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A Case Study on Pre-stimulus Effect on Face Processing in an Individual with Autism

Narjes Soltani Dehaghani[a], Burkhard Maess[b], Reza Khosrowabadi[a], Mojtaba Zarei[*c], Sven Braeutigam[d]

[a] *Institute for Cognitive and Brain Sciences, Shahid Beheshti University, Tehran, Iran.*
[b] *Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany.*
[c] *Institute for Medical Sciences and Technology, Shahid Beheshti University, Tehran, Iran.*
[d] *Oxford Centre for Human Brain Activity, University of Oxford, Oxford, UK.*

Abstract

Face perception recruits different neural mechanisms in comparison to other objects and individuals with autism show disruptions in facial processing in comparison to other objects. Scientists have reported multiple abnormalities in both early and late stages of face processing in people who suffer from autism. On the other hand, pre-stimulus oscillation could impact the perception of the incoming stimulus in healthy participants. Yet, the effect of pre-stimulus oscillations on post-stimulus activities in individuals with autism has rarely been investigated. Here we acquired magnetoencephalography (MEG) to explore the role of pre-stimulus alpha oscillations on the face and non-face perception in an autistic participant. Our results showed that the pre-stimulus alpha power in the lateral occipital cortex yielded to significant separation of post-stimulus activities in the fusiform face area as well as the intra-parietal sulcus in response to human face stimulus.

Keywords: Face Perception, Pre-stimulus Oscillation, Autism.

[*] Corresponding author
Email addresses: moj_zarei@sbu.ac.ir

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1. Introduction and preliminaries

Autism Spectrum Disorder (ASD) is a brain disorder characterized by deterioration in social skills. Individuals with autism usually have difficulties in social interactions including eye contact and obtaining the emotional cues from the people they encounter with. This is mainly due to the fact that they have multiple problems in facial processing (Dawson, Webb et al. 2005), however, impairments in face processing are not part of the disgnistic criteria. The human face is a very important for humans to look at since it carries much information about the owner. Hence, in psychophysiological experiments human faces constitute very special stimuli! In healthy people, faces can be speedily processed, although they convey an immense amount of information (Rossion 2014). On the other hand, these great abilities are usually absent or different in individuals with autism.

Numerous studies have investigated the electrophysiological correlates of face processing, indicating the first face selective component called P1, around 100 ms (in the 48– 120 ms time window) which is mainly assigned to top-down or attentional mechanisms (Halit, de Haan et al. 2000). This component tends to have longer latencies in autistic participants indicating slower processing in them in comparison to atypical development. Besides, individuals with autism did not show an effect in P1 in in response to inverted faces which is different from the pattern seen in healthy participants for whom amplitude of P1 increased in response to the same stimulus.

The most prominent face selective component happens around 170 ms after stimulus onset and is called N170. This component in responsible for structural encoding of faces. Participants diagnosed with ASD have shown longer latencies for this component (Hileman, Henderson et al. 2011, Neuhaus, Kresse et al. 2015). In addition, (Neuhaus, Kresse et al. 2015) showed that N170 amplitude is decreased in adults with ASD in comparison to healthy people. They have concluded that atypical N170 in response to face stimuli could be considered as a biomarker of social communication impairments in ASD.

Another component which is activated in response to face stimuli occurs around 250 after stimulus onset (for a review see Yovel 2016). The M250 is thought to encode face identity and is detected in the face selective region of fusiform face area (FFA) (Nasr and Esteky 2009).

In case of visual processing, an important event related component is the M400. This component is thought to reflect the categorization of visual stimulus and it usually peaks 300 to 400 ms after stimulus onset (Curran, Tanaka et al. 2002).

Beside the electrophyiological correlates of facial processing, another field of study which has recently attracted the researcher's attention is the effect of pre-stimulus oscillations on face processing. Pre-stimulus activities are brain oscillations immediately before stimulus onset which can influence post-stimulus activities (Milton and Pleydell-Pearce 2016). Multiple studies have investigated the role of pre-stimulus fluctuations in healthy participants through different kinds of challenging task conditions (Hesselmann, Kell et al. 2008, Esterman and Yantis 2009, Hsieh, Colas et al. 2012). However, to the best of our knowledge, no study has examined the effect of pre-stimulus oscillations in individuals with autism to this date. On the other hand, although multiple studies have investigated event related responses in the context of face/non-face processing in individuals with autism (Hileman, Henderson et al. 2011, Neuhaus, Kresse et al. 2015), how pre-stimulus activities could affect event related responses when an

individual with autism is confronted with face stimulus has never been explored.

