Physiology & Behavior 222 (2020) 112937

Contents lists available at ScienceDirect

Physiology & Behavior

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

Attractiveness and neural processing of infant faces: effects of a facial abnormality but not dopamine

Rens Huffmeijer[a,b,*], Yael Barak-Levy[c], Ralph C.A. Rippe[a]

[a] Institute of Education and Child Studies, Leiden University, P.O. Box 9555, 2300 RB Leiden, the Netherlands.
[b] Leiden Institute for Brain and Cognition (LIBC), Leiden University, P.O. Box 9600, 2300 RC Leiden, the Netherlands.
[c] Department of Early Childhood, Achva Academic College, R.D Shikmim 7980400, Arugot, Israel.

ARTICLE INFO

Keywords:
Infant faces
Dopamine
Cleft lip
ERP
N170
Attractiveness
Mediation

ABSTRACT

Adults' caregiving responses toward infants may have important origins in the perception and processing of infant cues as well as the motivation to attend to these cues. Moreover, some biological processes, such as dopaminergic neurotransmission, may be crucially involved. Although infant stimuli are generally experienced as cute and rewarding, infants with a visible disability may be regarded much less favorably than others, perhaps dependent on differences in perception, motivation, and neural processing. The current study investigated effects of administered dopamine on the perceived attractiveness and neurophysiological indices of attention and processing (i.e., the P1, P2, and N170 components of the event-related potential) of infant faces with and without a cleft lip. No evidence for effects of dopamine was found, but we replicated the finding that the decreased attractiveness of infants with a cleft lip was mediated by decreased configural face processing (smaller N170 amplitudes), but not more general attentional and/or executive processing (P2). The current findings show once again the unfavorable consequences of a cleft lip, but also highlight the importance of combining and relating measures across various levels of analysis and underscore the importance of replication.

1. Introduction

Adults differ in the way they respond to infant signals. Differences in the modality, timing, and appropriateness of caregiving responses may have important origins in the perception and processing of infant cues as well as the motivation to attend to those [47, 48]. As biological processes may be crucially involved, recent years have seen an impressive increase in attention for the neurobiological origins of human caregiving. Accumulating evidence has highlighted the essential role that reproductive hormones, such as estrogen, prolactin and testosterone, as well as the 'social' neuropeptides oxytocin and vasopressin play in the onset, maintenance and shaping of caregiving behavior (see e.g., [14, 77, 78]). Dopaminergic neurocircuitry has been critically implicated, particularly in animal studies (see e.g. [41, 78]). Specifically, hormonal effects on adults' responses to infants and children are thought to occur, at least in part, through interactions with dopaminergic pathways (see e.g. [77, 78]). Considering the above, the lack of administration studies focusing specifically on dopamine is striking.

Dopamine is a monoamine neurotransmitter important for neural signalling within several cortical and subcortical pathways. Dopaminergic neurons in the substantia nigra project to the caudate nucleus and putamen (dorsal striatum) to form the nigrostriatal pathway important for movement (e.g., [10, 43]). Mesocorticolimbic dopaminergic pathways arise from neurons in the ventral tegmental area (VTA) in the midbrain that connect to the nucleus accumbens (NA), limbic structures, and areas within the frontal cortices. These pathways are implicated in motivation and reward, addiction (e.g., [1, 9]), and higher-order cognitive functions, including (executive) attention and working memory (e.g., [18, 67, 87]).

Both attention and motivation, and the rewarding aspects of interacting with an infant are essential for successful caregiving (e.g., [47, 48, 49, 95]). Animal studies have provided evidence for the involvement of dopamine in caregiving behavior. In rats, dopamine release into the NA has been associated with maternal licking and grooming behaviour [16] and systemic administration of dopamine receptor antagonists resulted in disruptions in pup approach and retrieval [51, 52, 68, 71]. Evidence for the involvement of dopamine in human caregiving behavior is mostly indirect. Functional magnetic resonance imaging (fMRI) studies have revealed activity in dopaminergic areas as well as closely connected brain regions (including the ventral tegmental area, striatum, thalamus, amygdala, cingulate cortex, and the medial prefrontal and right orbitofrontal cortices) when mothers are presented

* Corresponding Author. Tel. +31 71 5274080, Fax +31 71 5273945.
E-mail addresses: rhuffmeijer@fsw.leidenuniv.nl (R. Huffmeijer), yael.barak.levy@gmail.com (Y. Barak-Levy), rrippe@fsw.leidenuniv.nl (R.C.A. Rippe).

https://doi.org/10.1016/j.physbeh.2020.112937
Received 28 November 2019; Received in revised form 9 April 2020; Accepted 23 April 2020
Available online 17 May 2020

with sounds [54, 85, 86], pictures [6, 50, 64, 93, 106], or videos [65, 75] of their own or other infants. Importantly, genetic variation in the dopamine receptor D1 and D2 genes has been related to maternal attention, with mothers with genotypes putatively resulting in more efficient dopaminergic signaling paying more attention to their infants [59].

The current study aims to gain insight into some of the neurocognitive mechanisms of dopamine involvement in caregiving behaviour. Specifically, the current study investigates effects of administered dopamine on neural indices of processing of and attention to infant faces as well as their perceived attractiveness. As mentioned above, the dopamine system is well known to regulate (executive) attention in general (e.g., [18, 67, 87]) and has been suggested to play a role in maternal attention more specifically [59]. Therefore, we expect dopamine to enhance attention to, and consequently processing of, the infant stimuli. Attentional effects may occur on several time scales, involving early and automatic capture of attention (enhanced salience) as well as later and more controlled resource allocation (e.g., [66]). Event-related potentials (ERPs) are ideally suited to study and distinguish between early, automatic, and later, more controlled, processes. The visual P1 component, a positive wave in the ERP peaking at occipital electrode sites at approximately 100ms post stimulus onset, represents an early stage of visual encoding (e.g., [28, 44, 56, 80]) and is sensitive to early saliency effects. Enhanced attention is reflected in larger amplitudes (e.g., [32, 102]). Later, more controlled processes should affect the P2, a positive-going ERP component that often peaks about 200ms post stimulus onset at posterior electrode sites. The P2 represents a later stage of encoding and processing visual stimuli (e.g., [44, 56]) and is sensitive to the operation of working memory [82] as well as (re)orienting of visuospatial attention [96]. To the extent that dopamine enhances both the early automatic capture of attention and later, more controlled attentional processes, we expect larger (more positive) P1 and P2 amplitudes in response to infant faces after dopamine administration. In addition, enhanced (early) attention may lead to more extensive stimulus processing in general. The N170, a negative wave in the ERP peaking at occipito-temporal electrode sites at approximately 170ms post stimulus onset, can be used to quantify face processing. Contrary to the P1 and P2, the N170 is a face-specific component representing the structural encoding of face configuration (i.e., forming a mental representation of the features, and their constellation, of a particular face; e.g., [37, 57, 91]). Changes to face configuration and facial features, including scrambling or inversion of features, and face inversion are well known to affect the N170 (e.g., [7, 12, 13, 23, 27, 36, 80, 84]). The amplitude of the N170 has been related to activity of the fusiform gyrus (a brain area extensively involved in face processing; [35]). If dopamine enhances attention to and processing of infant faces, we expect not only larger (more positive) P1 and P2 amplitudes, but also larger (i.e., more negative) N170 amplitudes after dopamine administration.

Dopamine administration has been associated with the activation and heightened activity of the reward circuitry [2, 69]. Hence, on a cognitive/perceptual level, dopamine may enhance the reward value and perceived attractiveness of infant faces. We therefore expect infant faces to be rated as more attractive after dopamine administration. Although it might be argued that neural processing precedes and underlies overt judgements, the question remains whether changes in P1, P2 and N170 amplitudes after dopamine administration should be expected to mediate effects of dopamine on attractiveness ratings. In previous research, we found that effects of a facial abnormality (a cleft lip) on ratings of attractiveness of infant faces were mediated by decreased N170, but not P2 amplitudes [34]. In addition, changes in ERP component amplitudes may depend mostly on attention and changes in attractiveness on reward. Attention and reward processing are distinct, although related processes, as reward is well known to bias attention (e.g., [3, 74]). Similarly, they depend on overlapping, closely connected, but also distinct, neural circuitry (e.g., [58, 70]). The current study, therefore, explored the possibility of mediation without formulating a directional hypothesis.

In addition, the current study investigates the potential moderational role of infant facial characteristics. Infant stimuli are generally experienced as cute and rewarding by adults, parents as well as non-parents, and attract attention (e.g., [15, 24]), raising the possibility of ceiling effects. However, some infants, in particular those with a visible disability, may be regarded much less favorably than non-disabled children. Children with a physical abnormality even run a greater risk of parental neglect or maltreatment (e.g., [26, 40, 63, 88, 94]). Thus, it is of great interest to investigate whether dopamine could mitigate some perceptual or evaluative bias. A cleft lip is an easily visible, as well as fairly common condition, affecting one to two per 1000 newborn infants in The Netherlands ([81]; similar to the WHO worldwide prevalence estimate of 1 in 700 live births; [61]). It is a purely physical condition and can often be remedied in (early) childhood (e.g., [62]). Nevertheless, negative consequences of being born with a cleft lip have been found for early parent-child interaction, and socio-emotional as well as cognitive development [17, 31, 63, 90].

Infants with a cleft lip are rated as less cute and less attractive than healthy infants [34, 73, 76, 104], and adults make less of an effort to prolong the viewing time of images of infants with a cleft lip [73], indicative of a diminished reward value. The presence of a cleft lip also seems to hamper normative processing of infant faces [34, 72]. Moreover, we have recently shown that reductions in perceived attractiveness of infants with a cleft lip were mediated by changes in face-specific neural processes (reflected in N170 amplitudes; [34]). In addition, studies of adults' fixation patterns on images of infants [76] and mothers' fixation patterns during face-to-face interaction [19] point toward differences in attentional processing of healthy infants and infants with a cleft lip. As both attentional and reward-related processes are likely implicated, effects of dopamine may well be moderated by the presence of a cleft lip, with potentially larger effects for the inherently less rewarding stimuli depicting infants with a cleft lip. This would result in reduced differentiation between infants with and without a cleft lip after dopamine administration, both in ratings of attractiveness and ERP component amplitude.

