Robustness of brain structural network analysis with respect to diffusion fiber tractography parameter settings in patients with dementia

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***Abstract*—Whole-brain tractography has shown promising results distinguishing patients with Alzheimer's disease from individuals without dementia. To assess whether the analytical results differ based on the parameter settings, the difference between healthy controls and dementia patients will be analysed when changing the different parameters and measurements of the connectomic analysis.**

The data employed during this research was obtained from the study performed by Reijmer et al., 2013, and consisted of a 3-T MRI scan and cognitive assessment of 59 dementia patients and 47 control subjects. DTI and CSD tractographies were obtained from every patient while changing the FA or FOD threshold, respectively, and the angle deviation. This data was then employed to perform two different network analysis approaches: based on the registration to the atlas or based on individual parcellation. Finally, the analysis were quantified by measuring the clustering coefficient, global and local efficiency, and distance from the binary connectivity matrices, and connectivity matrices weighted by the FA values and percentage of tracts.

The students t-tests (alpha 0.05) performed and the Cohen's D values calculated showed that the measurement decreased while the FA threshold was increased, been anatomically implausible a threshold higher than 0.3. With respect to the angle deviation, the measures were increased together with the threshold, and the analysis showed that, for angles higher than 15º, a change of the angle deviation does not have a significant change in the results.

Moreover, DTI tractography, network analysis based on individual parcellations, FA connectivity matrix and global efficiency have shown the higher discrimination performance when differentiating between healthy controls and dementia patients.

***Index Terms*—Tractography, Network analysis, Alzheimer's disease, Efficiency**

I. Introduction

DIFFUSION MRI (dMRI) is an MRI technique sensitive to the random microscopic motion of water molecules. A relevant application of dMRI is fiber tractography, a technique that reconstructs the white matter pathways of the brain by computing the local fiber orientations throughout a region of interest [7].

The study of brain connections with dMRI is often referred to as connectomics or connectome reconstruction. The full connectome of the brain presents valuable information about the brain's architecture but, more significantly, the functioning of the brain [7]. There is a wide range of fiber-tracking algorithms, but the most popular ones, and the ones we will be focusing on in the study, are Diffusion Tensor Imaging (DTI)-based tractography and Constrained Spherical Deconvolution (CSD)-based tractography. DTI-based tractography is a deterministic approach that estimates the diffusion of water within brain white matter tissue using only a 3x3 tensor. However, due to its simplicity, this technique cannot correctly estimate the regions of the brain where there are crossing fibers, therefore been necessary higher-order models to capture more complete information of the Diffusion-weighted (DW) image [19]. The spherical deconvolution approaches were proposed as a solution to the limitations present in DTI tractography. In general, spherical deconvolution is based on the idea that the DW signal measured for any fibre population is sufficiently similar that any differences can to all intents and purposes be ignored. Provided with a good estimate of the DW signal for a canonical fibre population, the problem can be expressed as a linear sum of the signals for all the fibre populations present in a given voxel. When these fibre populations are represented in terms of a more general distribution of fibre orientations (fODF), this mixture of signals becomes a spherical convolution. The problem of estimating the fibre orientations themselves is then solved by inverting the problem, to infer the fODF from the measured signal given a suitably calibrated response for a canonical fibre population. CSD-based tractography uses the spherical harmonic basis to represent the fODF, and applies a non-negativity constraint as a soft regularizer [5].

Once the white matter pathways have been estimated, the connectome can be quantified with well-defined connectivity metrics to assess brain performance. To this end, complex network analysis attempts to describe and quantify the properties of complex systems such as connectomics. Brain connectivity datasets comprise networks of brain regions connected by anatomical tracts or by functional associations. By performing network analysis one can obtain different information of the local and global brain connectivity [17]. In the literature, different approaches are employed when defining the network analysis, which are later quantified for an easier understanding of the results.

The quantification of connectomics is of great interest to the investigation of a wide range of neuroscience diseases including Alzheimer's disease. Alzheimer's disease (AD) dementia refers to a particular onset and course of cognitive and functional decline associated with age which ultimately results in death. It is the most common cause of neurodegenerative dementia [18].

Whole-brain tractography has shown promising results distinguishing patients with Alzheimer's disease from individuals without dementia [1]–[3], [8], [9], [12]–[14]. Reijmer et al., 2013 reveals a decrease in the measures of network efficiency

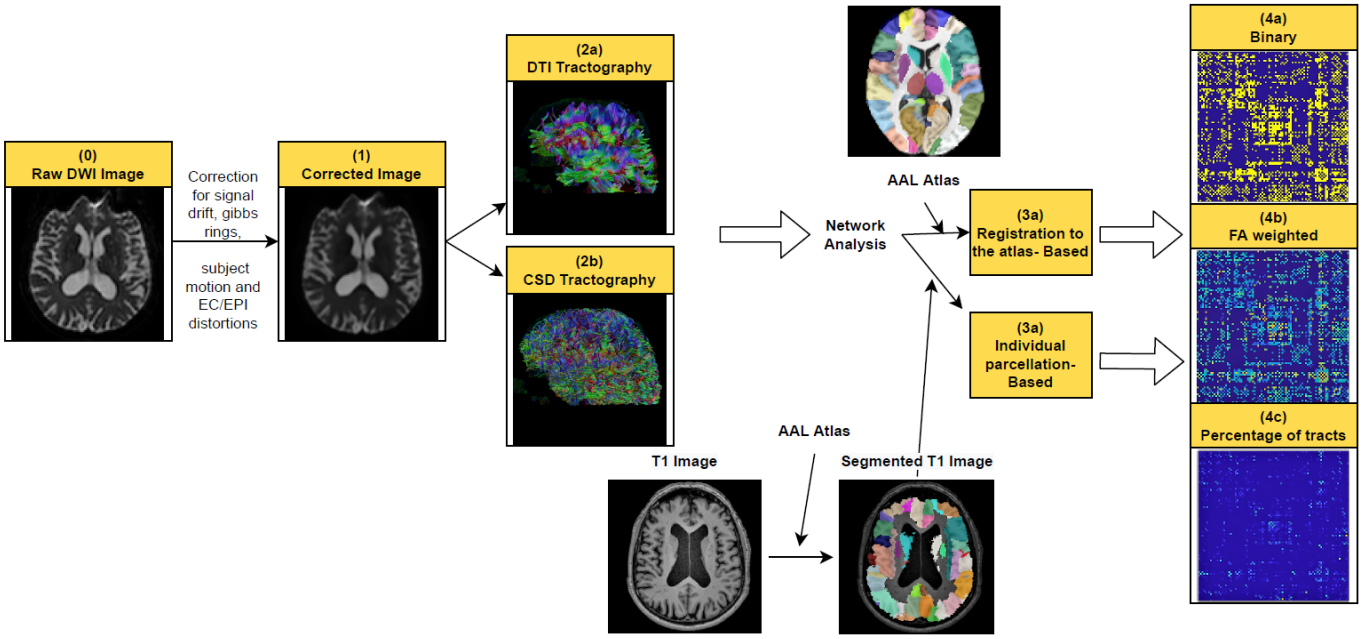

Fig. 1. Graphical overview of the image processing pipeline for a single subject.

in patients with Alzheimer's disease with respect to control patients [14].

