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Adeline Lacroix, Sylvain Harquel, Leonardo S Barbosa, Klara Kovarski, Marta I Garrido, et al.. Reduced spatial frequency differentiation and sex-related specificities in fearful face detection in autism: Insights from EEG and the predictive brain model. *Autism Research*, 2024, 17 (9), pp.1778-1795. 10.1002/aur.3209 . hal-04693490

**HAL Id: hal-04693490**

**<https://hal.science/hal-04693490v1>**


Submitted on 10 Sep 2024

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## RESEARCH ARTICLE

# Reduced spatial frequency differentiation and sex-related specificities in fearful face detection in autism: Insights from EEG and the predictive brain model

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## Funding information

The French Ministry of Higher Education, Research, and Innovation (France); MIAI @ Grenoble Alpes, Grant/Award Number: ANR-19-P3IA-0003; France Life Imaging Network, Grant/Award Number: ANR-11-INBS-0006; CBH Graduate School, Grant/Award Number: ANR-17-EURE-003; IDEX Investissement d'Avenir of EDISCE Doctoral School; GIS autism et troubles du neurodéveloppement

## Abstract

Face processing relies on predictive processes driven by low spatial frequencies (LSF) that convey coarse information prior to fine information conveyed by high spatial frequencies. However, autistic individuals might have atypical predictive processes, contributing to facial processing difficulties. This may be more normalized in autistic females, who often exhibit better socio-communicational abilities than males. We hypothesized that autistic females would display a more typical coarse-to-fine processing for socio-emotional stimuli compared to autistic males. To test this hypothesis, we asked adult participants (44 autistic, 51 non-autistic) to detect fearful faces among neutral faces, filtered in two orders: from coarse-to-fine (CtF) and from fine-to-coarse (FtC). Results show lower  $d'$  values and longer reaction times for fearful detection in autism compared to non-autistic (NA) individuals, regardless of the filtering order. Both groups presented shorter P100 latency after CtF compared to FtC, and larger amplitude for N170 after FtC compared to CtF. However, autistic participants presented a reduced difference in source activity between CtF and FtC in the fusiform. There was also a more spatially spread activation pattern in autistic females compared to NA females. Finally, females had faster P100 and N170 latencies, as well as larger occipital activation for FtC sequences than males, irrespective of the group. Overall, the results do not suggest impaired predictive processes from LSF in autism despite behavioral differences in fear detection. However, they do indicate reduced brain modulation by spatial frequency in autism. In addition, the findings

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highlight sex differences that warrant consideration in understanding autistic females.

### Lay Summary

Using EEG, the study investigated whether autistic individuals exhibit atypical prediction from coarse information during face processing compared to non-autistic (NA) individuals. Additionally, it examined whether autistic females demonstrate a more typical neurophysiological response to faces than males, potentially contributing to their superior socio-communicational abilities. The results revealed a reduced differentiation in the processing of coarse and fine information in autism compared to NA individuals. Furthermore, they unveiled a distinctive profile among autistic females, encompassing characteristics of both autistic males and NA females. These findings underscore the importance of considering neurophysiological sex differences in autism to gain a deeper understanding of autistic females.

### KEYWORDS

autism, EEG, emotion recognition, fusiform, sex differences, spatial frequencies

## BACKGROUND

Autistic individuals are characterized by the coexistence of socio-communicational difficulties, distinctive special interests, repetitive behaviors, and sensory specificities (American Psychiatric Association, 2013). However, recent research has uncovered enhanced socio-communicational abilities in autistic females compared to autistic males (for a review and meta-analysis, see Wood-Downie et al., 2021), that might help to camouflage their autism (Cook et al., 2021). The unique profile of autistic females potentially contributes to their delayed or missed diagnoses (Belcher et al., 2021; Gesi et al., 2021; Hull & Mandy, 2017), highlighting the importance of better understanding these differences. They might be explained by different phenotypic and brain trajectories, under the influence of genes, sex hormones, and education (Walsh et al., 2021; Walsh et al., 2023).

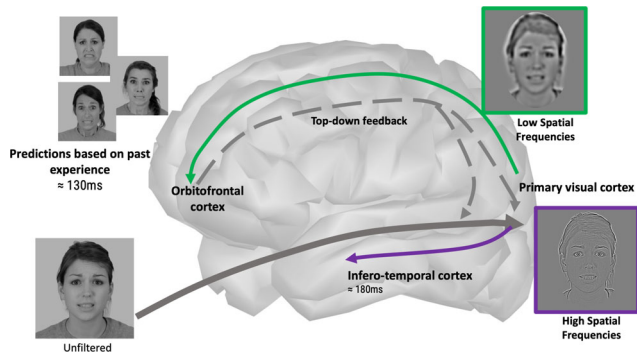
Critical to socio-communicational abilities is face processing and emotion recognition, both of which are atypical in autism and rely on social and sensory processing. The P100 and the N170 ERPs are two components with functional significance in the context of face processing. The P100, occurring around 100 ms post-stimulus, has generators located in the extrastriate areas of the occipital lobe, as well as in temporal regions such as the fusiform gyrus, crucially involved in face processing (Herrmann et al., 2005). The P100 is typically associated with the initial stages of sensory processing, including the detection of basic visual features and the allocation of attentional resources. However, electroencephalography (EEG) and magnetoencephalography (MEG) studies have demonstrated that responses in face-selective regions, such as the lateral occipital cortex, the fusiform gyrus, the inferior parietal cortex, and the superior temporal sulcus, can also discriminate between basic

expressions from as early as 100 ms post-stimulus (Dima et al., 2018; Muukkonen et al., 2020; Zhang et al., 2023). Nonetheless, the N170, peaking between 130 and 200 ms after stimulus onset, is considered the major face-responsive component and is thought to reflect holistic processing and higher-level identity representations (Bentin et al., 1996; Hinojosa et al., 2015; Muukkonen et al., 2020). Its neural generators have been identified in the fusiform gyrus and the superior temporal sulcus (Hinojosa et al., 2015; Itier & Taylor, 2004), which is particularly involved in interpreting emotional expression on faces (Iidaka, 2014).

In non-autistic (NA) individuals, infant and adult females present advantages in emotion recognition compared to males (for reviews and meta-analyses see, Forni-Santos & Osório, 2015; Kret & De Gelder, 2012; McClure, 2000; Proverbio, 2021). In addition, adult females also show larger (Lee et al., 2017; Pfabigan et al., 2014; Proverbio et al., 2006a, 2006b) or faster (Nowparast Rostami et al., 2020; Proverbio et al., 2006b; Ran, 2018; Ran et al., 2014; Sun et al., 2017) electrophysiological responses to faces.

Nevertheless, limited research has explored face processing differences between autistic males and females, a gap that could contribute to understanding socio-communicational sex differences in autism. No differences were found between autistic women and men in the reading the mind in the eyes test, while correct response rates were higher in NA women than men (Baron-Cohen et al., 2015). In contrast, autistic females, compared to autistic males, were faster in emotion recognition in context as shown in adult participants (Lacroix, Dutheil, et al., 2022) and presented greater attention to faces in both children and adults (Del Bianco et al., 2022; Harrop et al., 2018, 2020; Harrop et al., 2019).

At the neurophysiological level, a study on autistic children showed a more positive P100 response to faces,



**FIGURE 1** Bar's model applied to emotional face stimuli (inspired from Lacroix et al., 2024). Low spatial frequencies (LSF) would be quickly extracted and sent to the orbitofrontal cortex (OFC), triggering predictive processes. Then, predictions would be top-down projected to infero-temporal and posterior areas to facilitate the integration of high spatial frequencies (HSF) and face recognition.

compared to houses, in autistic boys (but not girls), who also displayed shorter N170 latencies than autistic girls across conditions (house/faces, upright/inverted) (Coffman et al., 2015). In contrast, a study on adults revealed that Mismatch Response, P100, and N170 responses to faces in autistic females were intermediate between those of autistic males and NA (Lacroix et al., 2024). While the opposite sex differences between children and adults can potentially be explained by increased compensation mechanisms in females over time, longitudinal studies would be required to investigate sex differences in developmental trajectories.