In summary, the current study investigated effects of administered dopamine on the perceived attractiveness and several neural indices of attention and processing of infant faces with and without a cleft lip. We hypothesized that dopamine enhances the perceived attractiveness and neural processing (as reflected in larger P1, N170 and P2 amplitudes) of infant faces, particularly of infant faces with a cleft lip (this would reduce differentiation between healthy infants and infants with a cleft lip). Moreover, we explored whether effects of dopamine on ratings of attractiveness are mediated by changes in neural processing.

2. Material and Methods

2.1. Participants

A total of 74 female students, aged 18-41 years (M = 21.76, SD = 3.27) were invited to participate in two experimental sessions. Exclusion criteria included neurological or psychiatric disease, use of psychoactive medication, cardiovascular disease, pregnancy, non-Caucasian ethnicity, uncorrected visual impairments, and alcohol or drug abuse. None of the participants were parents or had a cleft lip or palate themselves. Of the 74 participants, 11 did not participate in the second session, 2 turned out to meet exclusion criteria after starting the study, 2 were excluded from analyses because of medication errors, 4 had missing EEG (n = 2) or rating data (n = 2) due to technical errors, and 4 provided insufficient artifact-free EEG data. The final sample thus consisted of 51 participants (aged 18-41 years, M = 22.18, SD = 4.12; excluded and included participants did not differ in age, $t(72) = 1.50$, $p > .10$). The power to detect a moderate-size main effect of dopamine using this sample size is .93. In case of substantial mediation, power to

detect the indirect effect is at least as large as the power to detect the main effect [39]. Thus, the current sample size is sufficient to test for mediation. Participants received 10 euros after participation in the first session and 25 euros after participation in the second session. The study was approved by the ethics committee of the Leiden University Medical Center and the local IRB. All participants signed informed consent.

2.2. Procedure

Participants came to the laboratory for two identical 3.5-hour experimental sessions. At the start of each session, participants self-administered two capsules containing either 25 mg carbidopa and 100 mg levodopa (Sinemet; dopamine condition) or a placebo (containing only a filler substance, no active ingredient). Levodopa/carbidopa and placebo were administered using identical capsules, and the order of administration (i.e., levodopa/carbidopa during the first and placebo during the second session or vice versa) was counterbalanced across participants. Within the current sample, 27 participants participated in the dopamine condition first and 24 participated in the placebo condition first. After drug administration participants completed several questionnaires and then performed two blocks of tasks in one of two orders: half the participants first performed several tasks while their encephalographic (EEG) activity was recorded (an infant face processing paradigm, a sound processing paradigm, and a mirror-neuron task) and then participated in a block of behavioral tasks (including an observation of interactive behavior and computerized tasks assessing empathy and ratings of infant faces). The other half of the participants performed the task blocks in the opposite order. The first block started approximately 60 minutes after drug administration. The current study uses EEG data from the infant face processing paradigm and behavioral data from the task assessing participants' ratings of infant faces. The infant face processing paradigm took about 6 minutes to complete and the rating task took about 10 to 15 minutes to complete. These same tasks were used in our previous study comparing the processing and evaluation of infant faces with and without a cleft lip (see [34]).

2.3. Stimuli

The same 6 photographs of healthy infant faces and 6 photographs of infant faces with a cleft lip were used in the face processing paradigm and the rating task. Pictures were obtained from a set of grey-scale images (with a black background) of infant faces included in an existing database [72, 73]. All pictures showed an infant's face with direct gaze at the observer, a forward-oriented head position (i.e., not turned away or tilted), and a neutral facial expression. All infants were rated between 9 and 18 months old, and pictures of healthy infants and infants with a cleft lip were matched on perceived gender of the infant and luminosity. The face processing paradigm also included 12 scrambled stimuli created from the 12 infant faces as a visual control (see [34] for a detailed description of stimulus selection and creation of the scrambled stimuli).

2.4. Experimental tasks

Ratings. Participants viewed each of the 12 infant faces ($4.06 \times 5.00^{\circ}$ visual angle) on a computer screen. To rate infants' cuteness and approachability, visual analog scales (VAS; subtending $10.20 \times 2.29^{\circ}$ visual angle) were presented below each image. Cuteness was rated on a 500-point VAS ranging from "not at all cute" to "very cute". The 500-point VAS to rate approachability ranged from "I would turn and look away from this baby" to "I would turn and look toward this baby". Participants provided ratings by dragging a cursor onto the desired position on each VAS using the mouse. Ratings of cuteness and approachability (all $rs \geq .62$, $ps < .001$) were averaged together into a single, composite attractiveness score as in [34].

Infant face processing paradigm. Participants sat behind a computer monitor in a sound attenuated, dimly lit room. Images of healthy infant faces, faces of infants with a cleft lip, and scrambled faces (all $6.60 \times 8.10^{\circ}$ visual angle) were presented on a black background for a total of 144 trials (48 healthy, 48 cleft, 48 scrambled [sufficient for reliable amplitude measures of the relatively early P1, N170 and P2 components; see e.g. [33]]). Images of healthy faces and faces of infants with a cleft lip were each presented 8 times and each of the 12 scrambled faces was presented 4 times in quasi random order. Images from the same category (healthy, cleft, scrambled) could not be presented more than 4 times in a row. Each trial consisted of the presentation of a fixation cross for 800 – 1200ms (varying randomly) after which an image was presented for 1000ms. No responses were required from the participants.

2.5. ERPs

The same procedures were followed as described in [34]. During the infant face processing paradigm, participants' EEG was acquired using 129-channel hydrocel geodesic sensor nets. The signal was amplified using a NetAmps300 amplifier, low-pass filtered at 200 Hz, and digitized at a rate of 500 Hz using NetStation software (Electrical Geodesics, Inc.). Impedances were kept below 50 kΩ and Cz was used as the online reference. Before exporting the data for further offline processing using Brain Vision Analyzer 2.0 software (BVA; Brain Products GmbH), the EEG was high-pass filtered at 0.3 Hz (99.9% pass-band gain, 0.1% stop-band gain, 1.5 Hz roll-off). Using BVA, the EEG was low-pass filtered at 30 Hz (-3 dB, 48 dB/octave), rereferenced to the average of activity in all channels, and segmented into segments extending from 200 ms before to 1000 ms after the onset of each image. Independent components analysis (ICA) was used to correct ocular artifacts, and segments containing residual artifacts were removed (if the difference between the maximum and minimum activity within a segment exceeded 100 μV within a 200ms window in the vertical EOG channels [channel 8-channel 126 and channel 25-channel 127] or 60 μV within a 200ms window in the horizontal EOG channel [channel 128-channel 125] the whole segment was removed, and individual channels were removed from a segment if the difference between the maximum and minimum activity in that channel during that segment exceeded 150 μV). The remaining segments were averaged per category (healthy infant faces, faces of infants with a cleft lip, and scrambled faces), per condition (dopamine, placebo). Participants contributed an average number of 43.9 (SD = 5.49, range: 25-48), 44.1 (SD = 5.83, range: 26-48), and 43.7 (SD = 6.14, range: 25-48) artifact-free trials in response to healthy, cleft, and scrambled faces respectively in the dopamine condition, and 44.7 (SD = 5.03, range: 27-48; Healthy), 44.7 (SD = 4.45, range: 31-48; Cleft), and 44.5 (SD = 5.20, range: 25-48; Scrambled) in the placebo condition.

Time windows and electrodes for quantification of P1, N170, and P2 amplitudes were selected a-priori. Because the current study used the same paradigm, procedures, and apparatus among a similar (though independent) sample, we quantified ERP components the same as reported in [34]. P1 amplitude was quantified as the average amplitude within the 96-124ms window across channels 70 (O1), 75 (Oz), and 83 (O2). N170 amplitude was quantified as the average amplitude in the 132-162ms time window across electrodes 58 (T5), 64, and 65 (left N170), and 90, 95, and 96 (T6; right N170). P2 amplitude was quantified as the average amplitude in the 184-244ms time window across electrodes 59, 65, and 66 (left P2) and 84, 90, and 91 (right P2). Figure 1 illustrates scalp topographies of the P1, N170 and P2.

2.6. Analyses

The MEMORE-macro for SPSS [60] was used to test whether dopamine affects ratings of infant attractiveness and P1, N170, and P2 amplitudes in response to infant faces, and whether effects on attractiveness ratings are mediated by ERP component amplitudes. Because it

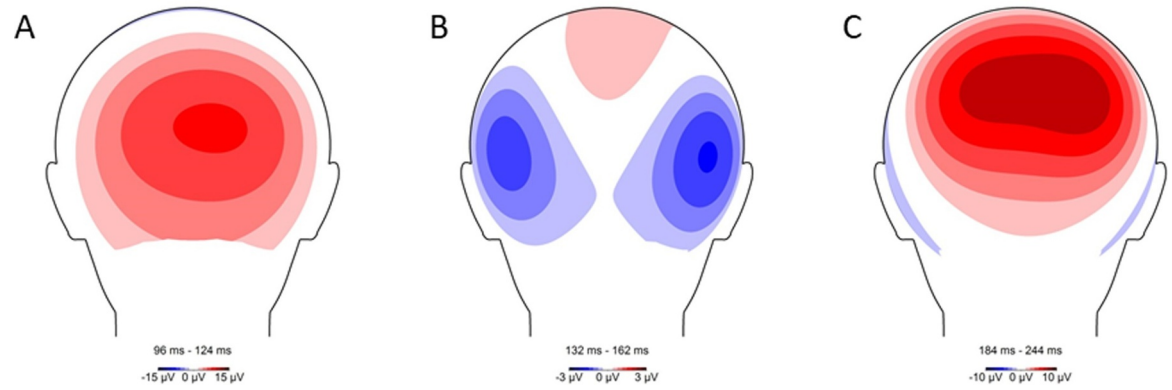

Figure 1. Scalp topographies of the P1 (A), N170 (Faces – Scrambled; B), and P2 (C).