However, the connectomics framework is still a state-of-art technique. There is a lack of consensus on the way to perform it, and it is, at the same time, composed of a large variety of parameter settings of choice, having great differences in the outcome of the investigations. In this study, we will explore the differences in analytical results for Alzheimer's disease, based on the different parameter settings, in order to perform more reliable investigations in the future. To this extent, the difference between healthy controls and dementia patients will be analysed when changing the parameters during tractography, the way to define the nodes when performing network analysis and the different metrics to quantify the results.

II. Materials and Methods

THE data employed during this research was obtained from the study performed by Reijmer et al., 2013. Note that the acquisition and preprocessing steps were developed during the previous investigation and are beyond the scope of the following research.

A. *Participants*

The data consisted of patients with early-stage AD dementia and amnesic Mild cognitive impairment (aMCI; considered a transitional stage between normal aging and AD). In addition, a group of functionally independent age-, sex-, and education-matched elderly individuals were recruited to evaluate whether the patient brain networks differed from controls [14]. The participants included in the research were increased to a total of 59 dementia patients and 47 controls since 2013.

All participants were recruited from the University Medical Center Utrecht, and they underwent a standardized evaluation, including medical history, physical and neurologic examination, laboratory testing, and a 3-T MRI scan. All patients participated in a standardized cognitive assessment, although this is not relevant in our study as dementia patients are included in the same group [14].

B. *Image acquisition*

MRI data were acquired on a Philips 3.0 T scanner (Achieva and Ingenia, Philips, Best, the Netherlands).

For each subject, 3D T1-weighted images, fluid-attenuated inversion recovery (FLAIR) scans, and diffusion-weighted images were obtained during the same scanning session.

The following parameters were used for the 3D T1: 192 continuous slices, reconstructed voxel size 1.00 x 1.00 x 1.00 mm^3, repetition time 7.9 ms, echo time 4.5 ms, and a flip angle of 8°; and for the FLAIR: 48 continuous slices, reconstructed voxel size 0.96 x 0.95 x 3 mm^3, repetition time 11,000 ms, echo time 125 ms, inversion time 2,800 ms.

Diffusion MRI data were obtained using a single-shot spin-echo EPI sequence with the following parameters: 48 contiguous slices, reconstructed voxel size 1.72 x 1.72 x 2.50 mm^2, repetition time 6,638 ms, echo time 73 ms, flip angle of 90°, 45 isotropically distributed diffusion-sensitizing gradients with a b value of 1,200 s/mm^2, and 1 b = 0 s/mm^2 (number of signal averages = 3).

C. *Image processing*

The complete image processing pipeline is summarized in Figure 1.

DTI scans were analyzed and processed in ExploreDTI (www.exploredti.com). To standardize and accelerate the connectomics analysis, the code from the ExploreDTI graphical

interface was customized and automatized by writing MATLAB scripts.

Step 1 consists of data preprocessing, which includes signal drift and Gibbs ring correction, correction of subject motion and EC/EPI distortions, and tensor estimation. In addition, T1 images were processed to obtain ROI segmentations in individual space, for each participant, using CAT12 [6] and the AAL3 atlas [16].

TABLE I
DTI TRACTOGRAPHY PARAMETERS

Tractography type	Parameters	Values
DTI	Seed FA	0.05:0.05:0.5
	FA track range	[0.05:0.05:0.5 1]
	Angle deviation	5:5:70º
	Step size	1 mm
	Seed point resolution	[2 2 2] mm
	Fiber length range	[50 500] mm
CSD	FOD	0.04:0.02:0.2
	Angle deviation	5:5:70º
	Step size	1 mm
	Seed point resolution	[2 2 2] mm
	Fiber length range	[50 500] mm

The second step of the pipeline consisted on a whole-brain tractography, which could be DTI or CSD. The parameters used to perform connectomics were changed from the default parameters in ExploreDTI, and are summarised in Table I.

Further, two approaches of network analysis were implemented during the research, which differ by the definition of the nodes. Step 3a defines the registration to the atlas-based network analysis, which employs Elastix [10] to register the tractography to the AAL3 atlas [16]. The network analysis shown in step 3b, however, is based on the individual parcellations of the T1 images to the atlas, previously done during the preprocessing of the images. Both analyses defined tract pathways between two ROIs when they ended in these ROIs.

The network analysis were evaluated using the Brain Connectivity Toolbox [17]. In order to decide which connectivity matrices and metrics will be present in the analysis, a literature research was performed to obtain the ones most often used in neuroscience. The chosen ones are described in the following paragraphs.

Binary connectivity matrices, and connectivity matrices weighted by the FA values and percentage of tracts, were therefore created and used to obtain the different metrics — step 4. Zeros were placed both at intersections without a streamline and on the main diagonal [11].

Finally, global and local efficiency, clustering coefficient and distance were calculated for every connectivity matrix using the Brain Connectivity Toolbox as defined in Rubinov et al., 2010 [17], and each metric was compared between the different participants and parameter settings.

D. *Statistical Analysis*

For each performed analysis, and every of the three connectivity matrices previously described, the different metrics were compared between healthy controls and dementia patients — subjects with aMCI or Alzheimer's disease were included in the same group.

For this purpose, the mean value of each measure —without taking NaN values into account— is calculated from every patient, and independent student t-tests (alpha 0.05) of these values are performed between the two groups. Two t-tests are performed for every parameter changed, each of which considers the controls group to be higher or lower, respectively. The data consists of two independent samples with unknown and different variances.

The Cohen's D value is calculated to measure the effect size between the two groups of subjects, according to the formula defined in (Cohen 1992) [4]. As the size effect is the same independently of the direction, the results have been analysed taking the absolute values.

A better outcome in discriminating between dementia patients and healthy controls is defined when the parameter has more statistically significant events and a higher Cohen's D value.

Due to the large number of parameters changed in the analysis, the results will be presented individually for each of them, while maintaining the rest in a fixed value. The order followed during the analysis will be the same as in the pipeline, showing the results when changing the type of tractography, network analysis approach, connectivity matrices and the metrics employed.

The results will then be obtained while changing the tractography parameters —FA or FOD, and Angle deviation— with the parameters that have been chosen in the previous analysis.

To examine whether there is a high difference in changing the tractography parameters, the percentage of change has been obtained when changing one value and the corresponding results with default values.

The statistics and final plots were performed in R.

III. RESULTS

FOR a better understanding of the results, the different steps of connectomics and metrics will be analysed separately and following the order described in the pipeline.

A. *Modifying the type of Tractography*

The results for both tractography types —DTI or CSD— have been obtained while changing the angle deviation, employing registration to the atlas-based network analysis, binary connectivity matrices and the clustering coefficient measure.

Figure 2 shows the box plots of the clustering coefficient as a function of the angle deviation threshold. Increasing the angle deviation results in an increase in the clustering coefficient values. This increment is higher for CSD tractography than for DTI. Moreover, there is a higher difference in the median values for DTI tractography in comparison to CSD, as well as a higher standard deviation for the clustering coefficient values in DTI. Notice that the median is higher for control subjects when performing DTI, but lower with CSD.

