Clinical Neurophysiology 130 (2019) 963–975

Contents lists available at ScienceDirect

Clinical Neurophysiology

journal homepage: www.elsevier.com/locate/clinph

Altered predictive contextual processing of emotional faces versus abstract stimuli in adults with Autism Spectrum Disorder

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ARTICLE INFO

Article history:
Accepted 22 March 2019
Available online 13 April 2019

Keywords:
Predictive local context
EEG
P3b
Graph theory
Autism

HIGHLIGHTS

- Processing of predictive context is altered in adults with Autism Spectrum Disorder (ASD).
- Abnormalities are more pronounced for emotional cartoon faces versus abstract triangles.
- Predictive context processing in ASD is associated with weaker fronto-parietal connectivity.

ABSTRACT

Objectives: We investigated the proposition that Autism Spectrum Disorder (ASD) is associated with predictive contextual processing deficits.
Methods: We recorded electroencephalography (EEG) in adults with ASD and controls during the performance of a predictive contextual processing task, using either triangles or emotional faces. Targets were preceded by either randomized sequences (R) or by sequences including a predictive sequence (P).
Results: ASD subjects showed an attenuated behavioral facilitation (P versus R) compared with controls (faces). P3b amplitudes of P, R and the predictive sequence (n-1) were attenuated in ASD compared with controls. However, the attenuation of n-1 was more pronounced during the processing of faces. Controls demonstrated shorter peak P3b latencies of P versus R, while this facilitation was absent in ASD subjects. ASD subjects demonstrated functional connectivity alterations during the processing of random (triangles and faces) and predicted targets (faces). These changes were associated with weaker, more randomised, functional connections between frontal and parietal regions in ASD.
Conclusions: We found predictive contextual processing alterations in ASD, which were more pronounced during the processing of emotional faces compared with abstract stimuli.
Significance: We provide novel evidence for the proposition that ASD is associated with deficits of top-down predictions.

1. Introduction

Autism Spectrum Disorders (ASD) are developmental disorders that occur with an estimated prevalence of 0.3–0.9% (Happé and Frith, 1996; Happé, 1999; Dakin and Frith, 2005). ASD have been associated with executive dysfunction (Happé and Frith, 1996; Hill, 2004; Nydén et al., 2010), working memory deficits (Hill, 2004; Koshino et al., 2008; O'Hearn et al., 2008; Barendse et al., 2013; Williams et al., 2014), impaired utilization of context (Beversdorf et al., 2007; Loukusa et al., 2007; Poirier et al., 2011; Maister et al., 2013; Wang et al., 2006) and deficits in prediction (Lawson et al., 2014). Deficits in working memory and dysfunction of prediction may affect diverse social and cognitive skills, including thinking and behaviour (Baddeley and Hitch, 1974; Unsworth and Engle, 2007), as well as contributing to social behaviour disturbances in ASD (Mundy, 2003). These deficits have been related to functional connectivity abnormalities within frontal circuits, suggesting a deficit in the integration of information (Courchesne and Pierce, 2005; Just et al., 2007; Koshino et al., 2008). Critically, cognitive deficits in attention and working memory persist throughout life in subjects with ASD (Geurts and Vissers, 2012). Recent propositions have suggested that subjects with ASD fail to

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https://doi.org/10.1016/j.clinph.2019.03.031
1388-2457/

instantiate top-down predictions during perceptual processing (Pellicano and Burr, 2012; Lawson et al., 2014). In other words, ASD can be seen as an inability to contextualize sensory information, so that sensory prediction errors are too precise and context insensitive (Lawson et al., 2014). However, there is still a lack of evidence as to whether ASD subjects have predictive contextual processing deficits.

The objective of the current study was to examine predictive contextual processing in adults with ASD, using electrophysiological and functional connectivity measures (Fogelson et al., 2009a,b, Fogelson et al., 2013, Fogelson, 2015). Specifically we evaluated processing of predictive top-down goal-directed contextual information, an important working memory process that sub-serves a wide range of higher cognitive functions (Cohen and Servan-Schreiber, 1992). The dorsolateral frontal cortex and top-down frontal networks have been shown to play a crucial role during the processing of predictive context (Fogelson et al., 2009a,b; reviewed in Fogelson, 2015). The paradigm that was utilized was previously used to evaluate specific deficits associated with predictive contextual processing in different patient populations (reviewed in Fogelson, 2015). The paradigm is an extended version of the well-established oddball paradigm (Squires et al., 1975), which measures P3b and cognitive processes associated with target detection (Squires et al., 1976; Donchin and Coles, 1988; Poulsen et al., 2005; Polich and Criado, 2006; Fogelson, 2015). Attenuated P3b amplitudes have been observed in subjects with ASD (Courchesne et al., 1989; Ciesielski et al., 1990; Salmond et al., 2007; Duncan et al., 2009; Maekawa et al., 2011). In the current study, we evaluated the ability of ASD subjects to detect different target conditions (random and predictable targets) and to process goal-directed information (a predictive sequence). To this end, we used the following electrophysiological measures (Fogelson et al., 2009a; reviewed in Fogelson, 2015): (1) peak P3b amplitudes of predicted and random targets, and of the stimuli consisting of the predictive sequence, compared to those of standard stimuli. (2) P3b latency differences between predictable and random target events, as well as the associated reaction time differences (context-dependent facilitation of predictive target detection). Importantly, we used two types of stimuli: abstract triangles and cartoon faces portraying emotional faces, since there is evidence showing that processing of faces and human emotions are altered or impaired in ASD (Koshino et al., 2008; Wong et al., 2008; Dichter et al., 2009; Khan et al., 2013). Our study is novel in that we are able to directly compare the same predictive contextual effects using these two types of stimuli.

To further investigate the mechanisms underlying the processing of predictive contextual information in ASD, we examined the event-related functional connectivity during the processing of the two target conditions and the predictive sequence. Specifically, we investigated whether changes within frontal networks underlie the hypothesized predictive contextual processing alterations in ASD, since top-down frontal networks have been shown to be critical for the processing of predictive context (Fogelson et al., 2009a, b; reviewed in Fogelson, 2015). Previous studies using the current paradigm have demonstrated functional connectivity changes that were specific to task-relevant stimuli in other patient populations (Fogelson et al., 2013; Li et al., 2018). In the current study we wanted to determine whether functional connectivity changes would be more pronounced during the processing of predictive stimuli. We used synchronization likelihood and graph theoretical analysis (Watts and Strogatz, 1998; Stam and Reijneveld, 2007; Fogelson et al., 2013; Li et al., 2018), to evaluate functional connectivity in ASD. Graph analysis evaluates the correlations between recorded signals of brain activity (Stam and Reijneveld, 2007; Stam et al., 2007; Bullmore and Sporns, 2009; He and Evans, 2010; Stam and van Straaten, 2012; Fogelson et al., 2013; Tan et al., 2013). Reduced functional connectivity in ASD subjects has been observed using functional magnetic resonance imaging (fMRI) (Just et al., 2007; Koshino et al., 2008; Weisberg et al., 2014; Denisova et al., 2016) and magnetoencephalography (MEG) (Khan et al., 2013; Ye et al., 2014). Other EEG studies have also demonstrated functional connectivity abnormalities in ASD (Murias et al., 2007; Barttfeld et al., 2011; Peters et al., 2013; Matlis et al., 2015; Urbain et al., 2016). However, only few of these were task-related studies, and these seem to be critical for the understanding of cognitive deficits in autism.

The objective of the present study was to determine whether subjects with ASD show alterations in the processing of predictive contextual information, and if these are, generalized across or specific to, emotional faces versus abstract stimuli. Our hypothesis was that ASD will be associated with P3b amplitude attenuations of task-relevant, predictive stimuli, as well as a reduced context-dependent facilitation of predictive target detection (Fogelson et al., 2009a,b; Fogelson, 2015). We hypothesized that these changes would be more pronounced when processing stimuli consisting of emotional cartoon faces. In addition, we hypothesized that ASD would be associated with weaker functional connectivity within fronto-parietal networks, specifically when processing task-relevant stimuli.