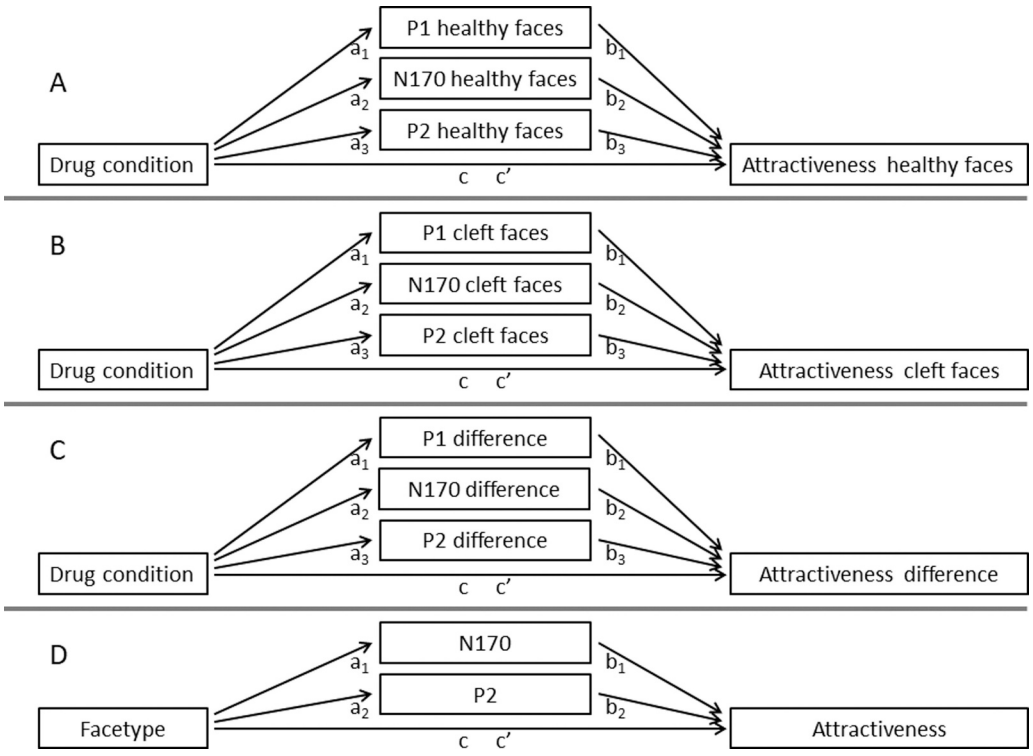

Figure 2. The mediation models: The current study examined whether effects of dopamine on the perceived attractiveness of healthy infant faces (A) and infant faces with a cleft lip (B), and the extent to which participants differentiate between these two types of faces (C) are mediated by effects of dopamine on P1, N170 and P2 amplitudes. We also examined whether differences in attractiveness of healthy infant faces and infant faces with a cleft lip are mediated by differences in N170 and P2 amplitudes (D).

is currently not possible to include a second independent variable or moderator in analyses using the MEMORE-macro, separate analyses were performed for 1) healthy infant faces, 2) faces of infants with a cleft lip, and 3) differences between healthy infant faces and faces of infants with a cleft lip. Figure 2 (panels A, B, and C) provides a visual illustration of the models tested. The MEMORE-macro performs a series of regression analyses to test the total effect of the independent variable (drug condition) on the outcome variable (attractiveness ratings; path c), the effect of the independent variable on the mediators (P1, N170, and P2 amplitudes; paths a_1, a_2, and a_3), the associations between effects on the mediators and the outcome variable (paths b_1, b_2, and b_3), and, finally, both the direct effect of the independent variable on the outcome variable (path c') and its indirect effects through each mediator (paths a_1*b_1, a_2*b_2, and a_3*b_3). Drug condition (dopamine vs. placebo) was the independent variable in all three analyses. Attractiveness ratings of healthy infants, attractiveness ratings of infants with a cleft lip, and the difference between attractiveness ratings of healthy infants and infants with a cleft lip (Healthy – Cleft) were the outcome variables in analyses 1, 2, and 3 respectively. The mediators were P1, N170 and P2 amplitudes in response to healthy faces, P1, N170 and P2 amplitudes in response to faces of infants with a cleft lip, and the difference between P1, N170 and P2 amplitudes in response to healthy infant faces and faces of infants with a cleft lip (Healthy – Cleft) in analyses 1, 2, and 3 respectively. N170 and P2 amplitudes were averaged across left and right electrode sites in all three analyses. Alpha was set to 0.05 and indirect effects were tested using the percentage bootstrap method with 10,000 runs in all three analyses.

In addition, repeated measures ANOVAs testing effects of drug condition (placebo, dopamine) and face type (healthy vs. cleft for attractiveness ratings; healthy vs. cleft vs. scrambled for ERP amplitudes) on attractiveness ratings, P1, N170, and P2 amplitudes were performed to examine effects of drug condition and face type in greater detail, both with and without including order of administration (dopamine first vs. placebo first) as additional between-subjects factor. Analyses of N170 and P2 amplitudes also included laterality (left vs. right) as within-subjects factor. Results of these analyses can be found in the supplementary materials.

Finally, we also used the MEMORE-macro to replicate our previous finding that reduced attractiveness ratings of infants with a cleft lip compared to healthy infants were mediated by reduced N170, but not

Table. 1
Descriptive statistics of attractiveness ratings and ERP amplitudes.

		Dopamine condition			Placebo condition		
		Healthy	Cleft	Scrambled	Healthy	Cleft	Scrambled
Attractiveness		309 (66)*	275 (83)		307 (78)	274 (79)	
P1		7.85 (3.05)	7.82 (3.35)	7.01 (3.37)	7.62 (3.62)	7.82 (3.74)	7.06 (3.88)
N170	Left	1.32 (2.93)	1.42 (2.96)	2.59 (2.77)	0.74 (2.85)	1.22 (2.77)	2.38 (2.74)
	Right	1.17 (3.49)	1.36 (3.45)	2.67 (3.11)	1.17 (3.26)	1.34 (3.22)	2.83 (3.50)
P2	Left	6.26 (3.04)	5.25 (3.37)	6.04 (3.33)	6.17 (3.52)	5.58 (3.54)	6.01 (3.57)
	Right	7.82 (3.98)	6.85 (4.13)	7.42 (3.78)	7.82 (4.25)	6.89 (3.96)	7.48 (4.34)

* Mean (SD)

P2 amplitudes (see Figure 2, panel D). Face type (healthy vs cleft) was used as the independent variable, attractiveness ratings were the outcome, and N170 and P2 amplitudes were the mediators. Because none of our analyses revealed any effect of drug condition (see below and supplementary materials), variables were averaged across the dopamine and placebo conditions, and because P1 amplitudes in response to healthy infant faces and infant faces with a cleft lip were not significantly different (replicating our previous findings; see supplementary materials), we did not include P1 amplitude as a mediator in this analysis. Alpha was set to 0.05 and indirect effects were tested using the percentage bootstrap method with 10,000 runs.

3. Results

Descriptive statistics of attractiveness ratings, P1, N170 and P2 amplitudes are presented in Table 1. Figures 3, 4, and 5 illustrate the P1, N170, and P2 respectively.

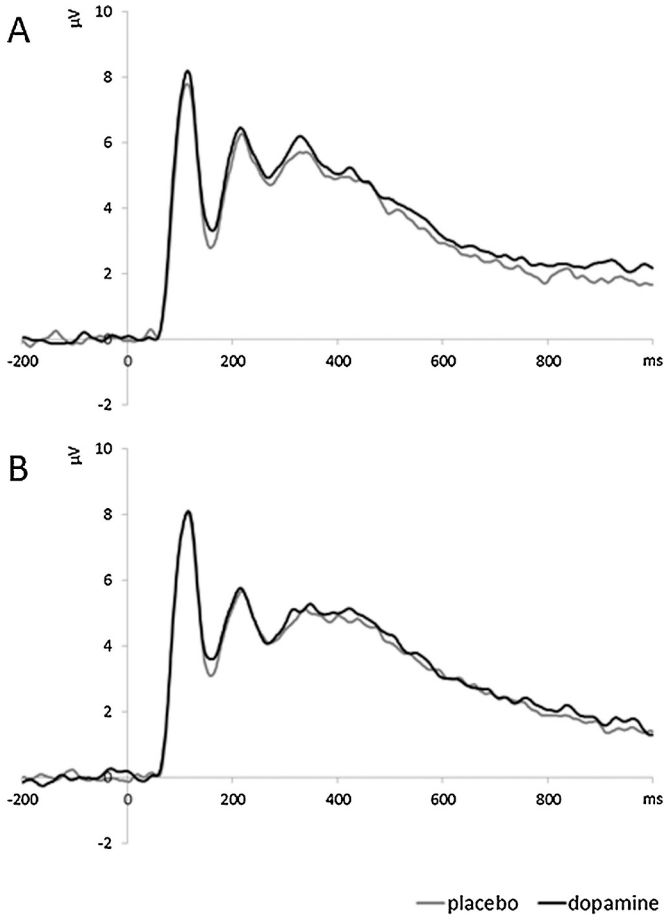

Figure 3. Grandaverage ERPs averaged across electrodes 70 (O1), 75 (Oz) and 83 (O2) illustrating the P1. Dopamine administration had no significant effects on the amplitude within the 96-124ms post-stimulus time window (P1) in response to pictures of healthy infant faces (A) and infant faces with a cleft lip (B).

3.1. Effects of dopamine on ERP component amplitudes and attractiveness of infant faces

Attractiveness ratings of and P1, N170, and P2 amplitudes in response to healthy infant faces and faces of infants with a cleft lip were approximately normally distributed (all standardized |skewness| < 3, standardized |kurtosis| < 3, except for the P1 amplitudes in the dopamine condition: standardized skewness = 3.05 [healthy], standardized skewness = 3.33 and standardized kurtosis = 3.16 [cleft]) without outliers (all |z| ≤ 3.29) in both the dopamine and placebo conditions.

Healthy infant faces. The analyses did not reveal a significant total or direct effect of drug condition on attractiveness ratings (total effect: b = 1.92, SE = 7.52, $t(50)$ = 0.26, p = .80; direct effect: b = 1.88, SE = 7.75, $t(44)$ = 0.24, p = .81). P1, N170, and P2 amplitudes were not significantly affected by drug condition either (P1: b = 0.22, SE = 0.33, $t(50)$ = 0.68, p = .50; N170: b = 0.29, SE = 0.21, $t(50)$ = 1.37, p = .18; P2: b = 0.04, SE = 0.33, $t(50)$ = 0.14, p = .89) and there were no significant associations between effects of drug condition on ERP component amplitudes and attractiveness ratings (P1: b = -0.32, SE = 4.77, $t(44)$ = -0.07, p = .95; N170: b = 0.23, SE = 5.50, $t(44)$ = 0.04, p = .97; P2: b = 1.10, SE = 4.98, $t(44)$ = 0.22, p = .83). Moreover, none of the indirect effects of drug condition on attractiveness ratings through ERP component amplitudes were significant (P1: b = -0.07, bootstrapped SE = 1.93, bootstrapped 95% CI: -5.28 – 2.65; N170: b = 0.07, bootstrapped SE = 1.52, bootstrapped 95% CI: -3.55 – 2.86; P2: b = 0.05, bootstrapped SE = 1.97, bootstrapped 95% CI: -3.66 – 4.81).