A higher difference between healthy controls and patients for DTI is demonstrated when performing the t-test analysis, as

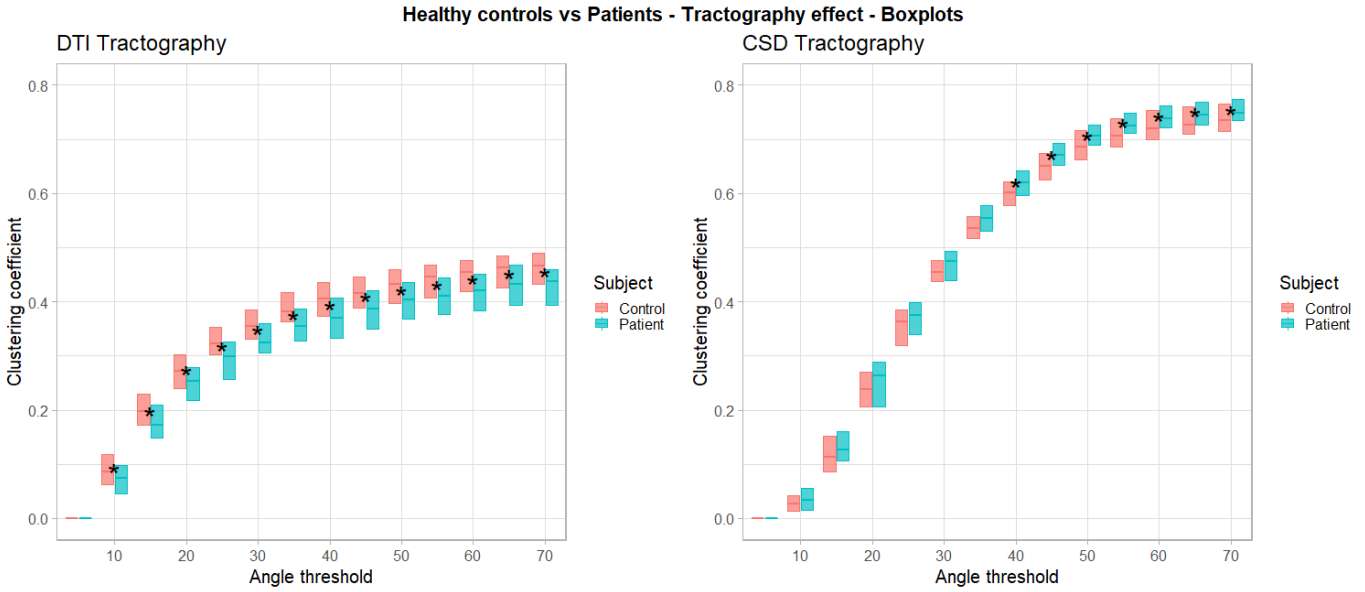

Fig. 2. Box plots of the clustering coefficient values for the two tractography types; showing the change on the angle threshold and discriminating between healthy controls and dementia patients. The symbol * is displayed on top of the threshold values in which the difference between healthy controls and patients is statistically significant. The figure shows the results for network analysis based on the registration to the atlas, binary connectivity matrix and clustering coefficient measure.

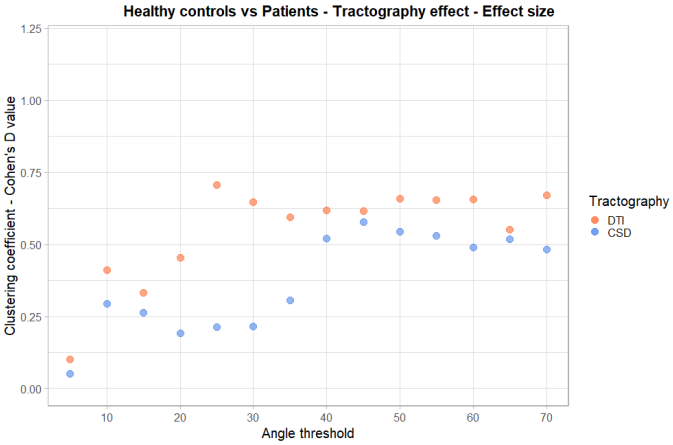

Fig. 3. Effect size of the clustering coefficient values when discriminating between healthy controls and dementia patients for the two tractography types; showing the change on the angle threshold. The figure shows the results for network analysis based on the registration to the atlas, binary connectivity matrix and clustering coefficient measure.

the difference is statistically significant for an angle deviation higher than 5 for DTI tractography, while for CSD, the difference is only statistically significant for angles higher than 40.

In Figure 3 the Cohen's D value represents the effect size between the two groups of subjects. It can be observed how the effect size is higher for DTI tractography.

From these figures we can conclude that DTI tractography has a better outcome in discriminating between healthy controls and patients for the lower angle thresholds, including the default angle value, 30º. Due to this event, the following analysis will only be presented for DTI tractography, and therefore, the results obtained when changing the FOD threshold will not be discussed. For further information, the box plots showing the statistically significant thresholds and the effect size can be examined in Appendix A.

B. Modifying the Network analysis approach

For all the FA thresholds, the two approaches of network analysis were performed with DTI tractography, binary connectivity matrices and the clustering coefficient measure.

In Figure 4, box plots were performed for the results of both approaches of network analysis, differentiating between the two groups of subjects and the FA threshold. The difference according to the choice of network analysis cannot be so easily observed as when differentiating by the tractography performed, although it is already detected a higher median value in the individual parcellations-based network analysis for both groups of subjects. This value is higher for controls with respect to dementia patients, except for FAs lower than 0.1 when performing the first network approach.

When examining the p-values, the network analysis based on individual parcellations has obtained a better performance in discriminating between the two groups of subjects, as the t-tests have resulted in statistically significant events for FAs lower than 0.3, except 0.1.

Finally, the Cohen's D values of the effect size for the two approaches of network analysis are displayed in Figure 5. It can be determined that the effect size is larger for the network analysis based on individual parcellations for FAs lower than 0.3.

The individual parcellations-based network analysis has therefore obtained better results when trying to distinguish between healthy controls and dementia patients.