2. Materials and methods

2.1. Participants

Fifteen adult subjects with ASD (mean age ± standard error of mean = 25.6 ± 2.6 years, 1 female) and fifteen age-matched controls (mean age ± standard error of mean = 25.7 ± 2.7, 1 female) participated in the study. All the subjects were right handed and had normal or corrected-to-normal visual acuity. ASD and control subjects had a mean of 13.1 ± 0.4 and 14.2 ± 0.5 years of education, respectively ($p = 0.103$). Demographics and clinical details of the ASD subjects are shown in Table 1. All the individuals with ASD received a diagnosis of ASD from a psychiatrist or a licensed clinical psychologist. The mean duration since the diagnosis was 7.3 ± 1.2 years, prior to participating in the study. ASD subjects had a total mean score of 11 ± 0.9 on the Autistic Diagnostic Observation Schedule-Generic, Module 4 (Lord et al., 2000), on the day of the experiment. Eight ASD subjects were administered medication on a regular basis (see Table 1), these eight ASD subjects were asked to take their regular medication on the day of the experi-

Table 1
Clinical details of subjects with Autism Spectrum Disorder.

Subject (Sex)	ADOS score	Duration since diagnosis (years)	Medication (daily dose in mg)
1 (M)	9	14	None
2 (M)	11	3	Aripiprazole 1, Sertraline 30
3 (M)	11	7	Methylphenidate 90, Risperidone 2.5
4 (M)	8	2	None
5 (M)	20	6	Topiramate 50
6 (F)	7	1	None
7 (M)	9	10	Aripiprazole 10
8 (M)	16	12	Aripiprazole 5
9 (M)	12	7	None
10 (M)	9	7	None
11 (M)	11	8	Risperidone 0.5
12 (M)	8	4	Risperidone 0.5
13 (M)	10	9	None
14 (M)	13	2	Fluoxetine 10
15 (M)	11	17	None

ADOS = Autism Diagnostic Observation Schedule (Lord et al., 2000).

ment. Control subjects had no history of psychiatric or neurological problems. Participation was voluntary and informed consent was obtained in line with a protocol approved by the local ethics committee of University of A Coruña.

The methodology including the task, the ERP and functional connectivity analyses have been previously utilized and reported in detail (Fogelson et al., 2009a, Fogelson, 2015).

2.2. Task

The task has been previously utilized and reported (Fogelson et al., 2009a, Fogelson, 2015). On the day of the recording, each subject performed two sessions, a session with visual stimuli consisting of triangles at different orientations, and a session consisting of cartoon faces portraying different emotions. The reason that we used cartoon faces portraying human emotions, but not actual faces of people, was to avoid potential confounds of gender, race or age that may arise when using photos of human faces. Thus, the stimuli that we used were unambiguous and were matched to the four unambiguous images of the triangles, thus allowing for a direct comparison of the two sessions. Each subject performed the two sessions on the same day, with a 15 minutes rest interval between each session. The order of the sessions was counterbalanced across the subjects. Subjects were seated 110 cm in front of a 21-inch PC-computer screen. Stimuli were presented to either the left or right visual field 6 degrees from a central point of fixation. Subjects were asked to centrally fixate throughout the recording. The stimuli consisted of black triangles or black cartoon faces on a grey background. Stimuli consisted of 15% targets (downward facing triangle or a cartoon figure with a crying face) and 85% of equal amounts of three types of standards (triangles facing left, upwards and right, at 90 degree increments, or faces portraying the following emotions: happy, neutral and sad). "In each block a total of 78 stimuli (12 targets, 22 of each standard type) were presented each for 150 ms and inter-stimulus interval (ISI) of 1 sec. Recording blocks consisted of targets preceded by either randomized sequences of standards or by sequences including a three-standard predictive sequence. Fig. 1 illustrates an example of a target preceded by a randomized sequence of standards and a target preceded by the predictive sequence of standards for each of the recording sessions. Each block consisted of 6 different randomized sequences of standards (3–8 standards long) preceding the target; and 6 sequences of standards (3–8 standards long) with a predictive sequence preceding the target in each. Each recording session consisted of 14 different blocks, displayed in randomized order, each approximately 1.6 minutes long. A single sequence of trials appeared on the right or left hemi-field in a randomized order within each block. Within a single sequence of trials (predictive or random) all stimuli were presented in one hemi-field." (Fogelson et al., 2009a). The predictive sequence always consisted of the three standards: triangles facing left, up and right; or happy, neutral and sad faces, always in that order. The predictive sequence was always followed by the target stimulus (downward facing triangle or a crying face, respectively). Subjects were asked to press a button each time a target was presented. Stimulus presentation and response recordings were controlled using E-prime (Psychology Software Tools, Inc., Pittsburgh, USA).

Before each experimental session subjects performed a brief training session. In the first practice block subjects were introduced to the stimuli (triangles or faces, depending on the recording session), and were asked to detect targets. Once all the subjects were able to detect the targets accurately, they were shown the predictive sequence and were told that it would be 100% predictive of a target, but that targets would also appear randomly throughout the block. Subjects then performed another brief training session to ensure that they were confident in the detection of both predictive and random targets, before the recording session began.

2.3. EEG recordings

EEG was recorded from a 64 Ag-AgCl electrode array using the ActiveTwo system (Biosemi, The Netherlands). Signals were amplified and digitized at 512 Hz. Post processing and ERP analysis of the data was performed using Brain Vision Analyzer (Brain Products GmbH, Germany). All channels were re-referenced to averaged linked earlobes.

2.4. Behavioral analysis

Accuracy was defined as the percentage of targets for which a button press was detected.

Reaction times were calculated by averaging correct trials for predicted and random targets in each subject for each session. Misses (no button press 150–1150 ms post-stimulus onset) were excluded from reaction time analysis. Premature responses were not taken into consideration in the analysis of reaction time. Reaction times were analysed using E-prime (Psychology Software Tools, Inc., Pittsburgh, USA).

2.5. ERP analysis

Prior to ERP analysis blinks were defined using independent component analysis (ICA) (64 EEG electrodes were included), and the component identified as a blink was removed using the linear derivation function in Brain Vision Analyzer. Epochs containing premature responses, misses (no button press 150–1150 ms post-stimulus onset) and eye saccades were excluded from further analysis. EEG signals were filtered at 0.1–30 Hz for subsequent analysis. EEG signals were sorted and averaged relative to the stimulus onset, with epochs set from −200 to 1000 ms relative to stimulus onset. EEG epochs with amplitude of more than 75 μV at any electrode were excluded.

2.6. P3b

P3b was determined as the most positive point in the latency range of 300–500 ms. "Detected peaks were then checked for their topographical map (using Brain Vision Analyser) and confirmed as a P3b component by determining a posterior–parietal scalp distribution (Sawaki and Katayama, 2006; Fogelson et al., 2009a,b). In order to restrict the number of comparisons, and since no lateralization effects of hemisphere or visual field were observed, all P3b ERP data were collapsed across visual fields (Fogelson et al., 2009a; 2011; 2014). In addition, we concentrated on midline electrode sites (AFz, Fz, FCz, Cz, CPz, and Pz) to explore anterior versus posterior topographical differences of P3b for the different conditions." (Fogelson et al., 2009a). Thus, for each subject the peak P3b amplitudes (measured in μV) were evaluated at electrode sites AFz, Fz, FCz, Cz, CPz, and Pz for six different conditions in each session (triangles and faces): targets after predictive sequences (predicted, P), targets after non predictive random sequences (random, R), random preceding standards (standards excluding those comprising the predicting sequence, S) and the three standards consisting of the predictive sequence: the last most-informative standard (n-1), the middle standard (n-2) and the first least-informative standard (n-3) of the predicting sequence. Each condition consisted of a minimum of 35 trials in each subject (Duncan et al., 2009).

Peak P3b latencies (measured in ms) were evaluated for predicted and random targets at the electrode site with the largest P3b amplitude (CPz).

