

# Incidental memory for faces in children with different genetic subtypes of Prader-Willi syndrome

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## Abstract

The present study examined the effects of genetic subtype on social memory in children (7–16 years) with Prader-Willi syndrome (PWS). Visual event-related potentials (ERPs) during a passive viewing task were used to compare incidental memory traces for repeated vs single presentations of previously unfamiliar social (faces) and nonsocial (houses) images in 15 children with the deletion subtype and 13 children with maternal uniparental disomy (mUPD). While all participants perceived faces as different from houses (N170 responses), repeated faces elicited more positive ERP amplitudes ('old/new' effect, 250–500ms) only in children with the deletion subtype. Conversely, the mUPD group demonstrated reduced amplitudes suggestive of habituation to the repeated faces. ERP responses to repeated vs single house images did not differ in either group. The results suggest that faces hold different motivational value for individuals with the deletion vs mUPD subtype of PWS and could contribute to the explanation of subtype differences in the psychiatric symptoms, including autism symptomatology.

**Key words:** ERP; face; memory; Prader-Willi syndrome; social

## Introduction

Prader-Willi syndrome (PWS) is a genetic disorder associated primarily with a deletion on paternal chromosome 15q11-13 (deletion subtype, 70% of cases) or duplication of the maternal chromosome (maternal uniparental disomy, mUPD, 25% of cases) (Butler, 1990; Nicholls et al., 1989). The PWS phenotype includes intellectual disabilities, compulsivity, hyperphagia, and increased risks of life-threatening obesity (Dykens and Cassidy, 1999; Milner et al., 2005). However, the specific characteristics vary across the two main genetic subtypes of PWS, as they are associated with distinct neuroanatomy (Honea et al., 2012), varied cognitive performance and adaptive skills (Copet et al., 2010; Stauder et al., 2005; Woodcock et al., 2009), behavioral problems (Holsen et al., 2008; Key and Dykens, 2008) and psychiatric illness (Dykens and Roof, 2008; Sinnema et al., 2011; Veltman et al., 2005; Vogels, 2003; Whittington and Holland, 2011), including

autism-spectrum symptomatology (Dimitropoulos and Schultz, 2007; Milner et al., 2005; Veltman et al., 2005). The majority of individuals with PWS do not meet full criteria for a diagnosis of ASD (Dankner and Dykens, 2012; Bennett et al., 2015), but their repetitive behaviors and social difficulties, especially in persons with the mUPD subtype, resemble those of persons with ASD (Dimitropoulos and Schultz, 2007; Dimitropoulos et al., 2013; Dykens et al., 2011; Rice and Einfeld, 2015).

Studies examining the social deficits in PWS and their overlap with ASD are just beginning (Koenig et al., 2004; Dimitropoulos et al., 2013; Dykens et al., 2011) and advocate for additional research using neural and behavioral methodologies previously established in the autism literature (Dykens et al., 2011). Prior studies noted that individuals with PWS may demonstrate atypical processing of faces and difficulties identifying emotional information (Halit et al., 2008; Key et al., 2013;

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Whittington and Holland, 2011), but findings regarding the influence of the genetic subtypes have been inconsistent. While individuals with either subtype of PWS performed similarly on behavioral measures of face detection and emotion identification (Halit et al., 2008; Whittington and Holland, 2011), compared to individuals with the deletion subtype, persons with the mUPD subtype may have more typical (Halit et al., 2008) or less typical (Key et al., 2013) neural responses to faces. The difference in the results may be due to relatively small sample sizes, stimulus type (neutral vs emotional faces), or task instructions (passive viewing vs active classification). Additionally, persons with PWS may have difficulties establishing social connections (Feinstein and Singh, 2007), and unlike others with or without developmental disabilities, their social competence does not appear to improve with age (Rosner et al., 2004).

In individuals with ASD, the focus of studies on the mechanisms underlying social deficits is shifting from the basic face perception processes, which may or may not be atypical (Jemel et al., 2006), to considering more complex questions related to social interest and motivation (Chevallier et al., 2012; Dawson et al., 2005). Persons with ASD often show reduced interest in faces (Klin et al., 1999; Moore et al., 2012; Riby and Hancock, 2009), and face processing deficits appear to be most pronounced in more cognitively demanding tasks (see Harms et al., 2010 for review). Similarly, examining more complex forms of social information processing in persons with PWS could provide new information regarding the role of genetic subtypes in the observed behavioral phenotypes.

Most face processing paradigms explicitly direct participants' attention to the stimuli for the purpose of comparison, identification, or description, and require an overt behavioral response. As such, intellectual ability and motivation to cooperate may confound the observed results and overestimate or underestimate social information processing skills. To reduce such potential confounds, this study examined spontaneous engagement of higher-order social information processing in persons with PWS.

Success of daily social interaction depends on the ability to detect, attend to, and interpret social information conveyed by faces without explicit directions to do so. Social interest underlies all forms of face processing, as 'without this natural influence there is little to prime us to look at faces with any more frequency than other objects' (Grelotti et al., 2002, p. 219). Behavioral and neuroimaging studies have repeatedly demonstrated that stimulus salience affects multiple stages of information processing, from basic orienting to more complex attention and memory (for reviews see Bromberg-Martin et al., 2010; Gabrieli, 1998; Corbetta and Shulman, 2002). Thus, even in the absence of external instructions, a more salient stimulus is expected to undergo more extensive cognitive processing than a less personally relevant stimulus. Measures of brain activity such as event-related potentials (ERP) offer excellent temporal resolution needed to document various stages of stimulus processing, from early sensory-perceptual responses to later cognitive evaluation. ERPs also provide interpretable data even without overt responses by the participant, making them ideal for use in individuals with intellectual disabilities by avoiding any confounds associated with motivation or cognitive ability.

