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Development and Aging

Affective decision-making in children prenatally exposed to opioids

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Although opioid maintenance therapy (OMT) is currently recommended for pregnant opioid-dependent women, potential effects on children's long-term development are still largely unknown. The current study assessed the long-term cognitive development of children born to women in OMT. Particularly, children's decision-making performance was assessed with a child-friendly version of the Iowa Gambling Task.

Using a prospective longitudinal design, a cohort of children was followed from birth to middle childhood. Data were collected in Norway between 2005 and 2017. Participants included 41 children (aged 9–11 years), 20 of whom had histories of prenatal methadone or buprenorphine exposure. Background data were collected from personal interviews and medical records in 2005–2006. Children's affective decision-making was assessed in 2016–2017. Results showed no main effect of group on the net scores in the gambling task, $F(1, 39) = 1.44$, $p = 0.24$, $\eta^2 = 0.04$, demonstrating no group differences in decision-making performance. A main effect of group was found on sensitivity to punishment, with children in the control group choosing the doors with the infrequent, but high punishment more often compared to children in the OMT group, $F(1, 39) = 4.90$, $p = 0.03$, $\eta^2 = 0.11$. No main effect of group on decision-making speed was found, although results showed a significant interaction effect between group and gain, $F(1, 8{,}194) = 4.09$, $p = 0.04$, $\eta^2 = 0.001$. Children prenatally exposed to opioids were found to have normal decision-making performance on an affective decision-making task and were able to consider future consequences when making decisions.

Key words: Methadone, buprenorphine, prenatal opioid exposure, opioid maintenance therapy, decision-making, Iowa Gambling Task.

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INTRODUCTION

Opioid maintenance therapy (OMT) is a widely used, well-established treatment in which patients dependent on short-acting opioids receive daily maintenance treatment with long-acting opioids such as methadone or buprenorphine (Tran, Griffin, Stone, Vest & Todd, 2017; Whelan & Remski, 2012). OMT can reduce the risk of relapse to illicit opioid use, help patients move away from a drug-dominated lifestyle and aid treatment of comorbidity (Zippel-Schultz, Specka, Cimander *et al*., 2016). Because of these benefits, opioid-dependent women who are pregnant are currently recommended to enroll in OMT (Zedler, Mann, Kim *et al*., 2016). While OMT has many benefits, concerns have been raised that exposure during pregnancy may affect fetal development (McCarthy, 2012). Although the direct effects of prenatal methadone and buprenorphine on birth outcomes have been well investigated (Brogly, Saia, Walley, Du & Sebastiani, 2014; Fischer, Ortner, Rohrmeister *et al*., 2006; Zedler *et al*., 2016), far less is known about the potential long-term developmental effects (Farid, Dunlop, Tait & Hulse, 2008; Konijnenberg & Melinder, 2011; Melinder, Konijnenberg & Sarfi, 2013).

The consequences of prenatal opioid exposure on children's development are hard to investigate due to the difficulty of ruling out the effects of other pre- and postnatal factors such as polydrug use, maternal mental health, and other social factors related to opioid dependence. Yet, concerns have been raised that prenatal opioid exposure may negatively affect development, particularly attention and executive function (EF), a set of higher-order cognitive processes that control complex goal directed behaviors (Konijnenberg & Melinder, 2014; Nygaard, Slinning, Moe & Walhovd, 2016; Sirnes, Griffiths, Aukland, Eide, Elgen & Gundersen, 2018; Sundelin Wahlsten & Sarman, 2013). Deficits in EF and attention have been observed even when children were adopted or placed in foster care at an early age, suggesting that they are not caused by the postnatal home environment (Ornoy, Segal, Bar-Hamburger & Greenbaum, 2001; Slinning, 2004).

Prenatal opioid exposure may affect the developing brain through several mechanisms. Since opioids suppress cell viability and increase cell death during development, excess exposure to opioids may interfere with normal brain development (Farid *et al*., 2008). Evidence from both animal and human studies suggests that prenatal exposure to opioids can affect myelination (Sanchez, Bigbee, Fobbs, Robinson & Sato-Bigbee, 2008; Walhovd, Watts, Amlien & Woodward, 2012). Since myelination facilitates inter-regional connectivity, alterations in myelin can affect higher-order cognitive functions, including EF (Nickel & Gu, 2018). In addition, animal studies have demonstrated evidence that prenatal opioid exposure affects dopaminergic neurons and reduce dopamine concentrations in the brain, particularly in the frontal cortex (McGinty & Ford, 1980; Robbins, 2000; Robinson, Maher, Wallace & Kunko, 1997). Consequently, there are several mechanisms by which prenatal opioid exposure may affect EF.

