Predicting irritable bowel syndrome (IBS) from brain MR imaging data using machine learning

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Introduction

Irritable bowel syndrome (IBS) is a common functional gastrointestinal disorder associated with abdominal discomfort and alternated defecation habits, and a majority of patients experience postprandial symptoms exacerbation. Dysfunction of the **brain-gut axis** has been suggested as an important mechanism in IBS. In this context, thickness of the cerebral cortex might be influenced by chronic pain conditions, and can therefore be increased or decreased in different brain regions. In the human brain, a core network is the **salience network**, responding to subjective salience of stimulus or the expectation of stimulus. In our study of IBS patients and healthy controls, machine learning classification methods were used to analyse cortical thickness in key nodes of the salience network (Fig. 1).

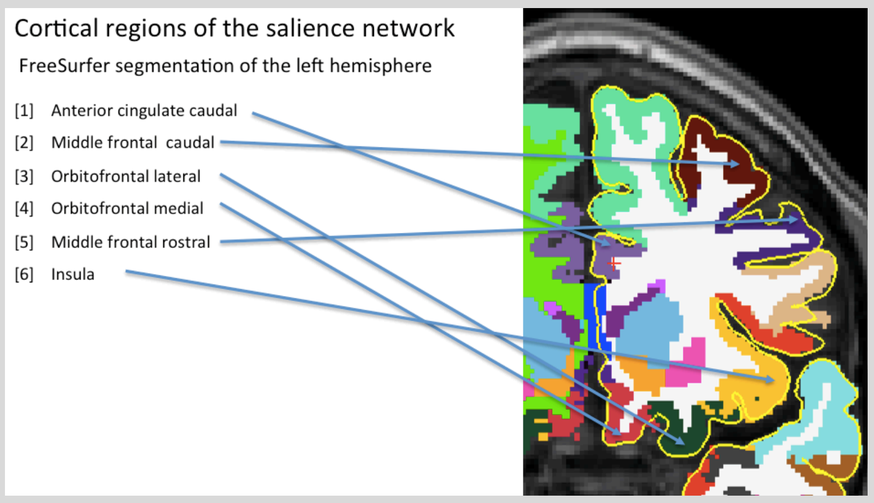

Figure 1. Segmentation and depiction of the cortical regions representing the salience network.

Methods and materials

From a multimodal MRI intervention study (Fig. 2), two successive 3D T1-weighted MRI acquisitions from 15 IBS patients and 15 healthy controls (HC) were recorded on a GE Sigma 3.0T MR scanner and segmented with FreeSurfer[1]. Mean cortical thickness values from 12 anatomical regions in the salience network were extracted and analysed in Python/scikit-learn[2] applying various machine learning classifiers (cf. Fig. 3) to the 60x12 dataset, with the goal of differentiating between HC and IBS. For training and evaluating a classifier we used cross validation with leave-one-out.