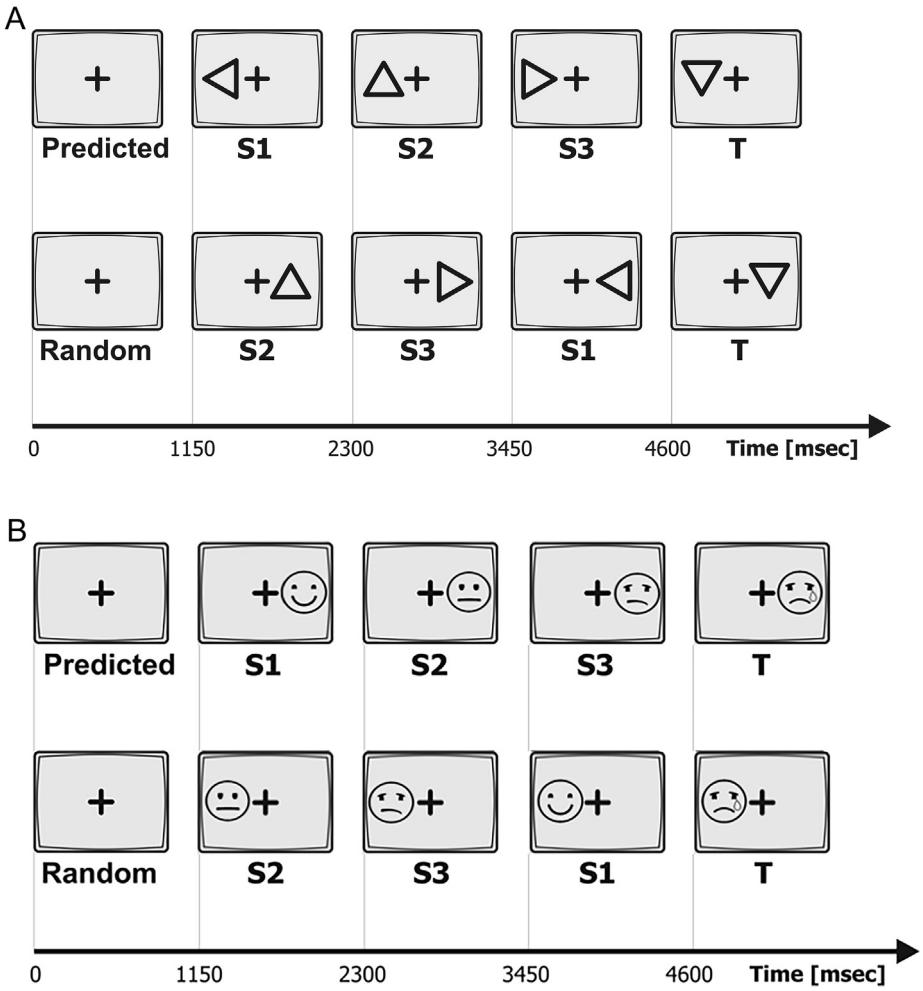

Fig. 1. Task timeline. Stimuli presented in the triangles (A) and faces (B) session. Sequences of standards S1, S2 and S3 with a predicted sequence (top) and in randomized order (bottom) preceding the target (T). The predictive sequence is always S1, followed by S2, and then S3 (n-1). The inter-trial interval (1000 ms) including the duration of the stimulus presentation (150 ms) is displayed. Each block consisted of 6 different randomized sequences of standards (3–8 standards long) preceding the target; and 6 sequences of standards (3–8 standards long) with the predictive sequence preceding the target in each.

2.7. Functional connectivity analysis

The functional connectivity analysis utilized in the current study has been previously used and reported (Fogelson et al., 2013; Li et al., 2018). "EEG signals were sorted and averaged relative to the stimulus onset, with epochs set from 200 to 700 ms relative to stimulus onset. EEG signals in each epoch in each subject were filtered with a two-way least-squares FIR bandpass filter (eegfilt.m from EEGLAB toolbox, Delorme and Makeig, 2004) between 4 and 8 Hz (theta band), 8 and 12 Hz (alpha band), and between 12 and 28 Hz (beta band). A current source density (CSD) toolbox (MATLAB) was used to estimate scalp current density with 4 as the spline interpolation constant for each trial in the three frequency bands (Perrin et al., 1989; Kayser and Tenke, 2006) and to minimize the contribution of volume conduction and remove spurious synchronization." (Fogelson et al., 2013; Li et al., 2018).

In each subject epochs were segmented for the following six conditions: predicted (P) and random (R) targets, random standards (excluding those comprising of the predicting sequence, S) and each of the three stimuli that consisted of the predictive sequence, that is, the last, most-informative stimulus (n-1), the middle stimulus (n-2), and the first, least-informative stimulus (n-3). In order to match trial numbers across subjects, we either randomly selected 60 trials for each condition in each subject for those blocks that had more than 60 trials, or kept all the trials for those blocks that had less than 60 trials. All conditions had a minimum of 20 trials. The signal segmented between 200–700 ms in each trial for each condition was then linked to create multi-channel signal matrices for further analysis.

2.8. Computation of synchronization likelihood

We used synchronization likelihood (SL), a method proposed by Stam and van Dijk (2002) to estimate the generalized synchronization for multi-channel signals. We utilized the following parameters to estimate the value of the synchronization likelihood (S): l, the lag of the embedding dimension, is 10, m, the embedding dimension, is 20, w_1, the Theiler correlation for autocorrelation effects, is 200, w_2, the time-resolution sharpening window of the synchronization measure, is 400, and P, the probability that embedded vectors are close to each other, is 0.05 (Stam and van Dijk, 2002; Micheloyannis et al., 2006; Stam et al., 2007; Rubinov et al., 2009). "After obtaining the S value, we averaged across the time index i, to obtain S_k, which evaluates how strongly channel k is synchronized to all the other channels. After this calculation, we obtained a 64 * 64 matrix for each condition in each frequency band in each subject (Posthuma, et al., 2005). SL takes on values

between 0 and 1, describing a continuum between no and perfect generalized synchronization (Stam and van Dijk, 2002)." (Fogelson et al., 2013; Li et al., 2018).

2.9. Computation of graph parameters

"The degree, clustering coefficient and path length are the most commonly used measures of graphs or networks. Networks consist of nodes and connections. Thus, the degree (K) evaluates the number of connections to each node, with larger K reflecting greater number of connections in a graph. The clustering coefficient (C) evaluates the number of connections between neighbors, thus providing a measure of the local structure of the network (local segregation) and its resilience to random attacks (Watts and Strogatz, 1998, Stam et al., 2007, Bullmore and Sporns, 2009). Path length (L) evaluates the number of steps from one node to another, and is thus an index of the network global properties and the overall integration of the network (Stam et al., 2007, Bullmore and Sporns, 2009, Stam and van Straaten, 2012). An SL matrix can be converted to a binary graph by obtaining different thresholds (T).)." (Fogelson et al., 2013; Li et al., 2018). We used T = 0.05:0.0001:0.5, for 4000 graphs; then calculated K, C, L. We selected $8 \leq K \leq 15$ (step 0.5) to demonstrate results ($K \geq 2 * \log(64) = 8.3$). After obtaining a graph from the synchronization matrix, the mean degree K, clustering coefficient C, and the shortest path length L were measured to characterize the functional connectivity (Watts and Strogatz, 1998, Stam et al., 2007, Bullmore and Sporns, 2009; Stam and van Straaten, 2012; Fogelson et al., 2013; Li et al., 2018).

2.10. Statistical analysis

Comparisons of the reaction time and the ERP variables were performed using analysis of variance (ANOVA) with the Greenhouse-Geisser correction. These were followed by post-hoc parametric paired t-tests, Sidak corrected for multiple comparisons unless otherwise stated. Partial eta squared (η_p^2) values are reported where applicable. Mean values with ± standard error of the mean (SEM) are used throughout the text. Since the distributions of the accuracy values were not Gaussian, non-parametric analysis was performed for the comparisons, using Mann-Whitney to evaluate group differences in each session for predicted and random targets. Correlations were calculated using Pearsońs Product Moment or Sprearman's rank correlation coefficient correlation coefficients for parametric and non-parametric correlations, respectively.

Graph parameters (C, L, gamma, and lambda) comparisons were performed using t-tests, across K values 8–15. In addition, the area under the curve (AUC) was evaluated for each measure across the range of K values, by calculating each small trapezoidal area (e.g K = 8–8.5), and then summing all 14 trapezoids (K = 8–15). Since the distributions of AUC values were not Gaussian, non-parametric analysis was performed for the comparisons, using Mann-Whitney to evaluate group differences in each condition.

