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Exploring the ERP time-course of associative recognition in Autism

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Abstract

Lay summary: Associative recognition of picture pairs relies on the same electrophysiological processes in autism as in typically developed individuals. Reduced behavioral performance in autism may however be related to the diminished early integration of perceptual and conceptual information implicated into the first stage of recollection.

Running title: ERP of associative recognition in autism

Keywords: autism, episodic memory, associative memory, recollection, EEG, Event-Related Potentials, Late Positive Component.

INTRODUCTION

Studies of episodic memory in Autism Spectrum Disorders (ASD) have consistently identified a dissociation between the relative preservation of recognition while diminished free recall, hypothesized to result from altered functional interactions between neurocognitive systems (see Cooper & Simons, 2019, for a review). This ability to correctly recognize previously seen items, in conjunction with preserved cued recall, has been theorized by Bowler, Gaigg, & Gardiner (2010) as the *Task Support Hypothesis*, that posits a normalization of memory performance in ASD in situations providing a memory support, which consist of part of the to-be-memorized information being available during retrieval (e.g. Phelan, Filliter, & Johnson, 2011; Ring, Gaigg, & Bowler, 2015).

In Typically Developed (TD) individuals, cognitive and neuroimaging studies converge to propose a model of recognition based on two successive and independent processes, being familiarity and recollection (*dual-process theory of recognition*, see Diana et al., 2006, Oberauer, 2008, and Yonelinas, 2002, for reviews). Familiarity is relatively automatic, more supported by the semantic memory system and associated with noetic awareness (knowing), hence enables recognition for single items or multiple items interactively encoded (see Oberauer, 2018, for a review and updated theory). In contrast, recollection appears as a more controlled process, associated with the episodic memory system and auto-noetic awareness, and requires the binding of information including contextual information for the successful remembering of an episode (Boywitt & Meiser, 2013).

The putative correlates of this relatively preserved recognition in ASD are intact familiarity (assessed in remember/know paradigms, e.g. Souchay et al., 2013), and intact functioning of the semantic memory system (Crane & Goddard, 2008; Gaigg, Bowler, & Gardiner, 2014). In contrast, the diminished remembering reported by Bowler, Gardiner and Grice, (2000) and Gaigg et al. (2015), in conjunction with reduced involvement of controlled cognitive processes (Camodeca & Voelker, 2015), and reduced binding abilities (Bowler, Gaigg, & Gardiner, 2014) in ASD, point towards a reduced functioning of the episodic memory system. As a consequence, it is not yet possible to extend the *dual-process theory of recognition* to ASD. Instead, other models have been postulated, such as *the fuzzy trace theory*, that suggests a lower reliance on general (fuzzy) rather than detailed memory traces in ASD relative to TD development (Miller, Odegard, & Allen, 2014).

The use of visual stimuli adds an additional layer of complexity to assess episodic recognition in ASD, since the degree of access to the semantic memory system can vary across stimuli, which in turn can contribute to inconsistent results. Ameli et al. (1988) first identified lower recognition for meaningless shapes yet similar performance on meaningful pictures in adolescents and young adults with ASD, relative to participants without ASD, and concluded that the ASD participants used semantic information to aid their visual memory. By contrast, in the same age category, Salmanian et al. (2012) showed that when Intelligence Quotient (IQ) was statistically controlled, participants with ASD performed similarly to matched comparison participants on memory for meaningful and meaningless shapes – this result being subsequently replicated in children by Semino et al. (2019) – and suggested that rather, recognition difficulties could be related to participants' general intellectual abilities. In a similar vein, some studies evaluated episodic recognition abilities for items from different semantic categories. Blair (2002) identified increased memory difficulties for living or non-living items capable of motion in adolescents and young adults with ASD compared to those without ASD. These authors

suggested this difference to be related to *theory of mind deficit* in ASD. Blair (2002) also report spared memory recognition for buildings and leaves. By contrast, Molesworth, Bowler, & Hampton (2005) showed that children with ASD were as sensitive as TD peers to the prototype effect – the individual’s tendency to display false recognition to an unstudied prototype of a category – which implies a similar level of integration of visual features. Similarly, Jiang et al. (2015) also report a high-level of object category recognition and a high-precision of recognition of specific exemplars in children with ASD, suggesting that their visual long-term memory was similarly structured to that of TD individuals. Other accounts, in line with the *enhanced perceptual functioning* account of ASD (Motttron & Burack, 2001; Motttron et al., 2006, 2009), have proposed that superior low-level processing interacts with locally oriented bias to produce enhanced visual or visuospatial episodic memory (Caron et al., 2004, 2006). Episodic visual memory appears as a preserved cognitive domain in ASD adults, as evidenced by Lever & Geurts (2016) in a large cohort of adult and elderly participants showing that visual recognition abilities persist across adulthood in ASD, while reducing in TD with old age (see Ring, Gaigg, & Bowler, 2016).

This relative preservation of general and visual recognition is however challenged by the observation of binding difficulties in ASD. Visual associative recognition paradigms have shown unexpected and contradictory results with regard to the *binding deficit hypothesis*, which argues for a specific impairment in hippocampally mediated relational and contextual memory, accompanied by intact item-specific and context-independent memory (Bowler et al., 2011; Gaigg, Gardiner, & Bowler, 2008). A binding deficit may explain memory difficulties in tasks involving relational processing, and also may constitute a possible explanation of the *complex information processing* theory (Williams, Goldstein, & Minshew, 2006), which suggests that difficulties arise when demand for integration of information increases (Bowler, Gaigg, & Gardiner, 2014), and to the *weak central coherence* theory (Happé & Frith, 2006), giving rise to difficulties in binding together the elements of a scene into a coherent representation (Lind, Bowler, & Raber, 2014). Difficulties with visual associative recognition in ASD have been shown in adults by Bowler et al. (2014) using an item-color and item-location paradigm, then by Cooper et al. (2015), also in adults in an item-scene paradigm, however other studies failed to support the *binding deficit* account when varying the experimental conditions, such as item-background (Lind et al., 2014) and picture-pairs (Semino et al., 2019) paradigms in children. Rather, Solomon et al. (2016) identified that adolescents with ASD performed similarly to TD peers for picture pairs associative recognition after relational encoding, with similar recollection awareness, while performing more poorly at single item recognition. Solomon et al’s paradigm has further been tested with functional Magnetic Resonance Imaging (fMRI) in a large cohort of adolescents and young adults with and without ASD by Hogeveen et al. (2019), who identified similar item and associative recognition performance in both groups. Relational encoding in ASD participants was marked by an increased hippocampal activity, which was thought to compensate for the diminished functional connectivity between the medial temporal lobes and the posterior medial network that supports relational memory. These results extend those of Cooper et al. (2017), who identified a similar precision for relational visual information, associated with reduced hippocampal connectivity with the fronto-parietal control network in adult participants with ASD relative to those without ASD.