Previous evidence suggests that EF may fall along a hot-cold continuum (Chaku & Hoyt, 2019; Zelazo & Carlson, 2012). Cool EF are elicited under relatively abstract, decontextualized, non-affective situations, while hot EF are evoked by emotionally laden tasks (Kerr & Zelazo, 2004; Nejati, Salehinejad & Nitsche, 2018). Though both cool and hot EF are important for everyday

functioning, previous research investigating the effects of prenatal exposure to opioids as well as other drugs has almost exclusively focused upon cool EF (Baldacchino, Arbuckle, Petrie & McCowan, 2014; Noland, Singer, Arendt, Minnes, Short & Bearer, 2003; Sirnes *et al*., 2018). More research investigating hot EF is needed, as hot EF may be an important link to explain the previously found association between prenatal opioid exposure and behavioral and emotion regulation (Alaedini, Haddadi & Asadian, 2017; Konijnenberg, Lund & Melinder, 2015; Nygaard *et al*., 2016).

A widely used measure of hot EF is the Iowa Gambling Task (IGT) which was designed to assess decision making and risk sensitivity (Bechara, Damasio, Damasio & Anderson, 1994). Performance on the IGT is not closely related to cool EF or general intelligence scores, suggesting that it might measure a separate construct (Toplak, Sorge, Benoit, West & Stanovich, 2010). While the task was originally designed to measure decision making in patients with ventromedial prefrontal cortex damage, it has also been used to measure decision making in patients with a substance use disorder (Barry & Petry, 2008) as well as children with fetal alcohol spectrum disorder (Kully-Martens, Treit, Pei & Rasmussen, 2013), attention deficit hyperactivity disorder (Geurts, Van der Oord & Crone, 2006), and prenatal cocaine exposure (Rasmussen & Wyper, 2007). However, to our knowledge, no study has investigated decision -making in children prenatally exposed to opioids.

The current study employed a child version of the IGT to assess: (1) whether there is a difference in decision-making strategy between children of women in OMT and children not prenatally exposed to drugs; (2) whether the OMT and control group differ in their sensitivity to punishment; and (3) whether the OMT and control group differ in their decision-making speed. Based on previous studies investigating the effects of prenatal opioid exposure on the frontal functioning, we expect children prenatally exposed to opioids to have a poorer decision-making performance on the IGT, choosing immediate rewards over long-term gains. In addition, we expect them to be more sensitive to punishment (losses in the game) and to have reduced decision-making speed.

METHODS

Study design and participants

The current study is part of a prospective longitudinal project investigating the development of children born to women in OMT from infancy to middle childhood (Bakstad, Sarfi, Welle-Strand & Ravndal, 2009). The original project was initiated in 2004, while the 10-year follow-up study was conducted during 2016 through 2017. Two groups were included in the study, one group of children born to women in OMT and one control group consisting of children from low-risk families whose mother reported having used no alcohol or drugs during pregnancy. Women in the OMT group were recruited through regional OMT centers and treatment facilities throughout Norway and contacted if they had a pregnancy due date between January 2005 and January 2007 and had used either methadone or buprenorphine during pregnancy. Of the 47 pregnant women in OMT in Norway identified at the start of the longitudinal project, 20 participated in the 10-year follow-up study, which is estimated to be 43% of the national target group. The other mothers contacted declined to participate at the start of the longitudinal project (n = 6), had a miscarriage (n = 2), withdrew from the study during the first 2 years (n = 3), were unable to be contacted by the researchers (n = 11), refused participation due to time restraints (n = 4), and one child was excluded at the start of the project due to a severe congenital disorder (n = 1). All women in the current sample started in an OMT program before conception and used prescribed opioids throughout their pregnancy. The mothers in the comparison group were recruited through local health care centers in and around the city of Oslo and selected based on corresponding due dates. Of the 36 comparison mothers that participated at the beginning of the project, 21 (58%) participated at the 10-year follow-up study, the others dropped out during the study period due to a lack of time (n = 15). Although an attempt was made at the beginning of the project, it was difficult to recruit families in the control group that matched the OMT group on socio-demographic characteristics. The comparison group, therefore, consisted mainly of families with a mid-to-high SES. The final sample for the 10-year follow-up included 20 children of women in OMT (10 girls and 10 boys) and 21 control children (13 girls and 8 boys), aged 9-11 years. Due to the limited number of participants, the study only has enough power to detect effect sizes of d = 0.69 or higher (which equals η^2 = 0.11) with a power of 0.80, which corresponds to moderate-to-large effects using Cohen's conventions (Cohen, 1988). Demographic, birth, and substance use characteristics are depicted in Table 1.