Overall, considering behavioral and neuroimaging data, the literature suggests that face processing in autistic females, compared to autistic males, is closer to NA individuals, although findings can be contradictory. Additionally, there is a lack of electrophysiological data on attentional face processing, particularly during emotion recognition. To address this gap and gain a deeper understanding of the unique profile of autistic females during facial emotion processing, we designed a study based on the predictive brain theory (Bar et al., 2006; Lacroix et al., 2024). This theory suggests that early visual processing involves rapid extraction of low spatial frequencies (LSF), conveying global information and supporting the extraction of configural cues for face recognition (Goffaux et al., 2005). LSF are transmitted from primary visual areas to frontal regions to feed association-based predictions (around 130 ms after stimulus onset). These predictions guide the integration of details, carried by high spatial frequencies (HSF), through feedback to posterior and inferotemporal areas (Kauffmann et al., 2015; Peyrin et al., 2010) (Figure 1). In NA adults, this coarse-to-fine (CtF) processing of faces is supported by EEG findings, showing a predominance of LSF processing in the earliest stages, followed by a predominance of HSF processing. This is evidenced by faster or larger P100 responses for LSF (Jeantet

et al., 2019; Mares et al., 2018; Nakashima et al., 2008; Obayashi et al., 2009; Peters & Kemner, 2017; Tian et al., 2018; Vlamings et al., 2009), despite the existence of contradictory results (e.g., Goffaux et al., 2003). On the contrary, the N170 component tends to be larger for HSF (Jeantet et al., 2019; Lacroix, Harquel, et al., 2022; Nakashima et al., 2008; Obayashi et al., 2009; Tian et al., 2018), even if inconsistencies have also been observed (Goffaux et al., 2003; Halit et al., 2006; Holmes et al., 2005). However, the N170 is usually found slower for HSF than LSF (Halit et al., 2006; Obayashi et al., 2009; Peters & Kemner, 2017; Vlamings et al., 2009; but Jeantet et al., 2019).

Autistic individuals are characterized by more detail-oriented visual processing (Kéïta et al., 2014; Mottron et al., 2006; Mottron & Burack, 2001), a trait also observed during face processing (Boeschoten, Kenemans, Engeland, et al., 2007; Deruelle et al., 2004; Kikuchi et al., 2013; Kovarski et al., 2019; Vlamings et al., 2010). However, it is unclear if autistic individuals exhibit enhanced HSF processing, as revealed in children by behavioral studies (Deruelle et al., 2004; Kikuchi et al., 2013) and EEG studies (Vlamings et al., 2010), or reduced LSF processing, as shown in adults by behavioral studies (Kätsyri et al., 2008). Notably, some behavioral studies in adults did not find differences between autistic and neurotypical individuals in processing LSF and HSF in faces (Lacroix et al., 2021; Rondan & Deruelle, 2004; Vanmarcke & Wagemans, 2017) and some studies suggested that the difference between autistic and NA individuals might actually come from a reduced modulation of brain activity by spatial frequencies in autism, as evidenced by EEG in children (Boeschoten, Kenemans, Engeland, & Kemner, 2007) and adults (Lacroix et al., 2024). Interestingly, this reduced brain modulation varied by sex, with autistic females showing an electrophysiological response to face more similar to NA adults as compared to autistic males during a mismatch paradigm with spatially filtered faces (Lacroix et al., 2024), investigating specifically predictive processes. This study also revealed similarities between autistic and NA females in the right fusiform activation during the mismatch response that were not present in autistic males. These results suggest a potential closeness in predictive processes of autistic females to those of NA individuals, although this has not been investigated during attentional face processing tasks, such as emotion detection.

In the current experiment, we forced CtF versus fine-to-coarse (FtC) processing by presenting neutral and fearful faces within sequences of images filtered from LSF to HSF (CtF) or vice versa (FtC). EEG activity of autistic and NA individuals was recorded while participants had to detect fearful faces. In line with the CtF hypothesis, NA individuals were expected to exhibit an earlier and larger P100 for CtF compared to FtC sequences, and a larger N170 for FtC compared to CtF

sequences. However, we hypothesized that decreased predictive processes from LSF, due to reduced modulation of brain activity by spatial frequencies in autism, would manifest as a reduced difference in the P100 response between CtF and FtC sequences compared to NA. Importantly, we also hypothesized better predictive processes in autistic females than in males, characterized by differences between CtF and FtC situated halfway between autistic males and NA individuals. In addition to our ERP hypotheses, we explored sources and behavioral responses. Bar's predictive brain model would predict higher activity for CtF than FtC sequences in the orbitofrontal cortex, which would be reduced in autism. Based on Lacroix et al. (2024), we also expected to find reduced spatial frequency differentiation between autistic and NA participants in the fusiform gyrus, possibly more pronounced in autistic males than females. Finally, we expected this reduced differentiation to be observable at the behavioral level, with autistic individuals showing a reduced difference in response time (RT) between CtF and FtC sequences compared to NA participants, who were expected to respond faster to CtF sequences.

## METHOD

### Participants

Forty-four autistic participants (Mean age =  $29 \pm 8$ ) participated in the study. They received a diagnosis based on DSM criteria (American Psychiatric Association, 2000, 2013) from a multidisciplinary clinical team before the study. Among them, 15 autistic participants reported psychiatric/neurodevelopmental diagnoses (e.g., anxiety, depression, dyslexia) and 10 reported medication use. Among 51 NA participants recruited (Mean age =  $30 \pm 7$ ), 2 reported an anxiety diagnosis and were under medication.

All participants completed the autism-spectrum quotient (AQ, Baron-Cohen et al., 2001). Intellectual quotient (IQ), and more particularly verbal and non-verbal abilities, were obtained from the diagnostic records or estimated if missing and for NA participants, using four subtests of the WAIS-IV (Vocabulary, Similarities, Block Design, and Matrix) (Grégoire & Schmitt, 2021; Grégoire & Wierzbicki, 2009; Wechsler, 2008). The description of the final sample is summarized in Table 1 and additional information about participants is provided in part 2.1 of Data S1. Autistic participants had lower levels of education than NA, more psychiatric and neurodevelopmental diagnoses, higher AQ scores (all  $p < .001$ ), and autistic females were diagnosed later than autistic males ( $p = 0.015$ ).

Participants received pre-study information, provided written informed consent, and received monetary compensation post-study. The Ethics Committee (Comité de Protection des Personnes Ile de France 1—IRB/IORG:

IORG0009918) approved the study under agreement number 2019A01145-52 and the study was pre-registered on Clinical Trials (<https://clinicaltrials.gov/show/NCT04069676>).

### Stimuli and procedures

Each experimental session contained 20 faces from the Chicago Face Database (Ma et al., 2015) (10 females and 10 males)  $\times$  2 emotions (fear and neutral)  $\times$  2 orders (coarse-to-fine/CtF—from LSF to HSF; fine-to-coarse/FtC—from HSF to LSF), repeated 3 times with different randomization (= 240 trials). Using MATLAB (MathWorks, Natick, MA), stimuli were filtered according to four band-pass filters with central frequencies of 1.04, 1.93, 3.72, 7.31 cycles per degree, and normalized to obtain a mean luminance of  $0.1 \text{ cd/m}^2$ . Task and frequencies were determined based on literature and pre-tests, detailed in part 1 of Data S1. Stimuli ( $768 \times 768$  pixels image/ $350$  pixels for the face width; 256-levels grayscale) were presented centrally on a CRT monitor (75 Hz refresh rate,  $1280 \times 1024$  pixels resolution) at a viewing distance of 87 cm. Trials started with a 1500 ms fixation dot, followed by filtered stimuli (25 ms each, 100 ms sequence) and a 25 ms mask. Participants were asked for fast and accurate fear detection within a 2000 ms limit, focusing on the fixation dot and blinking only between trials. Refer to Figure 2 for a trial schematic. Accuracy and RT were recorded.

### EEG data

#### EEG recording

EEG recordings were performed at the IRMaGe neurophysiology facility (Grenoble, France). Horizontal and vertical electrooculography (EOG) activity (hEOG and vEOG, respectively) was recorded using four electrodes placed at the left and right outer canthi of the eyes, and above and below the left eye, with the ground electrode at the left base of the neck. EEG recording utilized BrainAmp amplifiers and EasyCaps (Brain Products GmbH, Germany) with 96 active electrodes placed following the 10–5 standard system. Electrode impedance was maintained below  $25 \text{ k}\Omega$  and the signal was sampled at 1000 Hz (using anti-aliasing filtering tuned automatically by the system), with no additional filtering. FPz served as the ground electrode, and FCz as the reference.

#### EEG preprocessing

EEG preprocessing utilized Brainstorm software (Tadel et al., 2011) (<http://neuroimage.usc.edu/brainstorm>) and

**TABLE 1** Mean value, standard deviation and range for age, education, visual acuity (logMAR) and IQ (FSIQ, VIQ, PIQ) and AQ scores as well as percentage of participants with a diagnosis other than autism for each group, and group comparison.

