# Atlas-Based Segmentation Pipelines on 3D Brain MR Images: A Preliminary Study

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**Abstract**

Three dimensional structural MR imaging is a high-resolution imaging technique used in the detection and follow up of neurological disorders. Rigid changes in the brain are usually interpreted and reported manually by radiologists using MR images. The results of manual interpretation may vary with respect to the experts. At the same time, measurement and segmentation of the brain regions and the manual evaluation of the volume changes are a difficult process. With the increase of numerical methods, automated and semi-automated package programs have been developed for the analysis of brain measurements. These programs use electronic brain atlases or tissue probability maps. However, since the package programs have a lot of analysis time and give only certain outputs, they may be disadvantaged in the use of segmentation and measurement of brain regions. Hence, special pipelines are needed especially to obtain valuable features for artificial intelligence and classification studies. In this study, we propose pipelines to segment 3D certain brain regions, which will help to find the basic features such as volume changes, intensity variations, symmetry deteriorations, and tissue changes. With these pipelines, 3D segmentation of the brain regions defined in the atlas can be performed and normalized. It is aimed to use these studies as a preliminary study in order to quantitatively determine the basic changes in the brain by performing the volume of interest methods and to formulate a decision support system.

**Keywords :** Structural MR, 3D Atlas, 3D Segmentation, VOI.

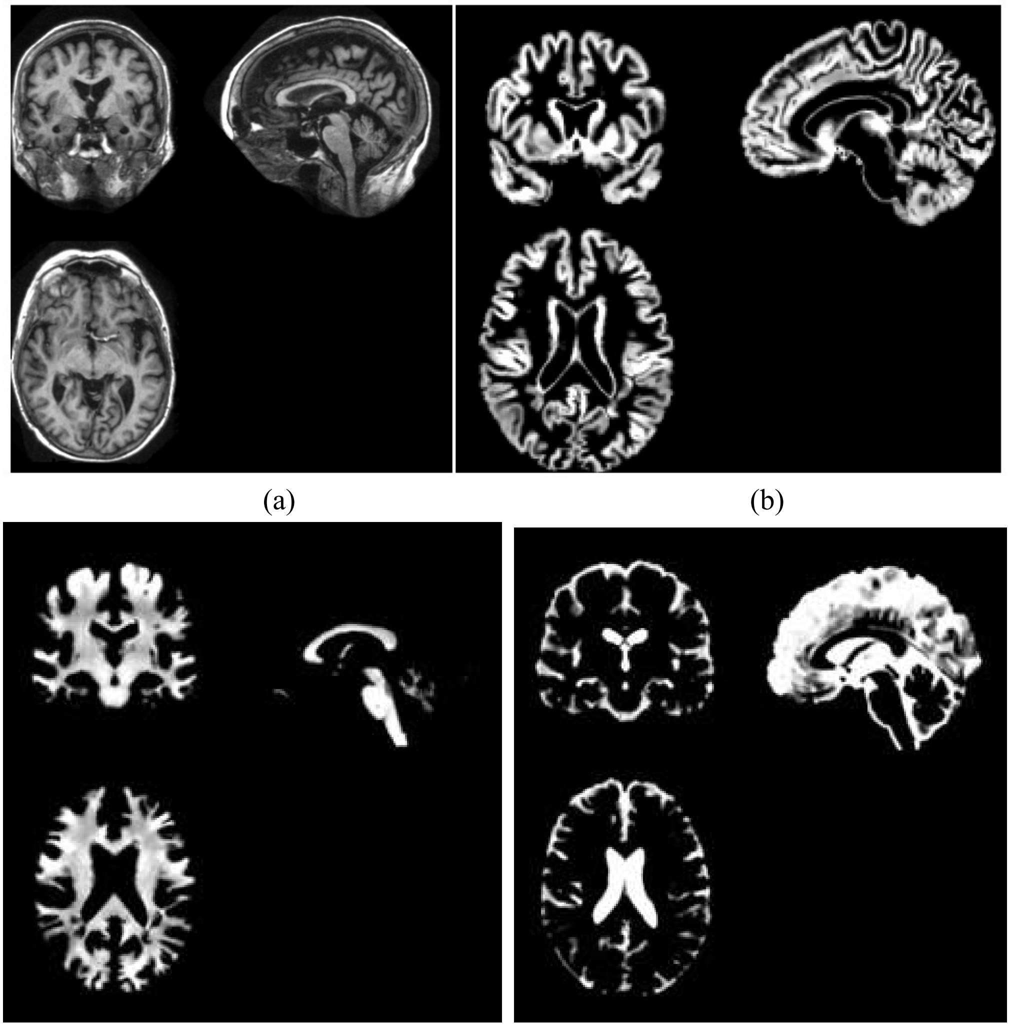
## 1. Introduction

Manual segmentation and absolute measurements of three-dimensional structural MR images, which are frequently used in the follow-up of neurological disorders, are a laborious process. It is necessary to evaluate and report the changes that occur in the brain using 3D MR images. However, the evaluation of the images may vary with respect to the experts (Despotović, Goossens, and Philips 2015). To overcome this problem, programs for automatic or semi-automatic analysis of structural MR images are being developed with the development of numerical methods (Bazin et al. 2007; Fischl 2012). These programs use pre-defined atlas and Tissue Probability Maps (TPMs) for the population (Evans et al. 1993; Lancaster et al. 1997; Fischl 2012; Tzourio-Mazoyer et al. 2002; Cabezas et al. 2011). The obtained outputs are used in the diagnosis and follow-up of the disease. Neurological diseases affect certain areas of the brain. Damage to these areas is due to volume loss or increase, cortical thickness change, symmetry deterioration or tissue disorders (Frisoni et al. 2010). For example, the first degeneration of Alzheimer's Disease (AD), which begins with memory problems, occurs in the hippocampus, amygdala and limbic brain regions as volume losses (Fennema-Notestine et al. 2009). The degeneration of Parkinson's Disease occurs in brain motor regions, where it begins with movement disorders (Xia and Mao 2012). In addition to volume losses in the AD, neurofibrillary tangles and senile plaques arise in brain regions, leading to tissue degeneration. This tissue defect cannot be observed in MR images but can be followed up by PET imaging (Vlassenko, Benzinger, and Morris 2012). In Multiple Sclerosis disease, each patient shows a different characteristic, and lesions arise in brain function regions (Milo and Miller 2014). In neurological diseases, each disease has its own characteristics in different regions of the brain, so it is necessary to analyze the only Volume of Interest (VOI) regions of disease-related areas of the brain. However, degeneration analysis may be relative because the pixel transition regions are not clear in the relevant regions. This problem is more obvious, especially in subcortical areas. The operations in these regions are completely dependent on the experience of the person. To overcome this problem, more precise and realistic measurements can be performed by using atlas-based methods which are determined for a general population. However, since these methods are not known by most radiologists and due to the limitations of digital programs, problems can arise in VOI analyses.