"Network-based statistic (NBS) was used to compare whole brain network differences between patients and control subjects, in order to control for the error rate when testing is performed at every connection comprising the graph (Zalesky et al., 2010). We used this approach to localize specific connected components that were significantly different between controls and patients. SL values were used to construct weighted networks. NBS analysis was performed on these weighted networks. Using this method we computed thresholded t-tests for each pair-wise association, identifying supra-threshold linked components." (Fogelson et al., 2013; Li et al., 2018). We selected the maximal threshold, which generated the first strongest connected component network difference. The null distribution of the connected component size was derived using a nonparametric permutation approach. Thus, 100,000 permutations were performed for each K value (K = 8–15) in each between-group comparison (for each condition and each frequency band), with p value < 0.05 as a significant threshold. We used two one-tailed tests to determine the components that were significantly different between controls and ASD subjects (controls > ASD and controls < ASD).

Furthermore, to avoid false-positive results for the functional connectivity analysis across multiple comparisons, for each variable we defined a significant result as that corroborated by all the three methods described above, i.e. significant group differences across K values, AUC values and NBS.

3. Results

3.1. Behavioral results

We used Mann-Whitney tests to evaluate group differences (ASD, controls) of target detection accuracy (predicted, random) in each session (triangles, faces). For the triangles session, we found no significant accuracy differences between ASD and control subjects for predicted (mean accuracies = 98 ± 0.6 and 99 ± 0.6 for ASD and controls, respectively, p = .08) and random targets (mean accuracies = 99 ± 0.3 and 99 ± 0.1, for controls and ASD, respectively, p = .186). For the faces session, we also found no significant accuracy differences between ASD and control subjects for predicted (mean accuracies = 99 ± 0.4 and 99 ± 0.2 for ASD and controls, respectively, p = .301) and random targets (mean

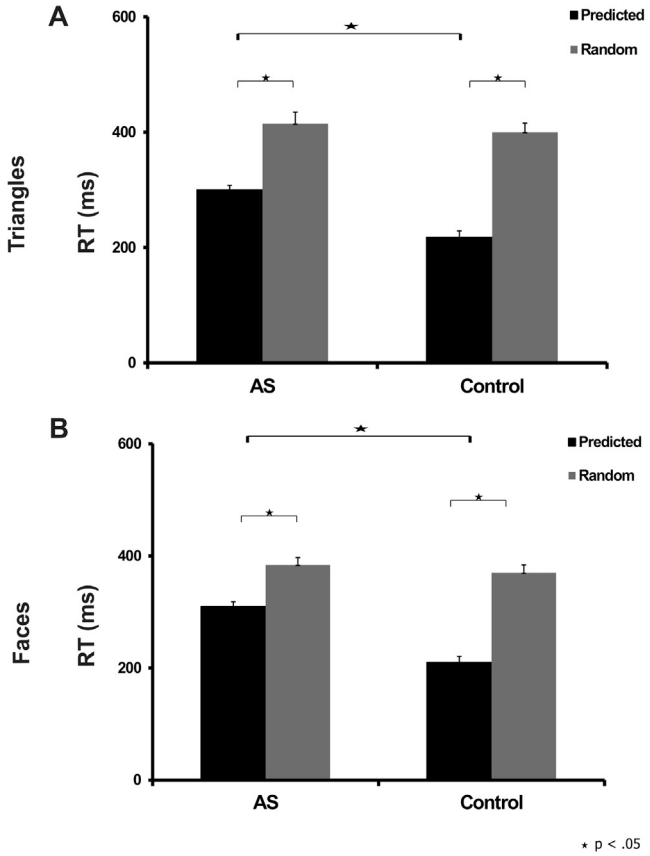

Fig. 2. Reaction times for predicted and random targets, in the triangles (A) and faces (B) sessions, for AS subjects and controls. Significant differences (p < .05) are highlighted with a star. Bars = SEM.

accuracies = 99 ± 0.2 and 99 ± 0.2, for controls and ASD, respectively, p = .674).

Reaction time (RT) comparisons are displayed in Fig. 2. To compare the RTs for the targets, and to test whether there is a behavioral facilitation in the sessions across the groups, we performed an ANOVA with condition (predicted, random targets) and session (triangles, faces) as the repeated measures factors, and with group (ASD, controls) as the between-subject factor. There were significant main effects for condition ($F(1,28) = 106.03$, $p < .000$, $\eta_p^2 = 0.79$) and session ($F(1,28) = 9.19$, $p = .005$, $\eta_p^2 = 0.24$), and a significant condition × group interaction ($F(1,28) = 8.88$, $p = .006$, $\eta_p^2 = 0.24$) and a session × condition interaction $F(1, 28) = 6.62$, $p = .016$, $\eta_p^2 = 0.19$. In the triangles session, both ASD and control subjects, showed faster RTs for predicted (mean RT = 300 ± 15 ms and 218 ± 14 ms, for ASD and controls, respectively) compared to random targets (mean RT = 414 ± 20 ms and 400 ± 16 ms, for AS and controls, respectively, $p \leq 0.001$). In the faces session, ASD and control subjects, also showed faster RTs for predicted (mean RT = 310 ± 12 ms and 210 ± 15 ms, for ASD and controls, respectively) compared to random targets (mean RT = 384 ± 13 ms and 365 ± 14 ms, for ASD and controls, respectively, $p \leq 0.0001$). However, the RTs for predicted targets were prolonged for ASD compared to controls in both sessions ($t(28) = 4.03$, $p < .0001$ and $t(28) = 5.24$, $p < .0001$, for triangles and faces, respectively), while there were no significant group differences for the RTs of random targets ($p = .574$, $p = .476$, for triangles and faces, respectively). The triangles session displayed longer RTs for random targets compared to the faces session, across conditions and groups ($p \leq 0.007$). In addition, RT differences between predicted and random targets were larger for controls (mean RT difference = 160 ± 17 ms) compared to ASD subjects (mean RT difference = 74 ± 16 ms, $t(28) = 3.7$, $p = .001$) only during the faces session, but did not reach statistical significance in the triangles session (mean RT difference = 182 ± 20 ms and 115 ± 26 ms, for controls and ASD subjects, $t(28) = 2.04$, $p = .051$).

3.2. P3b amplitude

The main P3b findings are displayed in Fig. 3, illustrating the waveforms of the grand-averaged ERPs in each of the sessions for ASD and control subjects, at electrode site CPz, elicited by predicted (P) and random (R) targets, n-1, and random standards (S). Fig. 3C illustrates the topographical maps of peak P3b amplitudes for P, R, and n-1.

We compared peak P3b amplitudes by performing an ANOVA with condition (P, R, n-1, n-2, n-3, and S), session (triangles, faces), and electrode site (AFz, Fz, FCz, Cz, CPz, and Pz) as the repeated measures factors, and with group (AS, controls) as the between-subject factor. There were significant main effects for condition ($F(5,140) = 55.86$, $p < .0001$, $\eta_p^2 = 0.67$), session ($F(1, 28) = 9.88$, $p = .004$, $\eta_p^2 = 0.26$) and electrode site ($F(5,140) = 59.64$, $p < .0001$, $\eta_p^2 = 0.68$), as well as significant condition × group, electrode × group, and session × electrode × condition × group interactions ($F(5,140) = 1140.94$, $p = .012$, $\eta_p^2 = 0.13$ and $F(5,140) = 4.46$, $p = .024$, $\eta_p^2 = 0.14$, $F(25,700) = 2.08$, $p = .031$, $\eta_p^2 = 0.07$, respectively).

Post-hoc t-tests corrected for multiple comparisons showed maximal and minimum peak P3b amplitudes at electrode sites CPz and AFz, respectively, across groups and sessions. For the triangles session, post-hoc tests corrected for multiple comparisons, showed that peak P3b amplitudes were larger for P, R and n-1 compared with n-2, n-3 and standards, across the groups. In addition, peak P3b amplitudes were larger for P, R and n-1 in controls compared with AS subjects ($p \leq 0.035$), during the triangles session. For the faces session, post-hoc tests corrected for multiple comparisons, showed that, in AS and controls, peak P3b amplitudes were larger for predicted and random targets compared with n-2, n-3 and standards. However only controls showed larger P3b amplitudes for n-1 compared with n-2, n-3 and standards, while ASD subjects showed no significant P3b amplitude differences between n-1 and the other standards, during the faces session. In addition, during the faces session, peak P3b amplitudes were larger for random targets and n-1 in controls compared to AS subjects, in ($p \leq 0.03$). There were no significant differences in P3b amplitude between random and predicted target stimuli across sessions and groups. Mean P3b amplitudes across conditions and sessions are displayed in Table 2.