Thanks to its high temporal resolution, EEG is a key method to explore the temporal profile of the cognitive processes implicated in memory recognition in typical and atypical population. Event-Related Potentials (ERP) have provided evidence for the *dual-process theory* of recognition in TD by

showing that familiarity and recollection processes are associated with two successive and independent old/new effects, consisting of a greater positivity for correctly recognized old as compared to correctly rejected new items. Greater mid-frontal negativity as well as a negative FN400 component (300–500ms) is an index of familiarity, whilst the LPC (*Late Positive Component* or *Late Parietal Component*; 500–800ms) indexes recollection (see Rugg & Curran, 2007, and Wilding & Ranganath, 2012, for reviews). Hence, the FN400 old/new effect can be elicited by the recognition of single items, as well as items unitized into a single item representation (e.g. Rhodes & Donaldson, 2007). This FN400 potential may reflect semantic processing during recognition testing (e.g. Voss & Federmeier, 2011), or be a specific marker of familiarity-based recognition (e.g. Bridger et al., 2012; Strózak, Abedzadeh, & Curran, 2016), more recent paradigms leading to a mixed model (Leynes et al., 2017). Consistently, the recollective nature of the LPC old/new effect has been confirmed during recollection awareness (e.g. Wynn et al., 2019), source memory (e.g. Addante, Ranganath, & Yonelinas, 2012), associative recognition (e.g. Borst, Ghuman, & Anderson, 2016; Opitz & Cornell, 2006), and simultaneous EEG–fMRI recordings identified posterior hippocampal and parahippocampal generators – areas being more related to the episodic memory system (Hopstädter et al., 2015). Hence, exclusion paradigms, that require discrimination of identical “old” pairs among rearranged and new pairs, are suited to assessing associative recognition and exploring the ERP correlates of the *dual-process theory*. Studies using exclusion paradigms both with verbal or visual paired items have consistently shown old/rearranged or old/new effects. These effects were seen on both the FN400 and LPC potentials for unitized pairs (due to independence of familiarity and recollection), and on the LPC potential only for non-unitized pairs (e.g. Donaldson & Rugg, 1998; Kriukova, Bridger, & Mecklinger, 2013).

Using visual stimuli, recognition paradigms have evidenced a more specific ERP signature, whether for single or paired items. Ally & Budson (2007) have proposed an ERP model of visual recognition memory as a succession of occipital perceptual priming (150–250ms), frontal familiarity (300–500ms) then parietal and predominantly right-sided recollection (variable latency and duration), ending by right-frontal post-retrieval processing (from 600–800 up to 1800ms). Using associative recognition of pairs of fractals, Speer & Curran (2007) identified the early P100 potential (100–175ms) as being sensitive to new stimuli, and added that swapping the position of items within a pair did not affect FN400 and LPC components. Comparing recognition for objects and non-objects, a more right-lateralized LPC old/new effect was found by Groh-Bordin, Zimmer, & Ecker (2006) for the former, and for both by Küper & Zimmer (2015), in accordance with fMRI study (Dalton, Hornberger, & Piguet, 2016) showing right perirhinal cortex and right hippocampus activations for episodic recognition of visual relative to verbal stimuli.

To date, only two studies have been conducted using ERPs to investigate episodic recognition in ASD. First, Massand et al. (2013) employed a single words recognition paradigm, and found a parietal rather than anterior early familiarity old/new effect in adults with ASD relative to non-ASD comparison participants. This was followed by parietal recollective process in both groups. To explain this lack of topographical difference in the ASD group, these authors hypothesized overlapping neural generators for the semantic and episodic memory systems, being possibly collapsed into a single memory system. Massand & Bowler (2015) conducted another more elaborated study, also in adults, designed to further distinguish the semantic and episodic systems, using a single-picture recognition test followed by a recall phase – recall of the color of the studied items – that relied more on episodic memory. The authors described successive old/new effects with a posterior only topographical distribution in the

ASD group and made similar arguments as Massand et al. (2013) in favor of a single non-differentiated memory system. Together, these ERP studies are not consistent with the dual-process theory in ASD memory, as postulated by cognitive studies. Instead, Massand and colleagues argued for the operation of a single recognition process in ASD.

Here, we conducted an EEG study investigating the ERP correlates of visual associative recognition for semantically unrelated picture pairs in participants with and without ASD. This task is an adapted version of a paradigm developed in our lab in TD young adults (Desaunay et al., 2017), that contrasted the associative recognition for semantically related and unrelated picture pairs, showing respectively a semantic and an episodic effect on the FN400 potential, followed by a recollective LPC old/new effect for both categories of stimuli, which supports the value of using picture pairs to assess the interaction of semantic and episodic processes in memory recognition in typical and atypical populations. In order for our sample to be representative of ASD individuals, participants with and without ASD were selected from late childhood to young adulthood, given the very moderate or even absent effect of age on this period in TD population, and the absence of age influence in memory difficulties in ASD (Desaunay et al., 2020). Developmental studies show that memory for associations emerges early in the TD population, with a pronounced increase until the age of 10, followed by a period of relative stability until adulthood (Guillery-Girard et al., 2013; Mastrogiuseppe et al., 2019), with similar visual associative memory performance between late childhood and adulthood (Baadte & Meinhardt-Injac, 2019). Congruent with these age-related differences, EEG studies have identified a greater reliance on recollection-based recognition during early childhood, while on familiarity-based recognition from late childhood to adulthood (Friedman et al., 2010, and Friedman, 2013, for a review).

Hence, our objectives were: (1) to compare the ERPs elicited by paired nameable pictures, especially the early potentials sensitive to perceptual and conceptual visual processes in participants with and without ASD; and (2) to determine whether the EEG recognition signature assessed during an associative recognition task reflects the operation of the *dual process theory*, as is seen in typical development, or whether it reflects a single process as argued by existing EEG studies of memory in ASD (Massand et al., 2013; Massand & Bowler, 2015).

METHODS

Participants

Twenty-two participants with ASD (2 female) and 32 participants with Typical Development (2 female) matched on age, IQ, and gender took part in this study. Participants with ASD were recruited through a database at *Autism Resource Centers* from Caen and Amiens. Clinical diagnoses were based on the Autism Diagnostic Interview-Revised (Rutter, Le Couteur, Lord, 2003) and/or the Autism Diagnostic Observation Schedule (Lord *et al.*, 2000), in accordance with DSM-5 and ICD-10 criteria.

For all participants, exclusion criteria were attention-deficit disorder with or without hyperactivity, schizophrenia, history of head trauma with loss of consciousness, recent or regular use of alcohol or drugs, chronic neurological or endocrine disorder, medication use likely to interfere with memory measures or EEG signal (evaluated on a case-by-case basis depending on drug and dosage), left hand dominance, mental retardation, and major deficit in associative memory (NS <5, 5th percentile subtest of Verbal Paired Associates Immediate and Delayed recall scores, Wechsler Memory Scale – fourth edition, 2012). All participants took part in this study on a voluntary basis, and written consent was obtained from children and their parents after being provided with detailed information about this study. This research was undertaken in accordance with the Declaration of Helsinki and approved by the regional ethics committee (CPP Nord Ouest III). This study was supported by the French Ministry of Health (PHRC, ID-RCB: 2014-A00481-46).

All participants were right-handed (assessed by the De Agostini & Dellatolas, 1988 checklist), and reported normal or corrected to normal vision. General functioning was evaluated by the Wechsler Intelligence Scales (Wechsler Intelligence Scale for Children-IV, and Wechsler Adult Intelligence Scale-IV). Participants characteristics are reported in Table 1.

Materials

Materials and methods were derived from the Desaunay *et al.* (2017) study. Three hundred and twenty simple, colored line drawings were used for this study. The items depicted were either objects or animals selected from 20 semantic categories (18 were selected from Marchal & Nicolas, 2003 according to their imageability, a 19th category – jewels – and a 20th category – prepared food – were generated based on a Wikipedia search), selected for their distinctiveness. All stimuli were drawn at to the same size (not scaled) on a same-color background in 300 x 300 pixel squares.

Stimuli were used to create 120 semantically unrelated picture pairs that were presented during the learning phase. We avoided supra-categorical pairings (e.g., pairing “pets” and “wild mammals”), and functionally associated items pairings (e.g., nail-hammer), to avoid familiarity-based recognition at test (e.g. Rhodes & Donaldson, 2007; Tibon & Levy, 2014).

For the retrieval phase, 80 target pairs of pictures were the same as those seen in the learning phase (identical pairs), 40 pairs of pictures were rearranged in order to differentiate item memory and relational memory, and 40 new pairs were also presented to test the classic old/new effect. In order to control for a purely perceptual association between paired items and a relational association

between items, the position of half the identical and rearranged pairs was swapped during the test phase.