Faces of infants with a cleft lip. The analyses did not reveal a significant total or direct effect of drug condition on attractiveness ratings (total effect: b = 1.75, SE = 7.38, $t(50)$ = 0.24, p = .81; direct effect: b = 1.63, SE = 6.63, $t(44)$ = 0.25, p = .81). P1, N170, and P2 amplitudes were not significantly affected by drug condition either (P1: b = 0.00, SE = 0.33, $t(50)$ = 0.00, p = 1.00; N170: b = 0.11, SE = 0.23, $t(50)$ = 0.46, p = .65; P2: b = -0.19, SE = 0.34, $t(50)$ = -0.55, p = .58) and there were no significant associations between effects of drug condition on ERP component amplitudes and attractiveness ratings (P1: b = 7.29, SE = 4.06, $t(44)$ = 1.80, p = .08; N170: b = 1.07, SE = 4.48, $t(44)$ = 0.24, p = .81; P2: b = -0.05, SE = 4.15, $t(44)$ = -0.01, p = .99). Moreover, none of the indirect effects of drug condition on attractiveness ratings through ERP component amplitudes were significant (P1: b = 0.00, bootstrapped SE = 3.21, bootstrapped 95% CI: -7.84 – 5.73; N170: b = 0.11, bootstrapped SE = 1.10, bootstrapped 95% CI: -1.83 – 2.88; P2: b = 0.01, bootstrapped SE = 1.44, bootstrapped 95% CI: -2.30 – 4.01).

3.2. Effects of dopamine on differentiation between healthy infant faces and faces of infants with a cleft lip

Difference scores (healthy – cleft) of attractiveness ratings and P1, N170, and P2 amplitudes were approximately normally distributed (all standardized |skewness| < 3, standardized |kurtosis| < 3) without

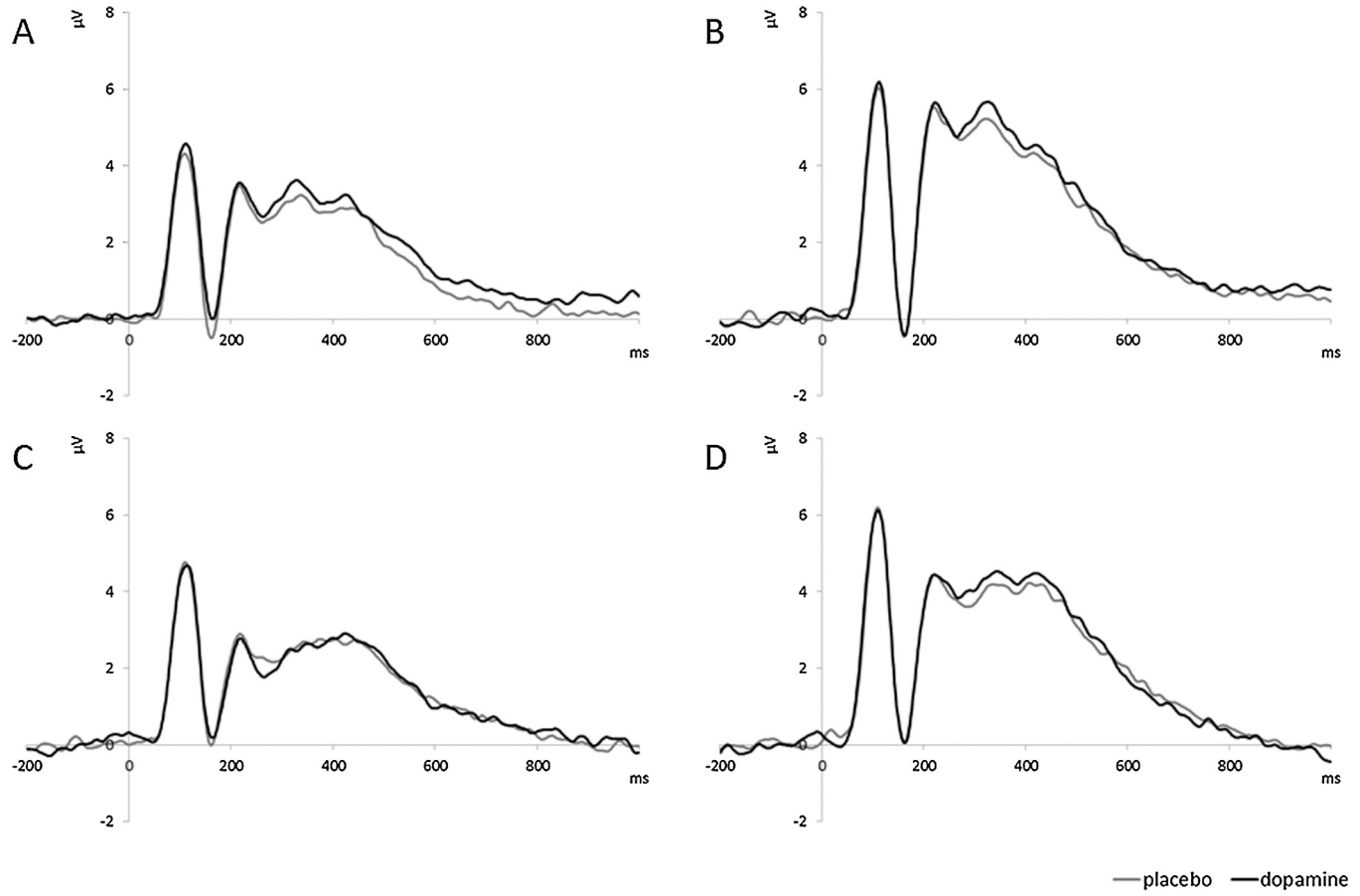

Figure 4. Grandaverage ERPs averaged across electrodes 58 (T5), 64, and 65 (left) and across electrodes 90, 95, and 96 (T6; right) illustrating the N170 in response to healthy infant faces (A: left N170, B: right N170) and infant faces with a cleft lip (C: left N170, D: right N170). ERP amplitudes within the 132-162ms post-stimulus time window (N170) were not significantly affected by dopamine administration, but were more negative in response to healthy infant faces compared to infant faces with a cleft lip.

outliers (all $|z| \leq 3.29$) in both the dopamine and placebo conditions, except for the attractiveness difference in the dopamine condition which showed one outlier ($z = 3.58$). After winsorizing the outlier the variable was normally distributed (standardized |skewness| < 3, standardized |kurtosis| < 3).

The analysis did not reveal a significant total or direct effect of drug condition on the attractiveness difference scores (total effect: $b = -1.56$, $SE = 7.28$, $t(50) = -0.21$, $p = .83$; direct effect: $b = -2.47$, $SE = 7.47$, $t(44) = -0.33$, $p = .74$). Difference scores for P1, N170, and P2 amplitudes were not significantly affected by drug condition (P1: $b = 0.22$, $SE = 0.21$, $t(50) = 1.06$, $p = .29$; N170: $b = 0.18$, $SE = 0.19$, $t(50) = 0.97$, $p = .34$; P2: $b = 0.23$, $SE = 0.22$, $t(50) = 1.06$, $p = .29$) and there were no significant associations between effects of drug condition on ERP component amplitude differences and attractiveness difference scores (P1: $b = 2.30$, $SE = 5.60$, $t(44) = 0.41$, $p = .68$; N170: $b = 2.08$, $SE = 6.61$, $t(44) = 0.31$, $p = .75$; P2: $b = 0.01$, $SE = 5.62$, $t(44) = 0.00$, $p = 1.00$). None of the indirect effects of drug condition on attractiveness difference scores through ERP component amplitude differences were significant either (P1: $b = 0.52$, bootstrapped $SE = 1.87$, bootstrapped 95% *CI*: -4.36 – 3.61; N170: $b = 0.38$, bootstrapped $SE = 1.40$, bootstrapped 95% *CI*: -3.01 – 2.98; P2: $b = 0.00$, bootstrapped $SE = 1.70$, bootstrapped 95% *CI*: -3.78 – 3.60).

3.3. Effects of face type

Attractiveness ratings of and N170 and P2 amplitudes in response to healthy infant faces and faces of infants with a cleft lip (averaged across the dopamine and placebo conditions) were all approximately normally distributed (all standardized |skewness| < 3, standardized |kurtosis| < 3) without outliers (all $|z| \leq 3.29$).

The analysis revealed a significant total effect of face type on attractiveness ratings ($b = 33.05$, $SE = 9.11$, $t(50) = 3.63$, $p = .00$). Healthy infants were rated as more attractive than infants with a cleft lip. However, the direct effect, when accounting for the mediators, was not significant ($b = 26.89$, $SE = 13.89$, $t(46) = 1.94$, $p = .06$). Face type also significantly affected N170 ($b = -0.23$, $SE = 0.11$, $t(50) = -2.16$, $p = .04$) and P2 amplitudes ($b = 0.87$, $SE = 0.13$, $t(50) = 6.88$, $p = .00$), with larger amplitudes (i.e., more negative N170 and more positive P2 amplitudes) elicited by healthy infant faces than faces of infants with a cleft lip. A significant association was observed between effects of face type on attractiveness ratings and N170 amplitude ($b = -26.26$, $SE = 12.30$, $t(46) = -2.14$, $p = .04$), but not P2 amplitude ($b = 0.03$, $SE = 10.88$, $t(46) = 0.00$, $p = 1.00$). As evidenced by a significant indirect effect of face type on attractiveness ratings through N170 amplitude ($b = 6.14$, bootstrapped $SE = 4.15$, bootstrapped 95% *CI*: 0.001 – 15.93), effects of a cleft lip on attractiveness ratings were mediated by its effects on N170 amplitudes. No evidence for mediation by P2 amplitude was obtained, as the indirect effect of face type on attractiveness ratings through P2 amplitude was not significant ($b = 0.02$, bootstrapped $SE = 11.56$, bootstrapped 95% *CI*: -17.64 – 27.14).