3.3. P3b latency

To test whether processing speed of the two target conditions was modulated across the sessions between the groups, we compared peak P3b latencies at electrode site CPz, and performed an ANOVA with condition (predicted, random targets) and session (triangles, session) as the repeated measures factors, and with group (AS, controls) as the between-subject factor. There were significant main effects for condition ($F(1,28) = 83.53$, $p < .0001$, $\eta_p^2 = 0.75$), and session ($F(1,28) = 8.34$, $p = .007$, $\eta_p^2 = 0.23$), as well as significant condition × group ($F(1,28) = 38.88$, $p < .0001$, $\eta_p^2 = 0.58$) and session × group ($F(1,28) = 4.46p = .044$, $\eta_p^2 = 0.14$) interactions. In controls, in both sessions peak P3b latencies were shorter for predicted targets (mean P3b latency = 336 ± 4 ms and 333 ± 10 ms, for triangles and faces, respectively) compared with random targets (mean P3b latency = 428 ± 16 ms, $t(14) = 6.47$, $p < .0001$, and 440 ± 11 ms, $t(14) = 12.38$, $p < .0001$, for triangles and faces, respectively). On the other hand, in ASD subjects, there were no significant peak P3b latency differences between the two target conditions in neither the triangles session (mean P3b latency = 361 ± 10 ms and 378 ± 11 ms for predicted and random targets, respectively, $t(14) = 1.54$, $p = .145$), nor in the faces session (mean P3b latency = 385 ± 12 ms and 406 ± 9 ms, for predicted and random targets, respectively, $t(14) = 2.12$, $p = .052$). These comparisons are displayed in Fig. 4. In addition, peak P3b latencies for predicted targets were prolonged in ASD subjects compared to controls across both sessions ($p \leq 0.029$), while peak P3b latencies for random targets were shorter in ASD compared to control subjects across both sessions ($p \leq 0.023$).

Furthermore, we evaluated the P3b latency shift for each subject between the two target conditions (subtraction of the peak P3b latency of random targets from that of predicted targets). To compare the P3b latency shift between groups and across sessions, we performed an ANOVA session (triangles, faces) as the repeated measures factor, and with group (ASD, controls) as the between-subject factor. There was no significant main effect for session, nor a significant session × group interaction. However, there was a significant overall effect of group ($p < .0001$), showing larger P3b latency shifts in controls (overall mean P3b latency shift = 99.6 ± 9 ms) compared to AS subjects (overall mean P3b latency shift = 18.8 ± 9 ms) across the two sessions.

3.4. Graph parameters

Figs. 5 and 6 display the significant functional connectivity comparisons between ASD and control subjects for the triangles and faces sessions.

We compared the clustering coefficient (C) and path length (L) between ASD and control subjects in each condition (P, R, n-1, n-2, n-3, S) for each of the sessions (triangles, faces) across three frequency bands (theta, alpha, beta).

In the triangles session we found significantly lower C values for random targets in the theta frequency band, in ASD compared to control subjects. These findings were corroborated using three dif-

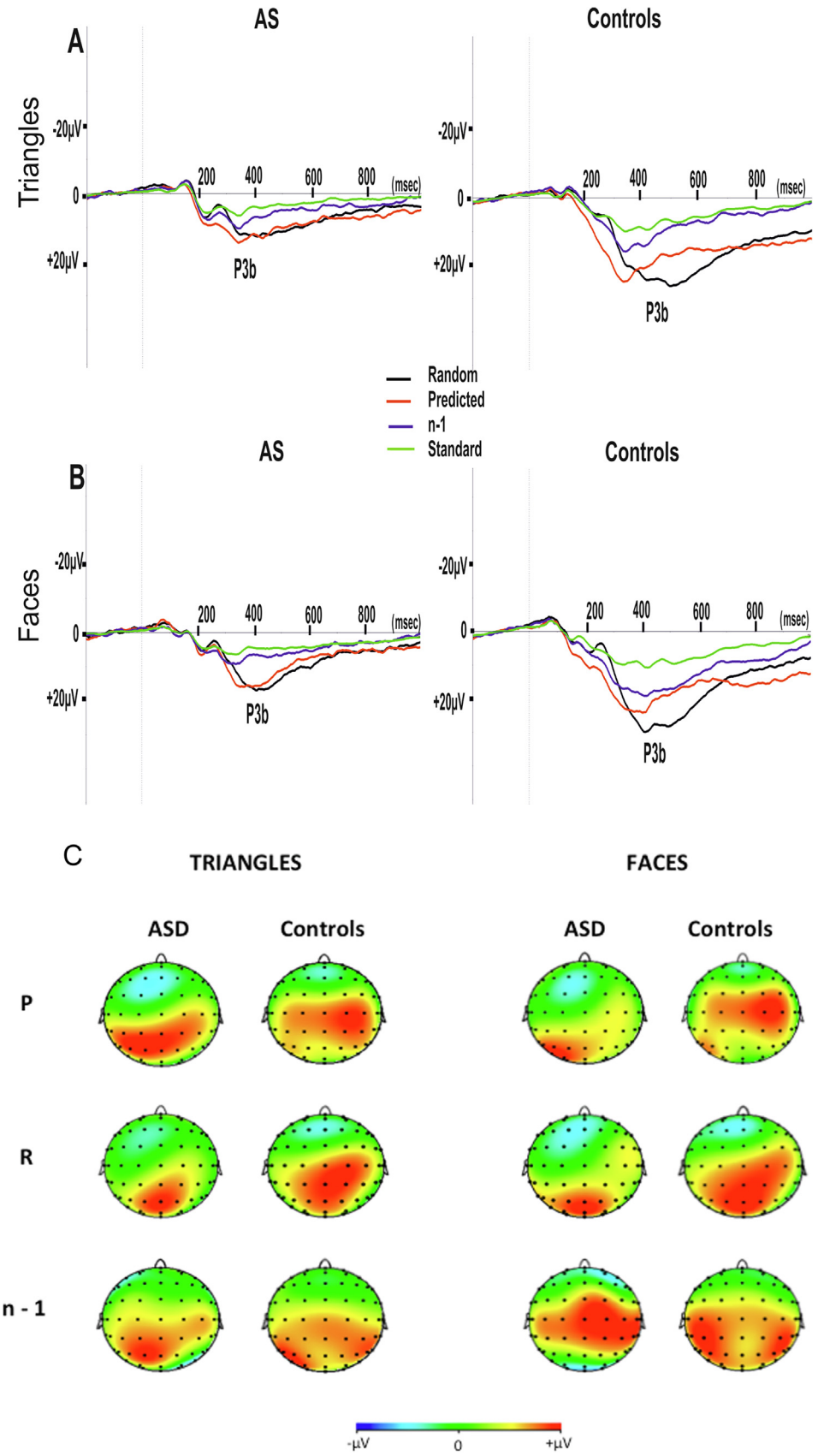

Fig. 3. Grand average at CPz for the 4 conditions: targets after random (Random) and predictive sequences (Predicted), the last most informative standard comprising the predicting sequence (n-1) and random preceding standards (Standard); for the triangles (A) and faces (B) sessions in AS subjects and controls. Vertical dotted lines indicate time of stimulus presentation onset. (Note that the grand averages for n-2 and n-3 overlap the signal of the grand average for random standards, and are thus not displayed, for the purpose of clarity of the figure). (C) Topographical maps of the peak P3b amplitudes of predicted (P), random (R) targets and the last most-informative stimulus of the predictive sequence (n-1) across groups and sessions.

Table 2
Mean P3b amplitudes at electrode sites CPz and AFz, for sessions consisting of either Faces or Triangles, in subjects with Autism Spectrum Disorders (ASD) and controls.