Procedure

Stimulus presentation was controlled by Eprime Pro on a 17" LCD screen with a 1280 x 1024 resolution. Participants were sitting comfortably 90-100cm from the screen in a dimly lit room during the whole experiment and were asked to try and minimize blinking and moving during recording.

At both study and test phases (Figure 1), a trial started with a white fixation cross presented on a black background for a pseudo-random interval of 1500 ± 200 ms. A pair of pictures then appeared on the screen for 3000ms, followed by a blank screen for 1000ms. Pairs were presented in pseudo-random order. For the incidental learning phase, participants were given the following instructions: "for each pair of drawings, you have to imagine a situation or an image that associates the two drawings presented on the screen. You must then decide whether this situation is plausible (possible) in reality or not. If you think the situation is possible (plausible), press the left button. If it is not plausible, press the right button". These instructions aimed to enhance a deep, relational encoding. There was no mention that participants would later be tested on their memory for the pairs, so learning was incidental. In recognition phase, participants were instructed to indicate whether or not they had seen both pictures together during the learning phase, regardless of the position of the images on the screen. In both cases participants responded by pressing one of two keys on a response box. They were instructed to respond as quickly as possible, and responses were collected only if they were produced either during the presentation of the stimulus or during the following blank (3000ms response interval). Both phases were preceded by a training phase using 5 mock items, which was repeated if necessary. An interval of 15min separated the learning phase and the test phase, during which participants did not engage in any particular task while the experimenter checked the impedances of the electrodes.

EEG acquisition

EEG activity was recorded continuously by GES 300 amplifier (Electrical Geodesics, INC.) using an EGI Hydrocel Geodesic Sensor Net (HGSN-130) with dense array of 128 Ag/AgCl sensors (Tucker, 1993). Impedances were kept under 100 k Ω (Ferree *et al.*, 2001), and EEG was measured with respect to a vertex reference Cz and ground to CPPZ (fixed by the EGI system). The signal was sampled at 20 kHz frequency with a 24-bit A/D and was online (hardware) amplified and low pass filtered at 4 KHz. The signal was later filtered using a 1Hz Kaiser FIR first order high-pass filter in order to discard DC and very slow waves. Electro-oculogram was recorded using 4 electrodes placed vertically and horizontally around the eyes.

The artifact in EEG stimulus signal was excluded of the analysis by visual inspection. No other corrections and electrodes reconstructions were applied. Recordings were re-referenced to a common average reference to minimize the effects of reference-site activity and accurately estimate the scalp topography of the measured electrical fields (Dien, 1998).

ERP waveforms were created by averaging the ERPs within each region and across participants. ERP analyses were performed on trials associated to correct behavioral responses (hits and correct

rejections) with a minimum of 15 artefact free trials per condition for each participant (number of trials for “identical pairs” ASD: 17–56, TD: 30–68; “rearranged pairs” ASD: 15–30, TD: 15–32; “new pairs” ASD: 15–34, TD: 18–39; Supplementary Table 1 in Annexes).

Analysis

Behavioral analyses were conducted using SAS software (SAS Institute Inc., version 9.4). We measured accuracy (proportion of correct responses in each condition), and calculated the associative discrimination index Pr (percentage of hits minus percentage of false alarms, Snodgrass & Corwin, 1988). We ran analyses of variance (ANOVAs) using a General Linear Model procedure. *Post-hoc* multiple comparisons were Tukey-corrected. We also conducted Pearson correlations to test the absence of association between age and behavioral performance in both groups.

For EEG analyses, groups of electrodes were averaged together to form each Region Of Interest (ROI) that increased signal/noise ratio and increased statistical power, with 4 to 8 electrodes per region (Kurikawa et al., 2019; Ross et al., 2015). We obtained 15 Regions Of Interest (ROIs, Figure 2): LpF left prefrontal, MpF midline prefrontal, RpF right prefrontal, LF left frontal, MF midline frontal, RF right frontal, LT left temporal, RT right temporal, MC midline central, LP left parietal, MP midline parietal, RP right parietal, LO left occipital, MO midline occipital, and RO right occipital. Statistical analyses were only realized on ROIs where components (P2, FN400, LPC) were visible. Statistical analyses of qEEG parameters were also performed with SAS software. Differences in qEEG indices were analyzed by the means of a General Linear Model (GLM) with age as a covariate.

We used *a priori* defined latencies of interest according to the literature and confirmed by visual inspection of ERP grand-average, resulting in three time-windows for the ERP analysis. First, visual inspection of ERPs revealed an unexpected amplitude and shape differences between ASD and TD groups on the posterior P2 potential. Hence, we realized between-group analyses on two time-windows, the former being 220–270ms that correspond to measures reported in literature (e.g. Wolff et al., 2014), and the latter being extended to 120–300ms to ensure that the difference in amplitude is not confused with a difference in latencies. Second, visual inspection of ERPs also revealed an unexpected amplitude difference between ASD and TD groups on the 350–470ms time-window, corresponding to the FN400 familiarity signal. Third, for the Late Positive Component (LPC), we began analyses focusing on 600-700ms time-window. Studies usually report that the LPC lasts longer with verbal material (e.g. Johnson *et al.*, 1998; Friedman & Johnson, 2000; Vilberg *et al.*, 2006; Woodruff *et al.*, 2006), but shorter time-windows lasting around 100ms are more often reported with pictures, either for single or associative recognition (Ally & Budson, 2007; Desauvay *et al.*, 2017; Tibon *et al.*, 2014). Besides, in order to better characterize the latencies of the LPC old/new effect in both groups, we run analyses on 50ms intervals, from 500ms to 800ms. In order to focus on associative processes and to have a sufficient number of trials per condition, data for unswapped and swapped pairs were therefore collapsed across each type of trial. According to Speer & Curran (2007), varying the position of visual stimuli within a pair from one trial to the next has no effect on the FN400 and the LPC old/new effect.

For the P2 analysis, electrode sites for analysis included left occipital (electrodes PO7, O1, PPO9h, POO9h, P11), right occipital (electrodes PO8, O2, PPO10, POO10, P12), and midline occipital

(electrodes POO1, POZ, OZ, POO2) ROIs. For the FN400 analysis, electrode sites for analysis included midline frontal (electrodes FFC1h, FFC2h, FCz, FCC3h, FCC4h, FCC1h, FCC2h) and midline central (electrodes CP1, CCP1h, CCP2h, CP2) ROIs. For the LPC analysis, electrode sites for analysis included midline parietal (electrodes CPZ, CCP2h, CPP1h, P1, PZ, P2), right parietal (electrodes CP2, CP6, TP8, P6, PO4, P8, P4, P10), midline occipital (electrodes POO1, POz, Oz, POO2) and right occipital (electrodes O2, PO8, POO10h, PPO10h, P12) ROIs, based on previous data (Desaunay *et al.*, 2017) and neuroimaging studies using visual stimuli (e.g. Achim & Lepage, 2005).

RESULTS

Behavioral results

Regarding to identical pairs, a 2 (group: ASD, TD) x 2 (condition: swapped, unswapped) ANOVA revealed a main effect of group only ($F_{(1,52)} = 15.34$, $p = .0002$; $\eta_p^2 = 0.126$), reflecting lower performance for participants with ASD when compared to without, but there was no main effect of condition ($F_{(1,52)} = 1.9$, $p = 0.17$; $\eta_p^2 = 0.016$) nor group x condition interaction ($F_{(1,52)} = 0.22$, $p = 0.64$; $\eta_p^2 = 0.002$). Hence, we collapsed these two conditions (as “identical pairs”). All accuracy results were significantly higher than chance level (0.50, all $ps < 0.05$) (Figure 3). A 2 (group: ASD, TD) x 3 (condition: identical, rearranged, new pairs) ANOVA revealed a main effect of group ($F_{(2,52)} = 5.3$, $p = 0.022$; $\eta_p^2 = 0.099$) and condition ($F_{(2,52)} = 33.94$, $p < .0001$; $\eta_p^2 = 0.59$) on accuracy. The group x condition interaction was also significant ($F_{(2,52)} = 3.33$, $p = 0.038$; $\eta_p^2 = 0.12$). *Post hoc* Tukey tests indicated that participants with ASD had lower scores than control participants on correctly identified identical pairs ($p = 0.01$), but groups did not differ on the correct rejection of rearranged and new pairs.

