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

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\textbf{A R T I C L E   I N F O}

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\textbf{A B S T R A C T}

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 configurational 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.

\section{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 these cues. 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., \textsuperscript{14, 77, 78}). Dopaminergic neurocircuitry has been critically implicated, particularly in animal studies (see e.g. \textsuperscript{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. \textsuperscript{77, 78}). Considering the above, the lack of administration studies focusing specifically on dopamine is striking.

Dopamine is a monoamine neurotransmitter important for neural signallng 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., \textsuperscript{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., \textsuperscript{1, 9}), and higher-order cognitive functions, including (executive) attention and working memory (e.g., \textsuperscript{18, 67, 87}). Both attention and motivation, and the rewarding aspects of interacting with an infant are essential for successful caregiving (e.g., \textsuperscript{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 \cite{16} and systemic administration of dopamine receptor antagonists resulted in disruptions in pup approach and retrieval \cite{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...
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 modulatory 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 × 5.00° visual angle) on a computer screen. To rate infants’ cuteness and approachability, visual analog scales (VAS; subtending 10.20 × 2.29° 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 ≥ .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 × 8.10° 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 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), referenced 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 (O2), and 83 (O2). N170 amplitude was quantified as the average amplitude in the 152-162ms 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...
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 a1, a2, and a3), the associations between effects on the mediators and the outcome variable (paths b1, b2, and b3), and, finally, both the direct effect of the independent variable on the outcome variable (path c’) and its indirect effects through each mediator (paths a1*b1, a2*b2, and a3*b3). 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.

| Attractiveness | Dopamine condition | Placebo condition |
|----------------|--------------------|-------------------|
|                | Healthy            | Cleft             | Scrambled | Healthy | Cleft | Scrambled |
| P1             | 309 (66)*          | 275 (83)          | 7.01 (3.37) | 7.62 (3.62) | 7.82 (3.74) | 7.06 (3.88) |
| N170 Right     | 1.32 (2.93)        | 1.42 (2.96)       | 2.59 (2.77) | 0.74 (2.85) | 1.22 (2.77) | 2.38 (2.74) |
| 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) | 8.99 (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

![Figure 3](image-url) Grandaverage ERPs averaged across electrodes 70 (O1), 75 (O2) 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).

P1, N170, and P2 respectively.

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
outliers \( (|z| \leq 3.29) \) 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 \((\text{standardized } |\text{skewness}| < 3, \text{standardized } |\text{kurtosis}| < 3)\).

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

### 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 \((\text{all standardized } |\text{skewness}| < 3, \text{standardized } |\text{kurtosis}| < 3)\) without outliers \((|z| \leq 3.29)\).

The analysis revealed a significant total effect of face type on attractiveness ratings \((b = 33.05, \text{SE} = 9.11, t(50) = 3.63, p = .00)\). 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 \((b = 26.89, \text{SE} = 13.89, t(46) = 1.94, p = .06)\). Face type also significantly affected N170 \((b = -0.23, \text{SE} = 0.11, t(50) = -2.16, p = .04)\) and P2 amplitudes \((b = 0.87, \text{SE} = 0.13, t(50) = 6.88, p = .00)\), 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 \((b = -26.26, \text{SE} = 12.30, t(46) = -2.14, p = .04)\), but not P2 amplitude \((b = 0.03, \text{SE} = 10.88, t(46) = 0.00, p = 1.00)\). As evidenced by a significant indirect effect of face type on attractiveness ratings through N170 amplitude \((b = 6.14, \text{SE} = 4.15, \text{bootstrapped 95% CI: } 0.001 - 15.93)\), 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 \((b = 0.02, \text{bootstrapped SE} = 11.56, \text{bootstrapped 95% CI: } -17.64 - 27.14)\).

### 4. Discussion

The current study investigated effects of administered dopamine on...
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 nul-liparous 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 laypeople’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 ([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.

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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.

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