Studies in typical populations identified the 'old/new' ERP response as a marker of memory, where previously studied (old) stimuli elicited more positive ERP amplitudes than novel (new) items (e.g. Curran and Cleary, 2003; Duarte et al., 2004). In particular, the frontal N400 response was observed between 300 and 500 ms and interpreted to reflect general stimulus

familiarity (Curran, 2004; Friedman and Johnson, 2000). The parietal P600 response within 400–900 ms was associated with recall of information (Nessler et al., 2001; Wilding, 2000) and depth of cognitive processing (Rugg et al., 2000). In studies utilizing face stimuli, this response was present within 300–500 ms (MacKenzie and Donaldson, 2007; Nessler et al., 2005).

Recently, we established that the 'old/new' ERP response previously used in the context of active memorization can also index incidental memory resulting from repeated exposures to stimuli during passive viewing, making it suitable to examine stimulus salience in individuals with developmental disabilities (Key and Dykens, 2014, 2016; Key and Corbett, 2014). In particular, we demonstrated that repetition of a socially salient stimulus (face) among other unfamiliar social and nonsocial images results in formation of a memory trace for the repeated face, as reflected by the increased parietal positivity within 300–500 ms in children aged 7–13 years (Key and Corbett, 2014). This memory trace for faces, however, was only observed in typical children, and not in children with ASD, consistent with low social interest in ASD. Strikingly, children with ASD who completed a social skills treatment program showed increased ERP evidence of incidental memory for the repeated faces compared to their baseline assessment, while no such changes were noted for children on the waitlist (Corbett et al., 2016). In all of these studies, ERP evidence of incidental memory for faces was independent of participants' IQ and did not correlate with early perceptual responses differentiating faces from nonsocial stimuli.

As no behavioral or neuroimaging studies have examined memory for faces in persons with PWS, the current study assessed incidental face memory as an index of spontaneous engagement in higher-order social information processing in children with PWS. Further, this study evaluated potential differences between deletion and mUPD genetic subtypes of PWS. To minimize possible effects of intellectual disability and short-term memory deficits associated with PWS (Dykens and Cassidy, 1999), no behavioral responses were required. The 'old/new' ERP marker of incidental memory for the repeated faces served as the dependent measure. Given their salience as social stimuli, we hypothesized that faces should attract attention and therefore be processed to a greater extent, resulting in a stronger memory trace, than nonsocial images (houses). Consequently, we expected to find that repeated faces elicit a greater (more positive amplitudes) 'old/new' ERP effect within 300–500 ms after stimulus onset. Further, as individuals with mUPD subtype are more likely to have ASD symptomatology, we predicted that they would generate a reduced ERP marker of face memory than those with deletions. Finally, as an exploratory aim, we examined the relationship between the old/new ERP responses to faces and the early perceptual responses to social vs nonsocial stimuli (occipito-temporal N170). The latter set of analyses has relevance for PWS in general, as information about brain processing of faces vs objects in this group remains limited.

## Materials and methods

### Participants

Twenty-eight children with PWS aged 7–16 years ( $M = 11.05$ ,  $s.d. = 2.70$  years) participated in the study. Fifteen of the participants ( $M$  age = 11.2,  $s.d. = 2.94$ ; 6 female) had the deletion subtype, and 13 had the maternal UPD subtype ( $M$  age = 10.96,  $s.d. = 2.52$ ; 9 female). Three additional participants (1 mUPD, 2

Deletion) were excluded due to insufficient number of artifact-free ERP trials. Three children were left-handed, the rest were right-handed (LQ  $M = .58$ ,  $s.d. = 0.64$ ) as determined by Edinburgh Handedness Inventory (Oldfield, 1971). All participants had normal or corrected-to-normal vision. The mean total IQ was 72.21 ( $s.d. = 17.44$ ) with better verbal than nonverbal performance ( $M$  verbal = 79.61,  $s.d. = 16.71$ ;  $M$  nonverbal = 71.50,  $s.d. = 17.48$ ,  $t(27) = 3.043$ ,  $P = 0.005$ ,  $d = 0.58$ ), assessed using Kaufman Brief Intelligence Test-2 (K-BIT-2; Kaufman and Kaufman 2004). The two groups did not differ in age or IQ.

Parents/guardians of participants provided written informed consent, and children with PWS indicated their assent for all study procedures. The study was conducted with approval from the Institutional Review Board of Vanderbilt University Medical Center.

### Stimuli

Stimuli included 51 color photographs of unfamiliar young adults displaying positive facial affect obtained from a standardized Radboud Faces Database set (Langner et al., 2010), 51 color photographs of unfamiliar houses (façade view, obtained from realtor websites), and a drawing of a yellow smiley face. The on-screen size of the stimuli was 30 cm high and 25 cm wide. From the viewing distance of 90 cm, the stimuli subtended visual angles of  $19^\circ(h) \times 16^\circ(w)$ . The yellow smiley face was  $14.5\text{ cm}$  ( $9.21^\circ$ ) in diameter.