The associative discrimination index for identical pairs was 0.54 (SD= 0.24) in the ASD group, and 0.68 (SD= 0.16) in the TD group. A one-way ANOVA ($F_{(1,52)} = 5.81$, $p = 0.019$; $\eta_p^2 = 0.1$) revealed this difference to be significant.

There were no between-group differences in reaction times (Figure 4). There was also no significant correlation between age and both behavioral performance and reaction times in the TSA and TD groups (for identical pairs, unswapped and swapped separately or pooled, rearranged pairs, and new pairs: all $p > .05$).

There was also no significant between-group difference on the responses during study phase (for “yes” responses for plausible situations “no” responses for implausible situations, out of time or absence of response: all $p > 0.05$; see Supplementary Table 2 in Annexes).

ERP results

P2 potential. To characterize the P2 potential on the 220–270ms time-window (Figure 5), we conducted a 2 (group: ASD, TD) x 2 (condition: identical, new pairs) ANOVA which revealed a main effect of group, unexpectedly indicating that P2 amplitude was lower across conditions in the ASD compared to the TD group, in each of the three ROIs: left occipital ($F_{(1,52)} = 10.79$, $p = 0.0014$; $\eta_p^2 = 0.18$), right occipital ($F_{(1,52)} = 5.44$, $p = 0.021$; $\eta_p^2 = 0.098$), and midline occipital ($F_{(1,52)} = 11.36$, $p = 0.001$; $\eta_p^2 = 0.18$). In line with the ERP literature on recognition identifying no old/new effect on early potentials,

there was no significant effect of conditions in these three areas ($F_{(1,52)} < 1$) nor interaction ($F_{(1,52)} < 1$). We then replicated these statistical analyses on the 120–300ms time-window. A 2 (group: ASD, TD) x 2 (condition: identical, new pairs) ANOVA confirmed the main effect of group, in the sense of a reduced amplitude for all pairs in the ASD relative to TD group, in left occipital ($F_{(1,52)} = 4.63$, $p = 0.033$; $\eta_p^2 = 0.042$) and midline occipital ($F_{(1,52)} = 9.66$, $p = 0.002$; $\eta_p^2 = 0.085$) ROIs, but we failed to replicate between-group difference on the right occipital ROI. There was also no significant condition effect of conditions in left occipital and midline occipital areas ($F_{(1,52)} < 1$) nor interaction ($F_{(1,52)} < 1$).

FN400 potential. To characterize the familiarity FN400 potential on the 350–470ms time-window (Figure 6), we conducted a 2 (group: ASD, TD) x 2 (condition: identical, new pairs) ANOVA which also revealed a main effect of group on the midline central ROI only ($F_{(1,52)} = 6.81$, $p = 0.01$; $\eta_p^2 = 0.061$), indexing a FN400 decrement across conditions in the ASD compared to the TD group. Congruently with ERP literature on unrelated and non-unitized paired stimuli, there was no condition effect, that is no old/new effect ($F_{(1,52)} < 1$) nor interaction ($F_{(1,52)} < 1$). There was no significant group, nor condition, nor interaction on the midline frontal ROI.

LPC potential. To characterize the recollection effect (Figure 7), we conducted a 2 (group: ASD, TD) x 2 (condition: identical, new pairs) ANOVA on the LPC potential.

First, we tested the LPC old/new effect on the 600–700ms time window. A significant condition effect was identified in four ROIs: right parietal ($F_{(1,52)} = 23.63$, $p < .0001$; $\eta_p^2 = 0.181$), midline parietal ($F_{(1,52)} = 8.14$, $p = 0.005$; $\eta_p^2 = 0.069$), midline occipital ($F_{(1,52)} = 14.76$, $p = 0.0002$; $\eta_p^2 = 0.123$), and right occipital ($F_{(1,52)} = 12.68$, $p = 0.0006$; $\eta_p^2 = 0.104$). A significant group effect was also identified in midline parietal ROI ($F_{(1,52)} = 4.51$, $p = 0.036$; $\eta_p^2 = 0.038$), and a tendency in the right occipital ROI ($F_{(1,52)} = 3.58$, $p = 0.061$; $\eta_p^2 = 0.029$). There was no significant group x condition interaction. Then, old-new effects were estimated using *post-hoc* Tuckey corrected comparisons between “identical” and “new” conditions in each group separately. In the ASD group, we identified a significant LPC old/new effect on right parietal ($p = 0.006$) and midline parietal ($p = 0.05$) ROIs, being marginally significant on the midline occipital area ($p = 0.076$), and non-significant in the right occipital area ($p = 0.22$). In the TD group, we identified an LPC old/new effect on the right parietal ($p = 0.002$), midline occipital ($p = 0.014$), and right occipital ($p = 0.008$) ROIs, being non-significant in the midline parietal ROI ($p = 0.53$). There was no group x condition interaction (all $F_{(1,52)} < 1$).

Second, to better characterize latencies of the LPC old/new effects in both groups, we extended the statistical analyses on the 550–600ms and 700–750ms time-window. From 550ms to 600ms, we found a significant condition effect on the right parietal ROI ($F_{(1,52)} = 5.07$, $p = 0.026$; $\eta_p^2 = 0.045$), and a trend on midline occipital ($F_{(1,52)} = 3.86$, $p = 0.052$; $\eta_p^2 = 0.035$) and right occipital ($F_{(1,52)} = 3.45$, $p = 0.066$; $\eta_p^2 = 0.031$) ROIs, without significant *post-hoc* analyses, that is no LPC old/new effects. On the 700–750ms time-window, a significant group effect was present on the right parietal ROI only ($F_{(1,52)} = 4.75$, $p = 0.031$; $\eta_p^2 = 0.042$), while only a trend on the right occipital ($F_{(1,52)} = 3.35$, $p = 0.07$; $\eta_p^2 = 0.031$) and midline occipital ($F_{(1,52)} = 32$, $p = 0.071$; $\eta_p^2 = 0.03$) ROIs, without significant *post-hoc* analyses, that is no LPC old/new effects as well.

DISCUSSION

Because of their dual perceptual and conceptual coding, picture stimuli enable the investigation of successive electrophysiological processes engaged in memory recognition. Here, picture pairs were used in an associative recognition paradigm, which is a well-validated method of assessing the ERP correlates of familiarity and recollection. Participants with ASD were less well able than matched TD comparison participants at correctly identifying identical “old” pairs, yet were as accurate as TD comparison participants at rejecting rearranged and new pairs. We observed the same succession of ERP waveforms in both groups, and an old/new effect on the LPC potential only, demonstrating the same recollection-based retrieval of associative information in ASD participants as was observed in the TD controls. However, amplitudes for all ERP waveforms was reduced in P2 and FN400 potentials in the ASD relative to the TD group, and the topographical distribution of the LPC old/new effect was larger on parietal areas, possibly reflecting compensatory processes. We conclude that there is a reduced conceptual processing of visual stimuli in memory in ASD, and that the LPC old/new effect is in line with the *dual-process theory* in ASD as in TD participants.