4. Discussion

The current study investigated effects of administered dopamine on

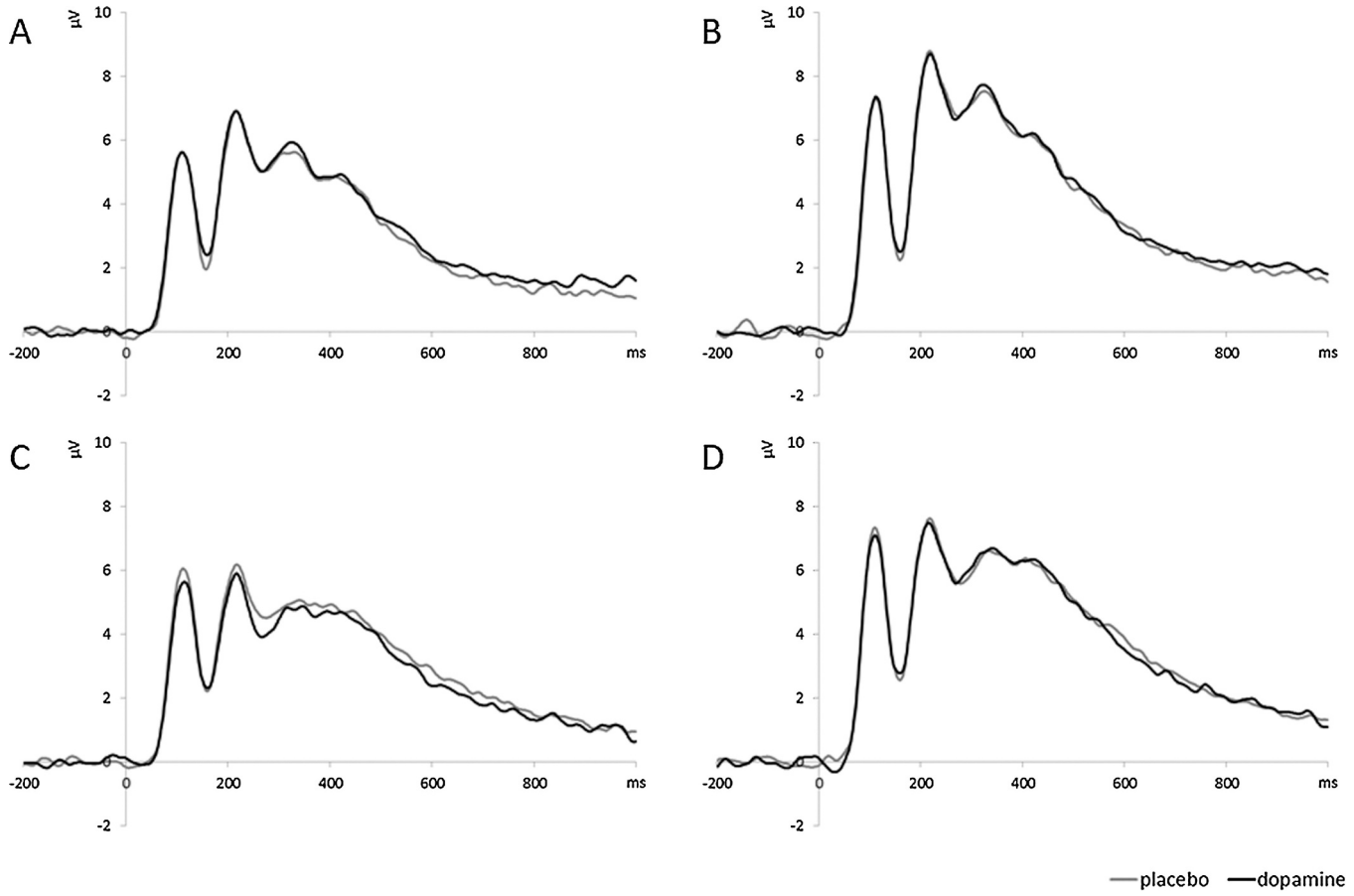

Figure 5. Grandaverage ERPs averaged across electrodes 59, 65, and 66 (left) and across electrodes 84, 90, and 91 (right) illustrating the P2 in response to healthy infant faces (A: left P2, B: right P2) and infant faces with a cleft lip (C: left P2, D: right P2). ERP amplitudes within the 184-244ms post-stimulus time window (P2) were not significantly affected by dopamine administration, but were more positive in response to healthy infant faces compared to infant faces with a cleft lip.

the perceived attractiveness of and P1, P2 and N170 responses to infant faces with and without a cleft lip. Contrary to expectations, we did not observe any effects of dopamine. However, we did replicate our previous finding that the presence of a cleft lip affects both the evaluation and neural processing of infant faces (see [34]). As before, and in accordance with other findings (e.g., [73, 76]), participants rated infants with a cleft lip as less attractive than healthy infants, highlighting once more the negative consequences of even a minor facial abnormality. In addition, and replicating our previous findings, both N170 and P2 amplitudes were found to be smaller in response to images of infants with a cleft lip than in response to images of healthy infant faces, but only reduced N170 amplitudes mediated the diminished attractiveness of infants with a cleft lip. Thus, the current findings add to the evidence that although the presence of a cleft lip interferes with both face specific (N170, see e.g. [7]) and more general attentional and/or executive (P2; see e.g., [28, 44, 56, 82, 96]) "normative" processing of faces, face-specific processing (N170) is likely to be specifically implicated in evaluative and behavioral effects of a cleft lip. Faces are highly salient social stimuli, providing information not only about an individual's identity, but also about a person's motivational and emotional state, and intentions. In fact, emotional facial expressions (characterized by a particular configuration) are well known to affect the N170 [4, 46, 57, 91, 101]. This inherently evaluative component of processing faces may well explain why we found face-specific neural processing to be particularly relevant for adults' judgements of infant faces.

It is important to note that some evidence for a relation between parental behavior and N170 indices of face processing has been found in several recent studies. Rutherford et al. [83] found that N170 amplitudes to infant faces were associated with parental reflective functioning (i.e., parents' ability to understand and interpret the mental state of an infant) in new mothers. Differences between neglectful mothers (not treated with an effective intervention) and control mothers in N170 amplitudes, in response to infants' faces, have also been found [8, 79]. Moreover, interventions aimed at improving sensitive parenting behavior have been found to affect the N170. Bernard et al. [8] compared neglectful mothers who received a control intervention or the Attachment and Biobehavioral Catch-up (ABC) intervention (that seeks to improve synchronous and sensitive responding to infant distress; [21]) to non-neglectful mothers. They found that infants' emotional expressions modulated N170 amplitudes similarly in non-neglectful mothers and in mothers who had participated in the ABC intervention, but not in those who had received a control intervention. Even more convincing intervention effects were obtained by Kolijn et al. [42], who compared mothers who received an intervention to enhance parental sensitivity and sensitive discipline with young children (the Video-feedback Intervention to promote Positive Parenting and Sensitive Discipline [VIPP-SD]; [38]) to mothers who received a control intervention, both before and after the intervention took place. These authors found that the VIPP-SD decreased mothers' N170 responses to children's faces, which they suggest may reflect more efficient face processing. Although all evidence cited here is suggestive of some relation between parental behavior and the N170 component, a caveat is in order. First, it should be noted that the nature of observed N170 effects varies across studies. This may, in part, be due to variations in e.g. sample characteristics, stimulus material, and attentional or motivational demands of the task or experimental setting. As argued in relation to our previous findings (see [34]) the task context may be particularly relevant. The attention, motivation and effort required by a

task or context might even codetermine whether changes in face configuration decrease or enhance N170 amplitudes. Second, correlations with actual parenting behavior are not often reported. Moreover, contrasting results have also been found. One recent study, for example, found that changes in mothers' P1 and P2, but not N170, amplitudes to faces from a prenatal to a postnatal assessment were related to mother-infant bonding [22]. Nevertheless, relations between face processing and parenting behavior clearly deserve attention in future research.

Thus, future studies could focus on mothers as well as fathers of both infants and older children. Parents of infants and children with a cleft lip deserve special attention. Whether results obtained with nulliparous adults generalize to parents of infants and children with a cleft lip, and whether parents' (neural) responses change over time (with increasing experience with their child) is important to investigate. Some evidence that experience with or exposure to individuals with a cleft lip may affect perception comes from studies that have found differences between professionals' (familiar with cleft lip) and lay-people's (unfamiliar with cleft lip) judgements of photographed faces after surgical treatment, although the direction of reported effects varies (see e.g., [105] for a review). Adults, whether or not they are parents, are sensitive and attuned to the infant schema – the characteristic features of an infant face ([45, 55, 92]) and evidence for the negative consequences of the disruption of this schema caused by a cleft lip is accumulating. To enhance understanding of the processes involved, future research could extend the focus to other types of facial abnormalities. Future research could also extend the focus from infants to older children and adults. Although manipulating attractiveness has been found to affect ERP responses to both infant and adult faces (e.g. [29, 97]) and decreased N170 amplitudes have been found in response to atypical, unattractive adult faces [30], it remains to be investigated whether the presence of a facial abnormality affects the processing and evaluation of faces similarly across ages. Moreover, our finding that changes in behavioral responses were mediated by changes in neural face processing, highlights the importance of combining various levels of analysis in a study. Directly investigating and relating neurophysiological and behavioral responses remains an important avenue for future research, and future studies should consider adding measures of interactive behavior with an infant or an infant-simulator (see e.g. [99]).

Although we replicated previous findings regarding the effects of a cleft lip, we did not find any effects of dopamine administration on ERP component amplitudes or evaluations of infant faces. One potential explanation is the dose administered. Even though significant effects of the same dose of L-Dopa on other (cognitive) functions have been found (e.g., [5, 11, 69]), null findings have also been reported (e.g., [53]) suggesting that the dose administered may not have been optimal for producing behavioral and neurophysiological effects. It has been suggested that effects of dopamine agonists on cognitive functions follow an inverted U shape, with optimal effects in the medium range and negative effects at very low and very high doses [67, 89, 98]. Thus, the dose administered in the current study may have been too low or too high to enhance neurophysiological responses to infant faces and ratings of attractiveness. Establishing what dose is effective in modulating signaling in dopaminergic areas to an optimal extent requires future fundamental research combining neurocognitive and/or behavioral assessments with measures of dopaminergic signaling. In addition, the ERP components under investigation are not generated in areas that are part of the dopaminergic circuitry, but rather in extrastriate visual areas (P1; [20, 28]), in parieto-occipital areas (P2; [25]), and in the lateral occipito-temporal cortex and posterior fusiform gyrus (N170; [12, 80]). Any effect of dopamine would therefore be indirect. Perhaps indirect effects are more difficult to observe.