Procedure

Written informed consent was obtained from the (foster) parents prior to participation and verbal consent was obtained from all participating children. Children were tested individually in a quiet testing room during one session. At the end of the session, children received a gift card worth approximately $10 for their participation. The study was approved by the local ethics committee and was conducted in accordance with the Declaration of Helsinki (1964).

Measures

Demographic information. Background data, including birth weight, birth length, gestational age, treatment for neonatal abstinence syndrome (NAS), living arrangements, education, employment and income, were collected from personal interviews and hospital medical records. The European Addiction Severity Index questionnaire (EuropASI), a structured interview designed to provide diagnostic information on substance use, was administered to all participants in the last trimester in order to measure substance use during pregnancy (McLellan, Kushner, Metzger *et al*., 1992). Table 1 shows the self-reported use of substances used during the last trimester of pregnancy, which were compared to the urine analyses from OMT centers during the last month of pregnancy. There was agreement in all but one case, and a mean number of 1.2 samples were collected per week (Bakstad *et al*., 2009). The Hopkins Symptom Checklist (HSCL-25) was used to assess symptoms of anxiety and depression during pregnancy in both the OMT and control group. Results of the HSCL-25 have been published previously (Bakstad *et al*., 2009). In addition, a questionnaire containing questions regarding pregnancy issues and birth data were administered in the last trimester and 3 months after delivery (Bakstad *et al*., 2009).

Gambling task. A child version of the Iowa Gambling Task, originally developed by Bechara *et al*., (1994) was administered to all participants (e.g., hungry donkey task: Crone & van der Molen, 2004). The task was administered on a PC fitted with a touch-screen monitor using Inquisit 4 (Millisecond Software, Washington, DC, USA). Participants were shown four doors (see Fig. 1) and instructed to open one of the doors by touching it on the screen, which resulted in a gain or loss of apples. The goal of the task was to collect as many apples as possible to feed a hungry donkey. Participants were instructed that they could choose any door they wanted and that they could switch doors at any time. After they made their choice, their gain was indicated by green apples and their losses by red apples with a cross through them. A red and green colored bar on the bottom of the screen presented the status of their gain. The task is

Table 1. *Demographic, birth, and substance use characteristics of the OMT and comparison group*

	OMT (n = 20)	Comparison (n = 21)	F/X^2	p	η^2/φ
Child characteristics					
Female sex, n (%)	10 (50.0)	13 (61.9)	0.59	0.44	0.12
Age, years*	10.94 (0.62)	10.57 (0.42)	4.92	0.03	0.11
Birth weight, gram*	3107.85 (728.55)	3548.90 (384.58)	5.97	0.02	0.13
Birth length, cm**	47.58 (3.67)	50.48 (1.40)	11.41	0.002	0.23
Gestational age, weeks*	38.96 (3.27)	40.00 (1.00)	1.93	0.17	0.05
Living with biological parent(s), n (%)**	13 (65.0)	21 (100)	8.86	0.003	0.47
Treated for NAS, n (%)	14 (70.0)	–			
Mother/fostermother characteristics					
Higher education, n (%)**	11 (55.0)	20 (95.2)	8.99	0.003	0.47
Employed, n (%)**	13 (65.0)	21 (100.0)	8.86	0.003	0.47
Yearly income < 37.000 euro, n (%)**	8 (40.0)	0 (0)	10.44	0.001	0.51
Single parenthood, n (%)**	11 (55.0)	2 (9.5)	87.55	0.006	0.43
Maternal substance use during pregnancy					
Tobacco, n (%)	19 (95.0)	0	–	–	–
Cigarettes, average per day	11.5 (6.4)	0	–	–	–
Alcohol, n (%)	2 (10.0)	0	–	–	–
Marijuana, n (%)	2 (10.0)	0	–	–	–
Amphetamine, n (%)	6 (30.0)	0	–	–	–
Benzodiazepine, n (%)	7 (35.0)	0	–	–	–
Opioids (other than meth/bup), n (%)	5 (25.0)	0	–	–	–
Methadone, n (%)	12 (60.0)	0	–	–	–
Buprenorphine, n (%)	8 (40.01)	0	–	–	–
Meth dose at delivery, mg, mean (range)[a]	101.8 (10–260)	0	–	–	–
Bup dose at delivery, mg, mean (range)	13.5 (3–24)	0			