In this study, we have used a one-back working memory task which is simpler task design compared to the task designs usually used for typical development. We recorded brain activities using magnetoencephalography (MEG) and concentrated on pre-stimulus alpha oscillations as they are the most common fluctuations in ongoing state of the brain which have the role of an inhibitory gating mechanism (Hanslmayr, Volberg et al. 2013).

Main questions:

1) Could the pre-stimulus alpha fluctuations have any impact on post-stimulus activities in an individual with autism?
2) Which event related components are influenced by pre-stimulus oscillations?
3) In case we found any effect, could we assign that to the inhibitory role of alpha oscillations?

1. Method

An individual with autism performed the after written consent was obtained from them. All procedures were in compliance with the Code of Ethics of the World Medical Association (Declaration of Helsinki), as well as approved by the Research Ethics Board of the University of Oxford (Ref. 07/H0605/124).

2. Experimental procedure and Data Acquisition

Images were static and grey-scale and the display time of each images was 200 ms. We used three different stimulus types, including human face, monkey face and motorbike. In each trial two images of the same type were presented sequentially. The onset of the presentation for the second image was after a delay of 1.2 ± 0.3 s, following the first presented image. Participant was asked to respond within a response window of 1 second if the second image was a repetition of the first or not. Essentially, our task features a simple 1-back working memory design probing face and object processing, where the actual task (i.e., deciding if same or not) is primarily meant to maintain task attendance. The image pairs were presented in random sequence, with 48 trials per category. In half of the trials the first image was repeated as the second image and in the other half not.

While participant was performing the task, the neuromagnetic responses were recorded with the VectorViewTM MEG system of the Brain Research Group at the Oxford Centre for Human Brain Activity. The system composed of 102 detectors, each having two gradiometer coils and a magnetometer coil. The sampling frequency was set to 1000 Hz (0.03 – 330 Hz bandwidth).

3. Data Preprocessing

We first preprocessed the data using the MEGIN/ Elekta Neuromag Maxfilter Maxfilter (Maxfilter Version 2.2.15, MEGIN, Helsinki and used the FieldTrip toolbox for EEG/MEG-analysis (Oostenveld, Fries et al. 2011) for our later analyses. Data was segmented such that each epoch started from 300 ms before stimulus onset and continued to 1000 ms after stimulus onset. In addition, we considered the pre-stimulus interval from 1300 ms before stimulus onset to 0 ms which was set as the stimulus onset. Trials were padded for filtering by setting the padding length to 10 seconds. We then used low-pass and then high-pass filters with cutoffs at 0.5 and 150 Hz b-y applying a single-pass, zero-phase windowed sinc FIR

filter and Kaiser window setting max passband deviation to 0.001. The number of coefficients were 93 and 3625 for low-pass and high-pass filters respectively. In order to reduce the heartbeat (ECG) and eye movement (EOG) artifacts, we used independent component analysis (ICA) and removed the contaminated components.

4. Source analysis

Based on previous literature stating that pre-stimulus activities are important in stimulus selective regions (Peelen and Kastner 2011, Ruhnau, Hauswald et al. 2014), we focused on the pre-stimulus alpha fluctuations in the fusiform face area (FFA), the occipital face area (OFA), the right superior temporal sulcus (rSTS) and the lateral occipital complex (LOC). We call this set of ROIs as the pre-stimulus nodes.

The level of pre-stimulus alpha power in these brain regions may influence event related responses in various parts of the brain including the same regions responsible for face/object processing along with higher-level brain regions that are thought to integrate bottom-up and top-down effects including the intra-parietal sulcus (IPS) and the frontal eye field (FEF) (Zelinsky and Bisley 2015). We call this set of ROIs as the post-stimulus nodes.

Due to the absence of individual MRI scans, defining of ROIs was done based on the Colin 27 brain (Holmes, Hoge et al. 1998). We scaled this surface for the participant. We then defined our regions of interest (ROI) based on previous studies(Marois, Yi et al. 2004, Pitcher, Walsh et al. 2011, Harris, Young et al. 2012). Each ROI filter was created using linear constrained minimum variance (LCMV) beamformer method and then multiplied by pre-stimulus and post-stimulus sensor space cleaned data to give the related time-courses in each ROI.