VOI analyses are a necessary step to perform classification and decision support systems in 3D biomedical images (Lilia et al. 2012; Ahmed et al. 2015). Rather than looking at the image as a whole, it is important to find only the affected regions, both in terms of time and in terms of extracting effective features. Many region of interest studies in the literature consist of two-dimensional images. However, looking at only one image in three-dimensional MR images can lead to loss of effective features. Since MR images occur in sequential slices, when looking at a slice, it is necessary to look at the previous and next slice of that slice. Because information about the disease is kept in sequential slices. Manual segmentation is a tedious and lengthy process (Despotović, Goossens, and Philips 2015). In order to solve this problem, in this study, a model has been followed and a MATLAB script has been proposed for fast, efficient and accurate segmentation by using electronic brain atlases. In order to perform this process, necessary preprocessing methods were performed in MR images. The size incompatibility between the MR images and the atlas was corrected. Both normalized space and native space segmentation have been implemented. This study is a preliminary work for extracting VOI features such as symmetry, texture, descriptive statistics, intensity changes, volume values which are necessary features for decision support systems to be performed with 3D MR images. Trials of segmentation have been made a 3D MR image freely taken from the OASIS database(Marcus et al. 2007).

## 2. Global Segmentation of 3D MR Images

The brain is basically divided into three global parts as Gray Matter (GM), White Matter (WM) and Cerebrospinal Fluid (CSF). GM forms the outer cortex of the brain in which the decision center is found. The WM is the region inside the relatively white-colored brain part that allows communication between body functions and GM. CSF is a fluid that surrounds the GM and WM regions and protects the brain from external hits. In MR images, pixel gray level transition for these three regions can be clearly seen. For the segmentation of these regions, priori TPMs (Ashburner and Friston 1997) are often used. These maps have been produced by taking averages of many MR images. The Statistical Parametric Mapping 8 (SPM8)(Ashburner et al. 2008) program developed by the University College of London, which is frequently used in the literature, uses these TPMs for segmentation of MR images. The VBM8 program running under the SPM8 program produces global segmentation results in Montreal Neurological Institute (MNI) space by performing necessary preprocessing on the raw images (Kurth, Luders, and Gaser 2010). VBM8 can do this in both native and normal space. Figure 1 shows the segmentation of the 3D raw image taken freely from the OASIS database and its GM, WM and CSF segmentation parts, respectively.



(a) (b)

(c) (d)

*Figure 1. (a) Raw 3D MR Image (b) GM normalized segmentation (c) WM normalized segmentation (d) CSF normalized segmentation*

With this segmentation process, necessary measurements can be made on the global scale. In particular, the changes that occur in GM can be easily measured by this process. However, GM has different functional centers. A separate process is required for the segmentation of subcortical centers. As shown in Figure 1b, the pixel boundaries of subcortical regions on GM are not clear. Therefore, at this stage, the previously defined electronic brain atlases must be registered to GM. However, there is a size incompatibility between the gray matter and the brain atlases. In order to perform the segmentation process, it is necessary to eliminate both the size incompatibility and to equalize the slice thickness.

