

## SDM tutorial, version Jul 2010

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The aim of this tutorial is to show, in a *step by step* basis, how to conduct a meta-analysis using SDM software. To this end, you will perform some of the analyses conducted in: *Radua J and Mataix-Cols D. Voxel-wise meta-analysis of grey matter changes in obsessive-compulsive disorder. Br J Psychiatry 2009; 195:393-402.* Please notice that this tutorial is distributed in the hope that it will be useful, but without any warranty on the accuracy of the text and data.

### Before executing the software

We have invested a lot of time and effort to improve accuracy of SDM method and software. However, calculations might be biased if the following exclusion criterion is not considered when conducting the searches and contacts with the authors:

*“Exclude studies in which statistically significant coordinates, at the whole-brain level and using the same threshold throughout the brain, are not available”*

This is of utmost importance because it is not uncommon in neuroimaging studies that some regions (e.g. a priori regions of interest) are more liberally thresholded than the rest of the brain.


### Preparation of the text files


For your convenience, the text files required for this tutorial have been already prepared in the folder containing this PDF. If you don't find these files please download the SDM software again from <http://www.sdmproject.com/software>. Take a look at the names and contents of the text files: the coordinates of each study are written in a separate text file, whose name is just a very short identification of the study (e.g. the name of the first author), plus a dot, plus the stereotactic space of the coordinates (“mni”, “mni2tal”, or “tal”), plus a dot, plus “txt”.

## Preparation of the SDM software

In this step you will first specify a working folder for the meta-analysis, as well as the folder containing your MRICron program. Finally, you should create an SDM table specifying the names of the studies and their sample sizes, as well as optional variables – this has been already prepared for you in this tutorial.

➔ Start the SDM software:

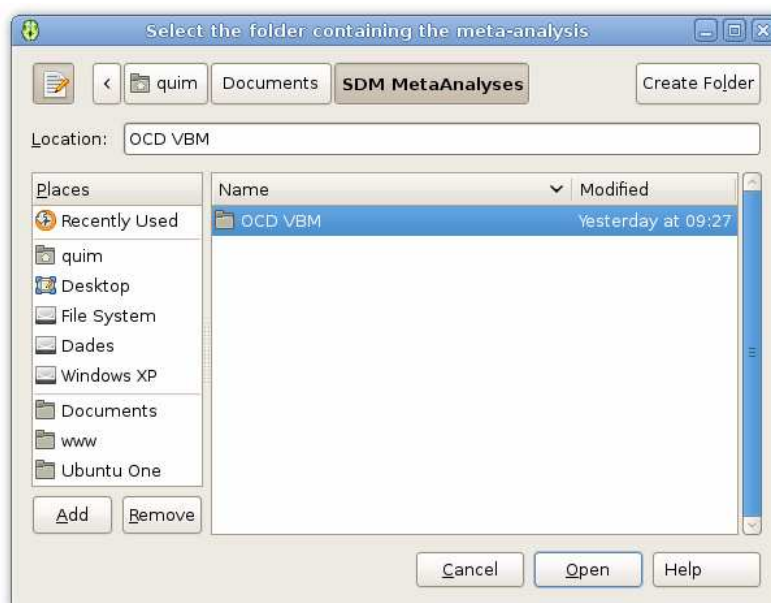
 *Linux users:* to start the software click a file called “sdm” in the SDM software folder. If the program does not execute follow the instructions to change file permissions which can be found at <http://www.sdmproject.com/software/?show=Linux>

 *Windows users:* to start the software click a file called “sdm.exe” in the SDM software folder. If you don't find this file, look for a file called “sdm” whose icon is a green brain.

Two red warnings might be printed in the screen if you haven't used this software before: one complaining about the working folder, and another complaining about the MRICron program.

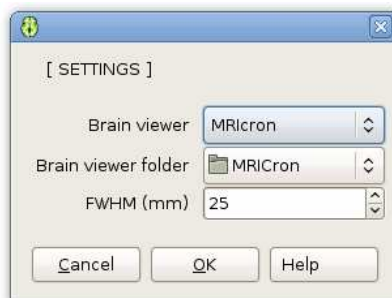
➔ To specify the working folder for the meta-analysis, click the button [Change folder / meta-analysis] button, look for the folder containing this PDF, and click [Open].