We used a Morlet wavelet approach for time-frequency analyses of pre-stimulus data and calculated average alpha (8-13 HZ) power in the pre-stimulus interval of each trial in each pre-stimulus node. We then separated the trials into two groups based on the median value of the pre-stimulus alpha power in any if the pre-stimulus nodes which led to the creation of the two conditions, i.e. low vs. high pre-stimulus alpha power (LPA vs. HPA) per stimulus type. The same grouping was then applied to post-stimulus source space time series in each trial yielding the event related activities in response to each stimulus type.

5. Statistical Analyses

We ran between trials cluster based permutation using a dependent-sample permutation t-test (Maris and Oostenveld 2007). This was done to evaluate whether pre-stimulus alpha in the pre-stimulus nodes can differentiate event related responses of the two conditions in our post-stimulus nodes per stimulus category. To this end, we first defined OFA and FFA as neighbors in each hemisphere and then applied Monte Carlo method for cluster-based permutation (number of iterations =5000). Temporal and spatial adjacent samples whose t values exceeded a critical threshold for an uncorrected level of 0.05 were clustered in connected sets. Cluster level statistics were calculated by taking the sum of the t-values within every cluster and then considering the maximum of the cluster-level statistic. The statistical test was defined as two-sided and was corrected for false alarm rate using a threshold value of 0.05.

As cluster based permutation only test the most extreme observation to reject the null hypothesis, additional analyses were needed to detect post-stimulus nodes and latencies at which the difference

between the two conditions was significant. To this aim, pre-stimulus nodes which led to significant effects were further examined by running separate two-tailed t-test on the event related responses of the post-stimulus nodes at the latencies were LPA vs. HPA difference considerably increased.

6. Results

Cluster based permutation revealed that there was a significant difference between the LPA and HPA conditions in response to human face stimuli. This effect was revealed based on the partitioning performed in the pre-stimulus node of the right LOC and was manifested in the post-stimulus node of right FFA from 198 ms to 239 ms after stimulus onset ($p=0.037$). In order to find the post-stimulus nodes and latencies at which the difference between the conditions were significant, we looked at the event related traces and observed multiple time intervals in which the difference between the two conditions was considerable in the right FFA and in the right IPS (candidate pre-stimulus ROIs and time intervals). Running two-tailed t-test on the candidate time intervals in the right FFA revealed that the amplitude for the HPA condition was significantly larger than the LPA condition from 110 ms to 125 ms, from 200 ms to 270 ms and from 330 ms to 450 ms after stimulus onset ($p<0.001$, for all of them). The following figure represent the traces of the two conditions in the right FFA.