Condition	Faces ASD	Faces controls	Triangles ASD	Triangles controls
Mean P3b amplitudes at CPz (mean ± SEM μV)				
P	20.2 ± 1.5	25.3 ± 2.1	17.2 ± 1.2	26.2 ± 2.5
R	20 ± 2.5	32.7 ± 3.3	16.1 ± 2.6	27 ± 2.9
n-1	12.9 ± 2.5	21.5 ± 2.9	12.6 ± 1.2	18.2 ± 2.2
n-2	10.1 ± 1.9	15.2 ± 2.1	8.3 ± 1.2	12.1 ± 1.5
n-3	9.7 ± 1.7	13.6 ± 1.6	8.6 ± 1.1	13.0 ± 1.6
S	8.6 ± 1.5	12.0 ± 1.3	8.0 ± 1.2	11.4 ± 1.3
Mean P3b amplitudes at AFz (mean ± SEM μV)				
P	13.7 ± 2.2	17.6 ± 1.6	11.7 ± 1.5	16.8 ± 1.8
R	12.8 ± 1.7	21.7 ± 2.3	11.1 ± 2.0	15.8 ± 1.8
n-1	10.0 ± 2	15.0 ± 2.2	9.7 ± 1.0	12.0 ± 1.5
n-2	8.8 ± 2.2	10.7 ± 1.7	5.8 ± 1.1	7.6 ± 1.2
n-3	7.4 ± 1.4	10.1 ± 1.3	6.7 ±1.2	9.3 ± 1.2
S	6.7 ± 1.4	9.2 ± 1.0	5.9 ± 1.0	8.0 ± 0.8

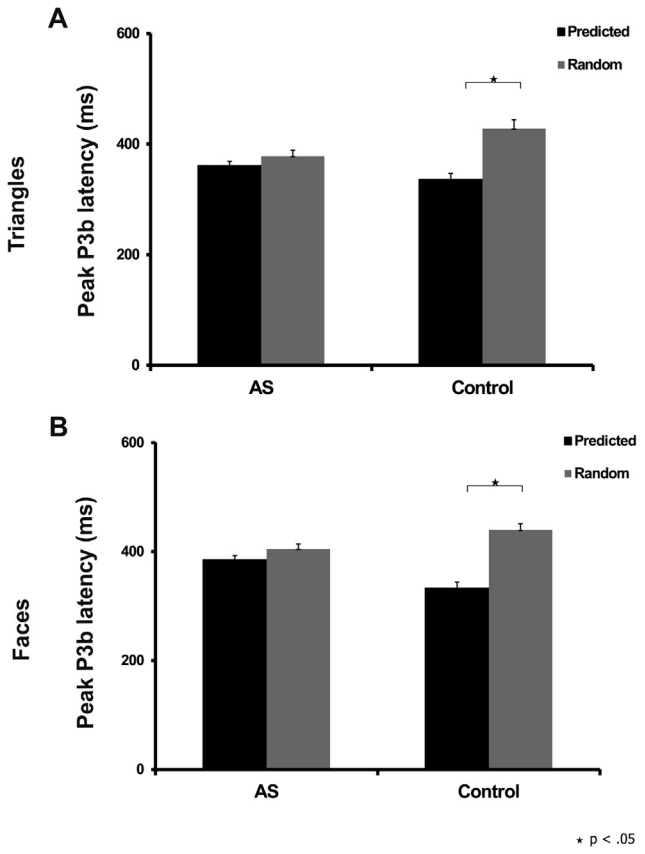

Fig. 4. Peak P3b latencies at electrode site CPz, for predicted and random targets, in the triangles (A) and faces (B) sessions, for AS subjects and controls. Significant differences ($p < .05$) are highlighted with a star. Bars = SEM.

ferent statistical comparisons. We found significant group differences for K values 8 – 13 ($p \leq 0.038$, see Fig. 5A), and using AUC values (mean AUC = 2.02 ± 0.05 and 2.20 ± 0.05, for AS and controls, respectively, p = .024). In addition, NBS showed that compared with ASD subjects, controls have stronger connections between frontal and parietal regions during the processing of random targets in the theta frequency range (see Fig. 5B).

In the faces session we found significantly lower C, and L values for predicted and random targets in the theta frequency band, in ASD compared to control subjects. These findings were corroborated using three different statistical comparisons. For predicted targets we found significant group differences of C for K values 9.5–14, 15 ($p \leq 0.046$, see Fig. 6A), and using AUC values (mean AUC = 2.05 ± 0.04 and 2.19 ± 0.05, for AS and controls, respectively, p = .033). L values also showed significant group differences, during processing of predicted targets, for K values 8.5–15 ($p \leq 0.026$, see Fig. 6C), and using AUC values (mean AUC = 14.01 ± 0.04 and 14.24 ± 0.07, for ASD and controls, respectively, p = .004). For random targets we found significant group differences of C for K values 8–15 ($p \leq 0.016$, see Fig. 6B), and using AUC values (mean AUC = 2.08 ± 0.05 and 2.34 ± 0.05, for ASD and controls, respectively, p = .002). L values also showed significant group differences, during processing of random targets, for K values 9.5–11, 12–15 ($p \leq 0.024$, see Fig. 6D), and using AUC values (mean AUC = 14.06 ± 0.06 and 14.26 ± 0.05, for ASD and controls, respectively, p = .005). In addition, NBS showed that, compared with ASD subjects, controls have stronger connections between frontal, central and parietal regions during the processing of predicted (see Fig. 6E) and random targets (see Fig. 6F), in the theta frequency range.

3.5. Correlations

In order to determine the association between the main behavioral and electrophysiological findings, and the clinical measures in the ASD subjects, we correlated the ADOS scores with the following variables in each session: RT of predicted and random targets, the RT difference (between the two target conditions), the peak P3b latencies for predicted and random targets, the P3b latency shift, peak P3b amplitudes of the targets and the predictive sequence, and AUC values of C and L. After a correction for multiple comparisons, we observed no significant correlations between the ADOS scores and the behavioral, ERP or functional connectivity measures.

4. Discussion

Our findings demonstrated altered processing of predictive contextual information in ASD subjects. Thus, compared to controls, ASD subjects showed prolonged reaction times for predicted targets, attenuated P3b amplitudes for targets and the last-most informative stimulus of the predictive sequence, and an absence of the electrophysiological facilitation in the detection of predictable versus random targets. Furthermore, we found that some of these alterations were more pronounced for stimuli that consisted of cartoon faces representing emotions, compared to abstract triangles. In addition, ASD subjects demonstrated functional connectivity alterations of graph network parameters within the theta frequency band during the processing of random targets across both sessions, as well as for predicted targets in the faces session.

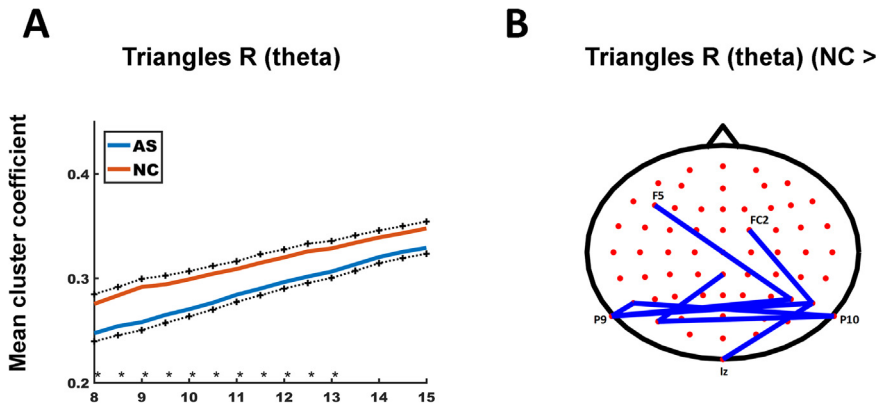

Fig. 5. Mean cluster coefficient for the triangles session as a function of degree K, in the theta frequency band, for random targets (A) in AS and control subjects (NC). Significant group differences ($p < .05$) are highlighted with a star. Dotted lines = SEM. (B) Topographic differences between the groups (NC – AS) for random targets during the triangles session (lines represent stronger connections in controls compared with AS subjects). Relevant electrode sites are highlighted in the topographic map.