Notes: OMT = Opioid Maintenance Therapy; Meth = methadone; Bup = buprenorphine.
Values are given as mean (standard deviation) unless otherwise specified.
[a]One outlier (660 mg methadone) was not included in this mean.
*$p < 0.05$; **$p < 0.01$.

designed to measure affective decision making by varying the net amount of apples gained or lost. The doors differed in the amount of gain that could be obtained, and the frequency and magnitude of loss (see description under Fig. 1). Door A was disadvantageous, with high gain, but frequent probability of intermediate-sized losses. Door B (most "risky" door) was disadvantageous, with high gain, but infrequent probability of high magnitude losses. Door C (the "safest" door) was advantageous, with smaller gain and frequent probability of small losses. Finally, door D was advantageous, with smaller gain and infrequent probability of intermediate sized losses. Participants with good decision-making abilities inhibit the response to go for the immediate reward (doors A and B), instead selecting the doors that are less immediately attractive (doors C and D), but much more advantageous in the long run.

Data analysis

All data were analyzed using IBM SPSS Statistics version 25 (SPSS Inc., Chicago, IL, USA). Demographic characteristics between the OMT and comparison group were analyzed using a one-way analysis of variance (ANOVA) or χ^2 test where appropriate. The main analysis was adopted from the Iowa Gambling Task literature in which net score differences were calculated between advantageous and disadvantageous choices (Antoine Bechara, Damasio & Damasio, 2000; Crone, Vendel & van der Molen, 2003; Fernie & Tunney, 2006). The difference score was calculated between the total number of choices for door C and D (advantageous choices) minus the total number of choices for door A and B (disadvantageous choices). Positive scores indicate an overall net gain while a negative score indicates an overall loss (Crone & van der Molen, 2004). To examine possible strategy changes during the task, net scores were calculated across 40 trials for five blocks (total of 200 trials). Preliminary analysis revealed no significant main effects or interaction effects involving gender, living arrangements (biological parents versus fosterparents), or type of opioid exposure (methadone versus buprenorphine). Data were, therefore, collapsed across these variables. In addition, no main or interactions were found of gestational age, birth weight, maternal education or opioid dose on test scores, all $p < 0.05$. These factors were, therefore, not included in subsequent analyses. The normality of the IGT data was checked using the Shapiro–Wilk test. In addition, data were checked for outliers by drawing box plots for the main study variables.

RESULTS

Decision-making strategy

Results of the gambling task are depicted in Table 2. The most popular choice for both groups was door B (high gain, infrequent high loss) followed by door D (low gain, infrequent high loss), then door C (low gain, frequent low loss), and finally, door A (high gain, frequent low loss). To investigate decision-making strategy, net scores were analyzed with a repeated measures ANOVA with group (OMT versus control) as a between subject factor and trial block as a within subject factor. No main effect of group $F(1, 39) = 1.44$, $p = 0.24$, $\eta^2 = 0.04$ or trial block $F(4, 156) = 0.93$, $p = 0.45$, $\eta^2 = 0.02$ were found. However, there was a significant interaction effect between group and trial block, $F(4, 156) = 2.83$, $p = 0.03$, $\eta^2 = 0.07$. This interaction effect can be seen in Fig. 2. Post-hoc comparisons yielded a significant group difference in net scores for trial block 4, $t(19) = 3.67$,