We chose to use smiling rather than neutral faces for the following reasons: (i) emotional stimuli attract greater attentional resources compared to neutral pictures, and thus would be more likely to demonstrate any repetition-related changes even during passive viewing (e.g. Codispoti, Ferrari, and Bradley, 2007); (ii) in social situations, faces are rarely if ever truly neutral, and therefore positive facial expressions would be more ecologically valid for investigating spontaneous attention to potential social partners; (iii) compared to other emotions, positive facial expressions are more likely to be accurately recognized by persons with developmental disabilities (PWS: Whittington and Holland, 2011; ASD: Uljarevic and Hamilton, 2013). Houses were selected as the non-social contrast condition due to structural similarity to faces in terms of the specific features (e.g. roof, windows, door) and their expected spatial arrangement (e.g. a roof above the windows, a door at the bottom). The choice of the smiley face as the attention probe was motivated by its general familiarity, positive affect, and distinct perceptual characteristics (shape, color, low image complexity) that would make it an easily detectable target.

### Electrodes

A high-density array of 128 Ag/AgCl electrodes embedded in soft sponges (Geodesic Sensor Net, EGI, Inc., Eugene, OR) was used to record the ERPs. Electrode impedance levels were at or below 40 kOhm as checked before and after testing. During acquisition, data were sampled at 250 Hz with the filters set to 0.1–100 Hz. All electrodes were referred to vertex and then re-referenced offline during data analysis to an average reference, the recommended reference for high-density arrays (Picton et al., 2000) that has also been used successfully in prior ERP studies of memory (e.g. Curran and Cleary, 2003), including incidental face memory (e.g. Key and Corbett, 2014; Key and Dykens, 2014).

### ERP procedure

All stimuli were presented in random order for 1500 ms with a varied inter-stimulus interval of 1300–1600 ms to prevent habituation and development of trial onset expectations. For each participant, one of the unfamiliar faces and one of the houses were randomly selected and repeated 50 times throughout the experiment, yielding a unique set of repeated images for each participant. The remaining stimuli were presented once. To encourage attention to the stimulus sequence, participants were asked to press a response button when they saw the yellow smiley face (10 trials, brain responses to this stimulus were not included in the analysis). Stimulus presentation was controlled by E-prime (v. 2.0, PST, Inc., Pittsburgh, PA). The entire task included 210 trials and lasted approximately 12 min. A researcher was present in the room to monitor participants' behavior. If participants became inattentive or restless, stimulus presentation was suspended until the participant was ready to continue with the task.

### Data analysis

#### Behavioral data

To support behavioral observations of participants' attention to the stimulus sequence, number and reaction time of the responses to the smiley face probes were submitted to a one-way ANOVA with the diagnostic group as the between-subject factor.

#### ERP data

Collected EEGs were filtered using a 30 Hz low-pass filter, segmented on stimulus onset to include a 100-ms pre-stimulus baseline and a 800 ms post-stimulus interval, and screened for ocular and movement artifacts using an automated algorithm in NetStation followed by a manual review. Data for electrodes with poor signal quality within a trial were reconstructed using spherical spline interpolation procedures. If more than 20% of the electrodes within a trial were deemed bad, the entire trial was discarded. The trial retention rates were comparable between conditions and groups, (Deletion:  $M = 15.87$ ,  $s.d. = 5.44$ ; UPD:  $M = 14.85$ ,  $s.d. = 4.36$ ;  $P$ 's  $> 0.05$ ).

Following artifact screening, individual ERPs for repeated and single presentations of faces and houses were averaged, re-referenced to an average reference, and baseline-corrected. To reduce the number of electrodes in the analysis, only data for the electrode clusters identified as optimal for the frontal N400 and parietal P600 old/new effects, as well as bilateral occipito-temporal N170 face response (see Figure 1) were used in remaining statistical analyses. These four clusters were selected a priori based on previously published ERP studies of face familiarity (Curran and Hancock, 2007) and our prior work on incidental repetition detection (Key and Dykens, 2014; Key and Corbett, 2014).

Next, to reduce the number of electrodes in the analysis, data were averaged within electrodes clusters previously identified as sensitive to incidental memory (Figure 1). Mean amplitudes for ERPs were calculated across the time windows reported in previous studies using the same paradigm in participants with developmental disabilities. The selected time windows corresponded to the occipito-temporal P1 (50–150 ms) and N170 (150–250 ms) responses reflecting face perception (e.g. Grice et al., 2001) and frontal and parietal 'old/new' responses (250–500 ms, 500–800 ms) indexing visual stimulus recognition and recall (e.g. Curran and Hancock, 2007; Key and Corbett, 2014).