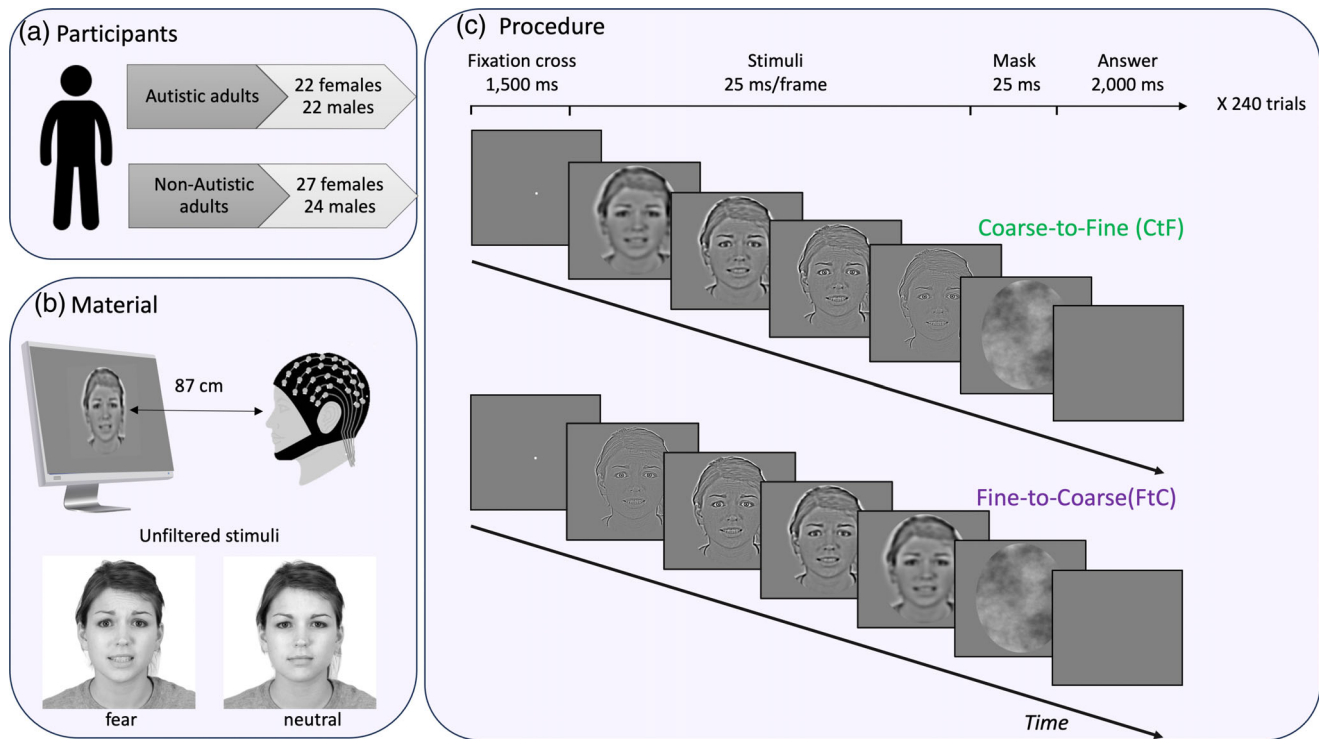
	Autistic F ( <i>N</i> = 22)	Autistic M ( <i>N</i> = 22)	NA F ( <i>N</i> = 27)	NA M ( <i>N</i> = 24)	<i>p</i> value
Age					0.721
Mean (SD)	30.4 (8.3)	28.3 (8.8)	30.7 (8.4)	29.5 (5.2)	
Range	18.4–44.2	18.1–46.0	19.5–46.1	21.2–43.0	
Education					< 0.001
Mean (SD)	14.4 (2.3)	13.1 (1.5)	16.2 (1.8)	15.6 (2.4)	
Range	11.0–20.0	10.0–16.0	14.0–20.0	11.0–20.0	
logMAR					0.974
Mean (SD)	−0.1 (0.1)	−0.1 (0.2)	−0.1 (0.1)	−0.1 (0.1)	
Range	−0.3–0.2	−1.0–0.2	−0.3–0.1	−0.3–0.1	
FSIQ					0.844
N-Miss	0	0	0	1	
Mean (SD)	117.8 (13.8)	115.4 (13.9)	118.6 (13.4)	116.9 (10.0)	
Range	92.0–149.0	87.0–136.0	92.0–147.0	100.0–135.0	
PIQ					0.958
N-miss	0	0	0	1	
Mean (SD)	108.0 (14.4)	107.8 (17.2)	108.9 (14.8)	106.6 (11.5)	
Range	84.0–136.0	64.0–140.0	82.0–140.0	80.0–134.0	
VIQ					0.879
N-miss	0	0	0	1	
Mean (SD)	125.0 (11.4)	122.9 (9.7)	124.7 (12.3)	123.2 (10.2)	
Range	100.0–146.0	103.0–141.0	98.0–147.0	100.0–144.0	
AQ					< 0.001
Mean (SD)	36.9 (4.1)	32.4 (8.5)	15.0 (8.3)	17.0 (5.6)	
Range	30.0–44.0	13.0–44.0	3.0–32.0	9.0–28.0	
PsyNeuroDiag					< 0.001
No	12 (54.5%)	17 (77.3%)	26 (96.3%)	23 (95.8%)	
Yes	10 (45.5%)	5 (22.7%)	1 (3.7%)	1 (4.2%)	
DiagAge					0.013
Mean (SD)	28.0 (8.5)	21.0 (9.4)			
Range	17.0–42.0	5.0–38.0			

Abbreviations: AQ, autism quotient; DiagAge, Age at diagnosis; FSIQ, full scale intelligence quotient; NA, non autistic; PIQ, performance intelligence quotient; PsyNeuroDiag, psychiatric or other neurodevelopmental diagnoses than autism (Yes/No); VIQ, verbal intelligence quotient.

MATLAB scripts (The MathWorks Inc.). Channels with a flat signal or deviant temporal dynamics of Welch's power spectrum were excluded. High-frequency periods (muscular artifacts) were removed and average reference was used for re-referencing the signal. Eye movements were targeted and corrected using signal-space projection (SSP), with visual inspection for each participant. The cleaned signal underwent a band-pass filter of 0.1–40 Hz, and trials were epoched from 1500 pre-stimulus to 600 ms post-stimulus, and baseline corrected from −200 to 0 ms. Trials with accidental blinks within −200 to + 600 ms were discarded. Ultimately, 6.5% of trials for NA participants and 6.8% for autistic participants were discarded during preprocessing.

## Event-related potentials

For each condition (CtF and FtC sequences in fear and neutral conditions), trials were averaged by subject, resulting in individual event-related potentials (ERPs), which were visually inspected. The remaining deviant electrodes were discarded and all rejected channels were interpolated using neighboring channels within a maximal distance of 4.0 cm, with weights assigned based on their distance. On average, two channels for NA and three channels for autistic participants were interpolated. In six participants with only 64 recorded electrodes, the 32 missing channels, evenly distributed on the scalp, were also interpolated.



**FIGURE 2** Study method—(a) Participants' characteristics. (b) Material utilized: Computer for stimuli presentation and EEG equipment, along with examples of the stimuli used (pre-filtering). (c) Procedure: example of a trial featuring a fearful face in both the coarse-to-fine condition and in the fine-to-coarse conditions.

## Source reconstruction

Source localization was conducted with Brainstorm and the ICBM152 template with a standard co-registered set of electrode positions. A realistic forward model was computed using the OpenMEEG software (boundary element method), and contained three layers: scalp, skull, and brain. These layers had conductivity ratios of 1, 0.0125 and 1, respectively. The source space was restricted to the cortical surface with 2500 dipoles, and the inversion kernel was computed using the standardized low-resolution brain electromagnetic tomography (sLORETA, Pascual-Marqui, 2002), assuming a SNR of three and unconstrained orientation. Noise covariance was individually computed using baseline activity (−200 to −1 ms).

## Statistics

### Electrode choice for ERP analysis

Electrode choice was guided by both visual inspection of the response and existing literature on ERPs for spatially filtered faces. For the P100 component, the most positive peaks were visually identified at electrodes P8, PO8, and PPO10h. Given that the P100 is typically investigated at occipital (O1/O2) and parieto-occipital (PO7/PO8) sites

(Goffaux et al., 2003; Jeantet et al., 2019; Lacroix, Harquel, et al., 2022; Vlamings et al., 2009), we selected PO7 and PO8 for our analyses. For the N170 component, the most negative peaks were observed at electrodes Oz, OI2h, and O2, with additional negative peaks at parieto-occipital sites (PO8, PO7). Since parieto-occipital sites are more commonly used for N170 analyses (Goffaux et al., 2003; Jeantet et al., 2019; Lacroix, Harquel, et al., 2022; Vlamings et al., 2009), we conducted two sets of analyses: one focusing on the largest peak (Oz) and another on the commonly used electrodes for N170 (PO7, PO8). Peak latencies and amplitudes were semi-automatically extracted from these electrodes using MATLAB scripts over the latency ranges of 60–140 ms for P100 and 130–200 ms for N170, with final checks performed through visual inspection.

### Behavioral and ERPs analyses

Analyses were conducted in R (R Core Team, 2020) and RStudio (RStudio Team, 2019) version 2023.12.1 + 402, using linear mixed models (for  $d'$  scores, ERPs and post-hoc tests on sources) or generalized linear mixed models with an inverse Gaussian function (for RT on correctly detected fearful faces) using *lme4* package (Bates et al., 2015).  $d'$  scores were calculated with the *dprime* function from the *psycho* package (Makowski, 2018).