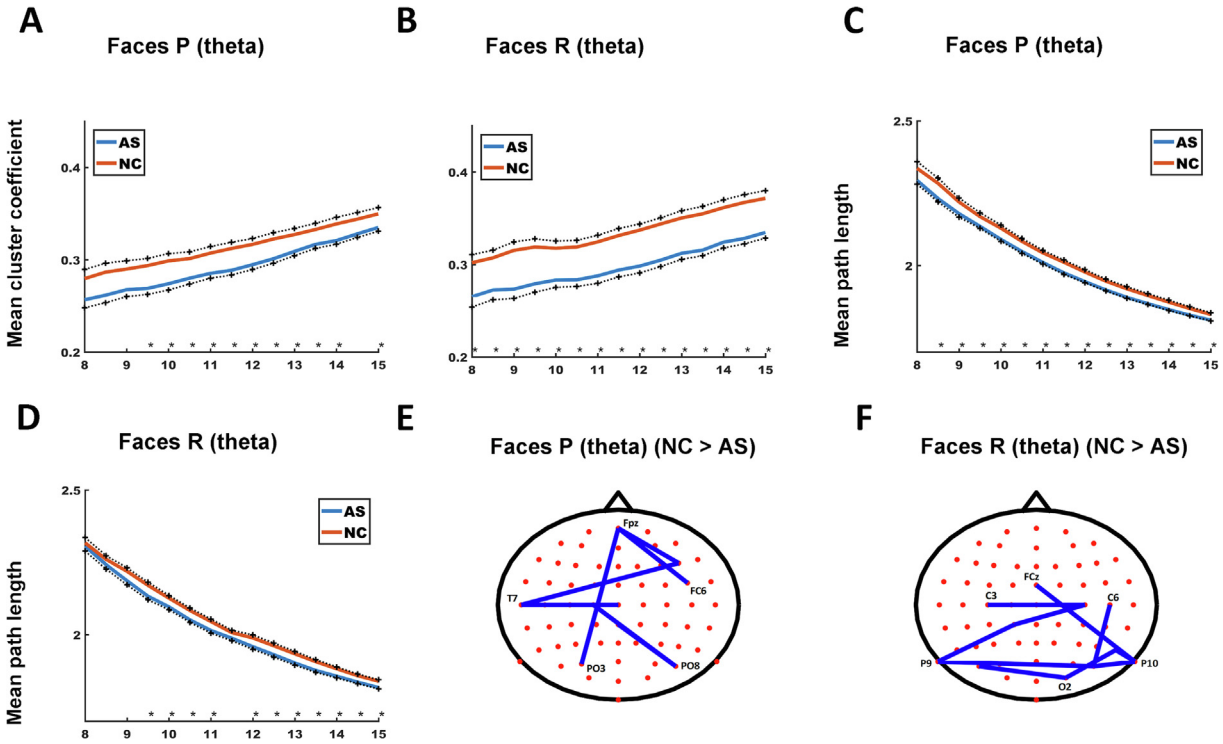

Fig. 6. Mean cluster coefficient for the faces session as a function of degree K, in the theta frequency band, for (A) predicted and (B) random targets in AS and control subjects (NC). Mean path length as a function of degree K, in the theta frequency band, for (C) predicted and (D) random targets in AS and control subjects (NC). Significant group differences ($p < .05$) are highlighted with a star. Dotted lines = SEM. Topographic differences between the groups (NC – AS) for predicted (E) and random (F) targets during the faces session (lines represent stronger connections in controls compared with AS subjects). Relevant electrode sites are highlighted in each topographic map.

4.1. Behavioral facilitation across the sessions

Both ASD and control subjects showed shorter reaction times for predicted versus random targets across the sessions. However, reaction times for predicted targets were prolonged in ASD subjects in both sessions, while there were no significant group differences for random targets. These results suggest that although both groups showed a behavioral facilitation in the detection of predicted versus random targets, this benefit was greater in controls, specifically due to faster RTs of predicted targets. Furthermore, we found that the magnitude of this facilitation (the RT difference) was larger in controls compared to ASD subjects in the faces session, but did not reach statistical significance in the triangles session, suggesting that processing of emotional faces was more affected in ASD.

4.2. P3b effects in ASD subjects

We demonstrated three main findings using the P3b component, to evaluate predictive contextual effects on target detection, in ASD and control subjects. First, ASD subjects showed attenuated P3b amplitudes of task-relevant stimuli, but not of standard stimuli. Thus, in the triangles session, P3b amplitude attenuations in ASD were observed for the last-most informative stimulus of the predictive sequence (n-1), and for predicted and random targets, while in the faces session these attenuations were observed for

n-1 and random targets. These P3b amplitude attenuations suggest a reduced ability to allocate attention to these stimuli compared to controls (Johnson, 1986; Kok, 2001). Reduced P3b amplitudes have been reported in ASD (Courchesne et al., 1989; Ciesielski et al., 1990; Salmond et al., 2007; Duncan et al., 2009; Maekawa et al., 2011), however, in the current study these attenuations were specific to task-relevant stimuli (especially to n-1 in both sessions). Thus, our findings suggest that attentional selection was specifically affected in ASD when the task required a higher degree of cognitive control, rather than being a generalized effect. This is in line with studies in ASD showing impaired processing of complex information (O'Hearn et al., 2008), specifically when greater demands on working memory are made (Barendse et al., 2013), and when tasks rely on internal control and self initiated effortful information processing (Wang et al., 2006; Williams et al., 2014). It has been suggested that ASD is associated with a selective difficulty in the storage of visual information in working memory (Williams et al., 2014). This is of relevance for the current study, where in order to perform the task, subjects were required to detect the stimuli comprising of the predictive sequence, extract the predictive information, manipulate and translate this information into a self-guided cue, and finally utilize this information to facilitate detection of predictable targets (Fogelson, 2015). Thus, the observed P3b amplitude attenuations for the predictive sequence in ASD subjects across both sessions may be due to working memory deficits associated with maintenance and manipulation of predictive contextual information.

Second, during the triangles session, we found that in both ASD and control subjects, significantly larger P3b amplitudes were generated by predicted targets, random targets, and the last most-informative stimulus of the predictive sequence (n-1) compared with standards, the middle (n-2), and first (n-3) least-informative stimuli of the predicting sequence. These findings are in line with earlier studies showing increases in peak P3b amplitudes, with increasing task-relevance (Sawaki and Katayama, 2006; Fogelson et al., 2009a,b, Fogelson, 2015). P3b amplitudes for n-1 have been shown to indicate how much attention was allocated to the sequence and whether it was detected (Johnson, 1986; Fogelson et al., 2009a,b; Fogelson, 2015). On the other hand, during the faces session, peak P3b amplitudes were larger for predicted and random targets compared with n-2, n-3 and standards in ASD and controls. However only controls showed larger P3b amplitudes for n-1 compared with n-2, n-3 and standards, while ASD subjects showed no significant P3b amplitude differences between n-1 and the other standards, during the faces session. These, findings suggest that when the stimuli consisted of emotional faces, the predictive sequence did not become a secondary target for ASD subjects.

Third, we found that in control subjects peak P3b latencies were shorter for predicted compared to random targets across both sessions, suggesting a facilitation in the processing speed of predicted targets (Kutas et al., 1977; Duncan-Johnson, 1981; McCarthy and Donchin, 1981; Duncan-Johnson and Donchin, 1982; Hillyard and Kutas, 1983; Fogelson et al., 2009a,b). However, in ASD subjects this facilitation was not observed in either session, showing non-significant P3b latency differences between the two target conditions across the sessions. These findings suggest a deficit in the differential processing of predicted versus target conditions, and of a limited ability to utilize the predictive information provided by the predictive sequence in order to facilitate detection of predictable targets (Fogelson, 2015) in ASD subjects.

Our findings support evidence of contextual deficits in ASD, in language (Wang et al., 2006; Beversdorf et al., 2007; Loukusa et al., 2007) and of difficulties processing relational contextual information (Maister et al., 2013) and the order of items (Poirier et al., 2011). In addition, our findings support the proposition of prediction deficits in ASD (Lawson et al., 2014). Other studies examining prediction effects in subjects with ASD have demonstrated altered processing of randomized sequences, while processing of predictable sequences remained intact (Johnson et al., 2007; Gonzalez-Gadea et al., 2015; Thillay et al., 2016). ASD has also been associated with a specific sensitivity to higher degrees of uncertainty during a task (Denisova et al., 2016). In contrast, our behavioural and ERP findings both showed specific alterations in the processing and utilization of predictive contextual information, in ASD compared to control subjects. These contrasting results may have been due the relatively lower degree of complexity of the predictive sequences that were utilized in previous studies, where either repetitions of the same stimulus were used for the predictive sequences (Johnson et al., 2007; Gonzalez-Gadea et al., 2015), or stimuli were presented at the centre of the field of vision (Johnson et al., 2007; Thillay et al, 2016). In the current study, prediction was generated through the introduction of a predictive sequence, consisting of a specific order of three different lateralized stimuli of either triangles or faces. Processing of this type of complex information is more effortful and demanding (O'Hearn et al., 2008; Wang et al., 2006; Barendse et al., 2013; Williams et al., 2014), and may have been more sensitive in the detection of significant group differences that were associated with the processing of the predictive sequence. In previous studies (Fogelson et al., 2011, 2014), using the triangles version of the paradigm, we also showed specific alterations of the electrophysiological indices of contextual processing in other psychiatric disorders. Thus, schizophrenia patients showed deficits in their ability to allocate attention and to utilize the predictive information provided by the predictive sequence (Fogelson et al, 2011), while patients with depression showed reduced decision confidence in the detection of predictive sequences (Fogelson et al., 2014).

