An fMRI study for Discovering the Resting-State Functional Changes in Schizophrenia using a Statistical and ML-based Approach

Abstract:
Schizophrenia is a severe mental illness in which people experience hallucinations and delusions. Reasons for happening schizophrenia are genetics, occur in a family, and it is heritable in nature. It can happen due to inappropriate development of the brain, due to complications at the time of birth, due to intake of drugs and an increase in the stress level in the environment. To diagnose critical psychological disorders like schizophrenia, functional magnetic resonance imaging (fMRI) is widely used. This technique measures the indirect neural activity of the brain tracing the oxygenation level of the blood flow. Resting-state fMRI measures the same in the rest condition of the patient while doing no cognitive task. This paper aims to study the resting-state fMRI data to identify the brain regions showing differences in functional activation using a two-stage feature selection approach.
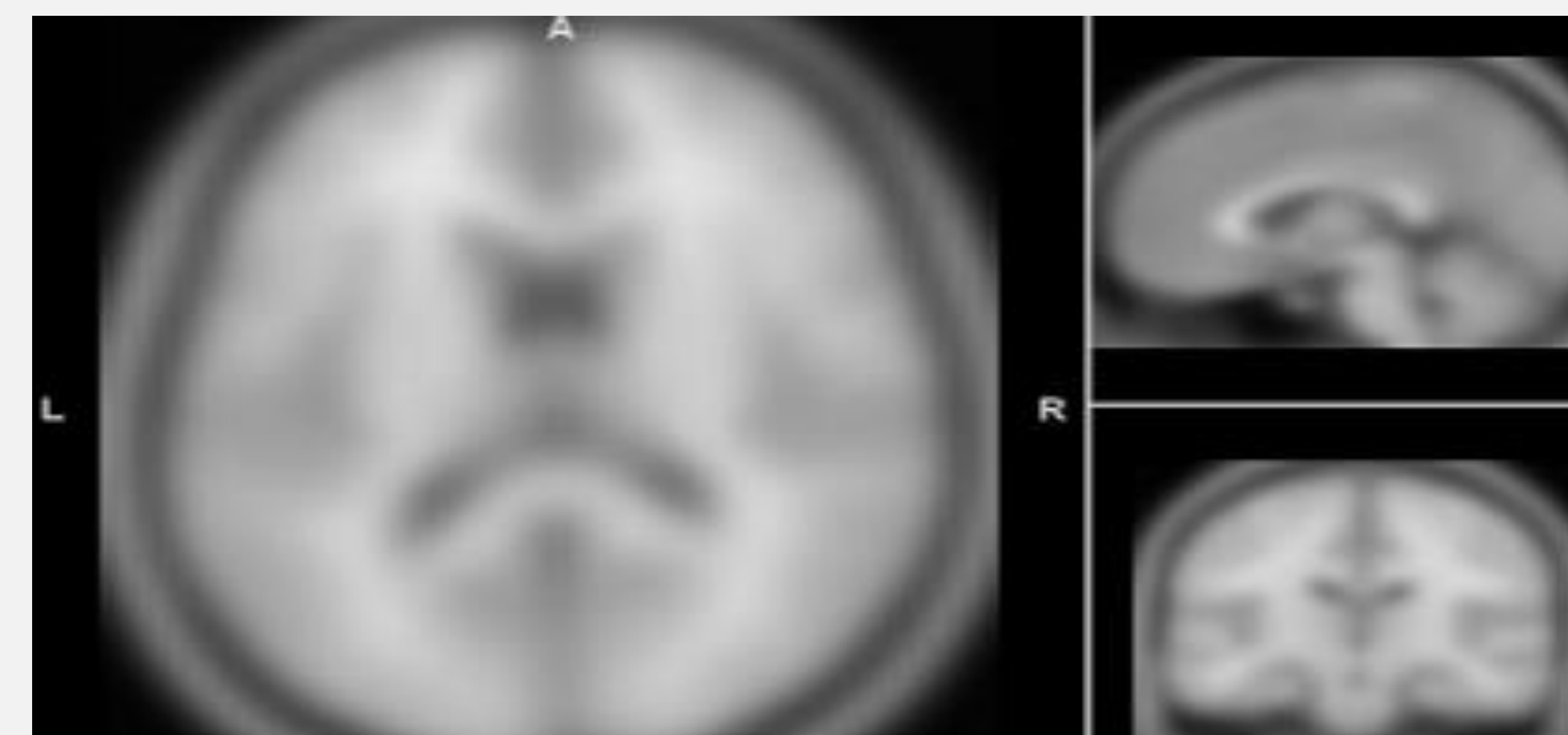
Background and Objective of the Study:

Schizophrenia is always a fascinating research area among the other psychological disorders due to its complexity of severe symptoms and neuropsychological changes in the brain. The diagnosis of schizophrenia mostly depends on identifying any of the symptoms, such as hallucinations, delusions and disorganized speech, entirely relying on observations. Researches are going on to identify the biomarkers in the brain affected by schizophrenia. Diverse machine learning approaches are applied to identify brain changes using fMRI studies. However, no conclusive clue has been derived yet. Recently, resting-state fMRI gains importance in identifying the brain's patterns of functional changes in patients having resting-state conditions. This paper aims to study the resting-state fMRI data to identify the brain regions showing differences in functional activation using a two-stage feature selection approach.

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Materials:

- Resting-state fMRI data obtained from The Center for Biomedical Research Excellence (COBRE) repository.
- 72 Schizophrenia patients
- 72 Healthy Subjects
- Ages ranging from 18 to 65 in each group.
- TR: 2 s, TE: 29 ms, matrix size: 64x64, 32 slices.
- Voxel size: 3x3x4 mm^3 (corrected to 3x3x3 mm^3)
- Preprocessed the data using SPM12 toolbox

Methodology:

Stage – 1:

Instead of applying the popular GLM approach to convert 4-D timeseries data into 3-D activation maps; Here a new mean deviation-based approach is applied (Chatterjee, F1000Research, 7:1615 (v2), 2018) to select the voxels showing functional activations.

This approach uses statistical measures such as mean and median for finding the significant functional changes in each voxel over time.

The voxels showing the functional changes in each subject were selected. After that, considering a threshold 'α' on the mean-deviation values, the best set of voxels were treated as an input for the second stage of voxel selection using Pearson's correlation coefficient.

Stage – 2

The voxel set obtained after the first stage was further reduced to select the minimal set of voxels to identify the functional changes in small brain regions.

Various state-of-the-art machine learning algorithms, such as Linear SVM and Extreme Learning Machine(ELM), were used to classify healthy and schizophrenia patients.

Results:

Obtained features (voxels) show the accuracy of around 88% with Support Vector Machine classifier and 85% with Extreme Learning Machine classifier. Subtle functional changes are observed in brain regions, such as the parietal lobe, prefrontal cortex, posterior cingulate cortex, superior temporal gyrus, lingual gyrus, cuneus and thalamus.

Algorithm 1. The proposed approach

Notations:

m (=34): the number of subjects in each group

n (=140): the number of observations in a run

V_i : time-series of ith voxel

i.e. $V_i = [v_{i,1} \; v_{i,2} \; v_{i,3} \cdots v_{i,n}]$;

μ_i : mean of V_i i.e. $\mu_i = \dfrac{\sum_{j=1}^{j=n} v_{i,j}}{n}$

Steps:

1. Calculate absolute mean deviation for each voxel using $\overline{V}_{d_i} = |V_i - \mu_i|$.

2. Find median M_i of $\overline{V}_{d_i}$.

3. For each subject $k \in \{1,2,...,m\}$, select the set V_{s_k} of voxels that show deviation higher than αM_i.

4. Find the group wise intersection of the voxels selected in step 3 for groups G1 and G2

   i.e. $V_{s_{G1}} = \cap_{k=1}^{m} V_{s_k}(G1)$

   $V_{s_{G2}} = \cap_{k=1}^{m} V_{s_k}(G2)$

5. Merge the two sets, obtained in step 4 to obtain set S

   i.e. $S = V_{S_{G1}} \cup V_{S_{G2}}$

6. Map S into the brain space to identify affected regions.

SUMMARY:

This study is the first-of-its-kind rs-fMRI study to employ the novel mean-deviation-based method to identify the potentially affected brain regions in schizophrenia, which eventually may help in better clinical intervention and cue for further investigation.

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