### 3. Electronic Brain Atlases and Package Programs

Package programs are frequently used in the literature for the structural MR analysis. Freesurfer(Fischl 2012), FSL(Jenkinson et al. 2012) and SPM(Ashburner et al. 2008) are three commonly used programs. Freesurfer and FSL are Linux based, and SPM is a MATLAB based program. The Freesurfer program can analyze the raw 3D MR image with a code script on the Linux terminal. However, the analysis continues for hours. The FSL program is analyzing only 15 regions as well as being relatively fast. The 3D MR image localized by Freesurfer atlas is given Figure 2, and the localization output by the FSL program is given in Figure 3.

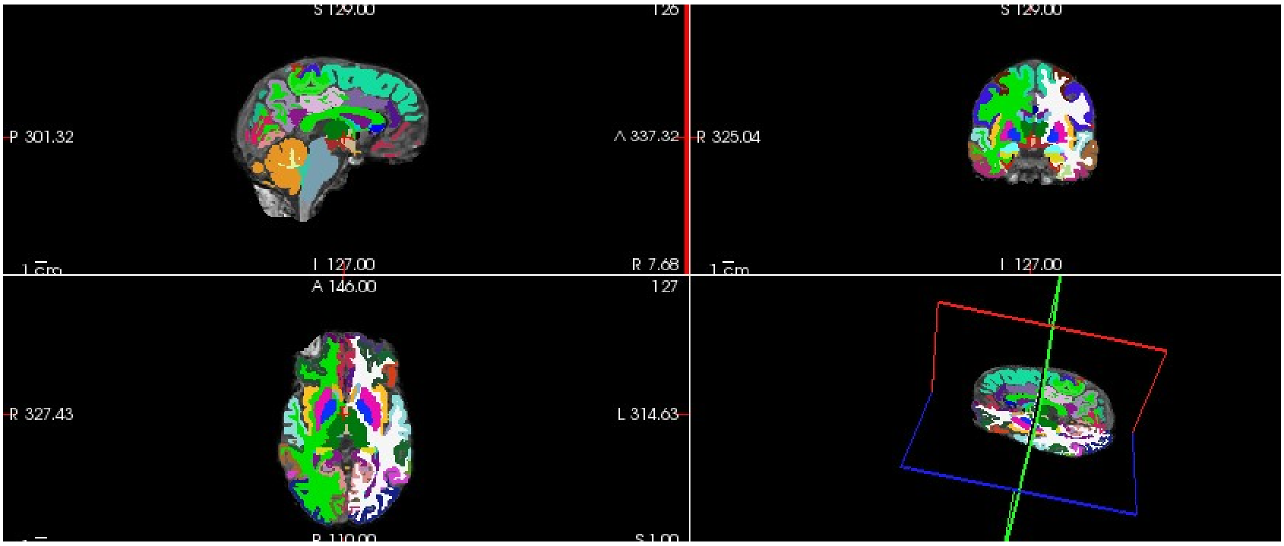



*Figure 2. Freesurfer outputs*

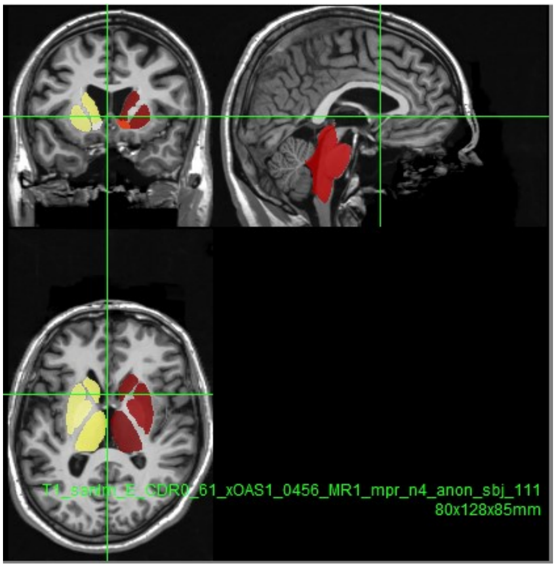



*Figure 3. FSL outputs*

The WFU Pick atlas program, running as a plug-in under the SPM8 program, provides binary masks for many regions using electronic brain atlases (Maldjian et al. 2003; Maldjian, Laurienti, and Burdette 2004). The program includes popular atlases such as AAL, Talairach, Lobe Regions. However, there is a size mismatch between the obtained masks and the 3D images. This incompatibility will be eliminated by performing a series of operations. Figure 4 shows the AAL Atlas, Talairach Atlas, and Lobe regions, respectively, and Figure 5 shows the output of superimposing these atlases with a raw 3D MR image respectively.