Diminished associative recognition for paired pictures

Diminished associative recognition of identical pairs for ASD relative to TD participants is in line with the *relational binding account* (Bowler *et al.*, 2011; Gaigg *et al.*, 2008), that posits a specific impairment in relational memory accompanied by intact item-specific memory. However, cognitive and neuroimaging models of associative recognition suggest that item and associative information are stored as distinct memory representations (Buchler, Light, & Reder, 2008; Ranganath, 2010), hence memory for either a picture within a pair or for the association may be diminished. A recent meta-analysis of episodic memory in ASD (Desaunay *et al.*, 2020) identified a medium deficit for visual material with a small deficit for verbal material in individuals with ASD, relative to TD controls. This observation contrasts with the *pictorial superiority effect* over words usually observed in TD populations (Nelson *et al.*, 1976; Snodgrass & Asiaghi, 1977; also see Baadte & Meinhardt-Injac, 2019, in associative memory). We suggest that the dual coding of pictures interacts with *enhanced perceptual functioning* (Motttron & Burack, 2001) and *weak central coherence* (Happé & Frith, 2006) in ASD, resulting in visual memory being less conceptually-driven relative to TD population. As a consequence, visual memory may be less supported by the semantic system and so less encoded into episodic memory as argued by hierarchical models of memory (SPI model, Tulving, 1995; MNESIS model, Eustache *et al.*, 2016). Taking these points together, we hypothesize that the use of pictorial stimuli in the current study may have reduced memory for items within a pair, independently of memory for the association.

The contrast between our results and with those of Hogeveen *et al.* (2019), who found preserved visual associative recognition in ASD, may result from methodological differences. Their paradigm was composed of a study phase divided into 27 picture pairs requiring item-specific encoding and 27 others with relational encoding. All participants were given an item recognition phase, and only a subset of participants performed the associative recognition phase. First, participants in our study had to encode a greater number of picture pairs than did Hogeveen *et al.*'s participants, hence the ASD participants in the present study may have been disadvantaged by higher memory load, as noted in other memory domains (e.g. Desaunay *et al.*, 2019). Second, the item recognition phase may have

reinforced item memory during the subsequent associative recognition phase, as previously demonstrated in elderly TD participants who show binding difficulties (Fine, Shing, & Naveh-Benjamin, 2018). Third, only participants who did not show fatigue were tested on the associative recognition phase of Hogeveen et al.'s. (2019) study, which may limit their conclusion that all participants showed preserved relational memory.

For rearranged pairs, we observed similar between-groups accuracy and reaction times. Although this difference was not significant, higher reaction time for rearranged compared to identical and new pairs in both groups suggests an additional “recall-to-reject” process of recollective detail. This memory process is a slower but more accurate strategy enabling more effective rejection of lures (see Xu & Malmberg, 2007, with unrelated picture pairs). In addition, Cooper et al., (2015, 2017) suggested that this might also operate during visual associative recognition in ASD.

Reduced early processing of semantically-related visual information

We found a reduced amplitude for all pairs (i.e. identical and new) on the occipital P2 and mid-frontal FN400 components, for ASD relative to TD participants. Electrophysiological studies show a leftward lateralization of functional connectivity in ASD compared to TD (see O'Reilly et al., 2017, for a review), leading to a reduced global/local integration of information due to hemispheric brain specialization (i.e. left and right hemispheres being specialized towards local–featural, and global–configural processing, respectively), which is suggested to participate to memory deficits in ASD in line with the greater right hemispheric dependence on visual memory (Fiebelkorn et al., 2013)(.....). Here, our results extend these findings, by suggesting a reduced processing of semantically-related visual information on the early stages of recognition.

The occipital P2 potential is thought to index an intermediate processing stage linking elementary perceptual processes with higher-level semantic processes (De Cesarei, MASTRIA, & CODISPOTI, 2013). During picture categorization tasks, the P2 potential has been associated with the perception of shape (Lee *et al.*, 2018; Schendan & Kutas, 2007), while higher-order between- and within-category information processing are associated with the later N300 and N400 potentials respectively (Hamm, Johnson, & Kirk, 2002). In visual episodic recognition, the P2 potential has been linked to the perceptual overlap between encoding and recognition of fragmented objects, corresponding to memory reactivation or priming (Schendan & Kutas, 2007), and to the processing of metric distances between facial features (Latinus & Taylor, 2006). During short-term memory for meaningless shapes, Cepeda-Freyre et al. (2020) showed its amplitude to increase with stimulus complexity, reflecting a visual attentional process. Here, we suggest that attenuation of the P2 amplitude for all pairs in the ASD relative to the TD group may correspond to a reduced early processing of perceptual visual information of pictures within a pair. Consistent with this account, Fiebelkorn et al. (2013) identified during a visual-target detection task, an attenuation of ERP waveforms in children with ASD relative to without in a close time-window (240–280ms), suggesting diminished selective attention and reduction of early categorization processing. Atypical electrophysiology in ASD on the P2 potential has also been found in audiovisual speech integration with a reduced amplitude, leading to the same conclusion of a reduced early semantic integration of information (Magnée et al., 2011; Megnin et al., 2012).

No old/new effect was observed on the FN400 potential in either group – i.e. no familiarity-based recognition – indicating that interactive encoding of picture pairs was not associated with unitization. Interestingly, we identified a reduced amplitude for all pairs in the ASD group relative to TD group. Given that the FN400 potential reflects both conceptual priming and familiarity during episodic recognition (see review and recent account in Leynes et al., 2017), this amplitude decrement in the ASD group may correspond to reduced semantic processing and familiarity signal elicited by pictures within a pair. Consistent with this account, Solomon et al. (2016) identified during the recognition of picture pairs after relational encoding a reduced level of familiarity awareness in their adolescent participants with ASD relative to those without ASD. In addition, Massand and Bowler (2015) showed that single-item recognition of line-drawings was associated with a reduced familiarity old/new effect (in the 300–650ms time-window) in adults with ASD relative to those without ASD.

Together, the sequence of amplitude decrement on the P2 then FN400 potentials suggests a reduced processing of both basic/perceptual and higher-order/semantic visual features of pictures in ASD participants, associated with a reduced familiarity-based memory. This conclusion fits with recent EEG results of atypical integration between low and high-level information with visual stimuli (Ortiz-Mantilla et al., 2019; Wang et al., 2017), and recent models of visual episodic memory being less supported by semantic knowledge than verbal memory in individuals with ASD relative to TD controls (Desaunay et al., 2020; Semino et al., 2019).

Similar neurophysiological process associated with recollection in ASD as in TD individuals

In both groups, we identified an old/new effect on the LPC potential only, highlighting that associative recognition in ASD is supported by the recollection process, just as in TD individuals (Donaldson & Rugg, 1998; Rugg & Vilberg, 2013). This finding may challenge previous ERP studies from Massand *et al.* (2013) and Massand & Bowler (2015), who suggested a single non-differentiated memory system in ASD, contrary to the semantic/episodic distinction observed in TD individuals (Tulving, 1972). In Massand *et al.*'s (2013) study, the FN400 and LPC potentials for the ASD group were located in overlapping parietal areas, preventing any clear distinction between these two potentials. In their following study, Massand & Bowler (2015) observed an attenuated familiarity old/new effect for the ASD group, but in a large time-window (300-650ms), less specific to the FN400 potential (see Rugg & Curran, 2007 for a review). These paradigms required single-item recognition, supported by the familiarity FN400 old/new effect, while the current paradigm was specifically designed to track the recollective LPC old/new effect, which may in part explain the different pattern of EEG results. Moreover, the LPC old/new effect identified in our study may instead suggest a distinctive recollective process, which supports the proposition of a relatively preserved *dual-process* account of recognition (Andrew P Yonelinas, 2002) in ASD. This argument may also help to resolve the apparent contradiction between existing EEG studies (Massand et al, 2013; Massand & Bowler, 2015), which appear to show diminished recollection and behavioral studies, which have shown that recollection and familiarity measures in ASD participants respond similarly to manipulations as do TD participants' responses (Bowler, Gardiner, & Gaigg, 2007). These last findings alongside those reported in the present study highlight that recollection can occur in ASD when the binding of information is required during episodic recognition.