A dialog similar to the following one should appear:



→ To specify the folder of your MRICron program, click the [Tools] menu, click [Settings], click the selection box at the right of [Brain viewer folder], select [Other...], look for the folder which contains your MRICron program (typically something like “C:\Program Files\MRICron” in Windows), click [Open], and click [OK].

A dialog similar to the following one should appear:



→ To create or edit the SDM table, click the button [SDM table editor] button.

A window similar to the following one should appear:

study	n1	n2	mean1	sd1	mean2	sd2	adults	YBOCS
Carmona	18	18	773.34	55.80	822.09	55.80	0	21.39
Christian	21	21	NA	NA	NA	NA	1	27.00
Gilbert	25	20	NA	NA	NA	NA	1	26.90
Gilbert_ped	10	10	NA	NA	NA	NA	0	26.50
Heuvel	55	50	685.00	74.00	708.00	72.00	1	22.83
Kim	25	25	849.80	83.30	834.40	71.10	1	24.20
Pujol	72	72	739.00	82.00	763.00	78.00	1	26.70
Rifkin	18	18	NA	NA	NA	NA	1	23.30
Soriano	30	30	NA	NA	NA	NA	1	21.00
Szeszko	37	26	776.00	69.00	747.00	68.00	0	24.90
Valente	19	15	826.78	43.59	836.47	62.79	1	24.60
Yoo	71	71	740.01	65.63	737.75	62.69	1	22.84

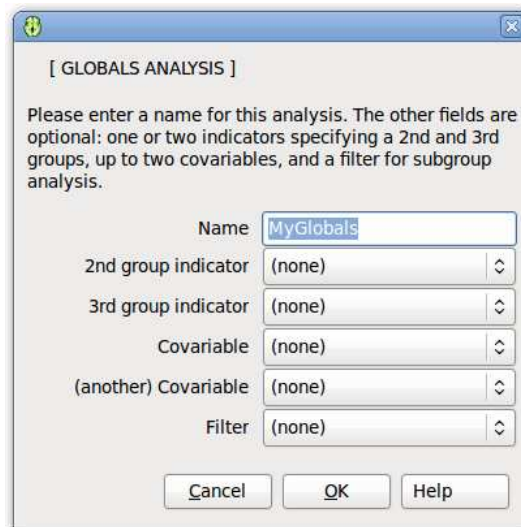
Each row in the SDM table is a study, first column is the identification of the study (exactly the same than in the text files), second column is the size of the patients' sample (“n1”), and other columns are optional variables.

## Globals analysis

Prior to the voxel-based meta-analysis, we will conduct an analysis of the global gray matter volumes. To this end, we need the following variables defined in the SDM table: “n1” and “n2” (sample size of the patients’ and the controls’ groups), “mean1” and “mean2” (global gray matter means), and “sd1” and “sd2” (global gray matter standard deviations).

➔ To conduct the globals analysis, click the button [Globals], and click [OK] twice.

A dialog similar to the following one should appear:



This will create a text file called “globals\_MyGlobals.txt” with many standard meta-analytic measures for global gray matter. The most important are the mean (Hedge’s  $\delta$  along with its corresponding  $Z$  and  $P$  values and the confidence interval) and the analysis of heterogeneity ( $\tau$  and its corresponding  $Q$  and  $P$  values). Heterogeneity should not be statistically significant.