Some of the characteristics of our study may also play a role. First, ERPs were elicited using a passive viewing paradigm, with clear and unambiguous facial stimuli. Thus, processing the stimuli did not require much attention or effort and enhanced attention after dopamine administration – if it occurred – may not have affected stimulus processing (i.e. a ceiling effect). Future studies could employ a more demanding task (e.g. requiring some kind of judgment of the stimuli) or a dual task situation in which attention is distracted away from the facial stimuli. This type of task would be ecologically valid, as having to focus on and attend to other things than the child is common in adult-child interaction. Second, all stimuli depicted infants with a neutral facial expression. Emotional expressions, however, may be very relevant with respect to engagement of attentional and reward systems, as well as motivational responses (see e.g., [100]). It would be interesting to include infant faces showing emotional expressions in future work. Third, one might wonder about the recruitment of reward systems by young adult nulliparous women when viewing infant faces. In fact, our participants were recruited through a university participant recruitment website frequented primarily by students of psychology and child and family studies. Therefore, young women with an interest in and empathy for infants and children may be over-represented in our sample, which might have consequences for the effects we observed (or did not observe) in the current study. We chose to focus on women only because of concerns for sample homogeneity and size in combination with well-known differences between men and women in the way they interact with, care for, and respond to infants (see e.g. [103]). Studies with larger and more diverse samples, directly comparing males and females and/or mothers and fathers are obviously welcome.

5. Conclusion

The current study did not provide any evidence for effects of dopamine on evaluations of attractiveness and neural processing of infant faces. However, we replicated the finding that the decreased attractiveness of infants with a cleft lip was mediated by decreased configural face processing (smaller N170 amplitudes), but not more general attentional and/or executive processing (P2). The current findings not only add evidence for the unfavorable consequences of a cleft lip, but also highlight the importance of combining and relating measures across various levels of analysis in a single study and underscore the, often underestimated, importance of replication.

Funding

The current study was funded by a grant from the Jacobs Foundation.

Declaration of Competing Interest

None.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.physbeh.2020.112937.

References

[1] A. Alcaro, R. Huber, J. Panksepp, Behavioral functions of the mesolimbic dopaminergic system: An affective neuroethological perspective, Brain Res Rev 56 (2) (2007) 283–321, https://doi.org/10.1016/j.brainresrev.2007.07.014.
[2] F.D. Alves, N. Schmitz, M. Figee, N. Abeling, G. Hasler, J. van der Meer, T. . . . van Amelsvoort, Dopaminergic modulation of the human reward system: a placebo-controlled dopamine depletion fMRI study, J Psychopharmacol 25 (4) (2011) 538–549, https://doi.org/10.1177/0269881110367731.
[3] B.A. Anderson, The attention habit: How reward learning shapes attentional selection, Ann NY Acad Sci 1369 (1) (2016) 24–39, https://doi.org/10.1111/nyas.12957.
[4] V. Ashley, P. Vuilleumier, D. Swick, Time course and specificity of event-related potentials to emotional expressions, NeuroReport 15 (1) (2004) 211–216.
[5] S.P. Barrett, R.O. Pihl, C. Benkelfat, C. Brunelle, S.N. Young, M. Leyton, The role of dopamine in alcohol self-administration in humans: individual differences, Eur Neuropsychopharmacol 18 (6) (2008) 439–447, https://doi.org/10.1016/j.