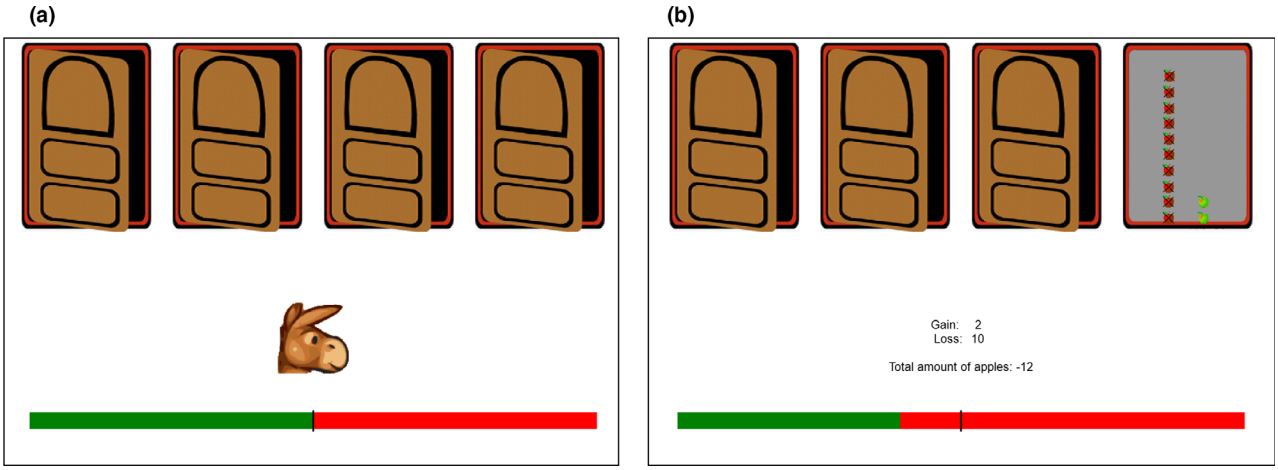

Fig. 1. Example of the door selection display (a) and outcome display (b). Each door selection resulted in a loss or gain of apples. Door A and door B were disadvantageous, resulting in a net loss over the long run, while door C and D were advantageous, resulting in a net win. The distribution of gains and losses for the four doors was: Door A (disadvantageous, frequent punishment): gain (4,4,4,4,4,4,4,4,4,4), losses (0,0,0,0,0,8,10,10,10,12), Door B (disadvantageous, infrequent punishment): gain (4,4,4,4,4,4,4,4,4,4), losses (0,0,0,0,0,0,0,0,0,50), Door C (advantageous, frequent punishment): gain (2,2,2,2,2,2,2,2,2,2), losses (0,0,0,0,0,1,2,2,2,3), and Door D (advantageous, infrequent punishment: gain (2,2,2,2,2,2,2,2,2,2), losses (0,0,0,0,0,0,0,0,0,10). [Colour figure can be viewed at wileyonlinelibrary.com]

Table 2. *Gambling task performance*

	OMT (n = 20)	Control (n = 21)
Door selection (%)		
Door A	16.0%	13.8%
Door B	33.2%	38.5%
Door C	23.1%	19.5%
Door D	27.8%	28.2%
Net scores		
Block 1	−0.50 (8.56)	0.95 (5.85)
Block 2	0.60 (9.22)	1.52 (11.78)
Block 3	−2.10 (12.51)	−2.86 (9.52)
Block 4	3.80 (10.68)	−6.29 (11.48)
Block 5	1.70 (14.16)	−2.48 (9.63)
Mean reaction time, ms (*SD*)		
Advantageous doors	873 (1,870)	831 (1,236)
Disadvantageous doors	796 (1,202)	878 (1,532)
Infrequent, high punishment doors	757 (1,325)	782 (1,157)
Frequent, low punishment doors	956 (1,900)	1,003 (1,777)

Note: *Net scores* = total number of choices for door C and D (advantageous choices) – total number of choices for door A and B (disadvantageous choices).

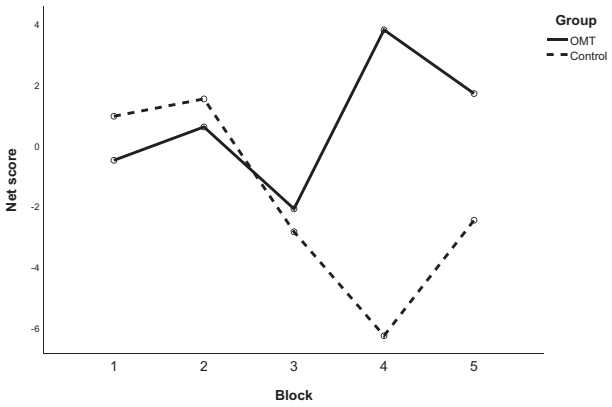

Fig. 2. Net scores as a function of trial block for the OMT and control group.

p = 0.002, d = 0.85, with children in the OMT group making more advantageous choices compared to the control group. Net scores did not differ between the two groups on any of the other trial blocks, all $p > 0.05$.