Analysis of the LPC old/new effect showed similar latency and duration in both groups, with a spatial extension to Midline Parietal ROI in the ASD compared to TD group. First, this additional parietal recruitment may suggest a compensatory process, that is effortful retrieval of associative information due to lower memory strength for individual items – indexed by the reduced FN400 familiarity signal. Second, the pattern of electrophysiological processes – i.e. reduced amplitude of the FN400 familiarity potential, while similar amplitude but parietal extension of the LPC recollective potential – may reflect an immature development of memory processes in ASD. Developmental EEG studies of verbal or visual recognition in TD individuals have consistently identified a greater reliance on the LPC recollective process than on the familiarity FN400 process in younger participants, with the opposite pattern occurring when age increases (e.g. Friedman et al., 2010; Sprondel, Kipp, & Mecklinger, 2011). Hence, reduced familiarity but enhanced recollection EEG signals in ASD compared to non-ASD participants, beyond the associative nature of our paradigm, may reflect an earlier developmental stage, possibly resulting from atypical structural and functional connectivity in ASD (see Rane et al., 2015, for a review). This conclusion is supported by a behavioral study by Solomon et al. (2016) showing greater visual memory both for items and associations in ASD when supported by recollection than familiarity. This may also explain to some extent the EEG results from the Massand et al. (2013) and Massand & Bowler (2015) studies, since single-item recognition led to a more reduced old/new effect on the FN400 than LPC potentials in ASD relative to TD participants in both studies. By contrast, we identified in the TD group a right occipital extension of the LPC old/new effect, suggesting a greater representation of individual items as suggested by fMRI studies (Yonelinas et al., 2001), possibly resulting from the greater familiarity signal.

Limitations of this study include absence of analyses on the rearranged pairs due to a lack of stimuli to generate their ERP waveforms in both ASD and TD groups. Statistical analyses on associative recognition paradigms generally include calculations on old/rearranged or old/new effects. However, it must be noted that visual association recognition studies – which remain scarce – sometimes do not evidence significant LPC old/rearranged effects (Tibon et al., 2014; Tsivilis, Otten, & Rugg, 2001), which may emerge from the LPC time-window being generally narrower for visual stimuli than for words, which reduces the statistical power.

To conclude, this ERP study provides insights into the time-course of associative recognition with visual material in individuals with ASD. Memory difficulties may emerge from the visual nature of paired stimuli, due to reduced integration between perceptual and conceptual visual features indexed by the P2 decrement. This may in turn lead to memory for individual items being less supported by the semantic memory system, possibly reflected by the FN400 decrement. This account is borne out by a recent meta-analysis of episodic memory showing greater difficulties for visual than verbal material in ASD (Desaunay et al., 2020), and a behavioral study reporting that memory for semantically-related pictures in ASD is enhanced by associating picture names to the pictures themselves, suggesting that words would foster item and inter-item conceptual processing, leading to better memory (Parra *et al.*, 2016). The same succession of potentials, in particular separable FN400 and LPC potentials in both groups, suggests that information processing during associative recognition in ASD is qualitatively similar to that seen in TD, and extends the *dual-process* theory of recognition in ASD condition. This interpretation seems consistent with Cooper *et al.*'s. (2017) fMRI study on visual recognition, which showed similar patterns of brain activity in ASD and TD individuals, reflecting the same processing of memory representations in the two groups. However, information processing differs quantitatively, and the greater parietal distribution of the LPC old/new effect in ASD may reflect either a compensatory process for reduced early processing of items or effortful retrieval of associative

information, either a more general reliance on the recollective LPC process in ASD, which may constitute an EEG marker of developmental immaturity of memory functioning in ASD. Overall, the present study challenges the possibility that recollective processes may function entirely atypically in ASD while having a largely common electrophysiological correlates. The operation of largely intact underlying neural processes, together with earlier evidence of intact response to experimental manipulations of recollection and familiarity (Bowler et al., 2007) suggests that there is scope for intervention to remediate diminished behavioral performance. Future studies could address the neural consequences of the provision of task support (Bowler, Gardiner, & Berthollier, 2004), which is known to enhance behavioral memory performance in this population.

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Table 1. Participant Characteristics and Independent Samples t-Test. FSIQ = full-scale intelligence quotient; VCI = verbal comprehension index; PRI = perceptual reasoning index; VPA – IR / VPA - DR = verbal paired associates immediate recall / delayed recall; AQ = autistic quotient (total).

	Autism Spectrum Disorders Group (n = 22)		Typical Development Group (n = 32)		p Value
	Mean	SD	Mean	SD	
Age (years)	16.51 (10.4–25.75)	3.56	17.95 (12.3–25.6)	3.97	0.178
FSIQ	101.4 (72–132)	14.65	106.22 (86–134)	12.38	0.199
VCI	106.72 (69–145)	17.32	110.06 (77–143)	17.11	0.487
PRI	105.68 (72–142)	18.22	104.40 (84–130)	12.51	0.761
VPA – IR	10.86 (5–18)	3.37	11.06 (5–16)	2.78	0.813
VPA – DR	10.4 (1–17)	3.59	10.46 (5–15)	2.43	0.942
AQ	34.42	8.57	12.28	6.45	<.0001
ADOS *	10.11	4.83			

* Nine participants with ASD received a diagnosis based on the ADOS.

Figure 1. Materials (left panel) and procedure (right panel).

Figure 2. Electrode grouping and localizations : LpF left prefrontal, MpF midline prefrontal, RpF right prefrontal, LF left frontal, MF midline frontal, RF right frontal, LT left temporal, RT right temporal, MC midline central, LP left parietal, MP midline parietal, RP right parietal, LO left occipital, MO midline occipital, RO right occipital

Figure 3. Accuracy scores per condition (means and standard deviations for identical, rearranged, and new pairs), in the ASD group and TD group.

Figure 4. Reaction times per condition (means and standard deviations for identical, rearranged, and new pairs), in the ASD group and TD group.

Figure 5. Event-Related Potentials and topographies for the P2 potential (signal in midline occipital area between 220–270ms). Yellow shaded areas correspond to significant differences between ASD and TD waveforms.

Figure 6. Event-Related Potentials and topographies for the FN400 potential (signal in midline central area between 350–470ms). Yellow shaded areas correspond to significant differences between ASD and TD waveforms.

Figure 7. Event-Related Potentials and topographies for the Late Positive Component – LPC potential (signal in right parietal area between 500–600ms). Yellow shaded areas correspond to significant differences between conditions, i.e. old/new effect in ASD and TD groups.

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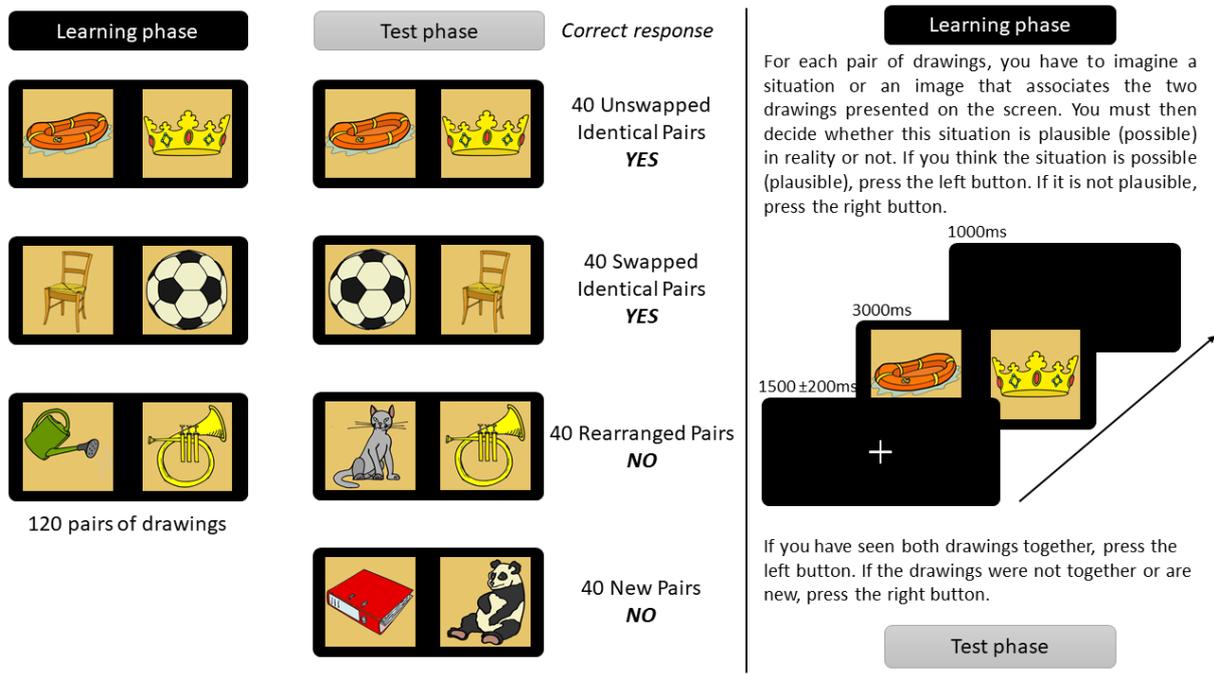