This sensitivity index corresponds to the  $Z$  value of the hit-rate minus that of the false alarm rate. Models included Group (ASD, NA), sex (female, male), order (CtF, FtC), emotion (Fear Neutral), and hemisphere (right, left; for analyses on PO7 and PO8) as fixed effects; medication and psychiatric and neurodevelopmental diagnosis other than autism were included as covariates. Random effects structures were kept maximal and reduced when the model did not fit (see, Barr et al., 2013). Significant interactions were described using estimated marginal means and 95% confidence interval (Garofalo et al., 2022). Post-hoc pairwise tests were conducted using emmeans (Lenth, 2021), applying Tukey correction for multiple comparisons. Due to the lack of a universally agreed-upon method for calculating standardized effect sizes in mixed models, unstandardized effect sizes are presented (corresponding to the  $\beta$  value, as each factor and covariates correspond to a dichotomous variable contrast-coded with  $-0.5$  and  $0.5$ ), adhering to recommendations for effect size reporting (Rights & Sterba, 2019). Two participants were excluded from behavioral analyses due to data recording failure, but were retained in EEG analyses, as camera monitoring confirmed task engagement, and they exhibited good ERPs responses.

## Sources statistics

Source statistics analyzed differences between order (CtF vs FtC), between group (ASD vs NA), and between sex (females vs males), during fear trials. Statistical analysis, conducted on the norm of each dipole, employed cluster-based permutation tests (“paired” for order differences, and “independent” for group or sex differences) using the `ft_timelockstatistics` (a Fieldtrip function, Oostenveld et al., 2011), with Monte-Carlo and 3000 randomizations. Cluster correction was applied with a significance threshold for sample selection of  $\alpha = 0.05$ . Signal averaging was performed over the two temporal windows of interest (i.e., 60–140 ms and 130–200 ms). The significant threshold for clusters was set to  $p_{\text{cluster}} < 0.05$ . Then, we used the Desikan-Killiany atlas to identify significant regions.

## Correlational analyses

Correlational analyses were conducted for exploratory purposes. We examined the correlations among autistic traits (AQ), diagnostic age (in the autistic group),  $d'$ , the difference in RT between CtF and FtC sequences, and (i) ERPs (P100 and N170) amplitudes and latencies for each order (CtF and FtC) within each group (Autism and NA), and (ii) the difference in average source activity between CtF and FtC sequences within each group. This second correlational analysis was performed for source

activity in cortical areas where a significant difference was observed between autistic and NA individuals. Holm’s method was employed to correct for multiple inferences.

## RESULTS

### Increased reaction time for fear detection in autism is modulated by sex and spatial frequency order

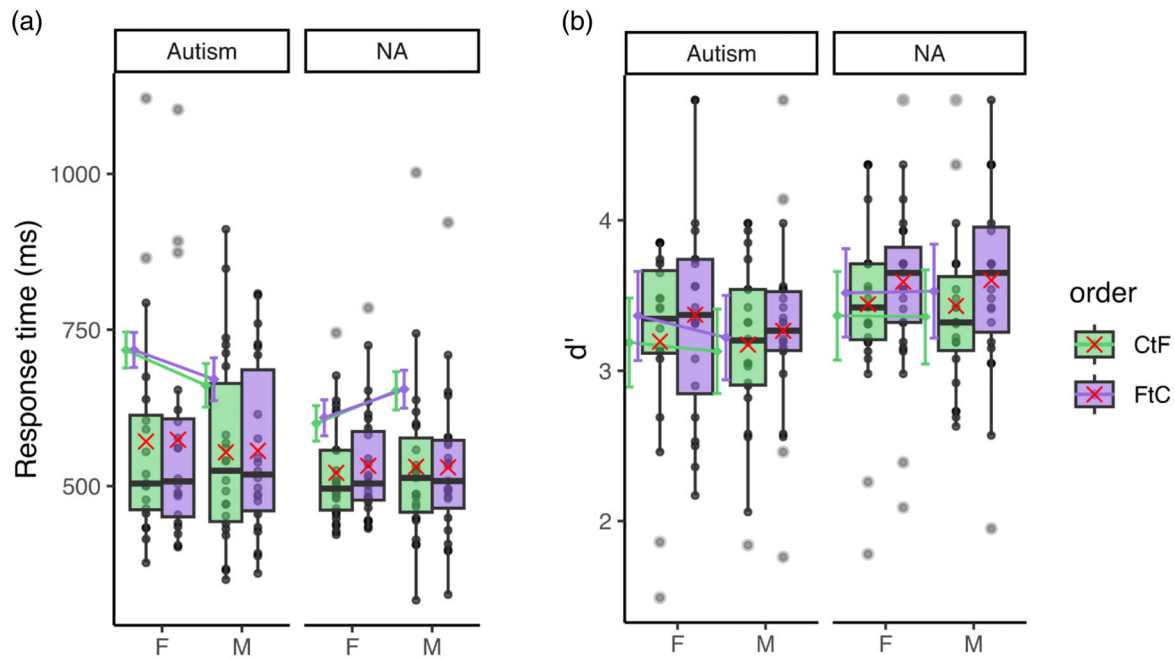
Mean RT and mean  $d'$  for fear detection according to group, sex, and order are represented on Figure 3. Analyses showed slower RT in autism compared to NA ( $\beta = -62.7$ , 95% CI  $[-82.59, -42.81]$ ,  $p < 0.001$ ), and for FtC than CtF sequences ( $\beta = 5.37$ , 95% CI  $[1.34, 9.4]$ ,  $p = 0.009$ ). These main effects were further explained by two and three-way interactions. The interaction between group and sex ( $\beta = 100.53$ , 95% CI  $[58.75, 142.31]$ ,  $p < 0.001$ ) indicated that the delayed RT in autistic females compared to NA females ( $\beta = 112.96$ , 95% CI  $[80.69, 145.24]$ ,  $p < 0.001$ ) was larger than those of autistic males compared to NA males ( $\beta = 12.43$ , 95% CI  $[-30.2, 55.07]$ ,  $p = 0.877$ ) and the interaction between group, sex, and order indicated that this effect was more pronounced in the CtF than FtC sequences (ASD vs. NA for CtF sequences in females:  $\beta = 117.43$ , 95% CI  $[77.41, 157.46]$ ,  $p < 0.001$ , in males  $\beta = 8.88$ , 95% CI  $[-43.07, 60.82]$ ,  $p = 1$ ; and for FtC sequences in females:  $\beta = 108.49$ , 95% CI  $[70.54, 146.45]$ ,  $p < 0.001$  and males:  $\beta = 15.99$ , 95% CI  $[-34.05, 66.04]$ ,  $p = 0.979$ ). In addition, medication delayed RT ( $\beta = 110.02$ , 95% CI  $[90.3, 129.74]$ ,  $p < 0.001$ ) while additional psychiatric or neurodevelopmental diagnoses fastened RT ( $\beta = -26.83$ , 95% CI  $[-47.4, -6.25]$ ,  $p = 0.011$ ). Analyses on  $d'$  showed one main effect of order only, with lower  $d'$  for CtF than FtC sequences ( $\beta = 0.15$ , 95% CI  $[0.04, 0.25]$ ,  $p = 0.007$ ).

### Event-related potentials

#### P100 response is modulated by order, sex, group, and hemisphere

P100 over PO7 and PO8 electrodes for each group, sex, and order as well as topographies are represented on Figure 4. Analyses on P100 latencies showed two main effects: there were earlier P100 for CtF sequences than FtC sequences ( $\beta = 2.5$ , 95% CI  $[0.46, 4.54]$ ,  $p = 0.017$ ), and for females than males ( $\beta = 4.58$ , 95% CI  $[0.59, 8.58]$ ,  $p = 0.025$ ). The main effect of order was further explained by an interaction between order, hemisphere and group ( $\beta = -6.66$ , 95% CI  $[-13.16, -0.16]$ ,  $p = 0.045$ ), indicating that the difference in P100 latencies between CtF and FtC sequences was larger at PO8 than PO7 in autism while it was larger at PO7 than PO8 in NA (CtF vs. FtC





**FIGURE 3** Response time (RT) and  $d'$  for fear detection. The boxplots represent the median RT (a) and  $d'$  (b) for fear detection with the interquartile range and individual data points (gray points are outliers) according to group (Autism = autistic individuals,  $N = 42$ ; NA = non autistic individuals,  $N = 51$ ), sex (F = females; M = males), and order (CtF = coarse-to-fine and FtC = fine-to-coarse). The red cross represents the mean. In addition, the colored points represent the estimated marginal means with their 95% CI.

in autism at PO8  $\beta = -4.81$ , 95% CI  $[-10.71, 1.1]$ ,  $p = 0.205$ ; at PO7:  $\beta = -0.61$ , 95% CI  $[-6.52, 5.29]$ ,  $p = 1$ ; in NA at PO8:  $\beta = -1.06$ , 95% CI  $[-6.55, 4.43]$ ,  $p = 0.999$ ; at PO7:  $\beta = -3.53$ , 95% CI  $[-9.02, 1.97]$ ,  $p = 0.508$ .