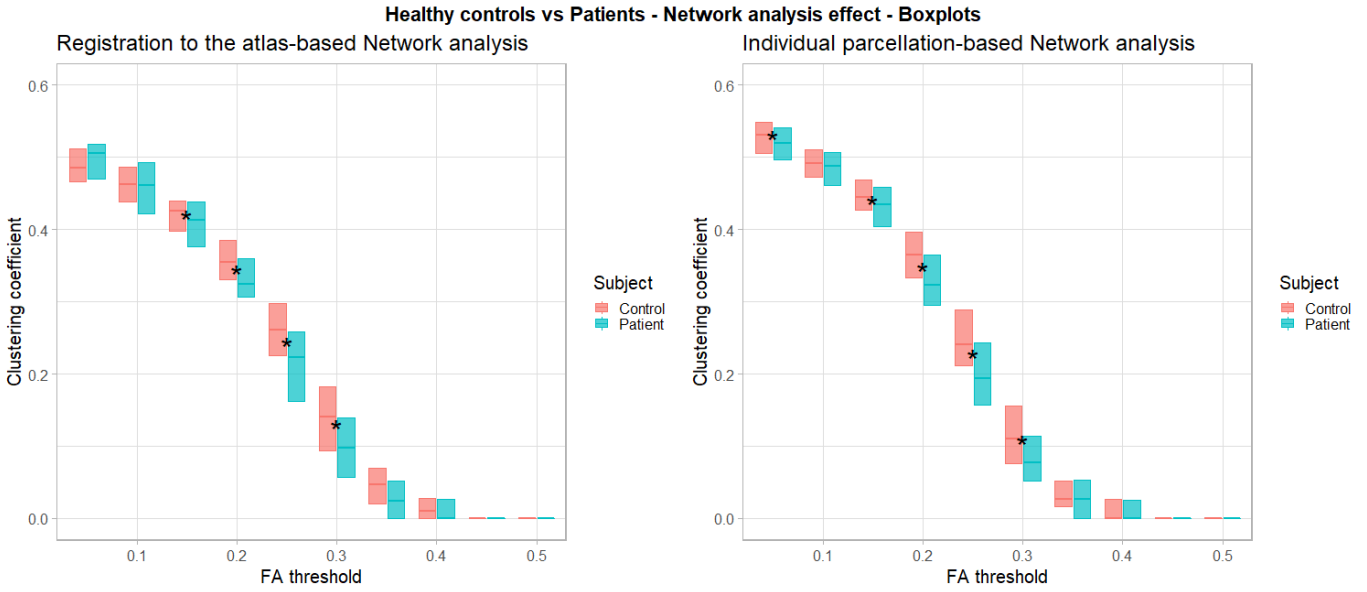

Fig. 4. Box plots of the clustering coefficient values for the two network analysis approaches; showing the change on the FA threshold and discriminating between healthy controls and dementia patients. The symbol * is displayed on top of the threshold values in which the difference between healthy controls and patients is statistically significant. The figure shows the results for DTI tractography, binary connectivity matrix and clustering coefficient measure.

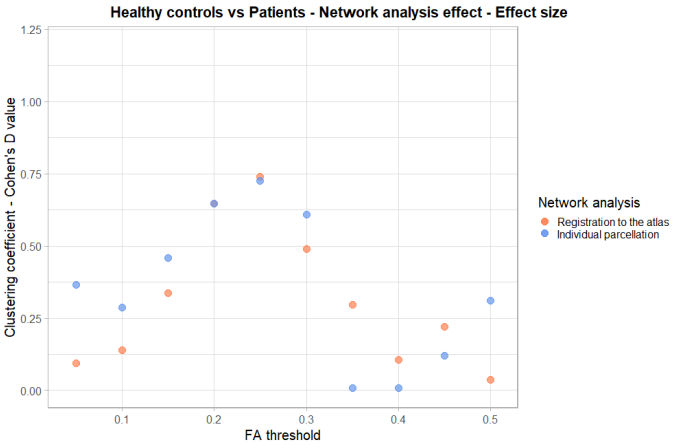

Fig. 5. Effect size of the clustering coefficient values when discriminating between healthy controls and dementia patients for the two network analysis approaches; showing the change on the FA threshold. The figure shows the results for DTI tractography, binary connectivity matrix and clustering coefficient measure.

C. Modifying the Connectivity matrix

In the next section, we report the results of the effect of changing the FA thresholds for the three types of connectivity matrices previously described. Analysis will be obtained with DTI tractography, network analysis based on individual parcellations and the clustering coefficient measure.

Figure 6 shows the box plots of the different types of connectivity matrices, distinguishing between healthy controls and patients, and for the different FA thresholds. Binary and FA connectivity matrices follow a similar tendency, although the clustering coefficient values are higher for the binary connectivity matrix. For these two types of connectivity matrices, the mean values for control subjects are higher and the standard deviation is similar for both types of subjects. The values for the percentage of tracts connectivity matrix, however, are almost zero for all the thresholds, and the standard deviation is very low, specially for the lower FA values. Notice that the clustering coefficient values increases until 0.3, and is higher for the patients group, contrary to the other matrices.

With respect to the t-tests performed, the results show that the FA connectivity matrix has more statistically significant events than the binary and percentage of tracts matrices, obtaining statistically significant results for FAs lower than 0.3.

Figure 7 shows the Cohen's D values of the effect size for the different types of connectivity matrices. This effect is very large for values lower than 0.2, for the matrix weighted by the percentage of tracts but shows an acute decrease as the threshold value increases. However, the change of this value for FA and binary matrices is softer. The Cohen's D value increases until 0.25 and decreases again for higher FA values. This effect is higher for the FA connectivity matrix than the binary one.

The FA connectivity matrix achieved a higher performance when comparing healthy controls and patients, as more thresholds have a significant difference, the effect size is high and the results are more easily interpreted than for the matrix weighted by the percentage of tracts.

D. Modifying the Connectivity measure

As mentioned before, there are four different connectivity measures widely employed in the study of neuroscience diseases: clustering coefficient, local and global efficiency, and distance. These measures have been compared for DTI tractography, individual parcellations-based network analysis and FA connectivity matrix, while changing the FA threshold values.

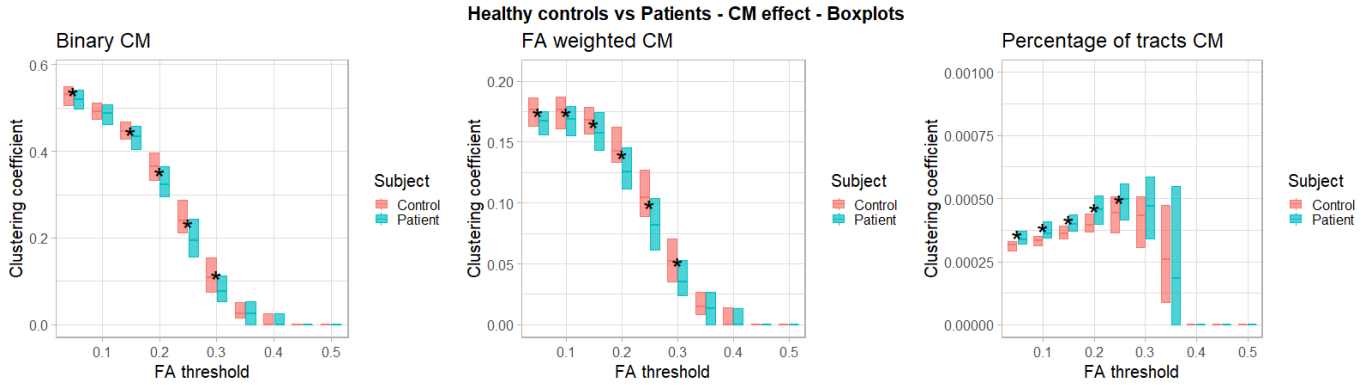

Fig. 6. Box plots of the clustering coefficient values for the three types of connectivity matrices; showing the change on the FA threshold and discriminating between healthy controls and dementia patients. The symbol * is displayed on top of the threshold values in which the difference between healthy controls and patients is statistically significant. The figures show the results for DTI tractography, individual parcellations-based network analysis and clustering coefficient measure.

