be used independently, as a module of the Functionnectome.

Simply type "**quickDisco -h**" in the terminal to display the help text for this program. In short, where the original Disconnectome method uses tractography to estimate the connectivity between a brain lesion and the rest of the brain (thus revealing the disconnection pattern of the lesion), quickDisco uses the white matter priors (derived from 100 tractograms) to do the same. The priors contain the connectivity map from every voxel of the brain, so using them to compute the disconnectome is relatively straightforward: it is the maximum projection, across the map of all the voxels in the lesion, for each brain voxel. For a given lesion, the equation would be:

$$P_{Disco}(v) = Max_{l \in lesion}(Pmap_l(v))$$

With v a given brain voxel, P_{Disco} the disconnectome (giving the probability of disconnection at each voxel), $lesion$ the lesion in question, l one voxel of the lesion, and $Pmap_l(v)$ the probability of connectivity between the voxel l and the voxel v, as per the priors (or, if you prefer, the value of the connectivity map of l ($Pmap_l$), at the voxel v).

Presence Score

The Presence score measures the involvement, or "proportional presence" ($Presence_{prop}$) of each RSN in a ROI by first computing a "raw presence" ($Presence_{raw}$), adding up the z-score value of all the RSN white matter map voxels in the ROI (Equation 1). This raw presence score is then normalised by dividing it by the sum of all z-scores in the RSN

(Equation 2), and finally converted into a proportional presence by dividing it by the sum of the normalised presence score of all the RSNs sharing part of the ROI (Equation 3):

For a given RSN and a given ROI,

$$Presence_{raw}(RSN, ROI) = \sum_{v \in ROI} z_{RSN}(v) \qquad [1]$$

$$Presence_{norm}(RSN, ROI) = \frac{Presence_{raw}(RSN, ROI)}{\sum_{v \in RSN} z_{RSN}(v)} \quad [2]$$

$$Presence_{prop}(RSN, ROI) = \frac{Presence_{norm}(RSN, ROI)}{\sum_{rsn \in Atlas} Presence_{norm}(rsn, ROI)} [3]$$

with v a voxel from the ROI, $z_{RSN}(v)$ the z-score of the voxel v in the white matter map of the studied RSN.

All these metrics are proposed in the output table for a more complete analysis of the atlas:
- The RSN normalised presence **Presence/RSN (%)**: The fraction of presence in the ROI of an RSN compared to the whole white matter map of the said RSN (i.e. how much of the RSN is in the ROI). (Eq. 2)
- The proportional presence **Presence prop. (%)**: Proportion of the presence of one RSN compared to the sum of the presence of all RSN in the ROI (Eq. 3)
- The "raw" presence score **Presence (raw)**: Sum of the z-score of all the voxels from the white matter map of one RSN in the ROI (Eq. 1)
- The ROI coverage **Coverage (%)**: The volume fraction of the ROI occupied by the RSN.

Essentially, the normalised presence score reflects how much of a network is intersecting with the ROI, and the proportional presence score can be used to compare the involvement of the affected RSNs. The Coverage indicates how much of the ROI is covered by a RSN.