Analyses on P100 amplitudes showed a larger P100 at PO8 than PO7 ( $\beta = 0.69$ , 95% CI  $[0.41, 0.97]$ ,  $p < 0.001$ ). This main effect was qualified by an interaction between hemisphere and group ( $\beta = -1.44$ , 95% CI  $[-2.01, -0.88]$ ,  $p < 0.001$ ), showing a larger difference between PO7 and PO8 on P100 amplitudes in autism ( $\beta = -1.41$ , 95% CI  $[-1.95, -0.87]$ ,  $p < 0.001$ ) than in NA, in whom the difference was not significant ( $\beta = 0.03$ , 95% CI  $[-0.47, 0.54]$ ,  $p = 0.999$ ). This effect was also qualified by an interaction between hemisphere, group, and sex, indicating that it was more pronounced in females (PO7 vs. PO8 in autistic females:  $\beta = -1.93$ , 95% CI  $[-2.84, -1.03]$ ,  $p < 0.001$ , NA females:  $\beta = 0.35$ , 95% CI  $[-0.47, 1.17]$ ,  $p = 0.897$ ; autistic males:  $\beta = -0.89$ , 95% CI  $[-1.79, 0.02]$ ,  $p = 0.059$ ; NA males:  $\beta = -0.29$ , 95% CI  $[-1.16, 0.58]$ ,  $p = 0.972$ ).

### N170 response is modulated by order, sex, group, hemisphere, and emotion

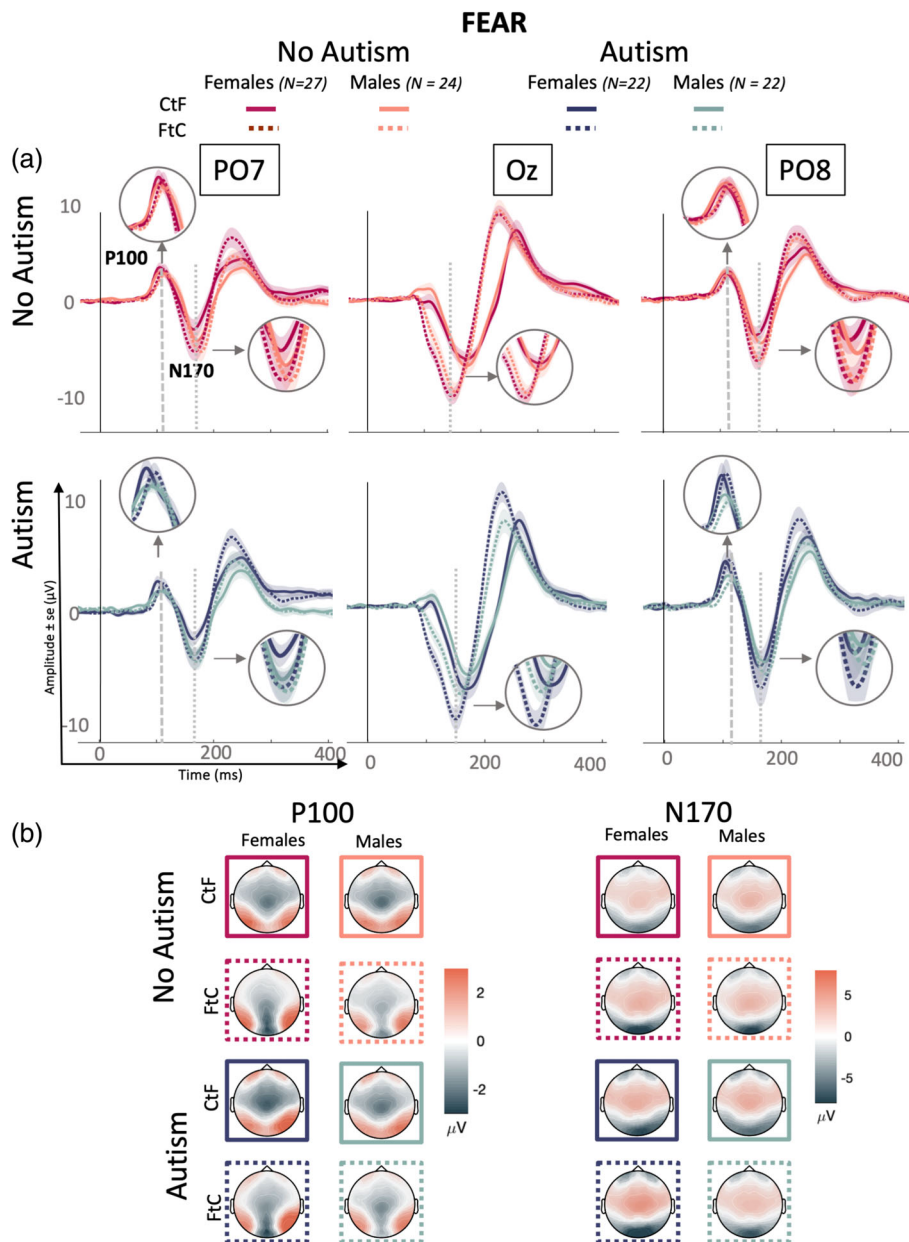
N170 over Oz electrode for each group, sex, and order as well as topographies are represented on Figure 4. Analyses on N170 latencies at Oz showed three main effects: N170 latencies were earlier for FtC than CtF sequences

( $\beta = -16.23$ , 95% CI  $[-19.15, -13.31]$ ,  $p < 0.001$ ), for females than males ( $\beta = 6.09$ , 95% CI  $[1.93, 10.24]$ ,  $p = 0.005$ ), and for fear-target than neutral-non-target faces ( $\beta = 2.09$ , 95% CI  $[0.51, 3.68]$ ,  $p = 0.01$ ). These effects were qualified by an interaction between order, group, and emotion ( $\beta = -10.44$ , 95% CI  $[-16.76, -4.11]$ ,  $p = 0.001$ ) indicating that the earlier N170 latencies at Oz for FtC than CtF sequences were more pronounced in NA than in autism in the neutral-non-target condition (CtF vs. FtC in NA neutral:  $\beta = 21.93$ , 95% CI  $[14.91, 28.94]$ ,  $p < 0.001$ ; autism neutral:  $\beta = 11.64$ , 95% CI  $[4.09, 19.18]$ ,  $p < 0.001$ ; NA fear:  $\beta = 15.6$ , 95% CI  $[8.59, 22.62]$ ,  $p < 0.001$ ; autism fear  $\beta = 15.75$ , 95% CI  $[8.21, 23.29]$ ,  $p < 0.001$ ).

Analyses on N170 latencies at PO7 and PO8 showed slightly different results. It revealed the similar main effects of sex ( $\beta = 7.15$ , 95% CI  $[3.04, 11.27]$ ,  $p = 0.001$ ). However, the effect of order was different, CtF leading to earlier N170 than FtC sequences ( $\beta = 2.26$ , 95% CI  $[0.63, 3.9]$ ,  $p = 0.007$ ). In addition, there was an effect of hemisphere ( $\beta = -1.19$ , 95% CI  $[-2.25, -0.13]$ ,  $p = 0.028$ ), with earlier N170 at PO8 than PO7.

Analyses on N170 amplitudes at Oz showed larger N170 amplitudes for FtC than CtF sequences ( $\beta = -3.37$ , 95% CI  $[-3.92, -2.82]$ ,  $p < 0.001$ ) and for fear than neutral condition ( $\beta = 0.18$ , 95% CI  $[0.02, 0.35]$ ,  $p = 0.027$ ). This main effect of emotion was further explained by an interaction between group and emotion ( $\beta = -0.45$ , 95% CI  $[-0.78, -0.13]$ ,  $p = 0.007$ ) indicating a larger difference in amplitude between fear and neutral stimuli in

**FIGURE 4** Event related potential (P100 and N170). (a) Grand average event-related potentials with standard error (shaded areas) for each group (Autistic individuals are in blue and NA are in pink), sex (Females are in dark colors and males in bright colors), and order (CtF are in plain lines, and FtC are in dotted lines) in the fear condition. (b) Scalp topographies show the mean activity of each group and sex in each order condition.



autism ( $\beta = -0.41$ , 95% CI  $[-0.73, -0.1]$ ,  $p = 0.005$ ) compared to NA ( $\beta = 0.04$ , 95% CI  $[-0.25, 0.34]$ ,  $p = 0.983$ ).