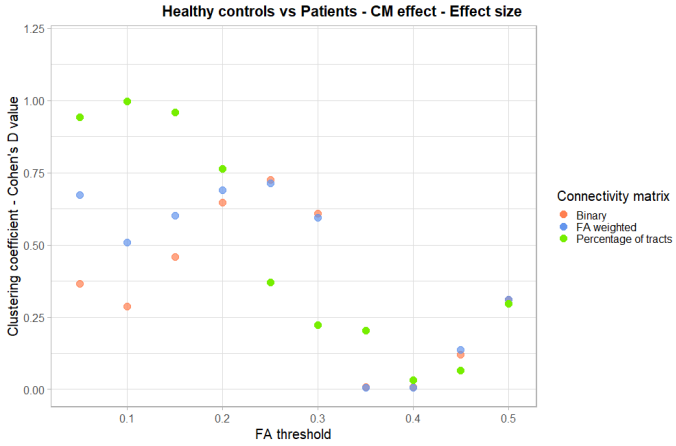

Fig. 7. Effect size of the clustering coefficient values when discriminating between healthy controls and dementia patients for the three types of connectivity matrices; showing the change on the FA threshold. The figures show the results for DTI tractography, individual parcellations-based network analysis and clustering coefficient measure.

In Figure 8, box plots for the four connectivity measures are plotted. Clustering coefficient, local efficiency and global efficiency values decrease while the FA threshold increases. However, the distance between nodes is increased until threshold 0.35, where the number of connections starts to decrease and this results in a lower distance mean value.

For the first three measures, the difference between the two groups of subjects is statistically significant for FA values lower than 0.3, and is also significant for 0.35 in the case of global efficiency. The distance measure, on the contrary, has statistically significant results for the FA thresholds 0.15 to 0.25, 0.35 and 0.4.

The Cohen's D values presented in Figure 9 represent the effect size of the measures' variation depending on the group of subjects. The distance measures have a lower effect with respect to the rest. The largest effect is indeed obtained by the global efficiency values of the FAs lower than 0.35, which corroborates that global efficiency is the best measure to discriminate between dementia patients and healthy controls.

E. Modifying the Threshold

Finally, the results of the effect of changing the FA and angle deviation thresholds are presented. The parameters and metrics employed during this analysis are the ones considered better in discriminating between the two groups of subjects during the previous sections —DTI tractography, individual parcellations-based network analysis, FA connectivity matrix and global efficiency.

Figure 10 shows the box plots of the global efficiency values obtained while changing the FA and angle threshold, separately. The global efficiency is reduced while increasing the FA threshold, contrary to a reduction of the measure when increasing the angle deviation. A higher median value of global efficiency for the healthy control subjects is also visible for both types of thresholds.

To identify if the difference between groups is statistically significant, a student t-test was performed for each threshold values. The results are presented in the box plots. FA thresholds values below 0.35 and every angle deviation have a significant difference between the two groups of subjects.

In Figure 11, the Cohen's D value is shown as an estimation of the effect size between the two groups. The effect is considered large for FAs below 0.3 and angles higher than 15 and does not have a big variability throughout these values.

Finally, to analyse to which extend the global efficiency measures vary with respect to the threshold value, the percentage of change was calculated for every threshold with respect to the default parameter —FA 0.2 and angle 30. The results are presented in Figure 12 in the shape of box plots. Here it can be noticed that changing the FA value has a bigger effect than changing the angle deviation. The standard deviation of this change is bigger for the dementia patients than the healthy controls, for both parameters. The change is below a 25% for FA values 0.05 to 0.15 and angle deviations 20 to 70º.

We can conclude that, when trying to discriminate between dementia patients and healthy controls, FA values between 0.05 and 0.30 will have a statistically significant difference and the results might change between 25-75%. For the angle deviation, the results values higher than 15º will change less

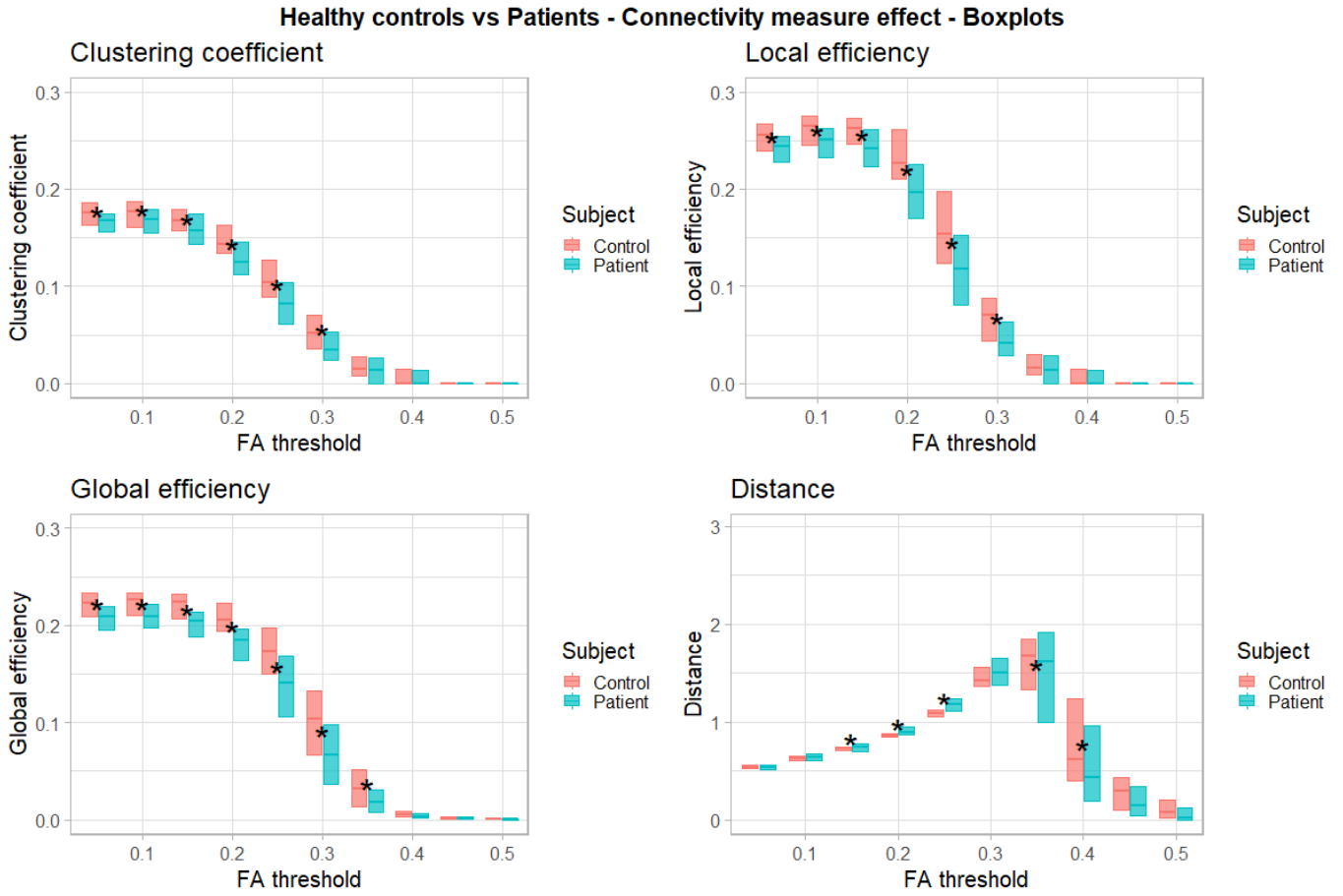

Fig. 8. Box plots of the considered connectivity measures; showing the change on the FA threshold and discriminating between healthy controls and dementia patients. The symbol * is displayed on top of the threshold values in which the difference between healthy controls and patients is statistically significant. The figures show the results for DTI tractography, individual parcellations-based network analysis and FA connectivity matrix.