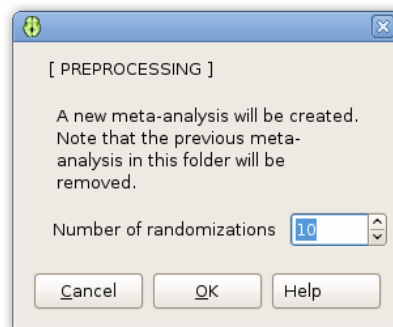
Note that you could have selected indicators for subgroup comparisons, covariates, and a filter for subgroup analysis. If one variable is selected, the program will create a coefficient called “0” which estimates the global gray matter volume at the minimum value of the variable, a coefficient called “1” which estimates the global gray matter volume at the maximum value of the variable, and a coefficient called “1m0” which estimates the difference in global gray matter volume between the maximum and the minimum values of the variable. If two variables are selected, “10” relates to the maximum value of the first variable and the minimum of the second, while “01” relates to the minimum value of the first variable and the maximum of the second. If two variables are selected, the two-variable  $Q$  is also computed, with a meaning similar to the  $F$  of an ANOVA.

## Pre-processing

In this step the coordinates will be used to create brain maps of the original studies. They will be also randomized and then used to create Monte Carlo brain maps, useful for finding the null distributions of the subsequent analyses.

➔ To pre-process the studies, click the button [Preprocessing], and click [OK].

A dialog similar to the following one should appear:



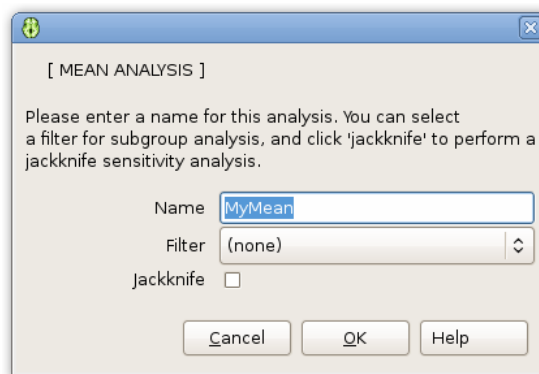
This will create a binary file called “sdm\_main.sdm” which contains the maps of the studies, a set of “pp\_\*.log” text files which contain the coordinates of the studies in Talairach space along with the corresponding brain regions according to the Talairach atlas, a binary file called “sdm\_nd.sdm” containing the null distributions of subsequent analyses, and a set of “sdm\_r\*.sdm” binary files containing the Monte Carlo maps. Notice that you have specified only 10 randomizations, but in a real meta-analysis 500 randomizations are recommended.

## Mean analysis

Now it's time to conduct the mean analysis, which is usually the main outcome of a meta-analysis. In this tutorial, the mean analysis represents the weighted mean differences in regional grey matter between patients with OCD and healthy controls.

➔ To conduct the mean analysis, click the button **[Mean]**, specify a name for this analysis (we will call it “mean”) and click **[OK]**.

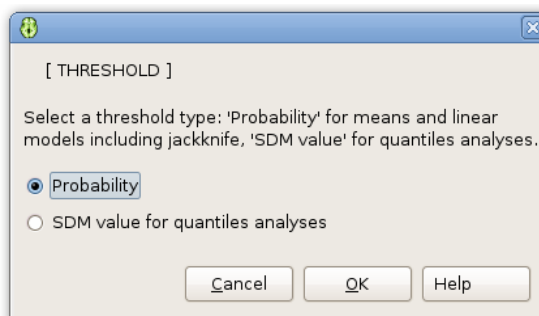
A dialog similar to the following one should appear:



This will create a mean map within the “sdm\_main.sdm” file, a null distribution for this map within the “sdm\_nd.sdm” file, and a new text file called “mean.log” with the statistical thresholds obtained after calculating the mean in each set of Monte Carlo maps.

➔ To threshold and see the results, click the button **[Threshold]**, click **[OK]**, select the “mean” map, and click **[OK]**.

A dialog similar to the following one should appear:



This will print the statistically significant differences in the SDM output window, will start the MRICron program to visually inspect them, and will create the following files: “mean\_p0.00100\_pos.txt” (a text file with positive statistically significant differences),

“mean\_p0.00100\_neg.txt” (a text file with negative statistically significant differences), “mean\_p0.00100\_pos.hdr/img” (a pair of NIfTI files with positive statistically significant differences) and “mean\_p0.00100\_neg.hdr/img” (a pair of NIfTI files with negative statistically significant differences).