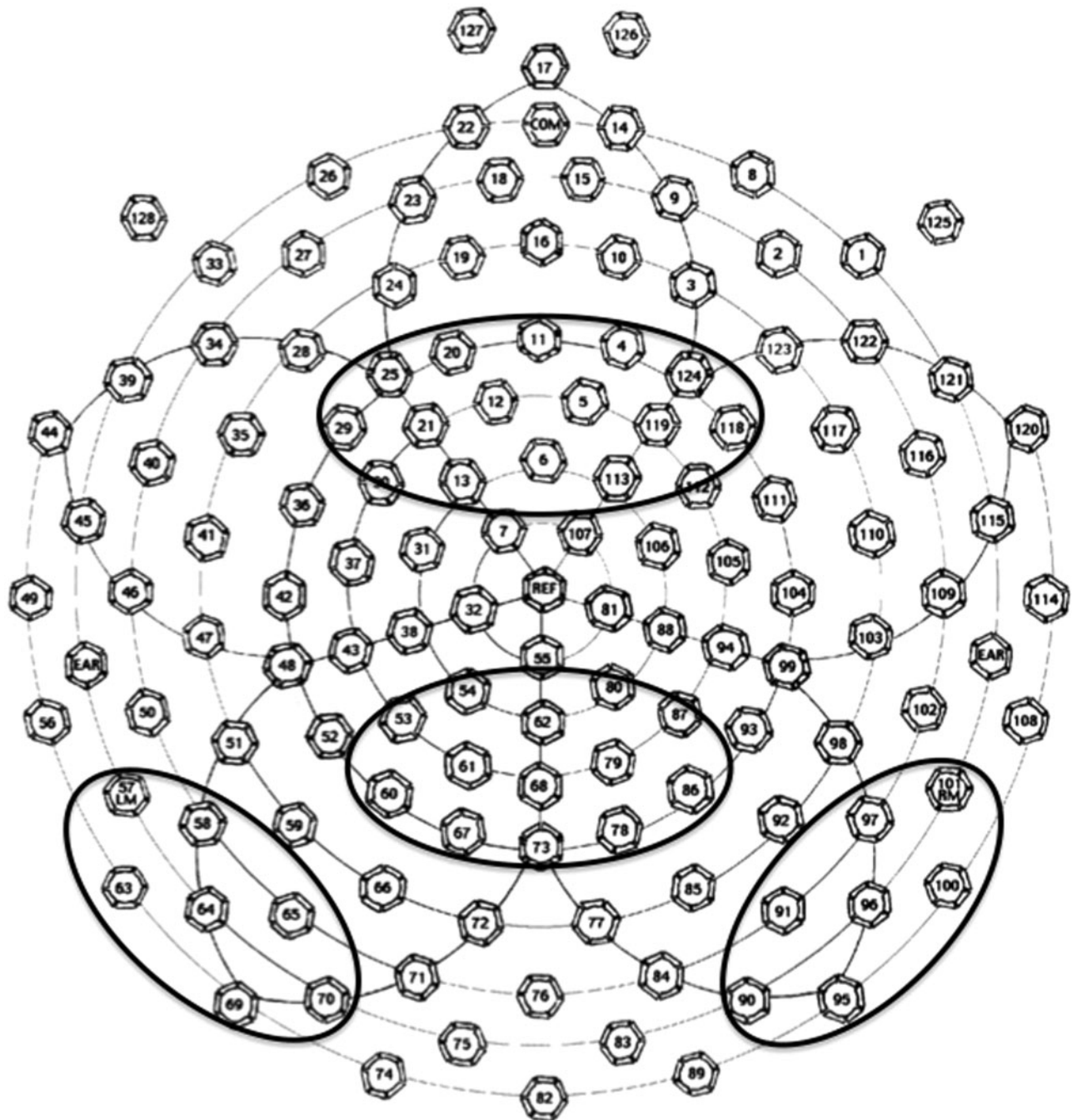


Fig. 1. Electrode layout and the selected electrode clusters used for data analysis.

The resulting values were entered into repeated-measures ANOVAs with Genetic Type (deletion, UPD) as the between-subject factor and Stimulus (2: faces, houses)  $\times$  Memory condition (2: single, repeated)  $\times$  Electrode (2: left vs right occipito-temporal or frontal vs parietal) within-subject factors with Huynh-Feldt correction. Significant interactions were further explored using planned comparisons (testing differences in response to repeated vs single presentations of faces within each group) as well as post-hoc one-way ANOVAs and pair-wise *t*-tests. To address the problem of multiple significance tests, false discovery rate (FDR; Benjamini and Hochberg, 1995) approach was used, and only those follow-up tests that remained significant based on the FDR criteria are reported. Unlike the

Bonferroni correction that adjusts alpha levels based on the total number of tests conducted, the FDR method controls for the proportion of incorrect rejections of the null hypothesis among the tests for which the null hypothesis was rejected (i.e. tests with *P* values  $< 0.05$ ) and has been used successfully in ERP analyses (Crowley et al., 2012; Key and Corbett, 2014).

## Results

### Behavioral data

Responses to attention probes (smiley face) revealed no group difference in the number of responses to the attention probe