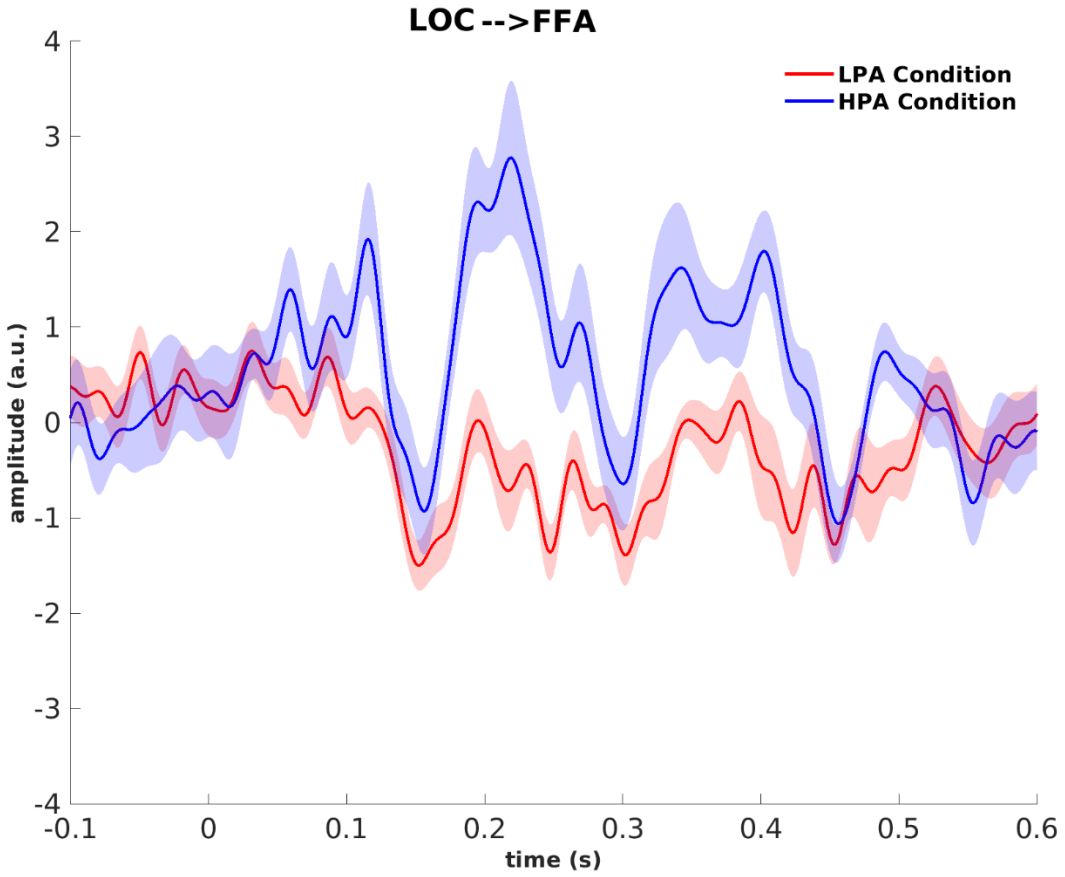

Figure 1. Evoked responses to human faces in the right FFA for the LPA (red curve) and the HPA (blue curve) conditions partitioned based on pre-stimulus alpha power in the right LOC.

Regarding the post-stimulus node of the right IPS, there was a significant difference between the two conditions from 340 ms to 380 ms after stimulus onset ($p<0.001$, two-tailed) in which the amplitude for HPA condition was significantly larger than the LPA condition. The comparison between the two conditions in the right IPS from 110 to 125 ms after stimulus onset however, was not significant ($p=0.07$). Figure 2. Shows the time courses of the two conditions in the right IPS.