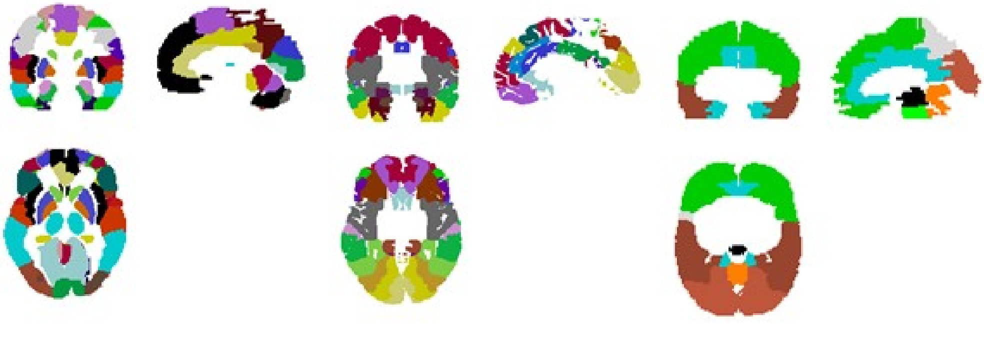


*Figure 4. 3D Brain Atlases (a)AAL atlas (b)Talairach Atlas (c) Lobe regions*

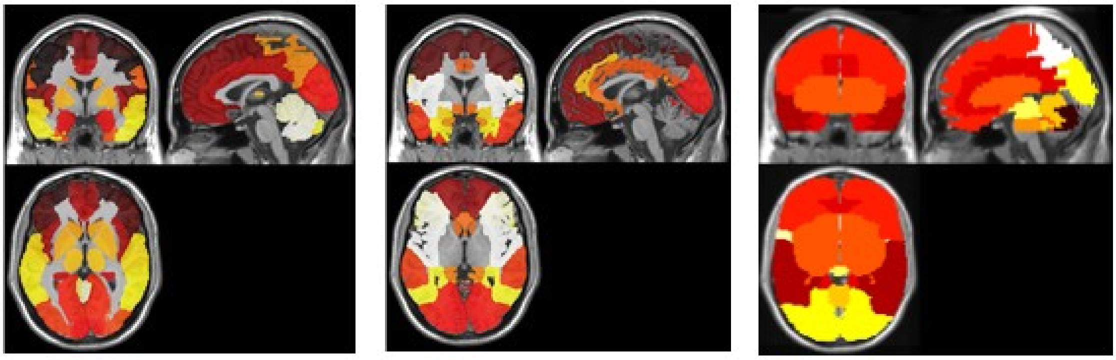


*Figure 5. Superimposing 3D MR Images with Atlas (a) AAL atlas (b) Talairach Atlas (c) Lobe regions*

## 4. Materials and Methods

### 4.1. 3D Raw MR Image

The 3D MR image used in the study was taken freely from the OASIS database. The OASIS database consists of healthy and AD-affected MR images of subjects aged 18 to 96 years. A mild stage 86 year old OASIS28 female 3D AD MR image labeled Clinical Dementia Rating 1 (CDR=1) was segmented in the study. Only the averaged sagittal axis prefixed with "OAS1_xxxx_MRy_mpr _ni_anon_sbj _111" was taken. The 3D MR image is a thin slice thickness and high-resolution MPRAGE volumetric three-dimensional image. However, some preprocessing needs to be performed in order to make analyzes on the images. The OASIS database imaging protocols are: TE: 4.0 msec, TR: 9.7 msec, TI: 20 msec, FA = 10, 128 sagittal slices, 1.25 slice thickness without gap, pixel resolution 256x256 (1x1mm) and T1 weighted MPRAGE extension with NifTi file format, 1.5 T vision scanner (Siemens, Erlangen, Germany) (Marcus et al. 2007).

### 4.2. Preprocessing

Preprocessing is a necessary preliminary step to resolve the size mismatch between 3D MR images and 3D masks. In order to be able to use the tools of the SPM8 program, the image was converted from the sagittal plane to the axial plane using the MRIcro program. However, Anterior Commissure (AC)/ Posterior Commissure (PC) line adjustment must be done because there was a coordinate shift on the image. This correction was done manually using the SPM8 program's reorientation tool. At this stage, only the coordinates of the voxels have been shifted and they have not been changed in content. Other necessary preprocessing was done automatically using the VBM8 library. For experiments that were to be performed in normalized space, the image was segmented into MNI space using the DARTEL method (Ashburner 2007). In the experiments to be made for normalized space there can be used modulated images which are preserving volume information, or normalized image which is preserving tissue concentration. This preference can be changed with respect to the flow of the work. For the experiments to be performed in the native space, no normalization process has been done. Since the masks used in both spaces were on the gray matter, there have been tested on only GM segmented images.

### 4.3. 3D Segmentation in Normalized Space

GM images were obtained in the MNI space to perform subcortical segmentation in normalized space. This image was 1.5*1.5*1.5 voxel size, 121*145*121 image size and center coordinates (x, y, z) = 0. Image dimensions obtained with Wfu Pick Atlas were 2*2*2 voxel size, 91*109*91 image size and center coordinates (x, y, z) = 0. Both voxel size and image size were incompatible. In order to overcome this incompatibility, "Coregister (Reslice)" tool under SPM8 was used. Under this tool, TPM GM image was given "Image Defining Space" part and a mask obtained by WFU Pick Atlas was given "Image to Reslice" part. The interpolation process was changed to "Nearest Neighbours". As a result, the 3D mask and the 3D MR image were equalized to the same size and were prepared for 3D masking in the normalized space.