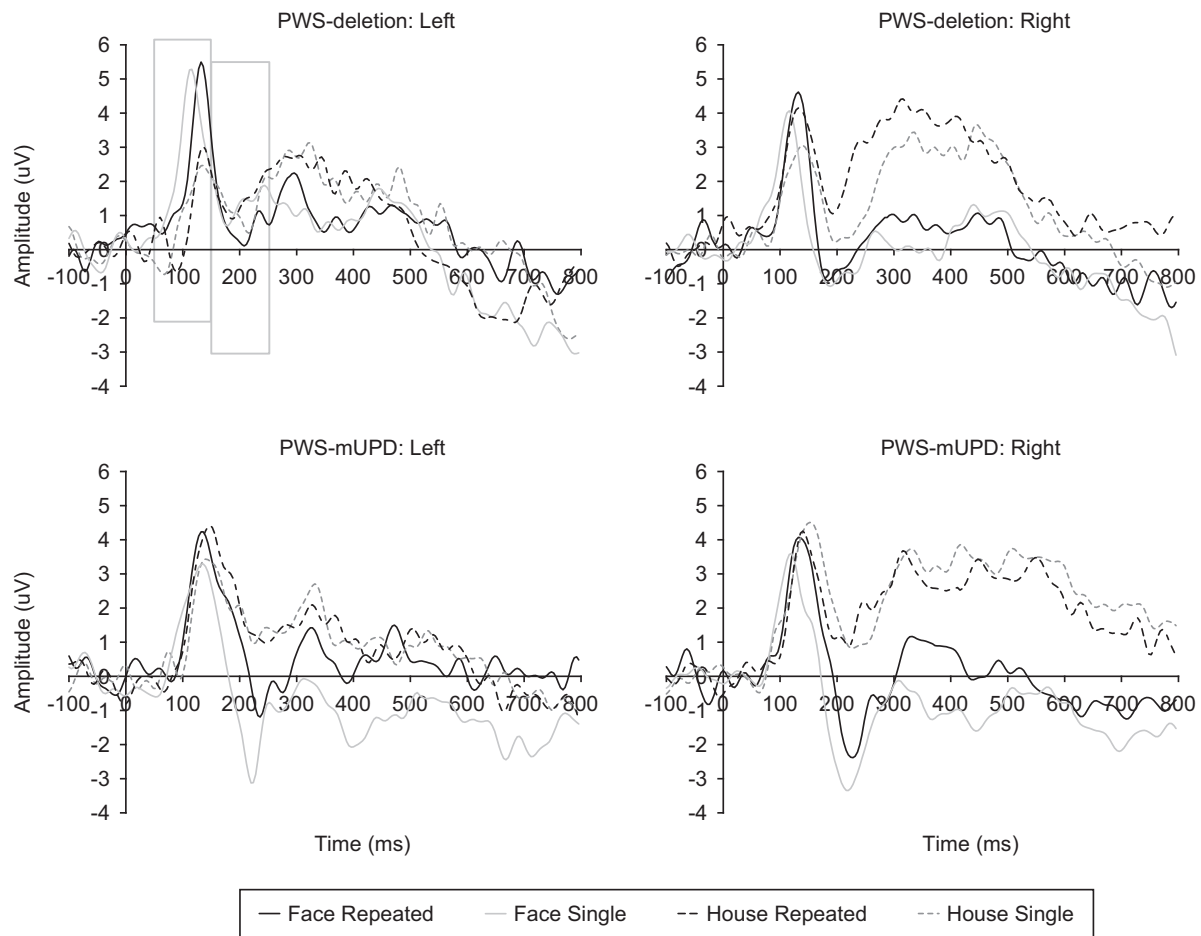


Fig. 2. Averaged ERP waveforms in response to repeated and single stimuli at left and right occipito-temporal clusters.

(Deletion:  $M = 8.60$ ,  $s.d. = 2.20$ ; mUPD:  $M = 7.69$  ms,  $s.d. = 2.06$ ,  $P = 0.272$ ) or in the reaction time (Deletion:  $M = 604.12$  ms,  $s.d. = 169.48$ ; mUPD:  $M = 639.92$  ms,  $s.d. = 120.16$ ,  $P = 0.531$ ). Neither of the response metrics correlated with IQ.

### ERP data

**Face perception (occipito-temporal responses).** 50–150 ms (P1): There were no significant effects for the 50–150ms temporal interval.

150–250 ms (N170): This interval was categorized by the main effect of Stimulus,  $F(1,26) = 19.208$ ,  $P < 0.001$ ,  $\eta_p^2 = 0.425$ . Post-hoc analysis indicated that larger (more negative) responses were observed for faces than houses,  $t(27) = 4.142$ ,  $P < 0.001$ ,  $d = 0.78$  (Figure 2).

**Face memory (frontal/parietal old/new response).** 250–500 ms: There was a main effect of Electrode,  $F(1,26) = 43.820$ ,  $P < 0.001$ ,  $\eta_p^2 = 0.628$ , and interactions of Memory  $\times$  Genetic Subtype,  $F(1,26) = 5.170$ ,  $P = 0.031$ ,  $\eta_p^2 = 0.166$ ; Stimulus  $\times$  Electrode,  $F(1,26) = 18.789$ ,  $P < 0.001$ ,  $\eta_p^2 = 0.420$ , and Stimulus  $\times$  Memory  $\times$  Genetic Subtype,  $F(1,26) = 6.750$ ,  $P = 0.015$ ,  $\eta_p^2 = 0.206$ . The follow-up analyses revealed a more positive response to faces than houses at frontal electrode locations,  $t(27) = 4.396$ ,  $P < 0.001$ ,  $d = 0.83$ . Additionally, planned comparisons indicated that participants in the Deletion subgroup showed the expected evidence of incidental memory for faces in the form of more positive ERP amplitudes for the repeated faces vs faces seen

once,  $t(14) = 4.342$ ,  $P = 0.001$ ,  $d = 1.12$  (Figures 3 and 4). This stimulus contrast was not significant for children in the mUPD group. Post-hoc one-way ANOVA indicated that the magnitude of the incidental memory for faces (quantified as the amplitude difference score for the repeated-single face) was significantly greater in the deletion than mUPD group,  $F(1,26) = 15.059$ ,  $P = 0.001$ ,  $d = 1.53$ . Neither group evidenced significant differentiation of repeated vs single houses ( $P$ 's  $> 0.38$ ).

500–800 ms: There was a main effect of Electrode,  $F(1,26) = 19.040$ ,  $P < 0.001$ ,  $\eta_p^2 = 0.423$ , and a Stimulus  $\times$  Memory  $\times$  Genetic Subtype interaction,  $F(1,26) = 10.584$ ,  $P = 0.003$ ,  $\eta_p^2 = 0.289$ . Follow-up planned comparisons analyses revealed that children in the mUPD group elicited more negative ERP responses for repeated vs single faces,  $t(12) = 2.705$ ,  $P = 0.019$ ,  $d = 0.76$ . No significant differences in face or house memory were observed for children in the deletion group.