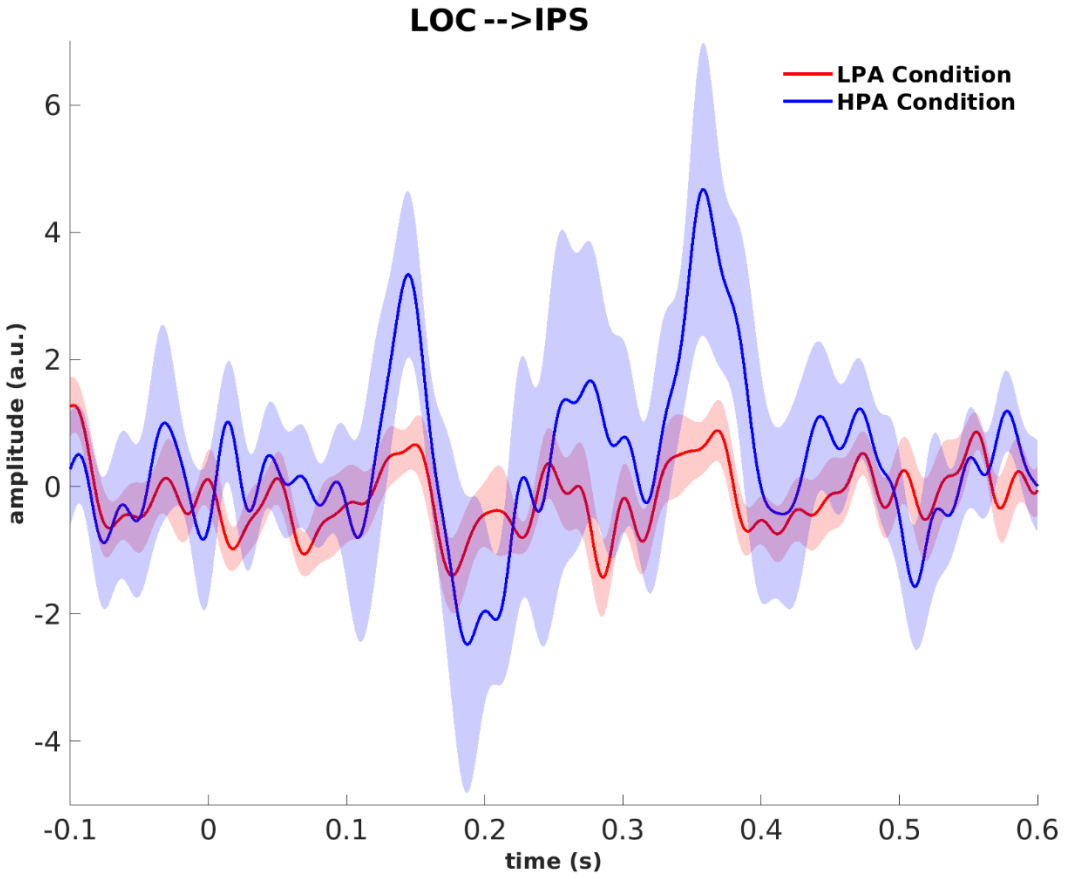

Figure 2. Time courses for the LPA (red curve) and the HPA (blue curve) conditions in the right IPS in response to human face stimulus.

There was not a significant result for the monkey face and neither for the motorbike stimuli.

7. Discussion

In this study we examined the effect of pre-stimulus alpha oscillations on post-stimulus activities in an individual with autism. To this aim we considered a set of stimulus selective brain regions as the pre-stimulus nodes and another set as the post-stimulus nodes. We partitioned the data based on the median value of pre-stimulus alpha power in pre-stimulus nodes and explored how this could affect event-related

activities in each stimulus category in post-stimulus nodes.

Our results suggest that partitioning the data based on the pre-stimulus alpha power in the right LOC could create a significant effect in the FFA in multiple time interval between the two conditions. The earliest effect seen in this region is around 100 ms after stimulus onset, resembling the M100 face selective component (Halit, de Haan et al. 2000). Thus this effect may be related to top-down mechanisms like attention. The difference between the two conditions was almost vanished over the M170 face selective component. This means that the pre-stimulus alpha oscillations do not have an influence on the structural encoding of faces which is assigned to M170 component (Rossion 2014).

The difference between the two conditions increased again and the next significant effect was detected around 250 ms after stimulus onset in the right FFA. The M250 components is also a face selective component which is responsible to identity encoding (Nasr and Esteky 2009). The next significant effect in right FFA was around 400 ms after stimulus onset which is likely to represent the stimulus categorization component of M400 (Curran, Tanaka et al. 2002).

Alpha oscillations are considered to play the role of an inhibitory gating mechanisms (Hanslmayr, Volberg et al. 2013). This means that in processing related a specific stimulus type, increase of alpha is seen in the brain regions which are selective for the other stimulus type. In this way, the brain regions unselective to a stimulus type would be inhibited and thus better resource management will be performed for the selective brain regions of that stimulus type.

LOC is considered as an object selective region in previous studies performed on healthy participants (Hesselmann, Kell et al. 2008, Peatfield, Muller et al. 2017). Thus, in face trials, more pre-stimulus alpha power in LOC, is interpreted as more inhibition of a stimulus unselective region. Interestingly, the significant difference between the two conditions is such that the group with HPA has significantly larger amplitude in comparison to the group with LPA in all the effect we found in the event related activity of the right FFA. This means that more inhibition of a stimulus unselective region (LOC) leads to a greater peak at post-stimulus processing in a stimulus selective region (FFA) and relevant time intervals.

In addition, the level of pre-stimulus alpha power in LOC yielded a significant dissociation between the two conditions in the IPS around 350 ms after stimulus onset. The pattern of difference in this component was the same as the effects seen in the FFA, i.e. the HPA condition has significantly larger amplitude than the LPA condition, which could be a sign for the same inhibitory mechanism of pre-stimulus alpha oscillations. Therefore, the higher activation of stimulus unspecific regions during pre-stimulus intervals leads to larger post-stimulus activity in a region which is responsible for merging top-down and bottom-up effects coming from pre-stimulus activation.

8. Conclusion

This study suggest that pre-stimulus modulation of post stimulus processing could happen in an individual with autism in response to human face stimulus. Furthermore, our results illustrates that such effect could be due to the inhibitory gating mechanism of pre-stimulus alpha oscillations. Although, the common procedure in neuroscience is that multiple subjects are examined in the same experimental paradigm, our study is confined to the data of a single subject, but it serves our purpose for answering the main questions.

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