ABSTRACT (Non utilizzare le parti in rosso per l’abstract)

One of the regions hindered by schizophrenia is the dorsolateral prefrontal cortex (DLPFC) which has been associated to the ability of task switching (TS), that is the realignment of perceptual, cognitive and motor goals in order to maximize process efficiency on the currently relevant task.

Nevertheless, literature suggests that people affected by schizophrenia (SCHZ) do not perform worse than a neuro-typical control population (CTRL). Apparently, SCHZ are simply slower in TS, but reach the same tasks’ performances as CTRL. The literature assumes that this latter fact is possibly due to some unknown compensation mechanism in the SCHZ’s brain.

The objective of our project was an exploration of the differences in brain activity between SCHZ and CTRL during TS. To this end we consider the results of 175 participants.   
  
An ANOVA and accuracy analysis of the subjects’ test scores shows that both groups apply similar speed/accuracy tradeoffs. SCHZ performances are poorer than the CTRL ones. However, while the CTRL scores decrease when the subjects are requested to switch, SCHZ subjects’ performances are not affected by the switching.

A PCA on the functional connectivity maps of the subjects yielded two results. First, SCHZ are more homogeneous in brain activity. Second, the distinction between SCHZ and CRTL is not given by a single region of the brain but by the interaction of multiple systems.

A LMM was fitted so as to take into account the intrinsic across-subject variability of the phenomenon.

HYPOTHESIS UNDER ANALYSIS

The literature holds true the following hypothesis:

*SCHZ are slower than CTRL but have comparable performance in the task switching test*

DATASETS (qua spieghiamo il test e i dati ottenuti)

The data considered for this work came from an experiment involving 175 participants (125 CTRL and 50 SCHZ). They provided general pieces of information like health, age, BMI, possible comorbidities, smoking habits, and behavioral traits (quantified through the Barratt Impulsivity Test).

While under fMRI, each participant was presented with a series of one of four possible geometric shapes and asked to respond to either the color or the shape of the image based on the task cue presented prior to, and above, the image. On 25% of trials the instructions switched, i.e., participants were instructed to switch from responding from shape to color, or vice versa.

Consequently, three sets of data were gathered for each participant:

1. Health-related data.
2. Functional connectivity maps, a table of >36000 values per participant, each corresponding to a node of the brain mesh on which the fMRI data was projected.
3. Event recordings, a time step dataset composed of all the readings from the test, such as: reaction time, cue, answer.

In particular, we kept only age and BMI of the health data, as the other ones were mainly missing or not consistent.

1 PRELIMINARY ANALYSES

We checked whether the data basic statistics matched the literature, and we identified the regressors that are statistically significant w.r.t. reaction time:

1. A T-test on the Scores of the Barratt Impulsivity Test (BIS) confirmed a significant difference between the means of SCHZ and CTRL scores (see Fig. 2).
2. A T-test on the means confirmed a significant difference in the distributions of the reaction timess in CTRL and SCHZ (see Fig. 1).

Then, the following Linear Regression Models (LRM) were fitted:

1. *Reaction.Time ~ Age + BMI + Diagnosis + Age:Diagnosis + BMI:Diagnosis.* Only age and Diagnosis resulted as the only statistically significant regressors (see Fig 5).
2. *Reaction.Time ~ BIS.* BIS did not turn out a statistically significant regressor, despite the previous results of the T-test on the BIS scores.

The above results suggest that SCHZ are indeed slower than CTRL. On the other hand, we cannot state the influence of impulsivity on performance.

2 ANALYSES OF THE PERFORMANCES

The performance of each participant is measured through the following four indexes (see Fig.9867):

1. Switch cost: |mu\_switch-mu\_noSwitch|
2. Correct cost: |mu\_correct – mu\_errors|
3. Accuracy rate: #\_correct/#\_total
4. Accuracy switch rate: #\_correctOnSwitch/#\_Switch

where, mu\_switch, respectively mu\_noSwitch, is the mean of the reaction times when a switch occurred, respectively did not occur, in a trial of the experiment; mu\_correct, respectively mu\_errors, is the mean of the reaction times taken by the participant to provide a correct, respectively mistaken, answer; #\_correct, respectively #\_correctOnSwitch, is the number of correct answers, respectively correct answers on switch trials; #\_total, respectively #\_switch, is the total number of trials, respectively of switch trials.

The analysis of the available dataset and of the above four indexes was performed as follows. We carried on an analysis of the Switch Costs and Correct Costs, an ANOVA, an analysis of error/accuracy rates.

2.1 ANALYSIS OF SWITCH AND CORRECT COSTS

The Box plots in Fig. 3989 indicated that the medians of SCHZ switch costs and correct costs were smaller than the corresponding CTRL medians.

2.2 ANOVA

An ANOVA on the mean of the reaction times of each participant according to different conditions of the experiment  
*Reaction.time* *~ diagnosis + congruent + switch + diagnosis\*congruent + diagnosis\*switch + congruent\*switch*  
showed a high significance of diagnosis and switch, but no interaction was statistically significant.  
A stepwise reduction led us to the additive model *Reaction.time* *~ diagnosis + switch* (see Fig. 46).