In summary, we showed alterations in the processing of predictive contextual information in ASD compared to control subjects, using both behavioural and electrophysiological indices of predictive contextual processing (Fogelson, 2015). Furthermore, these alterations were more pronounced for stimuli consisting of faces representing emotions versus abstract triangles. Our findings suggest a reduced ability of ASD subjects to utilize predictive contextual information, in order to facilitate detection of predicable versus unpredictable targets, compared to controls.

4.3. Functional connectivity in ASD subjects during contextual processing

ASD subjects demonstrated functional connectivity changes compared with controls across both sessions. Thus, ASD subjects demonstrated significantly lower C and L values for the two target conditions, when processing faces, while in the triangles session ASD subjects showed lower C values for random targets, in the theta frequency range. The observed decrease of the graph parameters in ASD subjects, suggest a reduced complexity and a shift towards a more randomised network organization (Watts and Strogatz, 1998, Stam et al., 2007, Bullmore and Sporns, 2009, Stam and van Straaten, 2012). These functional connectivity alterations were specific to task-relevant stimuli associated with target detection. In the faces session these alterations were more extensive as both global and local topological properties were altered in ASD subjects, while during the triangles session we only observed changes of the local network properties. Furthermore, functional connectivity changes in ASD subjects were observed during the processing of random targets across both sessions, while in the faces session these changes were also observed for predicted targets. Our findings support previous resting state EEG (Barttfeld et al., 2011; Peters et al., 2013) and fMRI (Itahashi et al., 2014; Ye et al., 2014) studies, showing reduced C values in ASD subjects. Our results of reduced path lengths in ASD subjects

are in line with several studies (Itahashi et al., 2014; Ye et al., 2014), and in contrast with others showing increased L values (Barttfeld et al., 2011; Peters et al., 2013) in ASD. Importantly, in a previous study using the triangles version of the paradigm in schizophrenia patients (Fogelson et al., 2013), we also observed reduced L values during the processing of task-relevant stimuli (P, R, n-1), suggesting that the randomization of functional connections within networks involved in processing contextual information and target detection may be a common feature of ASD and schizophrenia.

The observed alterations in functional connectivity related to processing of targets were associated with weaker long-range connections between frontal, central and parietal cortical areas in ASD subjects, across both sessions. These findings support evidence of reduced long-range connectivity in ASD (Belmonte et al., 2004; Courchesne and Pierce, 2005; Barttfeld et al., 2011; Urbain et al., 2016). Our findings show that this hypo-connectivity in ASD subjects was specifically observed during the processing of targets and may be associated with functional topological changes within top-down frontal networks (Fuster, 2009; Fogelson et al., 2009a,b; Mesulam, 2012; Fogelson, 2015).

The differences in network properties between ASD and controls were primarily observed in the theta frequency range. Synchronization in this frequency band is thought to be associated with cognitive processes engaging top-down control networks (von Stein and Sarnthein, 2000; Buzsáki and Draguhn, 2004, Wang, 2010), and the frontal-parietal network (Sauseng et al., 2005). Low frequency oscillations have been associated with entrainment of neuronal oscillations to task-relevant events (Lakatos et al., 2008), and with anticipatory mechanisms (Stefanics et al., 2010), in order to facilitate performance. The theta frequency band has been related to attention, processing of internal mental context (von Stein and Sarnthein, 2000; Sauseng et al., 2005), and to the organization of multiple items in working memory (Raghavachari et al., 2001).

4.4. Emotional faces versus abstract triangles

Our findings demonstrated altered processing of predictive contextual information in ASD subjects, across both the sessions. However, the group differences between ASD and controls across the behavioural, ERP and functional connectivity results were more pronounced for stimuli that consisted of cartoon faces portraying different emotions, compared with abstract triangles. Our findings are in line with other studies showing selective deficits in the processing of social stimuli in ASD, specifically of human emotions (Dichter et al., 2009; Khan et al., 2013; Weisberg et al., 2014). Thus, it has been proposed that subjects with ASD use feature-based strategies, associated with object perception, during face perception (Koshino et al., 2008; Khan et al., 2013; Weisberg et al., 2014). In addition, faces not only represent more complex visual patterns but also have social meaning, both of which are affected in ASD, requiring the recruitment of effortful cognitive control (Koshino et al., 2008; Dichter et al., 2009; Khan et al., 2013; Weisberg et al., 2014). In the current study, difficulty levels of the task may have been increased during the faces session, although this seems to be unlikely since accuracy levels were comparable across the sessions. However, it is of importance to note that unlike earlier studies we used cartoons portraying emotions rather than real human faces. These stimuli may have been less ambiguous and easier to process visually compared to photos of real human faces. Nevertheless we were able to demonstrate that these cartoon images induced more pronounced contextual deficits in ASD subjects, compared to abstract triangles. Thus, the reduced ability to utilize social predictive contextual information in ASD during the faces session, was likely due to difficulties in processing the emotional content of the stimuli. These findings are of specific relevance in the daily life of individuals with ASD, where compromised identification of relevant social cues may explain difficulties with social interactions (Happé and Frith, 1996).

Finally, we would like to point out the limitations of our experimental approach in the current study. First, the sample size used in the current study was small and findings need to be replicated in a larger sample, although other similar studies used comparable size samples (Ciesielski et al., 1990; Wong et al., 2008; Barttfeld et al., 2011; Maekawa et al., 2011; Peters et al., 2013; Matlis et al., 2015). Second, the effect of medication needs to be addressed since eight out of the fifteen ASD subjects were taking medication on a daily basis. Thus although medication effects cannot be precluded in the present study, the fact that ASD subjects displayed electrophysiological and functional connectivity changes that were specific to particular stimuli and that were more pronounced for emotional faces, suggests that these changes are likely related to the disorder, although the findings did not show significant correlations with the clinical scores. In addition, accuracy values were comparable across subjects, suggesting that the patients were alert during the performance of the task. Furthermore, we did not observe significant differences between medicated and non-medicated ASD subjects for the main findings of the study. Thus, although we cannot preclude medication effects, we propose that the observed changes are mainly due to ASD rather than an effect of the administered medication. However, it would be of importance to replicate the present findings in a cohort of unmedicated ASD subjects. Third, with regards to the functional connectivity analysis, although we used current source density measures (with high spatial resolution) to minimize spurious synchronization and to corroborate the connectivity findings, these should be interpreted with caution, since in functional connectivity studies of EEG volume conduction effects must be taken into account as a potential limitation.

In conclusion, the findings of the current study show altered processing of predictive contextual information in ASD subjects, showing a reduced ability to utilize this information in order to facilitate detection of predicable targets. We further showed functional connectivity changes in ASD subjects during the processing of targets that were associated with weaker connections within fronto-parietal networks. These alterations were more pronounced for stimuli consisting of faces representing emotions versus abstract triangles. Our findings may be of relevance for establishing objective mechanism-based electrophysiological markers for specific cognitive alterations in ASD, having potential implications for more efficient selection of treatment and rehabilitation.

Conflict of interest

The authors have no conflict of interest.

Acknowledgments

This work was supported by grants from the Spanish Ministry of Science and Innovation (PSI2015-65894-R to N.F), the Ramón y Cajal national fellowship program (to N.F) and by the NSFC (61473062 to L.L). We thank all the participants in the study and to Marisol Garcia Penalta from the "ASPERGA" association for help in recruiting AS subjects.

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