**Brain-behavior and brain-brain connections.** Correlational analyses examined the associations between the brain indices of stimulus repetition detection ('old/new' effects for faces and houses), perceptual processes (occipito-temporal N170 response to faces and houses), age, IQ, as well as number and RT of responses to the attention probe. No significant correlations were observed between the ERP responses and behavioral measures for the combined sample or for individual subtypes. However, in the combined sample, larger (more negative) N170 responses to faces were associated with larger (more positive) old/new

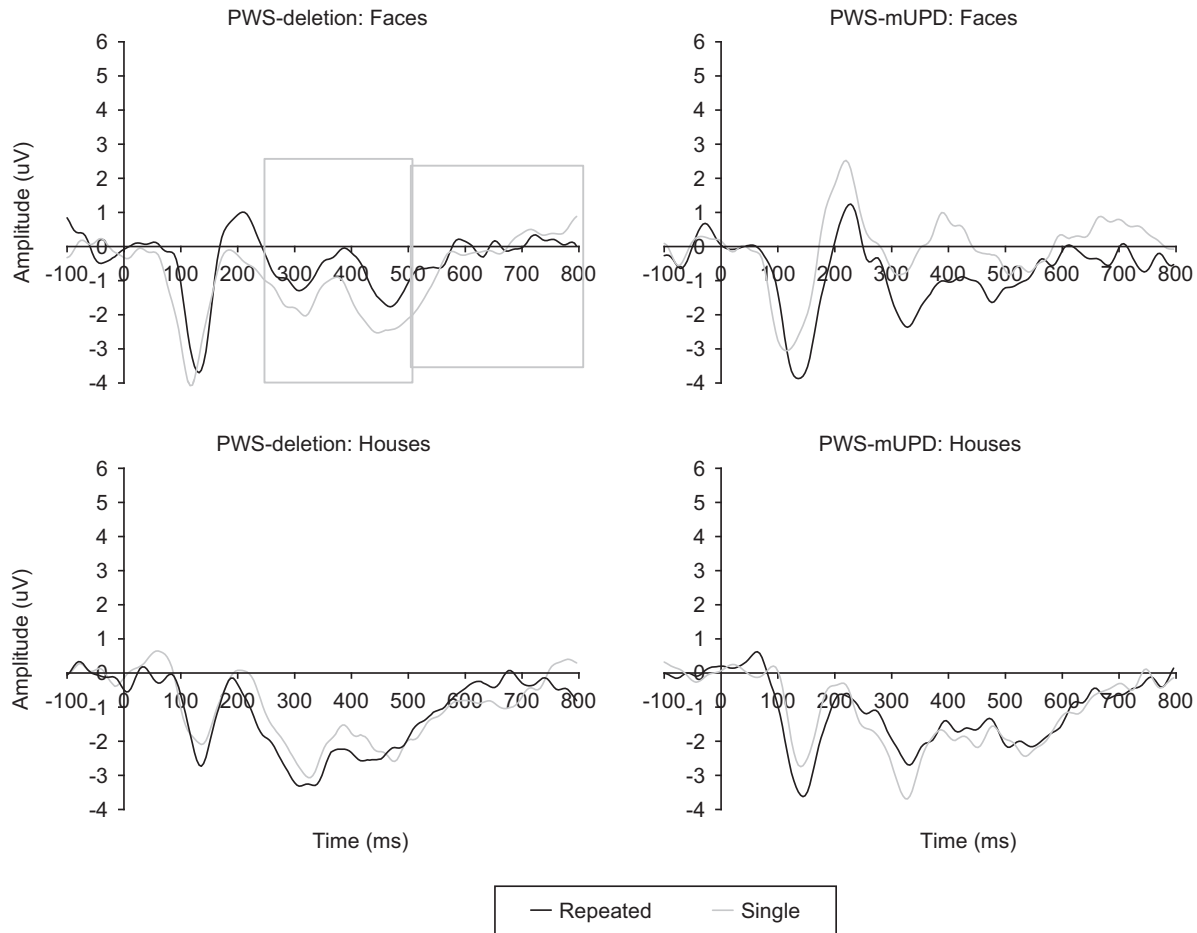


Fig. 3. Averaged old/new ERP responses to repeated and single stimuli at midline frontal locations.

response to repeated faces within 250–500 ms,  $r(27) = -0.571$ ,  $P = 0.002$ .

## Discussion

This study examined ERP responses indexing spontaneous social (faces) and nonsocial (houses) information processing in children with two different genetic subtypes of PWS. We observed that the participant groups did not differ in the perceptual responses to faces, as both generated larger N170 responses to faces than houses. However, only participants with the deletion subtype evidenced incidental memory for the repeated faces, reflected in the increased positive amplitudes of the ‘old/new’ ERP responses in 250–500 ms period. Conversely, participants with the mUPD subtype demonstrated evidence of habituation to repeated faces, indicated by the reduced ERP responses to the repeated faces within 500–800 ms. ERPs elicited by repeated vs single houses were not significantly different in either group.

Larger occipito-temporal N170 amplitude to faces than houses in children with PWS replicates findings in typical populations where larger ERP responses are observed for faces than other visual stimuli (Bentin and Deouell, 2000; Eimer, 2000; Jemel et al., 2003). However, the lack of subtype differences in the N170 response are in contradiction to our previous observation of reduced face-object differentiation in individuals with the mUPD subtype (Key et al., 2013). This inconsistency could be

due to the younger age of the present sample (7–16 years) vs 14–30 years in the Key et al. (2013). Indeed, social deficits in PWS appear to become more pronounced with increasing age (Dimitropoulos and Schultz, 2007; Rosner et al., 2004). Future longitudinal studies are needed to identify the potential time course of emerging perceptual difficulties associated with face processing, especially in those with the mUPD subtype.