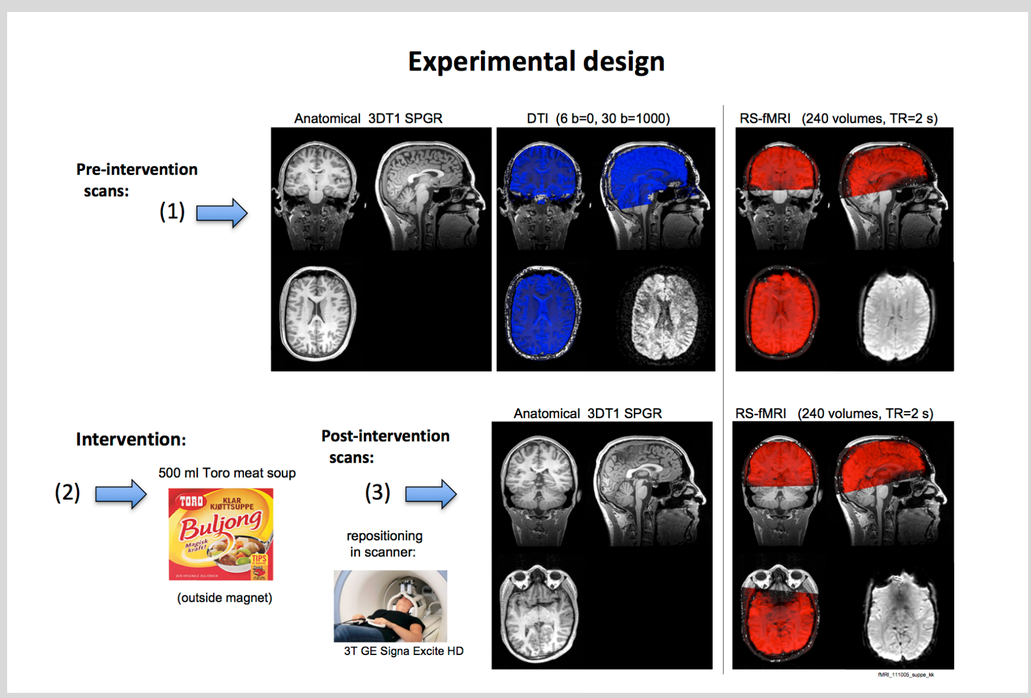

Figure 2. The multimodal MRI design with a meal intervention. Here we use only the 3D T1 data.

```
from sklearn.model_selection import LeaveOneOut
loo = LeaveOneOut()
```

```
from sklearn.neural_network import MLPClassifier
from sklearn.neighbors import KNeighborsClassifier
from sklearn.gaussian_process.kernels import RBF
from sklearn.ensemble import RandomForestClassifier, AdaBoostClassifier, ExtraTreesClassifier
from sklearn.naive_bayes import GaussianNB
from sklearn.discriminant_analysis import QuadraticDiscriminantAnalysis
from sklearn.neighbors import KNeighborsClassifier
```

```
classifiers = [
                RandomForestClassifier(n_estimators = 5, max_depth = 2),
                ExtraTreesClassifier(n_estimators = 5, max_depth = 2),
                MLPClassifier(alpha = 0.05, max_iter=10000),
                AdaBoostClassifier(learning_rate=0.1, n_estimators=50),
                GaussianNB(),
                QuadraticDiscriminantAnalysis(),
                KNeighborsClassifier(n_neighbors = 2)
                ]

names = [
         'Random forest',
         'ExtraTreesClassifier',
         'Neural net',
         'AdaBoost',
         'Naive Bayes',
         'QDA',
         'KNN'
         ]
```

Leave one out split, delete twin

```
def scoreLOO(clf, X):
    scores=[]
    trainscore=[]
    for train_index, test_index in loo.split(X):
            X_train, X_test = X.iloc[train_index,:], X.iloc[test_index,:]

            # Remove corresponding pair in X_train:
            y_train, y_test = y[train_index], y[test_index]
            if (y_test.index % 2 == 0): #even (pre meal)
                X_train = X_train.drop(y_test.index + 1)  #(after meal)
                y_train = y_train.drop(y_test.index + 1)
            else: #odd (after meal)
                X_train = X_train.drop(y_test.index - 1) #(pre meal)
                y_train = y_train.drop(y_test.index - 1)

            # Feature scaling
            sc = StandardScaler()
            sc.fit(X_train)

            # Classifier
            clfer=clf.fit(sc.transform(X_train), y_train)

            y_pred = clf.predict(sc.transform(X_test))
            y_train_pred = clf.predict(sc.transform(X_train))

            scores.append(accuracy_score(y_test, y_pred))
            trainscore.append(accuracy_score(y_train, y_train_pred))

    return np.mean(scores), np.mean(trainscore)
```

Figure 3. The classification scheme using scikit-learn. Excerpt from our Jupyter[3] notebook.

[1] https://surfer.nmr.mgh.harvard.edu [2] http://scikit-learn.org [3]http://jupyter.org

Results

Exploring the group-specific cortical thickness distributions, no single region was significantly different between IBS and HC (Fig. 4).