euroneuro.2008.01.008.
[6] A. Bartels, S. Zeki, The neural correlates of maternal and romantic love, NeuroImage 21 (3) (2004) 1155–1166, https://doi.org/10.1016/j.neuroimage.2003.11.003.
[7] S. Bentin, T. Allison, A. Puce, E. Perez, G. McCarthy, Electrophysiological studies of face perception in humans, J Cogn Neurosci 8 (6) (1996) 551–565, https://doi.org/10.1162/jocn.1996.8.6.551.
[8] K. Bernard, R. Simons, M. Dozier, Effects of an attachment-based intervention on child protective services-referred mothers' event-related potentials to children's emotions, Child Dev 6 (2015) 1673–1684 10.111/cdev.12418.
[9] K.C. Berridge, T.E. Robinson, What is the role of dopamine in reward: hedonic impact, reward learning, or incentive salience? Brain Res Rev 28 (3) (1998) 309–369.
[10] J. Booij, G. Tissingh, A. Winogrodzka, E.A. van Royen, Imaging of the dopaminergic neurotransmission system using single-photon emission tomography and positron emission tomography in patients with parkinsonism, Eur J Nucl Med 26 (2) (1999) 171–182, https://doi.org/10.1007/s002590050374.
[11] S. Both, W. Everaerd, E. Laan, L. Gooren, Effect of a single dose of levodopa on sexual response in men and women, Neuropsychopharmacol 30 (1) (2005) 173, https://doi.org/10.1038/sj.npp.1300580.
[12] K. Botzel, S. Schulze, S.R. Stodieck, Scalp topography and analysis of intracranial sources of face-evoked potentials, Exp Brain Res 104 (1) (1995) 135–143.
[13] L. Boutsen, G.W. Humphreys, P. Praamstra, T. Warbrick, Comparing neural correlates of configural processing in faces and objects: An ERP study of the Thatcher illusion, NeuroImage 32 (2006) 352–367, https://doi.org/10.1016/j.neuroimage.2006.03.023.
[14] R.S. Bridges, Neuroendocrine regulation of maternal behavior, Frontiers in Neuroendocrinology 36 (2015) 178–196, https://doi.org/10.1016/j.yfrne.2014.11.007.
[15] R.A. Cárdenas, L.J. Harris, M.W. Becker, Sex differences in visual attention toward infant faces, Evol Hum Behav 34 (4) (2013) 280–287, https://doi.org/10.1016/j.evolhumbehav.2013.04.001.
[16] F. Champagne, P. Chretien, C.W. Stevenson, T.Y. Zhang, A. Gratton, M.J. Meaney, Variations in nucleus accumbens dopamine associated with individual differences in maternal behavior in the rat, J Neurosci 24 (17) (2004) 4113–4123, https://doi.org/10.1523/JNEUROSCI.5322-03.2004.
[17] B.R. Collett, M. Stott-Miller, K.A. Kapp-Simon, M.L. Cunningham, M.L. Speltz, Reading in children with orofacial clefts versus controls, J Ped Psychol 35 (2010) 199–208, https://doi.org/10.1093/jpepsy/jsp047.
[18] L.C. Dang, J.P. O'Neil, W.J. Jagust, Dopamine supports coupling of attention-related networks, J Neurosci 32 (28) (2012) 9582–9587, https://doi.org/10.1523/JNEUROSCI.0909-12.2012.
[19] L. De Pascalis, N. Kkeli, B. Chakrabarti, L. Dalton, K. Vaillancourt, H. Rayson, S. Bicknell, T. Goodacre, P. Cooper, A. Stein, L. Murray, Maternal gaze to the infant face: effects of infant age and facial configuration during mother-infant engagement in the first nine weeks, Infant Behav Dev 46 (2017) 91–99, https://doi.org/10.1016/j.infbeh.2016.12.003.
[20] Di Russo, Martínez F., Sereno A., M. I., S. Pitzalis, S.A. Hillyard, Cortical sources of the early components of the visual evoked potential, Hum Brain Mapp 15 (2) (2002) 95–111, https://doi.org/10.1002/hbm.10010.
[21] M. Dozier, & the Infant Caregiver Project, Attachment and Biobehavioral Catch-up Intervention. Unpublished manuscript, Department of Psychology, University of Delaware, Newark, DE, 2006.
[22] J. Dudek, T. Colasante, A. Zuffianò, D.W. Haley, Changes in Cortical Sensitivity to Infant Facial Cues from Pregnancy to Motherhood Predict Mother–Infant Bonding, Child Dev. (2018), https://doi.org/10.1111/cdev.13182.
[23] M. Eimer, Effects of face inversion on the structural encoding and recognition of faces: Evidence from event-related brain potentials, Cognitive Brain Research, 10 (2000) 145–158, https://doi.org/10.1016/S0926-6410(00)00038-0.
[24] A.E. Ferrey, N. Santascoy, E.J. McCrory, C. Thompson-Booth, L.C. Mayes, H.J. Rutherford, Motivated attention and reward in parenting, Parenting 16 (4) (2016) 284–301, https://doi.org/10.1080/15295192.2016.1184928.
[25] R. Freunberger, W. Klimesch, M. Doppelmayr, Y. Höller, Visual P2 component is related to theta phase-locking, Neurosci Lett 426 (3) (2007) 181–186, https://doi.org/10.1016/j.neulet.2007.08.062.
[26] A.M. Frodi, Contribution of infant characteristics to child abuse, Am J Ment Def. (1981).
[27] N. George, J. Evans, N. Fiori, J. Davidoff, B. Renault, Brain events related to normal and moderately scrambled faces, Cognitive Brain Research 4 (1996) 65–76, https://doi.org/10.1016/0926-6410(95)00045-3.
[28] Gomez Gonzalez, C. M., V.P. Clark, S. Fan, S.J. Luck, S.A. Hillyard, Sources of attention-sensitive visual event-related potentials, Brain Topogr 7 (1) (1994) 41–51.
[29] A.C. Hahn, L.A. Symons, T. Kredel, K. Hanson, L. Hodgson, L. Schiavone, K.J. Jantzen, Early and late event-related potentials are modulated by infant and adult faces of high and low attractiveness, Social Neuroscience 11 (2) (2016) 207–220, https://doi.org/10.1080/17470919.2015.1059361.
[30] H. Halit, M. De Haan, M.H. Johnson, Modulation of event-related potentials by prototypical and atypical faces, NeuroReport 11 (9) (2000) 1871–1875, https://doi.org/10.1097/00001756-200006260-00014.
[31] F. Hentges, J. Hill, D.V.M. Bishop, T. Goodacre, T. Moss, L. Murray, The effect of cleft lip on cognitive development in school-aged children: a paradigm for examining sensitive period effects, J Child Psychol Psychiat 52 (2011) 704–712, https://doi.org/10.1111/j.1469-7610.2011.02375.x.
[32] S.A. Hillyard, E.K. Vogel, S.J. Luck, Sensory gain control (amplification) as a mechanism of selective attention: electrophysiological and neuroimaging evidence, Philos T Roy Soc B 353 (1373) (1998) 1257–1270, https://doi.org/10.1098/rstb.1998.0281.
[33] R. Huffmeijer, M.J. Bakermans-Kranenburg, L.R.A. Alink, M.H. Van IJzendoorn, Reliability of event-related potentials: the influence of number of trials and electrodes, Physiol Behav 130 (2014) 13–22, https://doi.org/10.1016/j.physbeh.2014.03.008.
[34] R. Huffmeijer, J. Eilander, V.R. Mileva-Seitz, R.C. Rippe, Changes in face-specific neural processing explain reduced cuteness and approachability of infants with cleft lip, Soc Neurosci 13 (4) (2018) 439–450, https://doi.org/10.1080/17470919.2017.1340336.
[35] T. Iidaka, A. Matsumoto, K. Haneda, T. Okada, N. Sadato, Hemodynamic and electrophysiological relationship involved in human face processing: evidence from a combined fMRI-ERP study, Brain Cogn 60 (2006) 176–186, https://doi.org/10.1016/j.bandc.2005.11.004.
[36] R.J. Itier, M.J. Taylor, Inversion and contrast polarity reversal affect both encoding and recognition processes of unfamiliar faces: A repetition study using ERPs, NeuroImage 15 (2002) 353–372, https://doi.org/10.1006/nimg.2001.0982.
[37] C. Joyce, B. Rossion, The face-sensitive N170 and VPP components manifest the same brain processes: the effect of reference electrode site, Clin Neurophysiol 116 (2005) 2613–2631, https://doi.org/10.1016/j.clinph.2005.07.005.
[38] Juffer, F., Bakermans-Kranenburg, M.J., & Van IJzendoorn, M.H. (2008). Promoting positive parenting: an attachment-based intervention. New York: Lawrence Erlbaum Associates.
[39] D.A. Kenny, C.M. Judd, Power anomalies in testing mediation, Psychological Science 25 (2) (2014) 334–339, https://doi.org/10.1177/0956797613502676.
[40] Kienberger Jaudes, L. Mackey-Bilaver, Do chronic conditions increase young children's risk of being maltreated? Child Abuse Neglect 32 (2008) 671–681, https://doi.org/10.1016/j.chiabu.2007.08.007.
[41] J. Kohl, A.E. Autry, C. Dulac, The neurobiology of parenting: a neural circuit perspective, Bioessays 39 (2016), https://doi.org/10.1002/bies.201600159.
[42] L. Kolijn, R. Huffmeijer, B.G. Van Den Bulk, C.I. Vrijhof, M.H. Van IJzendoorn, M.J. Bakermans-Kranenburg, Effects of the Video-feedback intervention to promote positive parenting and sensitive discipline on mothers' neural responses to child faces: A randomized controlled ERP study including pre-and post-intervention measures, Soc Neurosci (2019) 1–15, https://doi.org/10.1080/17470919.2019.1660709.
[43] A. Korchounov, M.F. Meyer, M. Krasnianski, Postsynaptic nigrostriatal dopamine receptors and their role in movement regulation, J Neural Transm 117 (12) (2010) 1359–1369, https://doi.org/10.1007/s00702-010-0454-z.
[44] E. Kotsoni, G. Csibra, D. Mareschal, M.H. Johnson, Electrophysiological correlates of common-onset visual masking, Neuropsychologia 45 (2007) 2285–2293, https://doi.org/10.1016/j.neuropsychologia.2007.02.023.
[45] M.L. Kringelbach, E.A. Stark, C. Alexander, M.H. Bornstein, A. Stein, On cuteness: unlocking the parental brain and beyond, Trends Cogn Sci 20 (7) (2016) 545–558, https://doi.org/10.1016/j.tics.2016.05.003.
[46] A. Krombholz, F. Schaefer, W. Boucsein, Modification of N170 by different emotional expression of schematic faces, Biological Psychology 76 (2007) 156–162.
[47] L.A. Leavitt, Mothers' sensitivity to infant signals, Pediatrics 102 (5) (1998) e1247, https://doi.org/10.1542/peds.102.5.SE1.1247.
[48] L.A. Leavitt, Research to practice: emotional development and maternal/infant attachment, J Pediatr Health Car 13 (3 Pt 2) (1999) S4–S7, https://doi.org/10.1016/S0891-5245(99)90048-2.
[49] E.M. Leerkes, Predictors of Maternal Sensitivity to Infant Distress, Parent-Sci Pract 10 (3) (2010) 219–239, https://doi.org/10.1080/15295190903290840.
[50] E. Leibenluft, M.I. Gobbini, T. Harrison, J.V. Haxby, Mothers' neural activation in response to pictures of their children and other children, Biol Psychiat 56 (4) (2004) 225–232, https://doi.org/10.1016/j.biopsych.2004.05.017.
[51] M. Li, R. Budin, A.S. Fleming, S. Kapur, Effects of chronic typical and atypical antipsychotic drug treatment on maternal behavior in rats, Schizophr Res 75 (2-3) (2005) 325–336, https://doi.org/10.1016/j.schres.2004.09.012.
[52] M. Li, P. Davidson, R. Budin, S. Kapur, A.S. Fleming, Effects of typical and atypical antipsychotic drugs on maternal behavior in postpartum female rats, Schizophr Res 70 (1) (2004) 69–80, https://doi.org/10.1016/j.schres.2003.09.013.
[53] J. Liggins, R.O. Pihl, C. Benkelfat, M. Leyton, The dopamine augmenter L-DOPA does not affect positive mood in healthy human volunteers, PLoS One 7 (1) (2012) e28370, https://doi.org/10.1371/journal.pone.0028370.
[54] J.P. Lorberbaum, J.D. Newman, A.R. Horwitz, J.R.J.R.J.R. Dubno, R.B.B. Lydiard, M.B. Hamner, M.S.M.S. … George, A potential role for thalamocingulate circuitry in human maternal behavior, Biol Psychiat 51 (6) (2002) 431–445, https://doi.org/10.1016/S0006-3223(01)01284-7.
[55] K. Lorenz, The innate forms of potential experience, Z Tierpsychol 5 (1943) 235–409.
[56] S.J. Luck, An introduction to the event-related potential technique, MIT press. (2014).
[57] W.B. Luo, W.F. Feng, W.Q. He, N.Y. Wang, Y.J. Luo, Three stages of facial expression processing: ERP study with rapid serial visual presentation, NeuroImage 49 (2) (2010) 1857–1867, https://doi.org/10.1016/j.neuroimage.2009.09.018.
[58] J.H. Maunsell, Neuronal representations of cognitive state: reward or attention? Trends Cogn Sci 8 (6) (2004) 261–265, https://doi.org/10.1016/j.tics.2004.04.003.
[59] V. Mileva-Seitz, A.S. Fleming, M.J. Meaney, A. Mastroianni, J.P. Sinnwell, M. Steiner, ... M.B. Sokolowski, Dopamine receptors D1 and D2 are related to observed maternal behavior, Genes Brain Behav 11 (6) (2012) 684–694, https://doi.org/10.1111/j.1601-183X.2012.00804.x.
[60] A.K. Montoya, A.F. Hayes, Two-condition within-participant statistical mediation analysis: a path-analytic framework, Psychol Meth (2016), https://doi.org/10.