### Subgroup analysis of adult samples

This is similar to the mean analysis, with the exception that when performing the mean analysis you will specify the “adults” filter in order that only studies with adult samples are included in the analysis.

- ➔ To conduct the subgroup analysis, click the button [Mean], specify a name for this analysis (we will call it “adults”), select the “adults” filter, and click [OK].
- ➔ To threshold and see the results, click the button [Threshold], click [OK], select the “adults” map, and click [OK].

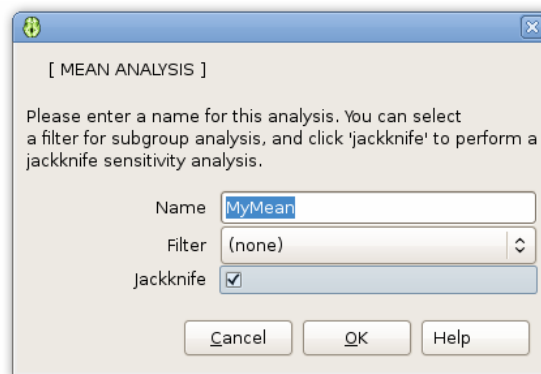
**Tip:** Please notice that you will be able to threshold any time any result from previous analyses, you do not have to conduct the calculations again!

## Jackknife sensitivity analysis

This is again similar to the mean analysis, with the exception that when performing the mean analysis you will select the “Jackknife” option.

→ To conduct the jackknife analysis, click the button **[Mean]** button, specify a name for this analysis (we will call it “mean” again), select the “Jackknife” option, and click **[OK]**.

A dialog similar to the following one should appear:



The software will repeat the mean analysis several times, including each time all the studies but one. The names of the resulting maps will be “mean”, plus “JK”, plus the name of the discarded study. E.g. the analysis including all the studies but “Carmona” will be called “meanJKCarmona”.

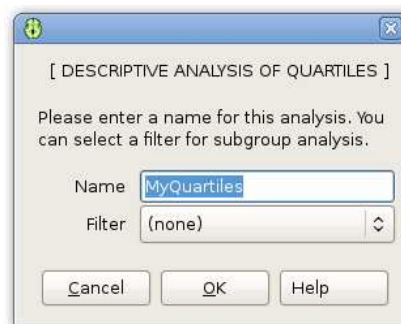
→ To threshold and see the results, click the **[Threshold]** button, click **[OK]**, select one of the maps (e.g. “meanJKCarmona”), and click **[OK]**.

## Analysis of quartiles

Now you will conduct a descriptive analysis of quartiles, i.e. finding the weighted proportions of studies in which differences were found between patients and controls. Please notice that this analysis is only descriptive, and thus no statistical thresholds are used.

- To conduct the analysis of quartiles, click the **[Quartiles]** button, specify a name for this analysis (e.g. “quartiles”), and click **[OK]**.

A dialog similar to the following one should appear:



This will create three maps: “quartiles25” (first quartile map, i.e. 25% of the patients with lower gray matter values), “quartiles50” (second quartile or median map) and “quartiles75” (third quartile).

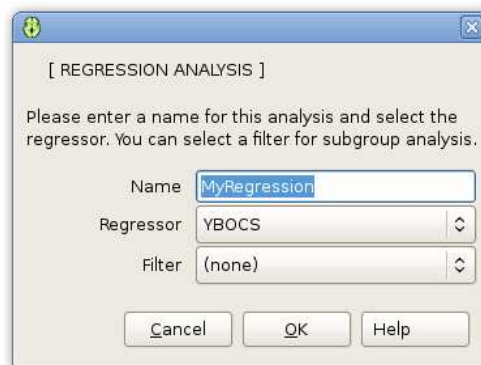
- To threshold and see the results, click the button **[Threshold]**, select “SDM value for quartiles analyses” instead of “Probability”, click **[OK]**, select one of the maps (e.g. “quartiles25”), specify an SDM value (0.001 for positive differences, -0.001 for negative differences), and click **[OK]**.