Figure 1. Materials (left panel) and procedure (right panel).

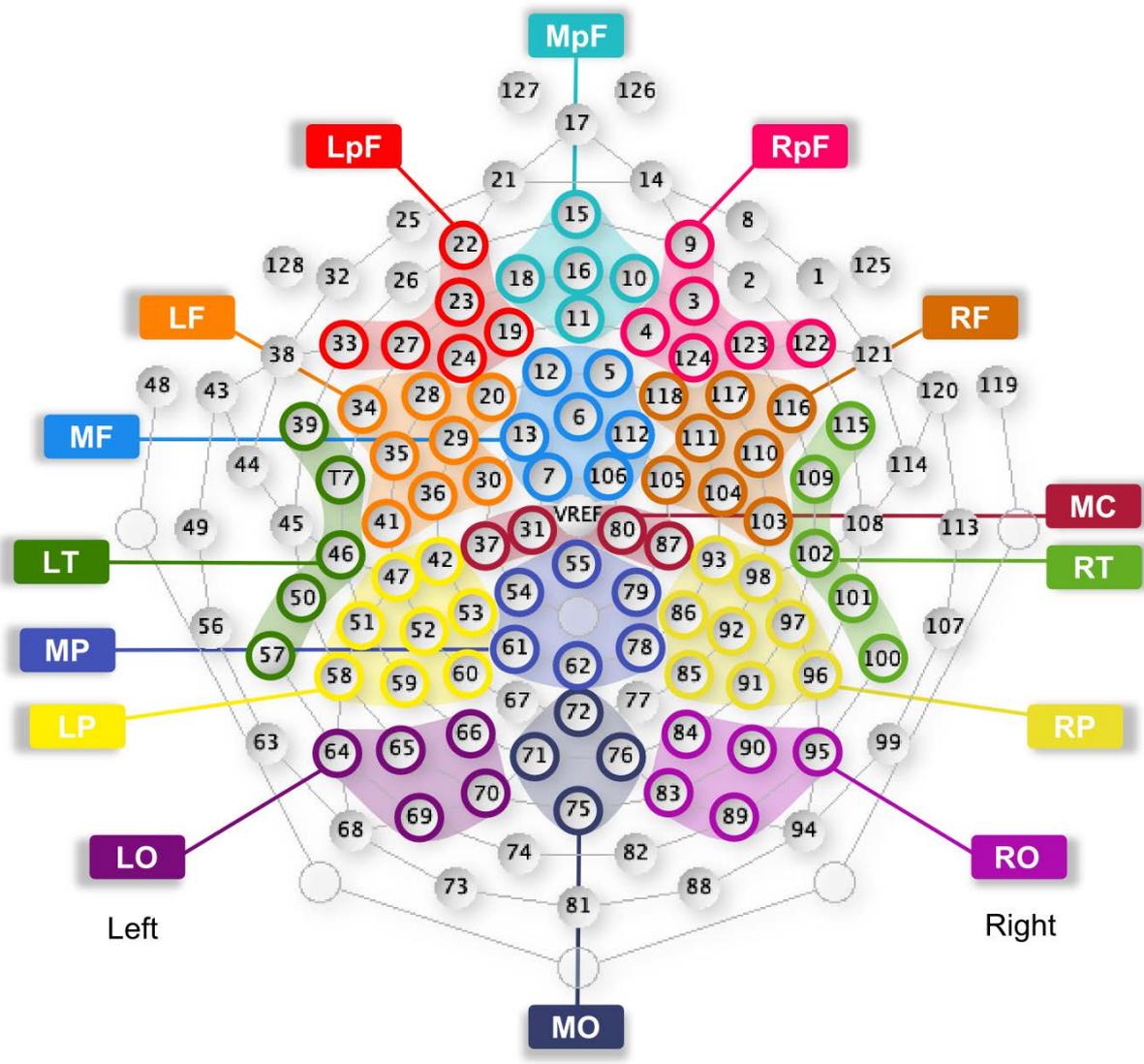


Figure 2. Electrode grouping and localizations : LpF left prefrontal, MpF midline prefrontal, RpF right prefrontal, LF left frontal, MF midline frontal, RF right frontal, LT left temporal, RT right temporal, MC midline central, LP left parietal, MP midline parietal, RP right parietal, LO left occipital, MO midline occipital, RO right occipital

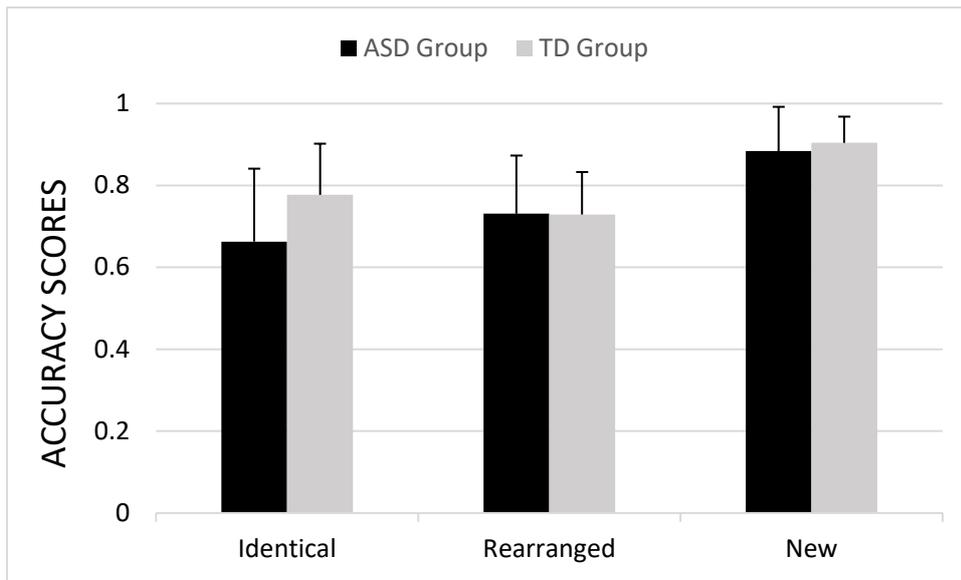


Figure 3. Accuracy scores per condition (identical pairs, rearranged pairs, new pairs), in the ASD group and TD group.