### 4.3. 3D Segmentation in Native Space

Native space is the original space from which the image is taken from the MR imaging device. In this space, real information of the image is protected. At this stage, the acquired atlas mask needs to be transformed into native space. The original dimensions of the image were 160*256*256 image size, 1*1*1 voxel size, (x,y,z = 0) coordinates. The size of the produced masks was 2*2*2 voxel size, 91*109*91 image size and center coordinates (x, y, z) = 0. The "Coregister (Reslice)" tool of the SPM8 program has been used again. Native GM segmented image was given "Image Defining Space" part and a mask obtained by WFU Pick Atlas was given "Image to Reslice" part. The interpolation process was changed to "Nearest Neighbours". Thus, the 3D mask and the 3D MR image were equalized to the same size and were prepared for 3D masking in the native space.

### 4.4. 3D Binary Masking

3D MR images and 3D masks can be masked after they are equalized to the same size. To perform this process, the MATLAB script in Table 1 was written. This script masks the same slices of the 3D image and 3D mask and then records them as Nifti file format with "*.nii" extension. These applications were performed only left cerebrum, limbic lobe and right hippocampus in this study but these regions can be increased desired VOI number using the proposed model. Figure 6 shows the flow diagram of the preprocessing and 3D binary masking for the normalized space, and Figure 7 shows the flow diagram for the preprocessing and 3D binary masking for the native space. In Figure 8, the left cerebrum, limbic lobe, and right hippocampus regions are given as masks, superimposing mask and image, after masked, and three-dimensional model, respectively, in normalized space. In Figure 9, the left cerebrum, limbic lobe, and right hippocampus regions are given as masks, superimposing mask and image, after masked, and three-dimensional model, respectively, in native space.

Table 1. Proposed MATLAB script for left cerebrum

```
V=spm_vol('GM.nii');
Y=spm_read_vols(V);

V_MASK=spm_vol('Left_Cerebrum.nii');
Y_MASK=spm_read_vols(V_MASK);
Y_MASK(Y_MASK>0)=1;

b=size(Y);
t=zeros(b(1),b(2),b(3));
for i=1:b(3)
t(:,:,i)= Y(:,:,i).* Y_MASK(:,:,i);
end
V1=V;
V1.fname='MASK_Left_Cerebrum.nii';
spm_write_vol(V1,t);
```