## Meta-regression by YBOCS

The last analysis will be a weighted regression of each voxel values across the studies and the YBOCS of the corresponding patients' samples.

→ To conduct the regression analysis, click the button [Linear model], select [Meta-regression] and click [OK], specify a name for this analysis (e.g. "ybocs"), select "YBOCS" as the regressor, and click [OK].

Dialog similar to the following one should appear:



This will create three maps: "ybocs\_1" (differences between patients with maximum YBOCS and healthy controls), "ybocs\_0" (differences between patients with minimum YBOCS and healthy controls), and "ybocs\_1m0" (differences between patients with maximum YBOCS and patients with minimum YBOCS).

→ To threshold and see the results, click the button [Threshold] button, click [OK], select one of the analyses (e.g. "ybocs\_1"), specify a lower probability, and click [OK].

Please remember that statistical significance of these meta-regressions should be taken with caution.

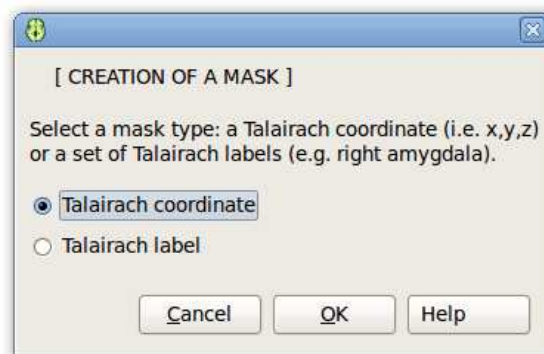
## Extraction of values

Extraction of values is useful for creating graphics with Microsoft Excel or similar software. You will first create a mask which will include the voxel or region from where you want to extract the values, and then extract these values using the mask. In this tutorial you will extract values from the voxel (20,14,0) located in right lentiform nucleus.

### a) Creation of the mask

- To create the mask, click the [Create a mask] button, click [OK], specify a name for the mask (e.g. "rLentif"), type the coordinate (X = 20, Y = 14, Z = 0), and click [OK].

A dialog similar to the following one should appear:

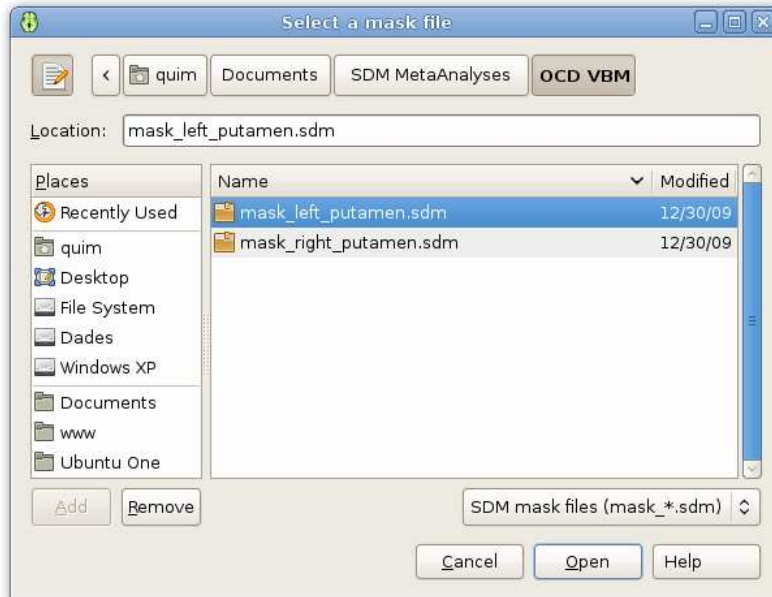


This will create a file called "mask\_rLentif.sdm" which contains the mask and can be used in other meta-analyses.

### b) Extraction of values

- To extract the values using this mask, click the [Extract] button, look for the “mask\_rLentif.sdm” file, and click [Open].

A dialog similar to the following one should appear:



This will create a file called “extract\_rLentif.txt” with the gray matter values of each map in this voxel.