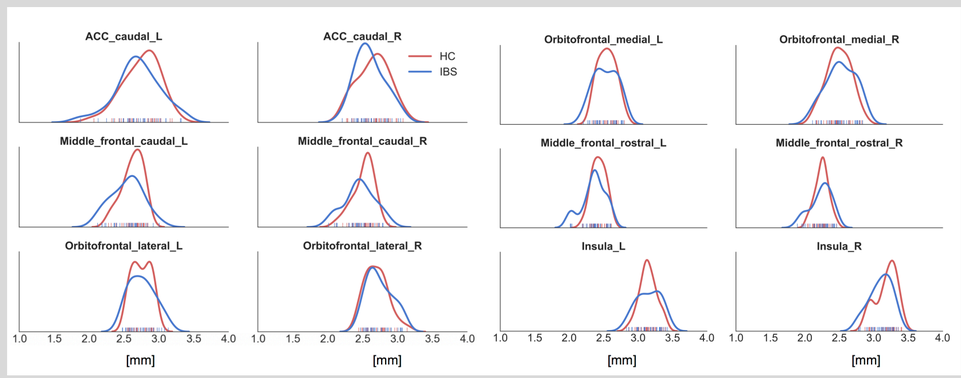

Figure 4. Group-specific feature densities in mean cortical thicknesses of the salience network.

Because the feature space is 12-dimensional and we only have 60 observations we shrank the feature space and performed the classification using only two features. These were selected according to recent literature and our previous findings of white matter microstructure differences (i.e. FA calculated from the DTI data) between IBS and HC in the **insular regions** (cf. left part of Fig. 5, and [6] in Fig.1).

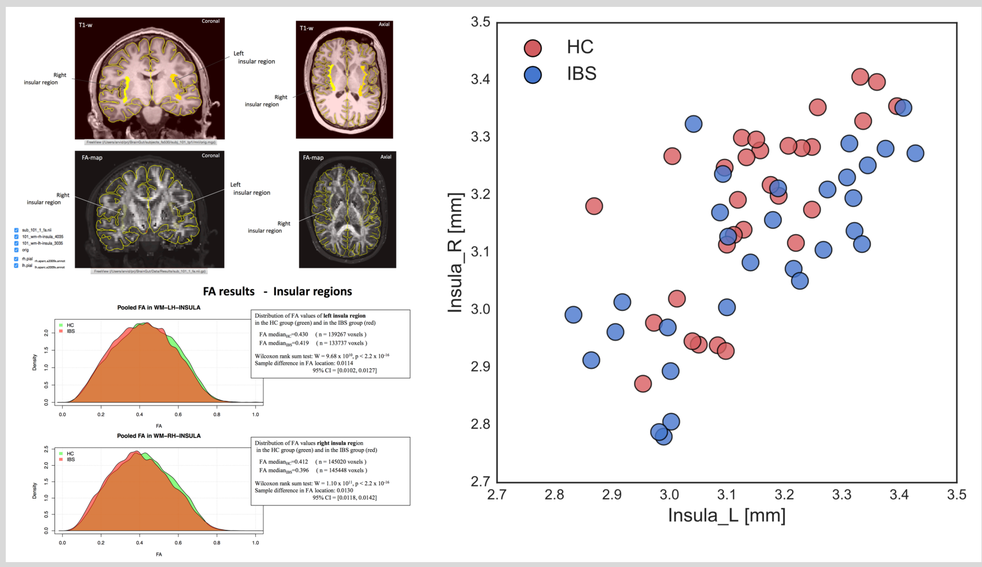

Figure 5. Left: Microstructural tissue properties in the insular white matter regions (from our previous DTI analysis). Right: The selected 2-dimensional feature space used in classification.

Classifier	Accuracy μ	Accuracy σ
RandomForest	0.48	0.045
ExtraTrees	0.45	0.061
Neural net (MLP)	0.63	0.013
AdaBoost	0.52	-
NaiveBayes	0.52	-
QDA	0.63	-
KNN	0.57	-

Figure 5. The seven machine learning classifiers being used and their performance (mean accuracy and its stand.dev.) using 50 repetitions of the leave-one-out cross validation scheme.

Discussion/conclusions/limitations

Patients with IBS are known to have brain signatures within the salience network that differs from healthy controls. Finding such patterns would make it possible to discriminate between the IBS and HC brain and is a highly interesting problem, both diagnostically and mechanistically. An overall change in the network could indicate an altered interoceptive function in IBS patients constituting of several minor non-significant findings.

The present study is part of an investigation into the salience network of IBS patients, using MRI and fMRI together with a meal intervention. The classification techniques studied here, using insula only, was not able to distinguish between patients and control in a significantly accurate manner. This is likely because the dataset is small and the variation of the cortical thickness patterns across the groups is subtle.

Using the fMRI data recorded pre and post meal intervention to construct activation graphs in the salience network, and use these networks to classify patients and healthy control would likely lead to better results. This approach is presently being investigated.