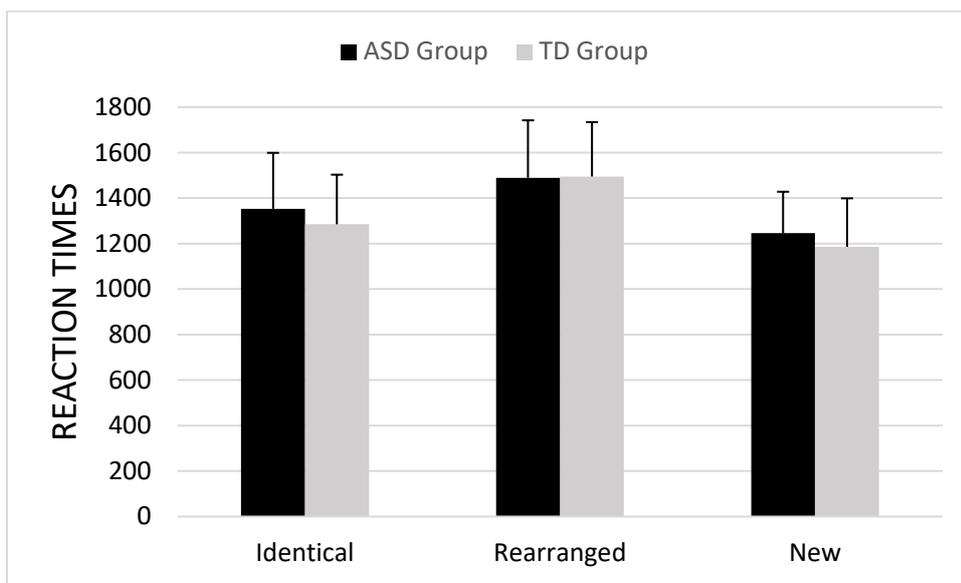


Figure 4. Reaction times per condition (identical pairs, rearranged pairs, new pairs), in the ASD group and TD group.

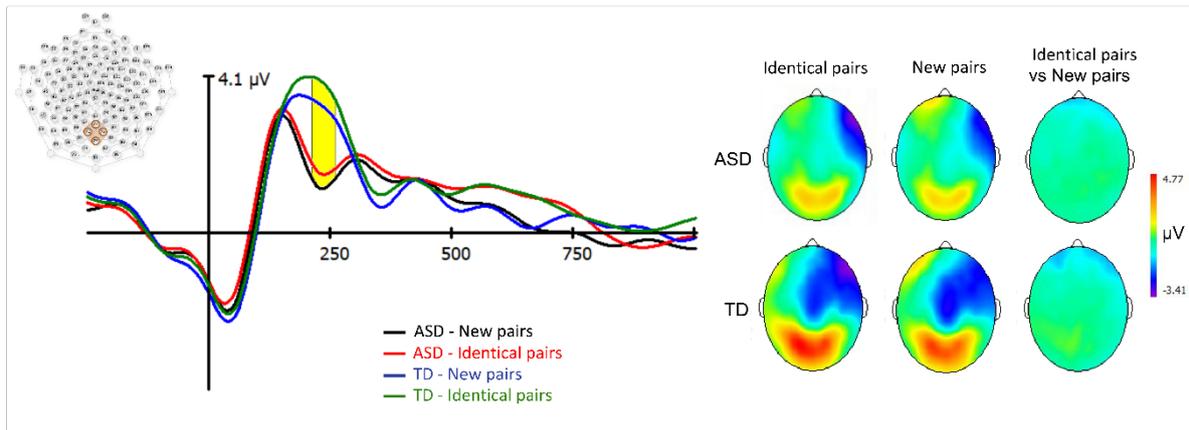


Figure 5. Event-Related Potentials (ERP) and topographies for P2 potential (signal in midline occipital area between 220-270ms). Yellow shaded areas correspond to significant differences between ASD and TD waveforms.

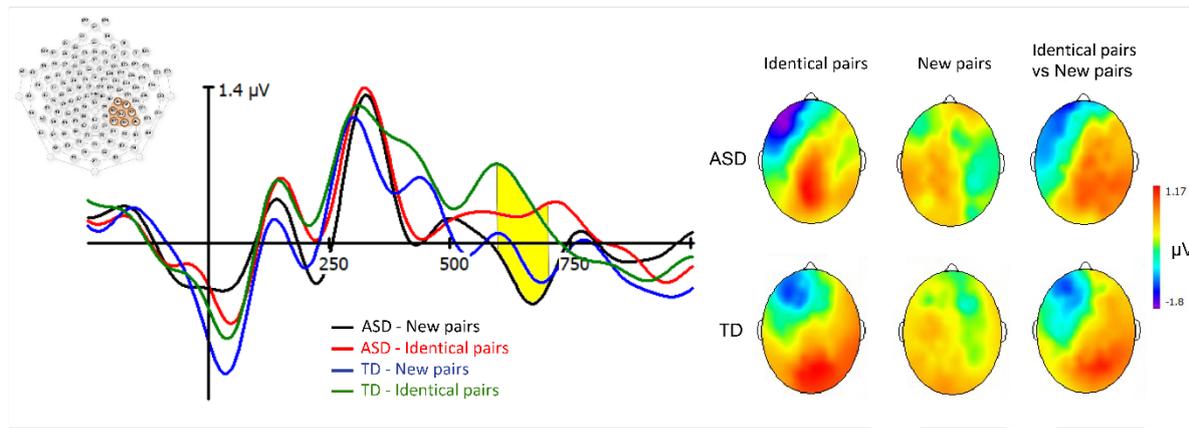


Figure 6. ERP and topographies for Late Positive Component – LPC potential (signal in right parietal area between 500–600ms). Yellow shaded areas correspond to significant differences between conditions, i.e. old/new effect in ASD and TD groups.

ANNEXES

Supplementary Table 1: average number of trials before, after rejection and discarded in each condition of interest (mean, minimum, maximum, standard-deviation) in the ASD and TD groups. We can observe that the difference between groups for identical pairs remains after artifact rejection. Otherwise, the total number of trials discarded in the ASD group did not differ from controls.

Before artifact rejection:

	Autism Spectrum Disorders Group (n = 22)		Typical Development Group (n = 32)		p Value
	Mean	SD	Mean	SD	
Identical pairs (/80)	53.09 (24-70)	14.27	62.75 (38-73)	9.89	0.0049
Rearranged pairs (/40)	29.23 (21-39)	5.70	29.19 (20-37)	4.15	0.976
New pairs (/40)	35.36 (21-40)	4.34	36.19 (29-40)	2.56	0.384

After artifact rejection:

	Autism Spectrum Disorders Group (n = 22)		Typical Development Group (n = 32)		p Value
	Mean	SD	Mean	SD	
Identical pairs (/80)	38.05 (17-56)	10.57	47 (30-68)	10.89	0.0041
Rearranged pairs (/40)	21.41 (15-30)	5.03	22.59 (15-32)	4.29	0.357
New pairs (/40)	25.32 (15-34)	4.88	27.97 (18-39)	6.16	0.098

Number of responses removed when rejecting artifacts (i.e. number of responses before artifact rejection minus number of responses after artifact rejection):

	Autism Spectrum Disorders Group (n = 22)		Typical Development Group (n = 32)		p Value
	Mean	SD	Mean	SD	
Identical pairs (/80)	15.05 (2-37)	8.49	15.75 (3-39)	10.21	0.791
Rearranged pairs (/40)	7.82 (1-23)	4.81	6.59 (0-15)	4.03	0.315
New pairs (/40)	10.05 (4-23)	4.66	8.22 (0-19)	5.46	0.207

Supplementary Table 2: number of “yes” responses, “no” responses, or error responses (out of time or absence of response) during the presentation of the 120 picture pairs at study.

	Autism Spectrum Disorders Group (n = 22)		Typical Development Group (n = 32)		p Value
	Mean	SD	Mean	SD	
“yes” responses (plausible)	29.45 (4-55)	14.35	38.38 (1-87)	19.94	0.078
“no” responses (implausible)	75.27 (27-104)	19.74	68.63 (15-107)	25.08	0.303
Errors	15.27 (0-68)	20.27	12.97 (0-68)	16.71	0.650