Group differences in incidental memory for faces but not houses, indexed by the ‘old/new’ ERP response, suggest distinct approaches to higher-order social information processing in those with deletions vs mUPD subtype. The more positive ERP amplitudes in response to repeated faces in the deletion group are consistent with previously reported findings in typically developing children (Key and Corbett, 2014) and adults (Key and Dykens, 2016). Due to their salience as socially relevant stimuli, pictures of faces received sufficiently extensive cognitive processing to develop a memory trace. Importantly, these memory traces were evident despite the passive viewing approach, and in the absence of instructions to detect, memorize or respond behaviorally to these stimuli. These findings are also in line with the report by Dimitropoulos et al. (2013) who noted less severe social difficulties (measured by Social Responsiveness Scale) in the deletion subtype compared to the mUPD and idiopathic autism groups. The deletion group thus demonstrated typical processing of social information during passive viewing.

Conversely, individuals with the mUPD subtype exhibited a reduction in the ERP amplitude to repeated faces compared to

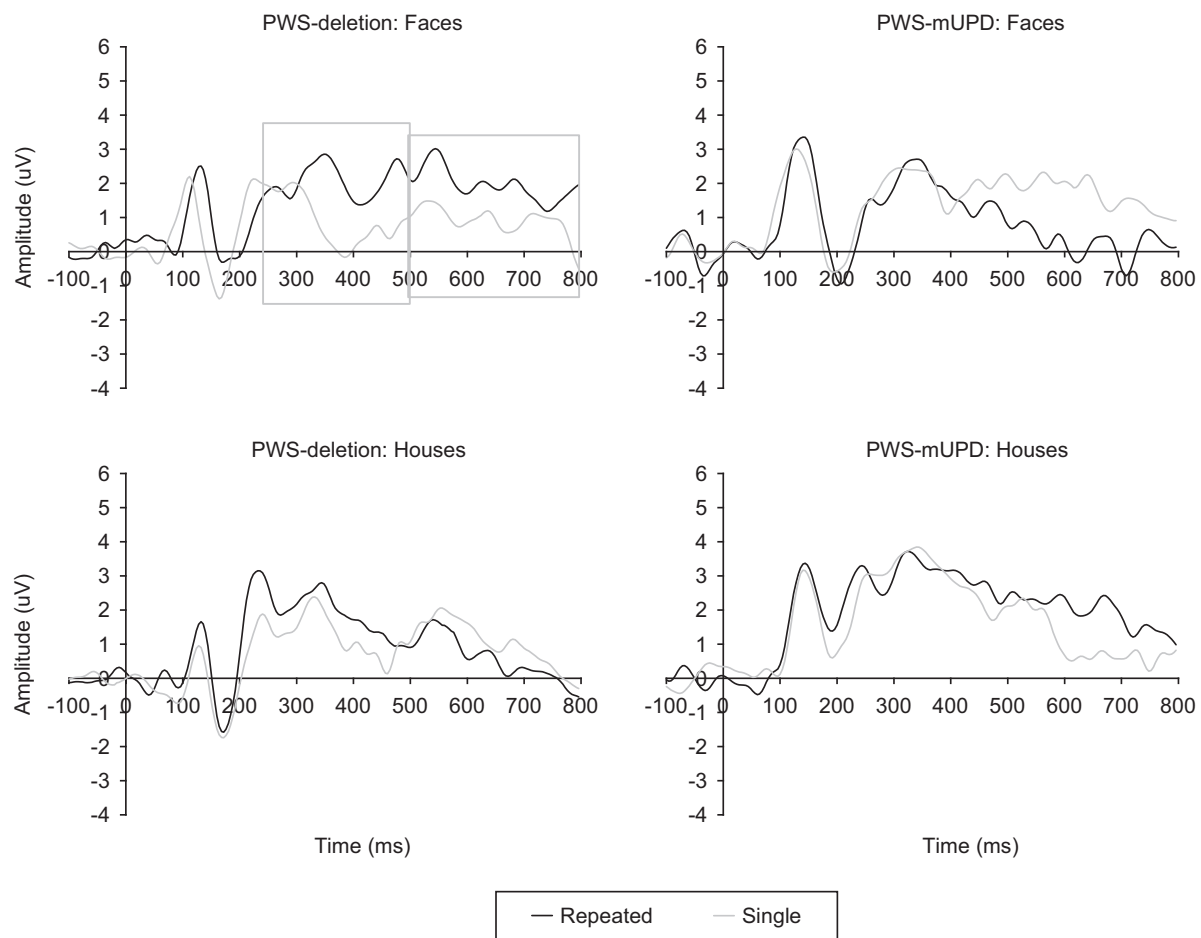


Fig. 4. Averaged old/new ERP responses to repeated and single stimuli at midline parietal locations.

those seen only once. Based on the idea that that the extent of stimulus processing is affected by motivational salience (Bromberg-Martin *et al.*, 2010), these results suggest that for children with mUPD, faces might not have been sufficiently salient to engage in extensive processing beyond the basic perceptual analysis. These results align well with the behavioral evidence of greater social difficulties and greater autism symptomatology in the mUPD group (e.g. Dimitropoulos *et al.*, 2013). Indeed, similar lack of ERP amplitude enhancement to repeated faces has been previously observed in children with ASD (Key and Corbett, 2014; Corbett *et al.*, 2016). The proposed interpretation linking the pattern of ERP responses to the extent of stimulus processing is further supported by fMRI findings of repetition-related enhancement of brain activity in cases of increased attention to the stimuli and incidental recall (see Segaert *et al.*, 2013 for review), while reduced activation was observed during repeated passive exposure to the less salient stimuli (Jessen *et al.*, 2002).