Analyses of N170 amplitudes at PO8 and PO7 showed slightly different results, as there was no longer an effect of emotion or any interaction involving emotion. However, analyses revealed a similar main effect of order, with larger N170 amplitudes for FtC than CtF sequences ( $\beta = -2.31$ , 95% CI  $[-2.72, -1.91]$ ,  $p < 0.001$ ), and a main effect of hemisphere, with larger amplitude at PO8 than PO7 ( $\beta = -1.95$ , 95% CI  $[-2.35, -1.54]$ ,  $p < 0.001$ ). These effects were qualified by interactions. The interaction between order and sex ( $\beta = 0.92$ , 95% CI  $[0.11, 1.73]$ ,  $p = 0.026$ ) showed a more pronounced difference between CtF and FtC sequences in females ( $\beta = 2.77$ , 95% CI  $[2.03, 3.51]$ ,  $p < 0.001$ ) than males ( $\beta = 1.85$ , 95% CI  $[1.09, 2.61]$ ,  $p < 0.001$ ). The interaction

between group and hemisphere ( $\beta = 1.21$ , 95% CI  $[0.4, 2.02]$ ,  $p = 0.003$ ) indicated a larger difference between PO7 and PO8 in autism ( $\beta = 2.55$ , 95% CI  $[1.78, 3.33]$ ,  $p < 0.001$ ) compared to NA ( $\beta = 1.34$ , 95% CI  $[0.62, 2.06]$ ,  $p < 0.001$ ), and the interaction between hemisphere and sex ( $\beta = 1.38$ , 95% CI  $[0.57, 2.19]$ ,  $p = 0.001$ ) showed a larger difference between PO7 and PO8 in females ( $\beta = 2.64$ , 95% CI  $[1.9, 3.38]$ ,  $p < 0.001$ ) than males ( $\beta = 1.25$ , 95% CI  $[0.49, 2.02]$ ,  $p < 0.001$ ). These two-way interactions were further qualified by a three-way interaction between hemisphere, group and sex ( $\beta = -1.68$ , 95% CI  $[-3.3, -0.06]$ ,  $p = 0.042$ ), showing that the increase difference between PO8 and PO7 in females than males was more pronounced in autism than in NA (PO7 vs. PO8 in autistic females:  $\beta = 3.66$ , 95% CI  $[2.37, 4.96]$ ,  $p < 0.001$ ; autistic males:  $\beta = 1.44$ , 95% CI  $[0.14, 2.74]$ ,

$p = 0.018$ ; NA females:  $\beta = 1.61$ , 95% CI [0.44, 2.78],  $p = 0.001$ ; NA males:  $\beta = 1.07$ , 95% CI [-0.18, 2.31],  $p = 0.153$ ).

### The modulation of source activity during fear detection in autism compared to NA differs between males and females

Cluster based statistics on sources activated during the processing of fear stimuli indicated a higher activity for FtC than for CtF sequences (Figure 5a), with two significant spatial clusters in the 60–140 ms time window (all  $p_{\text{cluster}} < 0.001$ ), on the right and left hemispheres. Clusters encompassed the lateral occipital cortices, the cuneus, the pericalcarine, the isthmus cingulate, the lingual gyri, the parahippocampal, and the fusiform areas. In the second time window (130–200 ms), spatial clusters were similar and extended to frontal areas, including orbitofrontal lobes and the rostral cingulate anterior cortices. The comparison of the CtF–FtC contrast between autistic and NA participants during the processing of fear stimuli showed one significant cluster in the right fusiform area during the 130–200 ms time window ( $p_{\text{cluster}} = 0.04$ ; Figure 5b). The analysis conducted on the mean activity in this area revealed a main effect of order, showing an increased activity for FtC than CtF sequences ( $\beta = 1.06$ , 95% CI [0.79, 1.32],  $p < 0.001$ ), and an interaction between order and group ( $\beta = 0.8$ , 95% CI [0.27, 1.34],  $p = 0.004$ ), indicating that this effect was more pronounced in NA ( $\beta = -1.46$ , 95% CI [-1.94, -0.98],  $p < 0.001$ ) than in autism ( $\beta = -0.66$ , 95% CI [-1.17, -0.14],  $p = 0.007$ ). Furthermore, comparing the CtF–FtC contrast between females and males during the processing of fear stimuli revealed a significant cluster in the 60–140 ms time window ( $p_{\text{cluster}} = 0.016$ ) located in the left hemisphere, including the lateral occipital cortex, the parahippocampal cortex, and the fusiform gyrus (Figure 5c). Analyses on the mean activity in the cluster revealed a main effect of order ( $\beta = 1.06$ , 95% CI [0.85, 1.27],  $p < 0.001$ ), FtC generating a higher activity than CtF sequences, and of sex ( $\beta = -0.65$ , 95% CI [-1.15, -0.14],  $p = 0.013$ ), females having a higher activity than males. These effects were further qualified by an interaction between order and sex ( $\beta = -0.75$ , 95% CI [-1.16, -0.33],  $p = 0.001$ ): the higher activity in females than males being more pronounced in the FtC condition ( $\beta = 1.02$ , 95% CI [0.3, 1.74],  $p = 0.002$ ), than in the CtF condition ( $\beta = 0.27$ , 95% CI [-0.45, 0.99],  $p = 1$ ). Finally, comparing the CtF–FtC contrast between ASD and NA during the processing of fear stimuli was performed separately for each sex. In females, during the second time window, two significant clusters were found (one in each hemisphere;  $p_{\text{cluster}} = 0.017$  on the right and  $p_{\text{cluster}} = 0.02$  on the left), encompassing the temporal poles (mainly on the right hemisphere), the rostral anterior cingulate cortices, the orbitofrontal cortices, the entorhinal cortices, and the

pericalcarine regions (Figure 5d). Analyses on the mean activity in this area revealed a main effect of order ( $\beta = 0.84$ , 95% CI [0.55, 1.14],  $p < 0.001$ ), indicating increased activity for FtC than CtF sequences, further qualified by an interaction between order and group showing that this effect of order was larger in NA females ( $\beta = -1.39$ , 95% CI [-1.91, -0.86],  $p < 0.001$ ), than in autistic females ( $\beta = -0.3$ , 95% CI [-0.88, 0.28],  $p = 1$ ). No significant clusters were found for the comparison between autistic and NA males.

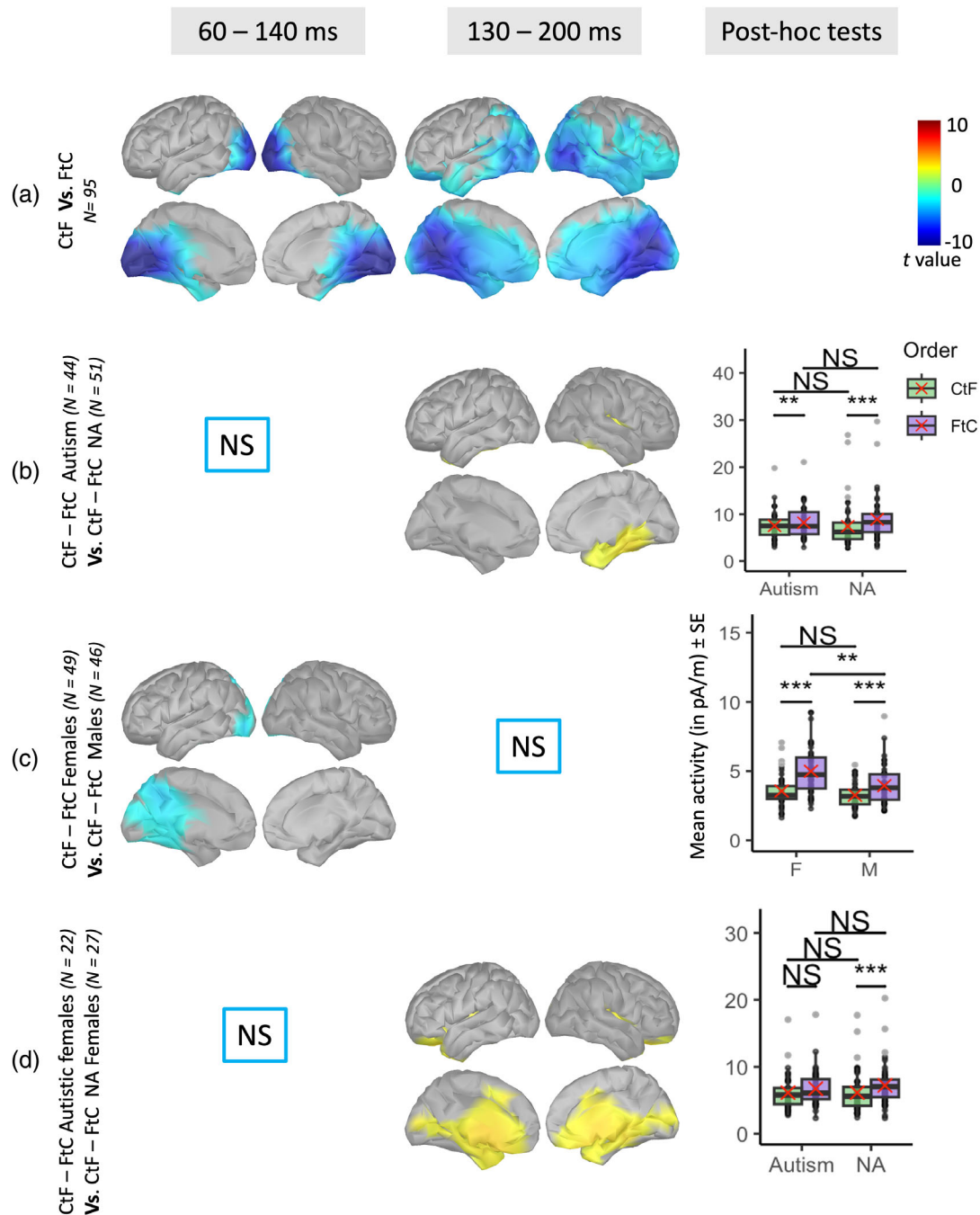
### No correlations among ERPs or source activity and behavioral or clinical measures

No significant correlation was observed among ERPs and AQ, diagnostic age or  $d'$ . However, we found that a later diagnostic age was associated with higher AQ scores in autistic males ( $r = 0.76$ ,  $p = 0.002$ ). This significant association was not present in autistic females.