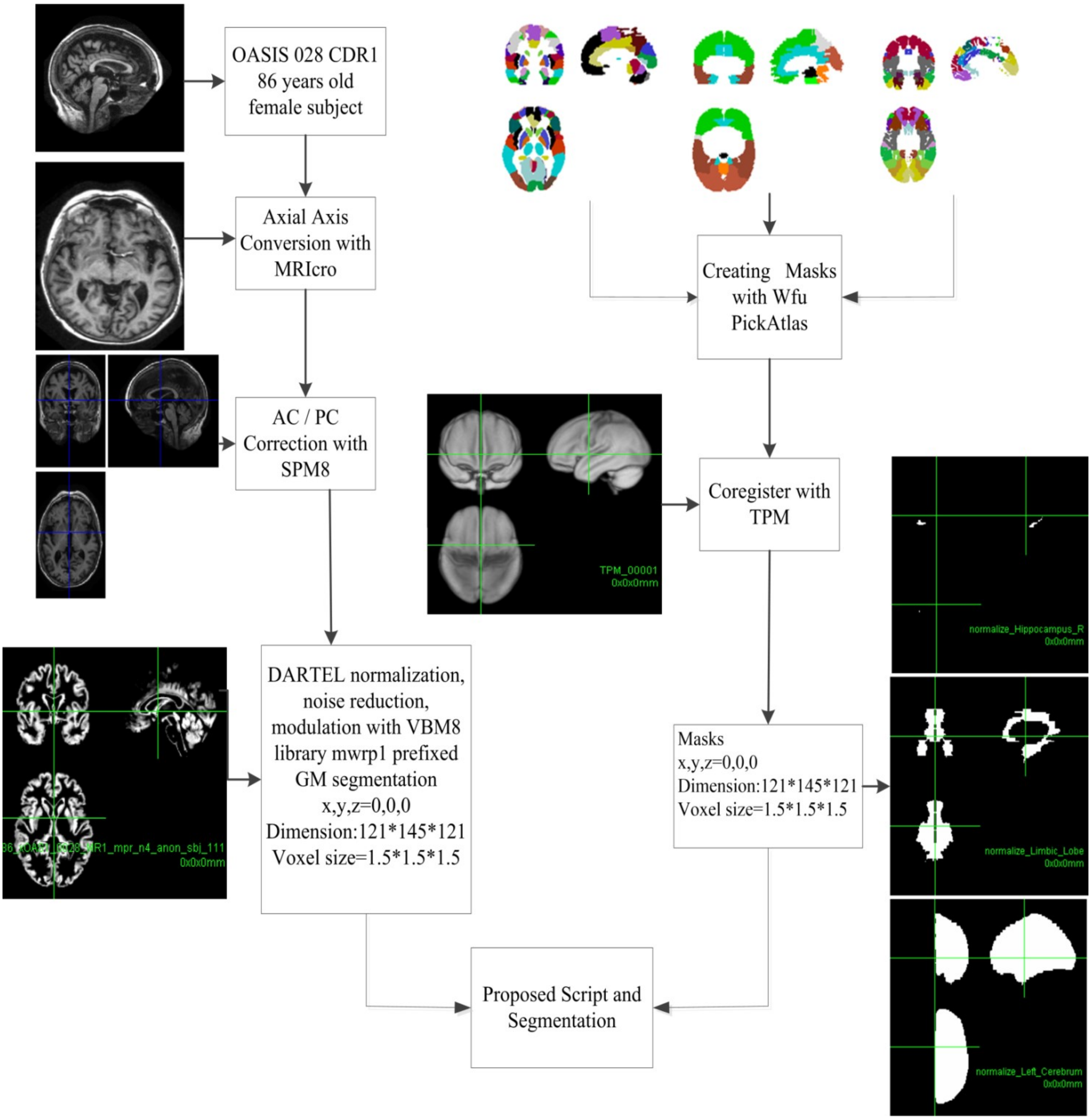



*Figure 6. VOI segmentation pipeline of normalized space*

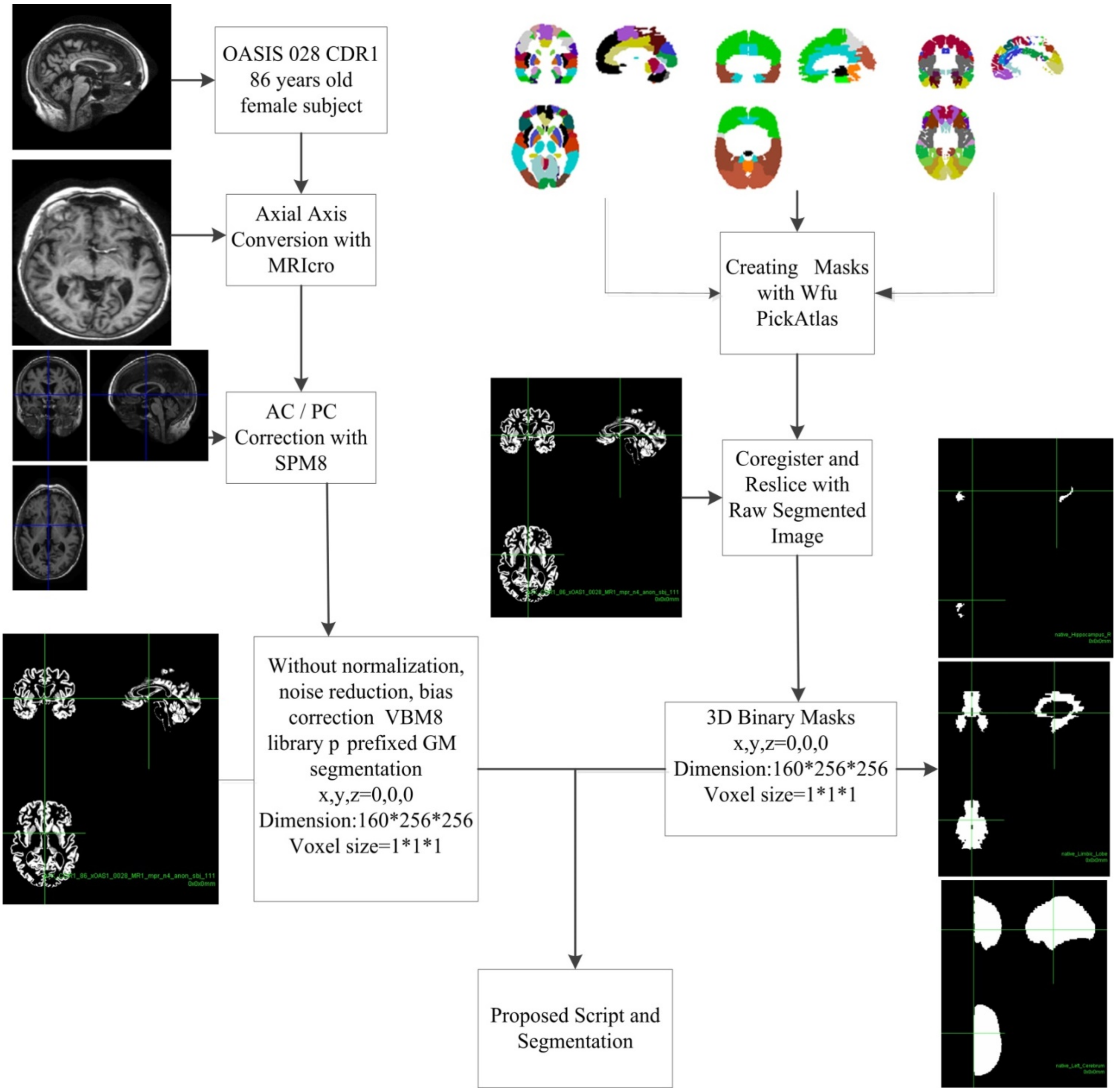



*Figure 7. VOI segmentation pipeline of native space*

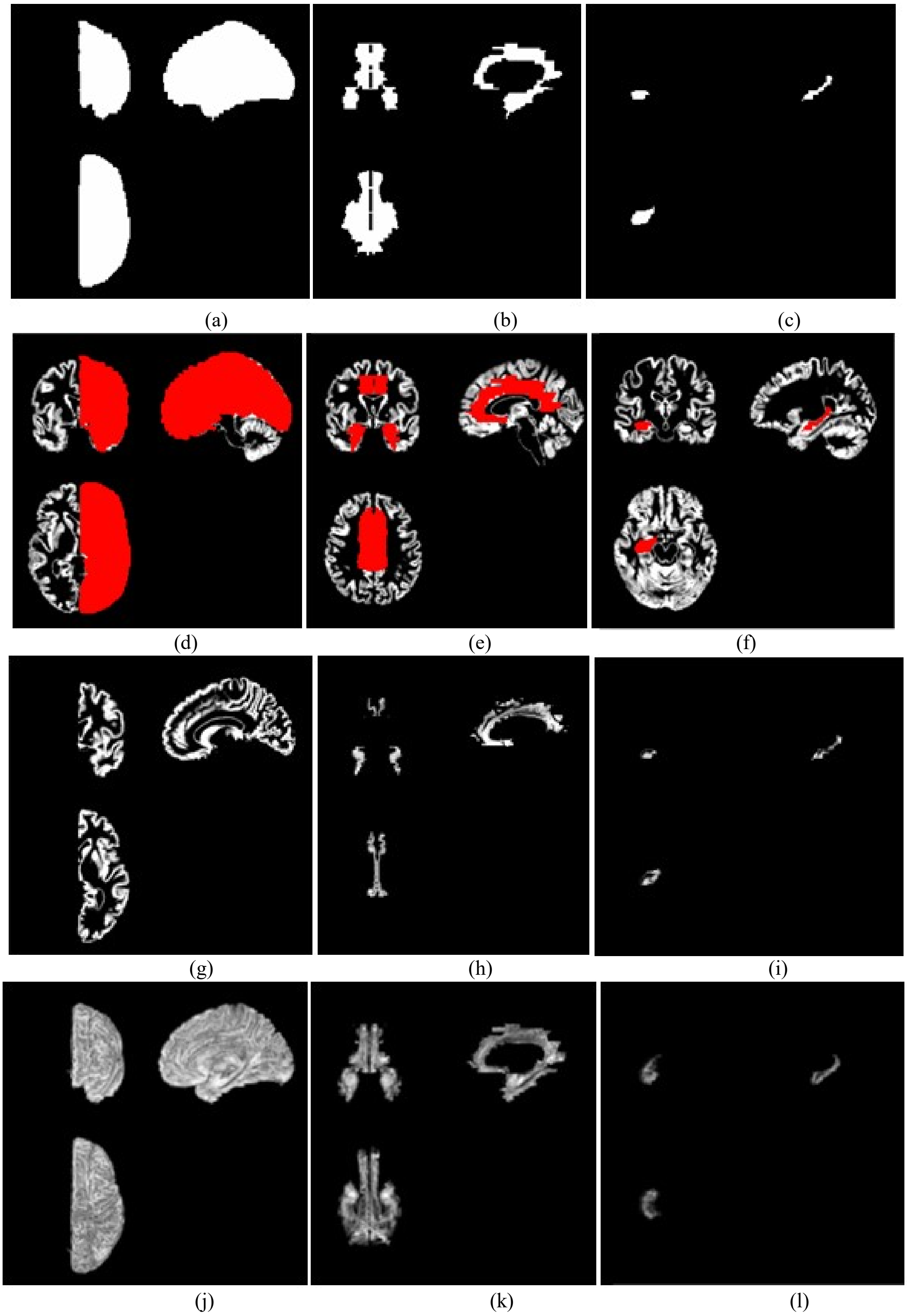



*Figure 8. Segmentation processes on Normalize Space (a)Left Cerebrum Mask (b) Limbic Lobe Mask (c) Right Hippocampus Mask (d)Superimposing Left Cerebrum Mask with GM (e) Superimposing Limbic Lobe Mask with GM (f) Superimposing Right Hippocampus Mask with GM (g) Masking GM with Left Cerebrum Mask (h) Masking GM with Limbic Lobe Mask (i) Masking GM with Right Hippocampus Mask (j) 3D Model GM Left Cerebrum (k) 3D Model GM Limbic Lobe (l) 3D Model GM Right Hippocampus*