Paired with the Box Plots in the analysis of switch and correct costs we can state that the difference between Switch Costs for SCHZ and CTRL are not statistically significant, switching seems not to hinder SCHZ’s reaction time more than CTRL.

2.3 ANALYSIS OF ERRORS AND ACCURACY OF ANSWER

The Box plots in Fig. 4782 showed a visible disparity in both the differences in accuracy rate and accuracy on switch between CTRL and SCHZ. In particular, the SCHZ accuracy rate is lower than the CTRL one. On the other hand, the SCHZ accuracy on switch is higher than the CTRL one.

The previous results falsify what has been proposed in literature. It appears that no compensating mechanism is necessary as the accuracy rate of SCHZ is lower than CTRL but seems independent of task switching.

3 PCA

We performed a PCA on the functional connectivity maps of the participants to see what the brain activity during the test was and (H0) whether the brain activity between SCHZ and CTRL differed enough to discriminate between the two groups.

Connectivity must be interpreted as a transformation of the correlation between Blood-Oxygenation level dependent (BOLD) signals, which are bio-electromagnetic in nature. In literature opposite signs in connectivity are interpreted either as two regions “competing” or as a delay of the signal if the regions belong to a same circuit.

Since the number of features was greater than the number of samples (p>n) we aggregated the >36000 nodes of our brain mesh into the 83 canonical regions. This method does not remove noise from the data, thus we decided to consider active only regions with loadings greater than a certain threshold.

3.1 FIRST PC

Weighted average of overall brain activation levels. Emphasis on regions specifically involved in learning, action, and prediction.

Cingulate gyrus (regions 24-27) involved in prediction. Caudate nucleus(34-35) regulates execution of movement and learning. Putamen (38) manages general cognitive functioning. Superior frontal gyrus (59) is key in maintaining working memory.

3.2 SECOND PC

The second PC highlights the brain’s prediction mechanism. Showing how the brain initially makes a prediction about external reality from biological signals (sensorial and emotional), rewarding itself if the prediction is accurate, also highlighting the delay between hand-eye coordination and the prediction.

(Inserire quanto segue come descrizione dell’immagine

*This graph represents the highlighted scores of the second PC.*

*Regions 62-63, manage hand-eye coordination. regions 24-25 reconstruct reality from biological inputs. Region 37 regulates emotional response. Regions 77-78 are responsible for regulating the reward mechanism).*

3.3 THIRD PC

The third PC highlights the regulation of dopamine release. It is the first PC where we can observe a visible difference in the scores between neurotypical and neurodivergent participants. Lower scores in the schizophrenic population show an unbalanced or ineffective production of dopamine (this is coherent with literature).

Nucleus accumbens (37) stimulates motivation and action reinforcement. Lateral ventricle (45-46) is mainly responsible for dopamine production. Substantia nigra (76) coordinates motor planning and reward seeking. Subcallosal area (78-79).

3.4 CLASSIFICATION

Through a MANOVA we ascertained that projecting all participants on the first three PCs would not be sufficient to build a classifier. On the side, we observe that neurotypical people tend to be less homogeneous in brain activity, unlike what we saw in the analyses of performances.

4 ANALYSES OF THE TRIAL CONDITIONS

We check whether the covariates related to the trial conditions influenced the reaction times.

A first LRM fitted reaction time vs the two categorical variables Diagnosis, Switch, deemed relevant from the previous ANOVA:

*reaction.time ~ diagnosi + switch.*

This method, however, does not take into account the interdependence of observations taken on the same participant. Then, the subjects were used as Random Effect (random intercept) to fit the following Linear Mixed Model (see Fig. 4358).  
*reaction.time ~ diagnosi + switch + (1 | Subject)*

Finally, the PVRE was checked and the result was extremely high.

The value of the PVRE suggests that most of the real variability must be assigned to the intrinsic differences between participants rather than the difference between two groups (see Fig. 45672).

CONCLUSIONS

The analyses of task performances falsify the hypothesis under concern as it appears SCHZ do not employ a compensatory mechanism in task-switching, rather displaying an insensitivity to task switching and overall worst results, modulated by a comparable speed-accuracy tradeoff with respect to CTRL.

Indeed, our results indicate that SCHZ exhibit a higher reaction time and a lower accuracy rate than CTRL, but both results seem to be independent of task switching. This may occur because of the general difficulty of SCHZ to maintain and implement a task-set (configuration of perceptual, cognitive and response biases that serve to optimize task performance). According to this view, schizophrenic participants would retain less information and cognitive configuration across tasks, substantially making each trial independent of the previous one.

Our PCA fails to identify any significant difference in brain activation between SCHZ and CTRL. This suggests that the differing cognitive functioning between the two groups (in our case mostly evident as a general slowing) is to be seeked in the complex interaction between brain networks, rather than in the anomalous activation of just one or few selected regions.

Finally, our LMM analysis sheds light on the non-negligible impact of variability across individuals. Specifically, the noticeable estimate we have obtained for PVRE advises caution over the possibility of attributing experimental variability to diagnosis alone.

OBJ: The literature has found contradictory results regarding the following hypotheses:

•SCHZ are slower than CTRL but have comparable performance in the task switching test

•The brain activity between SCHZ and CTRL differ in specific region activity.

Our objective was to determine if these would hold up to further investigation.

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