Correlational analyses including sources activity were performed for cortical areas where a significant difference was observed between autistic and NA individuals (i.e., the right fusiform area, where a difference was observed between autistic and NA individuals; and the right and left temporal pole and frontal areas, where a difference was observed between autistic and NA females). The results did not show significant correlations.

## DISCUSSION

The study aimed to investigate whether autistic adults exhibit atypical predictive processes related to reduced spatial frequency differentiation, which may contribute to difficulties in processing emotional faces. Additionally, we studied whether autistic females demonstrate more typical responses in these processes, potentially enhancing their socio-communicational abilities. While the findings align with the CtF hypothesis of visual perception at the ERP level, analyses did not show impaired CtF processing during fearful face detection in autism. Nevertheless, source activity suggested a reduced differentiation of spatial frequencies processing in the right fusiform gyrus in autism compared to NA. This reduced spatial frequency differentiation in autism compared to NA was more spatially distributed in females, extending to the left cortex and orbitofrontal regions. Furthermore, behavioral responses were slower in autistic females than in NA females, but no significant group difference was observed in males. Lastly, we observed that females, regardless of group, exhibited earlier P100 and N170 components and larger parieto-occipital activity for FtC sequences compared to males. Overall, the present findings highlight both characteristic features of autism and typical sex differences in autistic females during fearful face processing.



**FIGURE 5** Modulation of face-detection evoked activity in cortical generator according to sequence order, group, and sex. Statistically significant differences in sources in the 60–140 ms and 130–200 ms time windows, between (a) coarse-to-fine (CtF) and fine-to-coarse (FtC) sequences, (b) autistic and non autistic (NA) individuals in the CtF–FtC contrast, (c) females (F) and males (M) in the CtF–FtC contrast, (d) autistic females and NA females in the CtF–FtC contrast. The box plots on the right represent the post-hoc tests for each interaction effect. They include the observed median with interquartile range, the mean (red cross), and individual data points. Significance levels for simple effects of interest on marginal means are also displayed. \* $p < 0.05$ , \*\* $p < 0.01$ , \*\*\* $p < 0.001$ .

### Intact coarse-to-fine processing but reduced spatial frequency differentiation in autism

Aligned with prior research, the ERP analysis supported the CtF processing model for early perceptual processes, with earlier P100 for CtF sequences (Peters & Kemner, 2017; Vlamings et al., 2009) observed at

PO7/PO8. The N170, observed at Oz, PO7, and PO8 and representing the integrative processes along the ventral stream, was larger for FtC sequences (Jeantet et al., 2019; Mares et al., 2018; Nakashima et al., 2008; Obayashi et al., 2009; Peters & Kemner, 2017; Tian et al., 2018). This confirms a primary global parsing, which might enable prediction in line with Bar's model (Bar et al., 2006),

followed by attention to fine details during fearful face detection. This CtF processing might have an adaptive role, aimed at reacting rapidly to threats. This is evidenced by the expected faster response times for CtF compared to FtC sequences during the present task, in line with studies showing decreased RT for LSF compared to HSF faces in NA adults (Goffaux & Rossion, 2006; Winston et al., 2003). Nevertheless, this rapid detection might be at the expense of accuracy, as we also observed a decreased detection rate for CtF compared to FtC sequence (consistent with Stein et al., 2014). This can be explained by the fact that, in the context of a threat, it is often safer to react quickly to a false positive than to respond too slowly to a false negative.

It should be noted that N170 latencies were earlier for FtC sequences than for CtF sequences at Oz, but this pattern was reversed at PO7/PO8, where CtF sequences were earlier than FtC sequences. This aligns with previous findings showing that N170 response to HSF-filtered face is slower than for LSF-filtered face (Halit et al., 2006; Obayashi et al., 2009; Peters & Kemner, 2017; Vlamings et al., 2009). This result may reflect the slow transmission of information along the ventral pathway, which includes occipital areas like the occipital face area and more ventral areas such as the fusiform face area (Gao et al., 2019). The ventral stream receive major parvocellular inputs (Merigan & Maunsell, 1993), which are more sensitive to HSF information (Tootell et al., 1988), presented first during FtC sequences. This could explain why FtC sequences activate the ventral pathway more than CtF sequences (Vuilleumier et al., 2003), reflected by a shift in the peak of the N170 from more occipital electrodes to more ventral electrodes (i.e., during FtC sequences, the N170 peak seems earlier at Oz than PO8—see Figure 4). However, the ventral stream also receive magnocellular inputs, which are faster and more sensitive to LSF (Tootell et al., 1988), explaining why CtF sequences activate parieto-occipital regions faster than FtC sequences.

At the source level, these results are accompanied by increased activation for FtC compared to CtF sequences in the two time windows. In the first time window (60–140 ms), this increase is observed in several temporo-parieto-occipital regions. These regions included the lateral occipital cortices, which are bidirectionally connected to the occipital face area and the fusiform face area, and play a role in the early perception of facial features and face/non-face discrimination (Haxby et al., 2000; Nagy et al., 2012); the cuneus, involved in basic visual processing and whose activity is modulated by fear (Zhao et al., 2017); and the fusiform gyrus, strongly connected with occipital and frontal regions via the inferior longitudinal fasciculus and inferior fronto-occipital fasciculus (Palejwala et al., 2020), and known for its specialization in processing the invariant aspects of faces (Haxby et al., 2000). In the second time window, the difference extends to orbitofrontal areas and anterior

cingulate cortices, involved in facial expression representation (Rolls, 2023). Higher activity for FtC than CtF sequences does not support our hypothesis that predictions from LSF would manifest by higher orbitofrontal activity for CtF sequences. However, the current pattern of results might highlight the critical need for detailed information (appearing first in FtC sequence) in the cortical face processing network during fearful face detection, whereas subcortical areas, including the amygdala, might be more responsive to coarse information as previously suggested by Vuilleumier et al. (2003). Another possible explanation could be that the brain is more efficient at processing predictable sequences (CtF), where the progression aligns with natural visual processing, leading to faster initial responses at the ERP level. In contrast, FtC sequences, being less predictable, might require additional neural resources (Mermillod et al., 2010) to integrate the unexpected high-to-low spatial frequency information, leading to higher source activity. Finally, since predictive processes are typically better observed in ambiguous situations (Bar et al., 2006), it is also possible that our task lacked sufficient ambiguity to induce higher activity in LSF in frontal areas.

Contrary to our expectations, although autistic individuals responded slower than NA participants, no reduced difference between CtF and FtC sequences was found in autism in behavioral responses and ERPs (P100, N170). Behavioral results may conflict with the local bias typically reported in autistic children during face processing (Deruelle et al., 2004; Kikuchi et al., 2013). Nevertheless, they align with behavioral results showing no differences between autistic and NA adults in spatial frequency processing of faces (Rondan & Deruelle, 2004; Vanmarcke & Wagemans, 2017), potentially indicating normalization with age. At the ERPs level, results on latencies are consistent with previous studies showing earlier P100 responses to LSF compared with HSF-filtered faces in autistic and NA children (Boeschoten, Kenemans, Van Engeland, & Kemner, 2007; Vlamings et al., 2010). However, this contrasts with our recent study, involving the same participants, showing that autistic adults, particularly males, exhibited a reduced difference between HSF and LSF P100 amplitudes and latencies during an oddball paradigm (Lacroix et al., 2024). This difference might be explained by the constrained spatial frequency processing sequence in the present task, suggesting that the default/automatic spatial frequency processing in autistic adults could be biased toward details but can be normalized when constrained.

Nevertheless, a diminished difference in source activity between CtF and FtC sequences was observed in the right fusiform area during the 130–200 ms time window in autism compared to NA. This result slightly differs from a previous study demonstrating a reduced response of the fusiform area to HSF in autism compared to NA, rather than a reduced difference between HSF and LSF,

in a gender discrimination task (Corradi-Dell'Acqua et al., 2014). However, the observed reduced difference in source activity between CtF and FtC sequences in autism aligns with our hypothesis of a reduced modulation of brain activity by spatial frequency contained in faces in autism (Boeschoten, Kenemans, Van Engeland, & Kemner, 2007; Lacroix et al., 2024). Given the functional role of the fusiform gyrus in holistic face processing and more specifically in facial expression processing during this time window (Muukkonen et al., 2020), this result potentially explains the delayed behavioral response in autism.