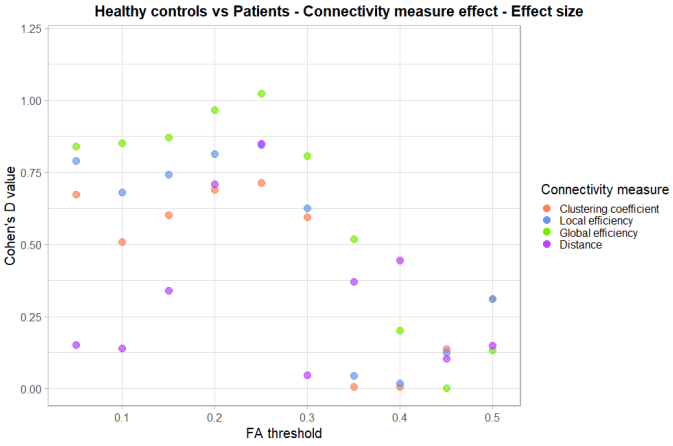

Fig. 9. Effect size of the considered connectivity measures when discriminating between healthy controls and dementia patients for the four different connectivity measures; showing the change on the FA threshold. The figures show the results for DTI tractography, individual parcellations-based network analysis and FA connectivity matrix.

than a 50% with respect to the default threshold, and will be able to differentiate between the two groups.

For further information, the box plots and effect size plots, when changing the FOD and angle deviation for CSD, and all the results for registration to the atlas-based network analysis are presented in Appendix A and B for the FA connectivity matrix and global efficiency measure.

IV. Discussion

THE results have proven to obtain different outcomes when differentiating between healthy controls and dementia patients depending on the choice of the different parameters and metrics.

In the first place, Figures 2 and 3 demonstrate that DTI has a higher discrimination power between the two groups when compared to CSD. For DTI-based tractography, all the events with an angle deviation higher than 5º are statistically significant, while this only occurs for angles higher than 40º when performing CSD.

In addition, for DTI tractography the clustering coefficient in patients with dementia is higher than for healthy controls, as opposed to CSD.

CSD is potentially more accurate given that the model is more elaborate. CSD-based tractography has indeed demonstrated to increase the sensitivity to detect white matter abnormalities within the tract for patients with Alzheimer's

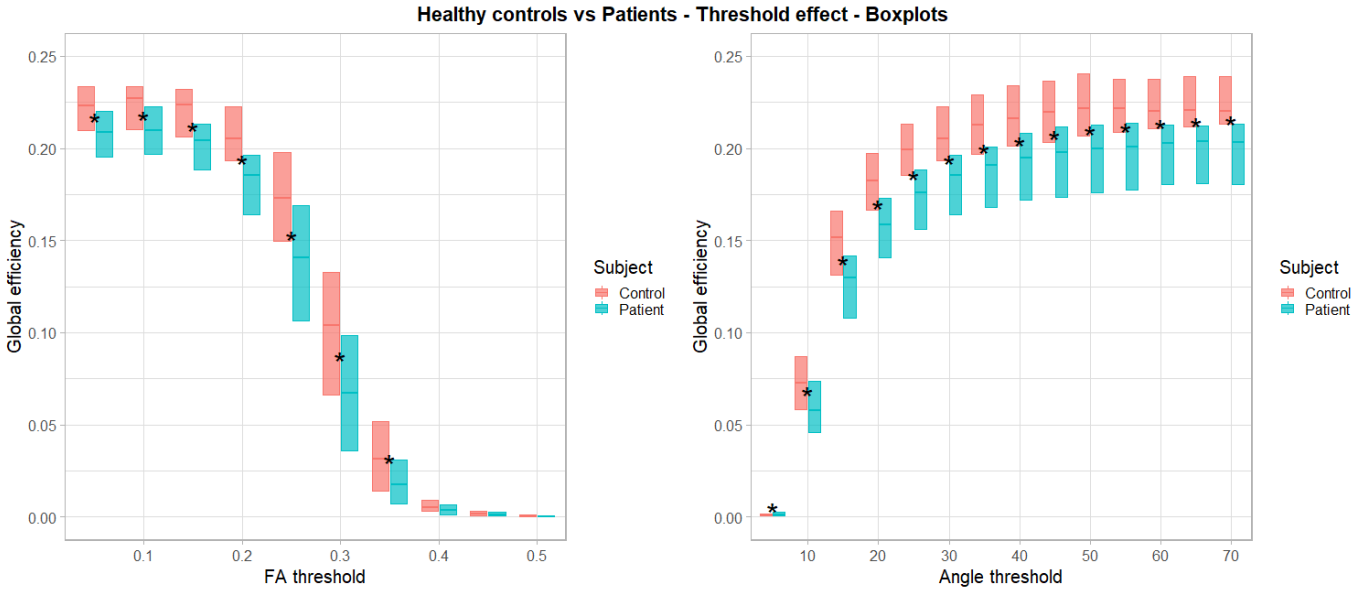

Fig. 10. Box plots of the global efficient values when changing the FA and angle thresholds; discriminating between healthy controls and dementia patients. The symbol * is displayed on top of the threshold values in which the difference between healthy controls and patients is statistically significant. The figures show the results for DTI tractography, individual parcellations-based network analysis and FA connectivity matrix.