1037/met0000086.
[61] Mossey, P.A., & Catilla, E.E. (2003). Global registry and database on craniofacial anomalies: report of a WHO Registry Meeting on craniofacial anomalies.
[62] P.A. Mossey, J. Little, R.G. Munger, M.J. Dixon, W.C. Shaw, Cleft lip and palate, Lancet 374 (2009) 1773–1785, https://doi.org/10.1016/S0140-6736(09)60695-4.
[63] L. Murray, F. Hentges, J. Hill, J. Karpf, B. Mistry, M. Kreutz, P. Woodall, T. Moss, T. Goodacre, The effect of cleft lip and palate, and the timing of lip repair on mother-infant interactions and infant development, J Child Psychol Psychiat 49 (2008) 115–123, https://doi.org/10.1111/j.1469-7160.2007.01833.x.
[64] J.B. Nitschke, E.E. Nelson, B.D. Rusch, A.S. Fox, T.R. Oakes, R.J. Davidson, Orbitofrontal cortex tracks positive mood in mothers viewing pictures of their newborn infants, NeuroImage 21 (2) (2004) 583–592, https://doi.org/10.1016/j.neuroimage.2003.10.005.
[65] M. Noriuchi, Y. Kikuchi, A. Senoo, The functional neuroanatomy of maternal love: mother's response to infant's attachment behaviors, Biol Psychiat 63 (4) (2008) 415–423, https://doi.org/10.1016/j.biopsych.2007.05.018.
[66] D.A. Norman, T. Shallice, Attention to Action - Willed and Automatic-Control of Behavior, Bull Psychonom Soc 21 (5) (1983) 354.
[67] B. Noudoost, T. Moore, The role of neuromodulators in selective attention, Trends Cogn Sci 15 (12) (2011) 585–591, https://doi.org/10.1016/j.tics.2011.10.006.
[68] M. Numan, M.J. Numan, N. Pliakou, D.S. Stolzenberg, O.J. Mullins, J.M. Murphy, C.D. Smith, The effects of D1 or D2 dopamine receptor antagonism in the medial preoptic area, ventral pallidum, or nucleus accumbens on the maternal retrieval response and other aspects of maternal behavior in rats, Behav Neurosci 119 (6) (2005) 1588–1604, https://doi.org/10.1037/0735-7044.119.6.1588.
[69] N.Y. Oei, S.A. Rombouts, R.P. Soeter, J.M. Van Gerven, S. Both, Dopamine modulates reward system activity during subconscious processing of sexual stimuli, Neuropsychopharmacol 37 (7) (2012) 1729, https://doi.org/10.1038/npp.2012.19.
[70] I. Opris, C.J. Bruce, Neural circuitry of judgment and decision mechanisms, Brain Res Rev 48 (3) (2005) 509–526, https://doi.org/10.1016/j.brainresrev.2004.11.001.
[71] M. Parada, S. King, M. Li, A.S. Fleming, The roles of accumbal dopamine D1 and D2 receptors in maternal memory in rats, Behav Neurosci 122 (2) (2008) 368–376, https://doi.org/10.1037/0735-7044.122.2.368.
[72] C.E. Parsons, K.S. Young, H. Mohseni, M.W. Woolrich, K Romer Thomsen, M Joensson, L. Murray, T Goodacre, A. Stein, M.L Kringelbach, Minor structural abnormalities in the infant face disrupt neural processing: a unique window into early caregiving responses, Soc Neurosci 8 (4) (2013) 268–274, https://doi.org/10.1080/17470919.2013.795189.
[73] C.E. Parsons, K.S. Young, E. Parsons, A. Dean, L. Murray, T. Goodacre, L. Dalton, A. Stein, M.L. Kringelbach, The effect of cleft lip on adults' responses to faces: cross-species findings, PLoS one 6 (10) (2011) e25897, https://doi.org/10.1371/journal.pone.0025897.
[74] C.J. Peck, D.C. Jangraw, M. Suzuki, R. Efem, J. Gottlieb, Reward modulates attention independently of action value in posterior parietal cortex, J Neurosci 29 (36) (2009) 11182–11191, https://doi.org/10.1523/JNEUROSCI.1929-09.2009.
[75] S. Ranote, R. Elliott, K.M. Abel, R. Mitchell, J.F.W. Deakin, L. Appleby, The neural basis of maternal responsiveness to infants: an fMRI study, NeuroReport 15 (11) (2004) 1825–1829, https://doi.org/10.1097/01.wnr.0000137078.64128.6a.
[76] H. Rayson, C.E. Parsons, K.S. Young, T. Goodacre, M.L. Kringelbach, J.J. Bonaiuto, E. McSorley, L. Murray, Effects of infant cleft lip on adult gaze and perceptions of "cuteness", Cleft Palate-Cran J 54 (5) (2017) 562–570, https://doi.org/10.1597/16-015.
[77] J.K. Rilling, J.S. Mascaro, The neurobiology of fatherhood, Current Opinion in Psychology 15 (2017) 26–32, https://doi.org/10.1016/j.copsyc.2017.02.013.
[78] J.K. Rilling, L.J. Young, The biology of mammalian parenting and its effect on offspring social development. science 345 (6198) (2014) 771–776, https://doi.org/10.1126/science.1252723.
[79] M.J. Rodrigo, I. León, I. Quiñones, A. Lage, S. Byrne, M.A. Bobes, Brain and personality bases of insensitivity to infant cues in neglectful mothers: an event-related potential study, Dev Psychopathol 23 (2011) 163–176, https://doi.org/10.1017/S0954579410000714.
[80] B. Rossion, C.A. Joyce, G.W. Cottrell, M.J. Tarr, Early lateralization and orientation tuning for face, word, and object processing in the visual cortex, NeuroImage 20 (3) (2003) 1609–1624, https://doi.org/10.1016/j.neuroimage.2003.07.010.
[81] A.M. Rozendaal, A.D. Mohangoo, A.J.M. Luijsterburg, M.K. Bakker, E.M. Ongkusowito, Vermeij-Keers, Prevalentie van schisis in Nederland en Noord-Nederland in 1997-2007: trendanalyse van gegevens uit drie Nederlandse registraties, Tijdschrift voor Kindergeneeskunde 79 (1) (2011) 16–25, https://doi.org/10.1007/s12456-011-0003-1.
[82] J.A. Rushby, R.J. Barry, S.J. Johnstone, Event-related potential correlates of serial position effects during an elaborative memory test, Int J Psychophysiol 46 (1) (2002) 13–27, https://doi.org/10.1016/S0167-8760(02)00037-5.
[83] H.J. Rutherford, A.N. Maupin, N. Landi, M.N. Potenza, L.C. Mayes, Parental reflective functioning and the neural correlates of processing infant affective cues, Soc Neurosci 12 (5) (2017) 519–529, https://doi.org/10.1080/17470919.2016.1193559.
[84] N. Sagiv, S. Bentin, Structural encoding of human and schematic faces: Holistic and part-based processes, Journal of Cognitive Neuroscience 13 (7) (2001) 937–951, https://doi.org/10.1162/089892901753165854.
[85] K. Sander, Y. Frome, H. Scheich, FMRI activations of amygdala, cingulate cortex, and auditory cortex by infant laughing and crying, Hum Brain Mapp 28 (10) (2007) 1007–1022, https://doi.org/10.1002/hbm.20333.
[86] E. Seifritz, F. Esposito, J.G. Neuhoff, A. Lüthi, H. Mustovic, G. Dammann, G. Tedeschi, Differential sex-independent amygdala response to infant crying and laughing in parents versus nonparents, Biol Psychiat 54 (12) (2003) 1367–1375, https://doi.org/10.1016/S0006-3223(03)00697-8.
[87] B.E. Schmeichel, F.P. Zemlan, C.W. Berridge, A selective dopamine reuptake inhibitor improves prefrontal cortex-dependent cognitive function: Potential relevance to attention deficit hyperactivity disorder, Neuropharmacol 64 (2013) 321–328, https://doi.org/10.1016/j.neuropharm.2012.07.005.
[88] H. Schuiringa, M. Van Nieuwenhuijzen, B. Orobio de Castro, W. Matthys, Parenting and the parent-child relationship in families of children with mild to borderline intellectual disabilities and externalizing behavior, Res Dev Disabil 36 (2015) 1–12, https://doi.org/10.1016/j.ridd.2014.08.018.
[89] J.K. Seamans, C.R. Yang, The principal features and mechanisms of dopamine modulation in the prefrontal cortex, Prog Neurobiol 74 (1) (2004) 1–58, https://doi.org/10.1016/j.pneurobio.2004.05.006.
[90] M.L. Speltz, M.C. Endriga, S. Hill, C.L. Maris, K. Jones, M.L. Omnell, Cognitive and psychomotor development of infants with orofacial clefts, J Ped Psychol 25 (2000) 185–190, https://doi.org/10.1093/jpepsy/25.3.185.
[91] R. Sprengelmeyer, I. Jentzsch, Event related potentials and the perception of intensity in facial expressions, Neuropsychologia 44 (2006) 2899–2906, https://doi.org/10.1016/j.neuropsychologia.2006.06.020.
[92] R. Sprengelmeyer, D.I. Perrett, E.C. Fagan, R.E. Cornwell, J.S. Lobmaier, A. Sprengelmeyer, H.B.M. Aasheim, I.M. Black, L.M. Cameron, S. Crow, N. Milne, E.C. Rhodes, A.W. Young, The cutest little baby face: a hormonal link to sensitivity to cuteness in infant faces, Psychol Sci 20 (2009) 149–154, https://doi.org/10.1111/j.1467-9280.2009.02272.x.
[93] L. Strathearn, J. Li, P. Fonagy, P.R. Montague, What's in a smile? Maternal brain responses to infant facial cues, Pediatrics 122 (1) (2008) 40–51, https://doi.org/10.1542/peds.2007-1566.
[94] P.M. Sullivan, J.F. Knutson, Maltreatment and disabilities: a population-based epidemiological study, Child Abuse Neglect 24 (10) (2000) 1257–1273, https://doi.org/10.1016/S0145-2134(00)00190-3.
[95] J.E. Swain, Baby stimuli and the parent brain: functional neuroimaging of the neural substrates of parent-infant attachment, Psychiat 5 (8) (2008) 28–36.
[96] D. Talsma, H.A. Slagter, S. Nieuwenhuis, J. Hage, A. Kok, The orienting of visuospatial attention: an event-related brain potential study, Cogn Brain Res 25 (2005) 117–129, https://doi.org/10.1016/j.cogbrainres.2005.04.013.
[97] L.T. Trujillo, J.M. Jankowitsch, J.H. Langlois, Beauty is in the ease of the beholding: a neurophysiological test of the averageness theory of facial attractiveness, Cognitive Affective and Behavioral Neuroscience 14 (2014) 1061–1076, https://doi.org/10.3758/s13415-013-0230-2.
[98] S. Vijayraghavan, M. Wang, S.G. Birnbaum, G.V. Williams, A.F. Arnsten, Inverted-U dopamine D1 receptor actions on prefrontal neurons engaged in working memory, Nat Neurosci 10 (3) (2007) 376, https://doi.org/10.1038/nn1846.
[99] A. Voorthuis, D. Out, R. Van der Veen, R. Bhandari, M.H. Van IJzendoorn, M.J. Bakermans-Kranenburg, One doll fits all: validation of the Leiden infant simulator sensitivity assessment (LISSA), Attach Hum Dev 15 (2013) 603–617, https://doi.org/10.1080/14616734.2013.820897.
[100] P. Vuilleumier, How brains beware: neural mechanisms of emotional attention, Trends Cogn Sci 9 (12) (2005) 585–594, https://doi.org/10.1016/j.tics.2005.10.011.
[101] L.M. Williams, D. Palmer, B.J. Liddell, L. Song, E. Gordon, The 'when' and 'where' of perceiving signals of threat versus non-threat, NeuroImage 31 (2006) 458–467.
[102] M.G. Woldorff, C.C. Gallen, S.A. Hampson, S.A. Hillyard, C. Pantev, D. Sobel, F.E. Bloom, Modulation of early sensory processing in human auditory cortex during auditory selective attention, P Natl Acad Sci USA 90 (18) (1993) 8722–8726.
[103] W. Wood, A.H. Eagly, A cross-cultural analysis of the behavior of women and men: Implications for the origins of sex differences, Psychol Bull 128 (5) (2002) 699–727, https://doi.org/10.1037//0033-2909.128.5.699.
[104] R. Yamamoto, D. Ariely, W. Chi, D.D. Langleben, I. Elman, Gender differences in the motivational processing of babies are determined by their facial attractiveness, PloS One 4 (2009) e6042, https://doi.org/10.1371/journal.pone.0006042.
[105] S Zhu, J Jayaraman, B Khambay, Evaluation of facial appearance in patients with cleft lip and palate by laypeople and orofessionals: a systematic literature review, Cleft Palate Craniofacial Journal 53 (2) (2016) 187–196, https://doi.org/10.1597/14-177.
[106] Barrett, et al., Maternal affect and quality of parenting experiences are related to amygdala response to infant faces, Social Neuroscience (2011), https://doi.org/10.1080/17470919.2011.609907.