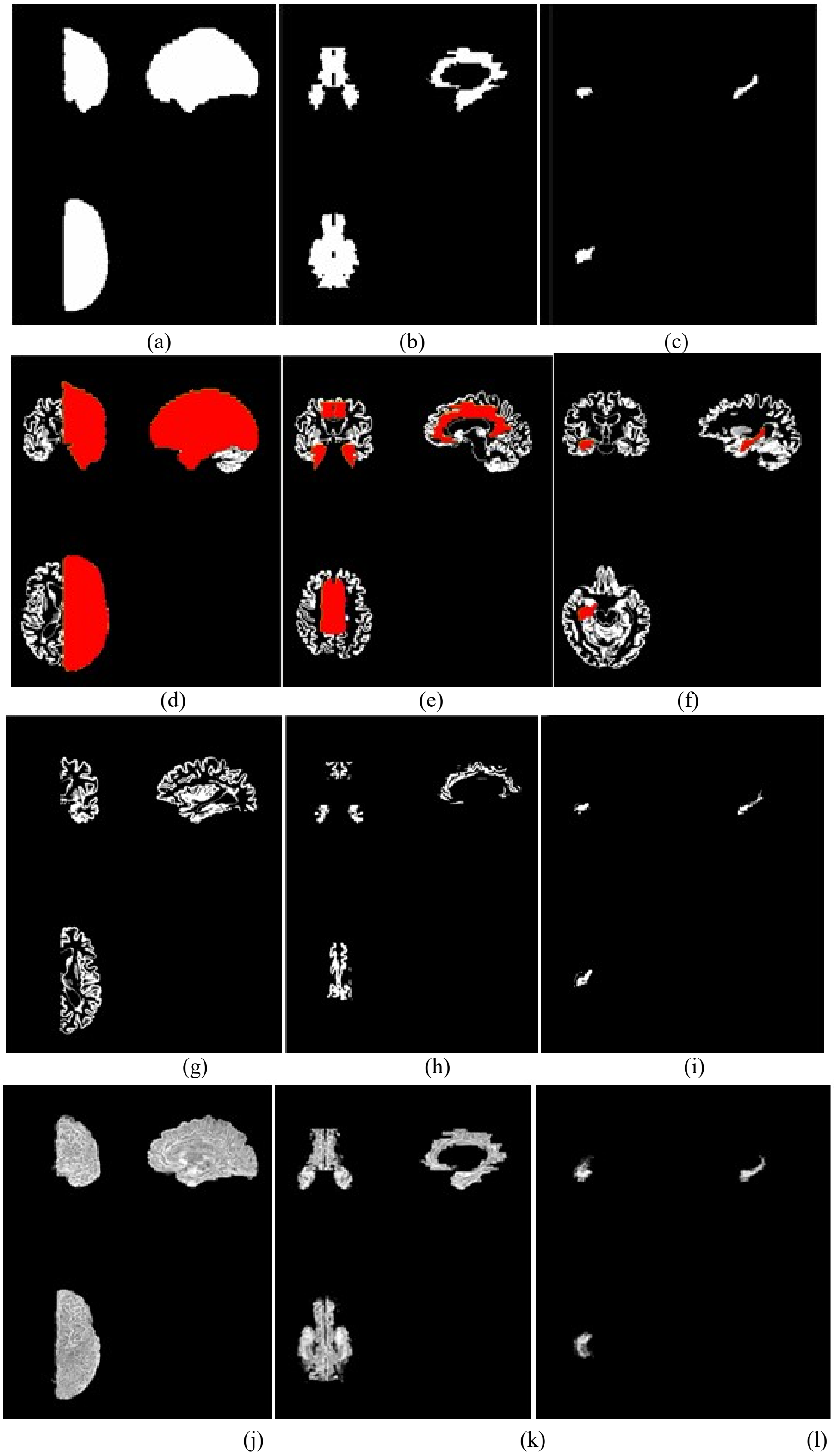


*Figure 9. Segmentation processes on Native Space (a)Left Cerebrum Mask (b) Limbic Lobe Mask (c) Right Hippocampus Mask (d)Superimposing Left Cerebrum Mask with GM (e) Superimposing Limbic Lobe Mask with GM (f) Superimposing Right Hippocampus Mask with GM (g) Masking GM with Left Cerebrum Mask (h) Masking GM with Limbic Lobe Mask (i) Masking GM with Right Hippocampus Mask (j) 3D Model GM Left Cerebrum (k) 3D Model GM Limbic Lobe (l) 3D Model GM Right Hippocampus*

## 5. Conclusion

Segmentation of the brain regions in 3D MR images is an important process for evaluating local and global changes that caused by neurological disorders. In 3D MR images, segmentation of the subcortical regions manually can give relative results because of experience. Along with the increase of digital sources, automatic or semi-automated package programs are preferred instead of manual measurements. These package programs automatically perform the necessary measurements, and these measurements are often used in the interpretation of diseases and features of decision support systems. These programs have practical uses because they perform the necessary preprocessing and segmentation automatically. However, these programs have some limitations to use in VOI analyses in terms of time and regions limit. To overcome this problem, it is necessary to carry out the steps of the special segmentation pipelines and models independently to obtain the desired brain region outputs in three dimension.

This study has been proposed a pipeline and a script to segment of subcortical regions for the normalization and native space in 3D MR images. By performing these pipeline and script, the left cerebrum, limbic lobe, and right hippocampus regions were segmented and then validated by a specialist neurologist. How to perform necessary preprocessing in 3D images is shown both in normalized space and in native space with flow diagrams in detail. This study is a preliminary study to extract features such as volume, intensity, descriptive statistics, texture, asymmetry in disease-related VOI of 3D MR images. Thus, instead of dealing with the entire image, by extracting features only from VOI can be obtained more valuable features. With these features, decision support systems will be designed with the machine learning and the artificial intelligence methods in the future studies.

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