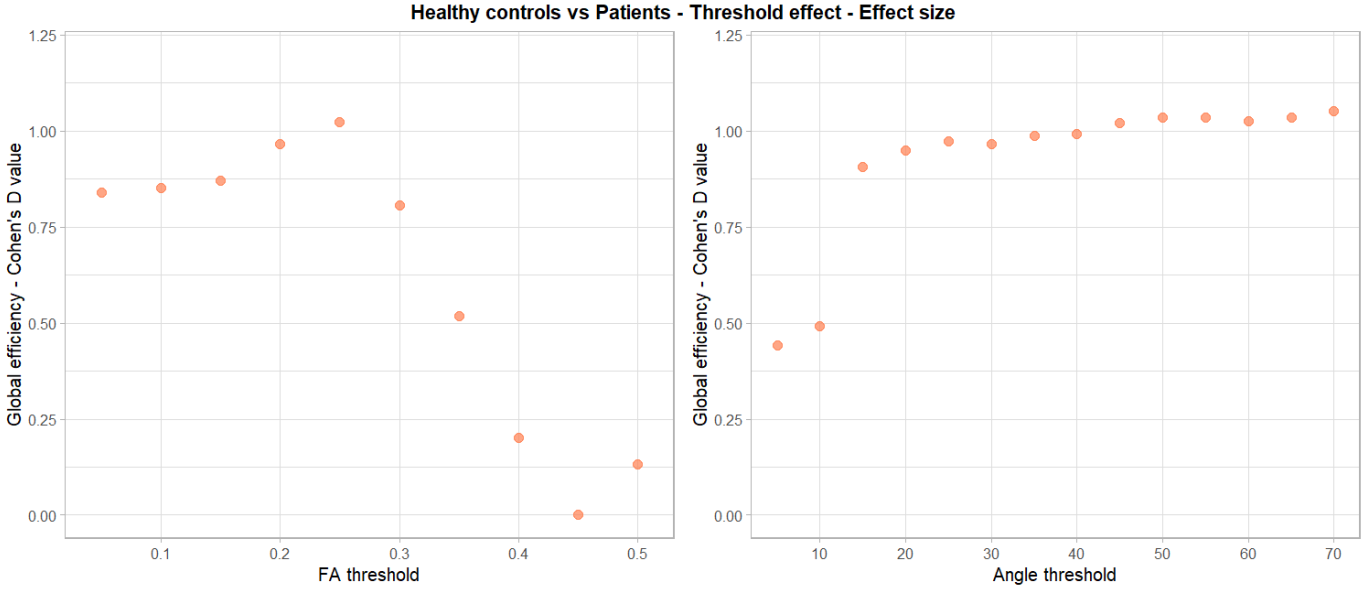

Fig. 11. Effect size of the global efficiency values when discriminating between healthy controls and dementia patients; showing the change on the FA and angle thresholds. The figures show the results for DTI tractography, individual parcellations-based network analysis and FA connectivity matrix.

disease. However, there are also adverse effects of the crossing fibers on the interpretation of diffusion measures that may result in contra-intuitive results in regions with crossing fibers, demonstrating higher FA values in patients compared to controls [15]. These findings suggest that CSD fails in distinguishing between the two groups, having an improper response function.

DTI-based approached, however, may be sufficient to observe the difference in the structural organisation of the white matter network between the two groups.

In Figures 4 and 5, both network analysis approaches have obtained very similar outcomes, as expected. However, the registration approaches have introduced additional variability as compared to individual parcellations, which results in a lower capability of the first network analysis approach.

Figures 6 and 7 make evident that increasing the FA threshold results in less tracks until none of them are found. Thresholds higher than 0.3 result in very low sensitivity, and they do not make sense from a physiological perspective, as they include very small parts of the white matter.

Indeed, none of the connectivity matrices show a difference between healthy controls and dementia patients above a threshold of 0.3, as there is too much variability inside the groups. These estimates are no longer reflecting anything anatomically

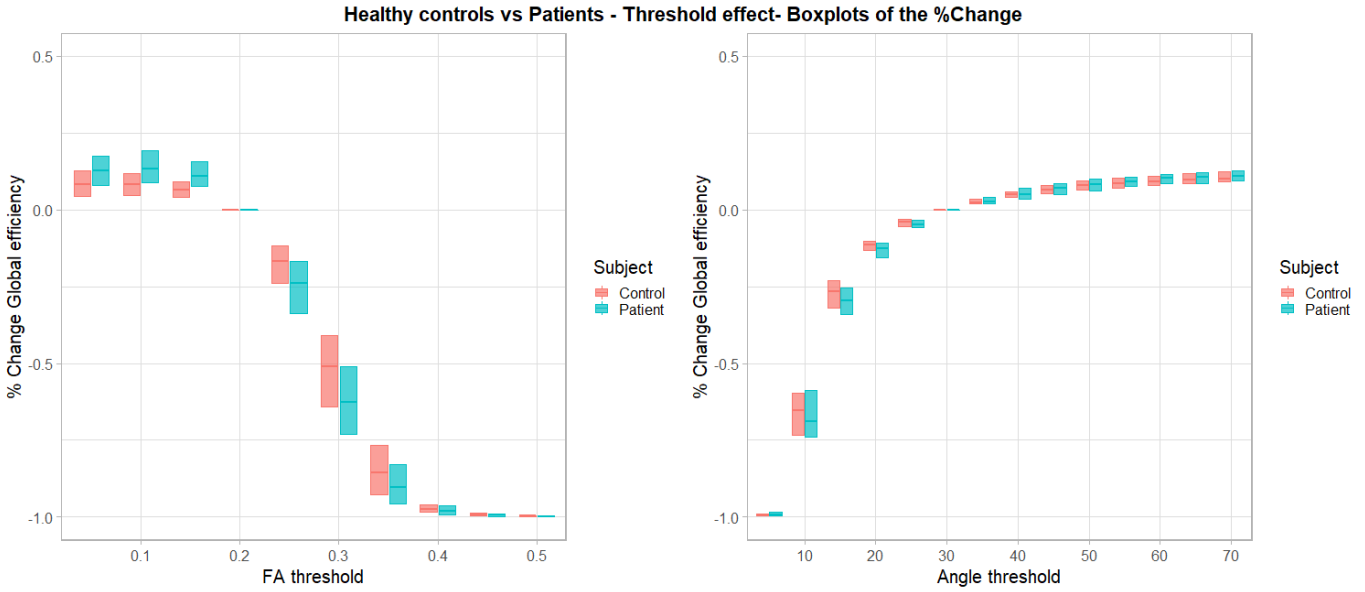

Fig. 12. Box plots of the percentage of change of the global efficient values when changing the FA and angle thresholds; discriminating between healthy controls and dementia patients. The figures show the results for DTI tractography, individual parcellations-based network analysis and FA connectivity matrix.

plausible.

In particular, the results obtained weighted by the percentage of tracts are not expected, having higher values for dementia patients than for controls. Further research needs to be done if this matrix is intended to be used.

A better outcome in FA values lower than 0.3 is also demonstrated for Figures 8 and 9. The effect size shows a constant increase in the values until 0.3, when they start to fluctuate across each other.

When comparing the measures, global efficiency has proven to obtain the best discrimination performance, and it is one of the most chosen in literature due to its simplicity and clear interpretation [11], [13], [14].

For this reason, global efficiency is calculated when changing the FA and angle thresholds, and the results are plotted in Figures 10 and 11.

As shown before, global efficiency decreases while the FA threshold goes up, as the nodes with lower FAs are discriminated and less connections are made. The results are physically implausible for values higher than 0.3. On the contrary, the angle deviation turns less restrictive when increasing its value, allowing higher deviations between the nodes and thus resulting in more connections and higher global efficiency.

Figure 12 depicts that the results are very robust when changing the thresholds. Increasing the angle threshold does not have a notable change in the results for angles higher than 30º, so the false negatives —the pathways missing due to a low threshold— have a bigger effect than including the false positives due to increasing the angle threshold.