### Both typical and specific sex differences in autism for fearful faces

The present study also revealed sex differences in ERPs to faces, with females displaying earlier P100, consistent with studies in NA (Proverbio et al., 2006a, 2006b; Yoon et al., 2016) and earlier N170 at Oz and PO7/PO8 (in line with Sun et al., 2017), regardless of group. While this finding does not align with Coffman et al. (2015), who found earlier N170 peaks in autistic boys than girls, the differences may stem from age, IQ, and the specific autistic profiles of participants, mainly late diagnosed in the present study. At PO7/PO8, the result also showed an interaction effect between order and sex on N170 amplitude, indicating a larger difference between FtC and CtF sequences in females. This interaction was also found in source activity in regions including the left lateral occipital cortex and the fusiform gyrus, in the 60–140 ms time window. Overall, these results suggest that the left hemisphere of autistic and NA females rely more on details than males for fear detection. This result aligns with previous behavioral data highlighting that the left hemisphere in NA females (but not males) prioritizes HSF (Perilla-Rodríguez et al., 2013), fco and suggests some typical sex differences in autism.

In the second time window, increased source activity for FtC compared to CtF sequences in females was observed only in NA, and this activity was not only located in the right temporal pole but also in the right and left orbitofrontal cortices and rostral anterior cingulate cortices. The orbitofrontal cortex is a key brain area for emotions, but also for integrating sensory information, reward value, and decision-making (Rolls & Grabenhorst, 2008). The anterior cingulate cortex is involved in the emotional evaluation of faces and reactions to emotions (Stevens et al., 2011), and is connected to both the emotional limbic system, particularly the amygdala, and the prefrontal cortices. Interestingly, greater effective connectivity between the orbitofrontal cortex and amygdala would differentiate emotional expressions, including fear, that may lead to approach responses (Liang et al., 2009). Thus,

increased differentiation between FtC and CtF sequences in these regions in NA females compared to autistic females, could facilitate the differentiation of emotions and might contribute to their faster reaction times (RTs) compared to autistic females, whereas delayed performance in autism might be mediated by atypical amygdala activity to spatial frequencies of faces (Maekawa et al., 2023). While the hypothesis linking increased modulation of brain response by spatial frequencies and increased emotion differentiation is of interest, it is not supported by correlational analyses, which did not show a significant correlation. Further studies are needed to explore both this relationship, and connectivity patterns.

Alternatively, the behavioral differences could also be explained by hemispheric lateralization differences. Indeed, results showed a larger difference in the N170 amplitude between PO7 and PO8 in autism compared to NA, especially in females, indicating a reduced hemispheric lateralization in NA. In line with this reduced lateralization at the ERP level, there is an increased difference between FtC and CtF sequences in a more broadened and less lateralized network in NA females. This reduced hemispheric lateralization in NA females compared to males during face processing has been noticed in several studies (Godard & Fiori, 2010; Proverbio et al., 2006b, 2010), and the current results suggest that this difference might be related to the processing of fine information. Reduced lateralization in NA females than males might be explained by stronger inter-hemispheric co-activation, particularly in areas of social cognition such as temporo-parietal junction (Bonelli et al., 2022), and larger interhemispheric connectivity in females appearing early in the development (Ingalthalikal et al., 2014). Thus, autistic females might have reduced interhemispheric connectivity compared to NA females, in line with decreased interhemispheric functional connectivity in autism (Li et al., 2019), and the increased difference in the hemispheric lateralization profile in females might contribute to the interaction between group and sex at the behavioral level (i.e., delayed RT in autistic females compared to NA females larger than in males, could partly be related to this difference of brain lateralization).

Overall, results suggest that autistic females exhibit brain activity characteristics similar to NA females when attending to fearful faces but also display specific characteristics related to their autistic condition. This confirms an intermediate profile of autistic females (Lacroix et al., 2024), who exhibit significant difficulties associated with autism, though these difficulties are often less obvious than in autistic males. Their intermediate profile might be partly explained by camouflaging strategies, often higher in autistic females (Cook et al., 2021), potentially due to gender constructs, with females receiving more encouragement in socio-emotional skills than males. This could result in

changes at both the behavioral level, such as increased attention to faces (Del Bianco et al., 2022; Harrop et al., 2018, 2020; Harrop et al., 2019), and brain activation patterns over time, leading to neural responses that are closer to those of NA individuals compared to males, although different from NA females (e.g., differences in brain lateralization). The impact of biological factors should also be considered in this specific profile. Indeed, distinct neurodevelopmental trajectories and hormonal environments in males and females could contribute to the observed differences. Recognizing the unique profile of autistic females is important for their comprehension and for acknowledging their unique difficulties.

## Limitations

Our study was conducted on autistic adults, with high intellectual abilities, displaying heterogeneity in terms of age of diagnosis and visible autism characteristics. The AQ was the sole clinical scale available for all participants and those with lower AQ scores were typically diagnosed earlier (particularly in males), which can be unexpected. This underscores a limitation of the AQ, as individuals with early diagnoses often exhibit more visible characteristics and may have lower awareness of their characteristics, potentially leading to underreporting of their traits (Poon et al., 2020). This may explain the absence of an association between electrophysiological responses and the AQ, emphasizing the need for more objective scales in future studies to correlate ERP responses with clinical data. In addition, findings indicated a larger and earlier N170 for fearful faces compared to neutral faces at Oz, consistent with the N170's sensitivity to facial expressions (Hinojosa et al., 2015). There was also a greater difference in N170 amplitude between fearful and neutral faces in autism compared to NA, which is opposite to a previous study in autistic children (De Jong et al., 2008). Additionally, N170 latency was earlier for FtC than CtF sequences, with this effect being more pronounced in NA than in autistic individuals during the neutral condition. The earlier N170 latency in NA compared to autism for FtC sequences may contribute to the current literature indicating slower N170 responses in autism (Kang et al., 2018), suggesting that this delay might be more related to the processing of fine information than coarse information. The interpretation of the emotional effects is nevertheless limited, especially considering the lack of literature on N170 modulation by emotion in autistic adults, but also because the experiment included only one condition of fear detection among neutral faces and did not include the counterbalanced condition of neutral detection between fearful faces. Thus, further studies would be needed to investigate and interpret the effects of emotion.

## Conclusion

The present study revealed typical CtF processing in autism compared to NA during fearful detection and contrast with a previous study, investigating automatic face processing (Lacroix et al., 2024). Nevertheless, the present findings highlight a unique profile in autistic females and underscore the importance of exploring sex differences in autism compared to NA. While some neurophysiological responses appeared more typical in autistic females, potentially contributing to better apparent socio-communication abilities, they still differ more from their NA peers than autistic males, as suggested by our source data, and impaired behavioral results. A better understanding of their profile is critical to aid in their diagnosis and provide them with appropriate support.

## ACKNOWLEDGMENTS

We thank all participants for their implication in the study. We thank the Centre Expert Asperger, the C3R of Grenoble, the Centre d'Evaluation Savoyard de l'Autisme in Chambéry, and the Service Accueil Handicap of the Grenoble Alpes University for their help in recruiting the participants. We are grateful to Perrine Porte, Valentine Cuisinier, and Margot Fombonne for their precious help in data acquisition.

## FUNDING INFORMATION

AL was supported by grants of the French Ministry of Higher Education, Research, and Innovation (France), of the ANR-17-EURE-003 from the CBH graduate school, of IDEX investissement d'avenir from the EDISCE doctoral school and of the GIS autisme et troubles du neurodéveloppement. This work has been partially supported by MIAI @ Grenoble Alpes, (ANR-19-P3IA-0003). Data were acquired on a platform of France Life Imaging Network partly funded by the grant ANR-11-INBS-0006.

## CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

## DATA AVAILABILITY STATEMENT

The ERP data (mean by participant) is openly available on the Open Science Framework: <https://osf.io/vzpz5n/>. The raw data recorded for this study are not publicly available due to absence of public data sharing statement in the informed consent form signed by the participant. The data may be available on request from the corresponding author Adeline Lacroix, on the condition that a data sharing agreement between the academic buyer and Grenoble University Hospital is established.

## ETHICS STATEMENT

The Ethics Committee (Comité de Protection des Personnes Ile de France 1—IRB/IORG: IORG0009918) approved the study under agreement number

2019A01145-52 and the study was pre-registered on Clinical Trials (<https://clinicaltrials.gov/show/NCT04069676>).

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**How to cite this article:** Lacroix, A., Harquel, S., Barbosa, L. S., Kovarski, K., Garrido, M. I., Vercueil, L., Kauffmann, L., Dutheil, F., Gomot, M., & Mermillod, M. (2024). Reduced spatial frequency differentiation and sex-related specificities in fearful face detection in autism: Insights from EEG and the predictive brain model. *Autism Research*, 1–18. <https://doi.org/10.1002/aur.3209>