Reduced activation in response to repeated stimulation is often interpreted as habituation. While it is more frequently investigated in the context of the early, sensory ERP responses, Snyder and Keil (2008) and others argue that habituation can affect not only attention-getting properties of a stimulus (indexed by the obligatory ERP responses) but also attention-maintaining processes (indexed by the late ERP responses). Habituation associated with stimulus repetition can manifest as reduced allocation of attentional resources due to decreased stimulus novelty

or salience. Previously, studies of the P300 response, a well-accepted marker of attention and memory processes, noted fast habituation to task-irrelevant stimuli and absent or delayed habituation to particularly salient events during passive exposure (e.g. Bennington and Polich, 1999). Of particular relevance to the current study, Codispoti *et al.* (2007) demonstrated that passive exposure to repeating visual stimuli results in the amplitude reduction of the late parietal positivity, while the early sensory/perceptual processes (<300 ms) may not habituate at all because they reflect basic bottom-up processes necessary to categorize the stimulus as previously experienced. Our findings of no memory effects for the N170 response and reduced amplitudes to repeated faces in the 500–800 ms window for the mUPD group are consistent with that pattern.

An alternative explanation for the lack of increased 'old/new' response to faces in the mUPD group could be that they paid less attention to all stimuli. However, the absence of group differences in the attention probe responses (number or reaction time) or in the 'old/new' ERP response to the repeated houses argues against this possibility. It is also possible that the presentation sequence, in which instances of stimulus repetition were often separated by multiple novel images, could have exceeded the capacity of memory system in participants with the mUPD subtype. Previous ERP study in 10 adults with PWS (unknown subtype) suggested possible short-term memory deficits reflected in the reduced P3 amplitudes to targets in a visual target detection (oddball) task using simple line drawings of

faces with direct or averted gaze (Stauder et al., 2002). In a follow-up study using an inhibition task (Continuous Performance Test), Stauder et al (2005) reported subgroup differences, such that the reduced P3 response was observed in the mUPD group but not in the deletion group. However, the incidental memory paradigm used in our study placed minimal demands on the participants' memory system by including no explicit task, a very small 'memory set' (one face, one house), and a high number of repeated exposures (50 trials each). Thus, memory limitation is not a likely explanation.

Correlational analyses within the genetic subtype groups and in the combined sample demonstrated that the observed 'old/new' effect was not related to the participants' verbal, non-verbal, or composite IQ, replicating previous findings that ERP markers of repetition-based incidental memory are independent of intellectual functioning (Key and Dykens, 2014; Key and Corbett, 2014). However, our exploratory correlational analyses also revealed that the 'old/new' ERP responses to repeated faces could be related in part to the early perceptual responses to faces: larger N170 response to faces was associated with greater positivity of the 'old/new' response to repeated faces. Future studies will need to probe this finding to clarify whether improved perceptual processing contributed to greater memory for faces (bottom-up influence) or if greater interest in social information resulted in greater attention to and perceptual processing of faces (top-down modulation).

The observed difference in incidental memory for faces between participants with the deletion and mUPD subtype could contribute to broader phenotypic differences, in particular, those related to psychiatric disorders. Persons with PWS are described as preferring routines and predictability (Dimitropoulos et al., 2013; Moss et al., 2009). The ability to notice repeating stimuli or events would be integral to maintaining such predictability. The ERP evidence of habituation rather than more active memory trace formation in participants with mUPD subtype may reflect reduced allocation of cognitive resources to processing of the continuously changing social environment. The decreased predictability could impose greater cognitive demands and, when cognitive resources are low, lead to emotional outbursts and tantrums (Woodcock et al., 2009). This explanation fits with higher incidence of psychiatric problems in the mUPD subgroup, including psychosis with an affective component (e.g. Dykens and Roof, 2008; Dykens et al., 2011; Whittington and Holland, 2010).

Although our study resulted in novel findings, it has several limitations. We did not collect any objective recollection data that could verify memory for the repeated faces. Our goal was to keep the task maximally easy to avoid any confounds due to intellectual disability. However, in future studies, a post-task recognition probe for the repeated stimuli could help bolster our interpretation of ERP results. Also, we used static images, and it is possible that dynamic stimuli could facilitate memory trace development (e.g. Otsuka et al., 2009; but see O'Toole et al., 2002). However, the choice of static stimuli allowed for a direct comparison of incidental memory for social (faces) and nonsocial (houses) stimuli, with the latter more typically experienced as non-moving images. Although our paradigm was designed to examine spontaneous processing of social information in the absence of explicit instructions directing attention to the particular stimulus type, the use of a smiley face cartoon as the attention probe could have lead the participants to pay more attention to all faces. If such carry-over did occur, it would have affected both memory conditions and therefore is unlikely to alter the proposed interpretation of reduced salience of social

stimuli in children with the mUPD compared to the deletion subtype of PWS. Finally, relating ERP findings for social vs non-social stimuli to direct measures of social dysfunction in PWS will strengthen future studies.

In sum, this study expands neural evidence of genetic subtypes differences in the social information processing of children with PWS. While brain responses indexing incidental memory for faces in the deletion group resembled those previously observed in typical children, the lack of a similar memory trace for the repeated faces in the mUPD group suggested potential alterations in social interest, which may contribute to increased ASD symptomatology in this group. Although further work is needed, these results identify possible mechanisms underlying social information processing in persons with PWS, and also offer potential new treatment targets or outcome measures for future trials aimed at ameliorating social difficulties.

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