For FAs above 0.3, the tractograhy is composed by a sparse representation of the white matter, resulting in a high variability of the results and, therefore, a higher percentage of change with respect to the lower thresholds.

Despite the variability demonstrated while changing the parameters, this study has encountered some methodological considerations that are worth to mention. A multidimensional analysis may obtain the exact parameters and measurements that result in a higher difference between the two group of subjects, although it might be too complex and computationally expensive for the objectives of this study. The number of subjects, may also play a role in the upcoming results. The subjects could additionally be differentiated by the two groups of dementia disease —AD and aMCI—, sex, age and other parameters of interest. Moreover, this analysis could be performed for different neuroscience diseases to evaluate if there are some optimal results for the different cases.

V. Conclusions

In conclusion, changing the default parameters when performing a connectomics and network analysis has an effect on the statistical analysis when discriminating between healthy controls and patients. This effect is stronger for the FA threshold than the angle deviation, but it is specially important when choosing the type of tractography, network analysis and connectivity matrix.

The parameters that have obtained the best discriminating performance in this study are DTI tractography, network analysis based on individual parcellations, FA connectivity matrix, global efficiency, FA values lower than 0.3 and angle deviation higher than 15º.

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APPENDIX A
CHANGING THE THRESHOLDS FOR CSD TRACTOGRAPHY

The next figures are presented for the best results obtained from the analysis, and for CSD tractography.

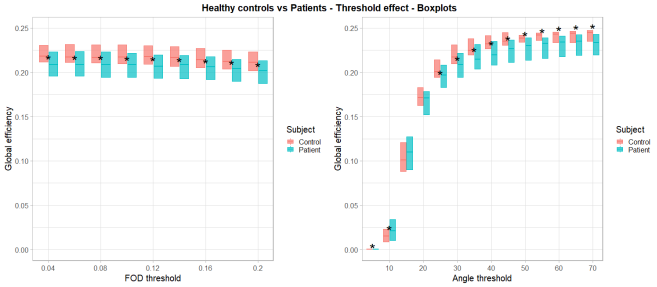

Fig. A.1. Box plots of the global efficient values when changing the FOD and angle thresholds; discriminating between healthy controls and dementia patients. * represent the threshold value in which the difference between healthy controls and patients is statistically significant for each threshold value. The figures show the results for CSD tractography, individual parcellations-based network analysis and FA connectivity matrix.

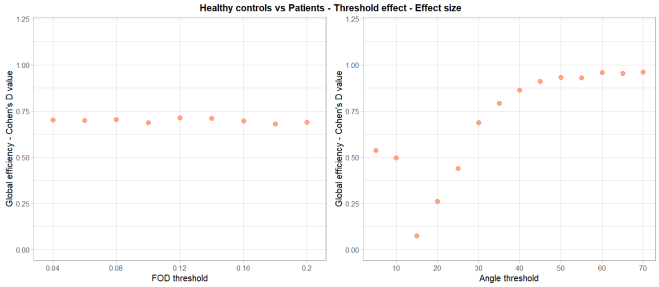

Fig. A.2. Effect size of the global efficiency values when discriminating between healthy controls and dementia patients; showing the change on the FA and angle thresholds. The figures show the results for CSD tractography, individual parcellations-based network analysis and FA connectivity matrix.

APPENDIX B
CHANGING THE THRESHOLDS FOR NETWORK ANALYSIS BASED ON REGISTRATION TO THE ATLAS

The next figures are presented for the best results obtained from the analysis, and for registration to the atlas-based network analysis.

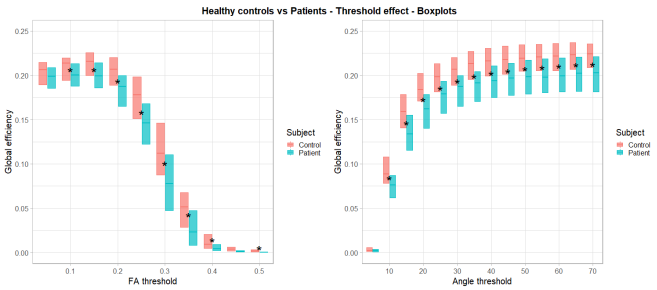

Fig. B.1. Box plots of the global efficient values when changing the FA and angle thresholds; discriminating between healthy controls and dementia patients. * represent the threshold value in which the difference between healthy controls and patients is statistically significant for each threshold value. The figures show the results for DTI tractography, registration to the atlas-based network analysis and FA connectivity matrix.

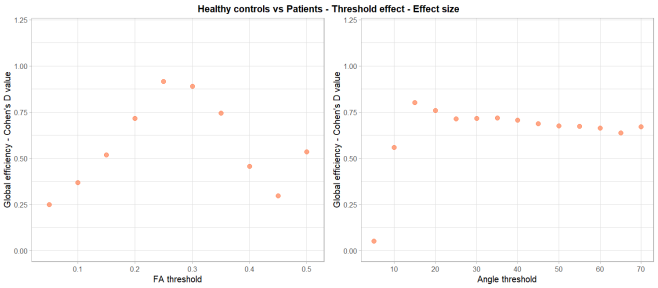

Fig. B.2. Effect size of the global efficiency values when discriminating between healthy controls and dementia patients; showing the change on the FA and angle thresholds. The figures show the results for DTI tractography, registration to the atlas-based network analysis and FA connectivity matrix.

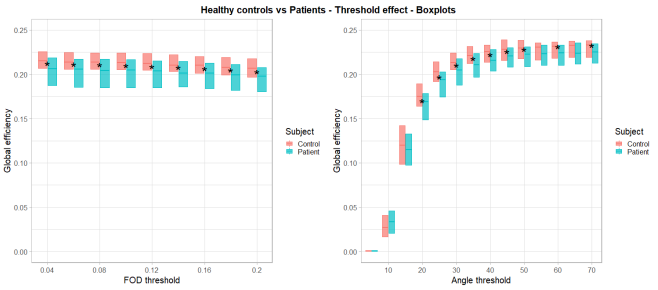

Fig. B.3. Box plots of the global efficient values when changing the FOD and angle thresholds; discriminating between healthy controls and dementia patients. * represent the threshold value in which the difference between healthy controls and patients is statistically significant for each threshold value. The figures show the results for CSD tractography, registration to the atlas-based network analysis and FA connectivity matrix.

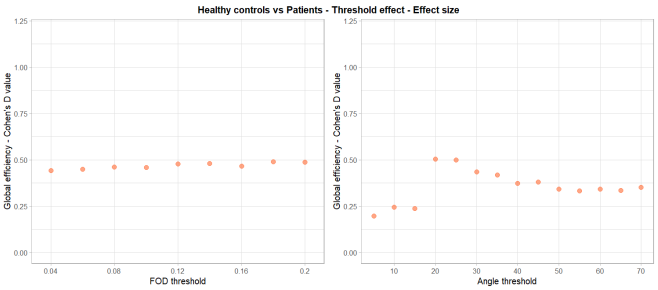

Fig. B.4. Effect size of the global efficiency values when discriminating between healthy controls and dementia patients; showing the change on the FA and angle thresholds. The figures show the results for CSD tractography, registration to the atlas-based network analysis and FA connectivity matrix.