Sensitivity to punishment

A second ANOVA investigated whether children choose doors associated with frequent, but lower punishment or doors with occasional, but higher punishment. A repeated measure ANOVA with Group as a between factor and Trial Block as a within subject factor revealed a main effect of frequency, F(4, 156) = 2.57, p = 0.04, η^2 = 0.06, showing that children chose the decks with infrequent, but high punishment more often than the decks with frequent, but low punishment (see Fig. 3). In addition, a main effect of group was found, F(1, 39) = 4.90, p = 0.03, η^2 = 0.11, with children in the control group choosing the doors with the infrequent, but high punishment more often compared to children in the OMT group. These results suggest that the OMT group avoided the doors with the high punishment more than the children in the control group. No significant interaction between trial block and group was found, $p > 0.05$.

Decision-making speed

Finally, reaction times were compared between the OMT and control group in an ANOVA with group as a between participant factor and gain (advantageous vs disadvantageous) and frequency (low versus high frequency punishment) as within-participant factors (see Table 2). Results yielded a significant main effect of frequency on reaction time, F(1, 8,194) = 38.02, p = < 0.001,

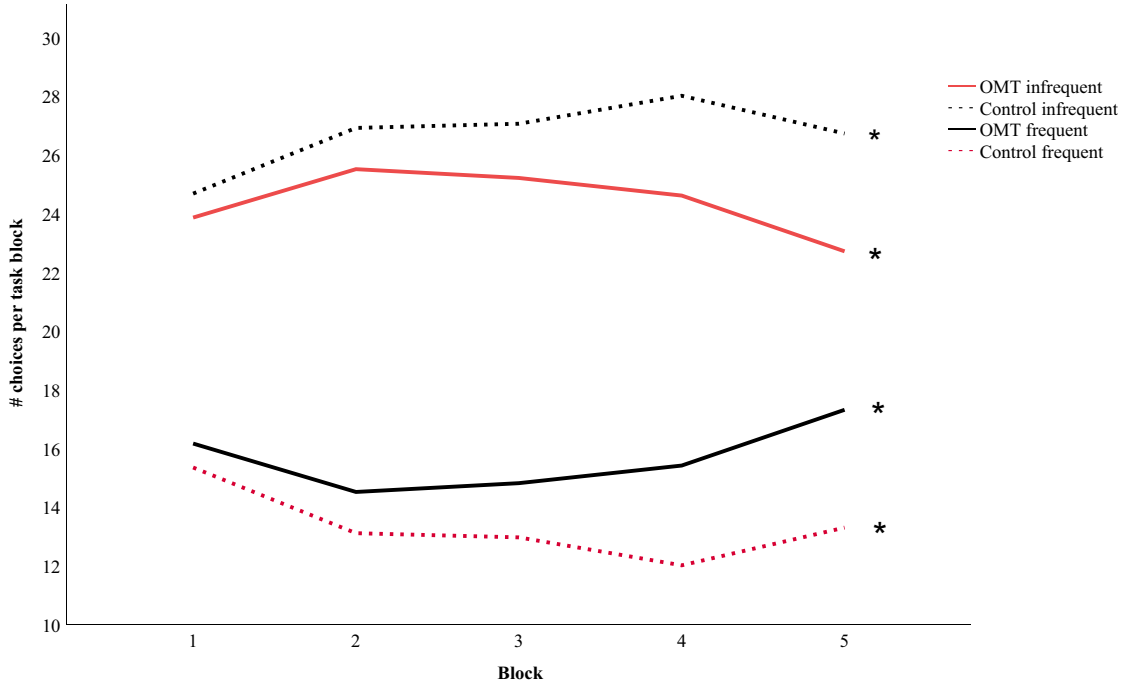

Fig. 3. Number of choices associated with high frequency punishment or low frequency punishment as a function of trial block, for each group separately. *Note*: *$p < 0.05$. [Colour figure can be viewed at wileyonlinelibrary.com]

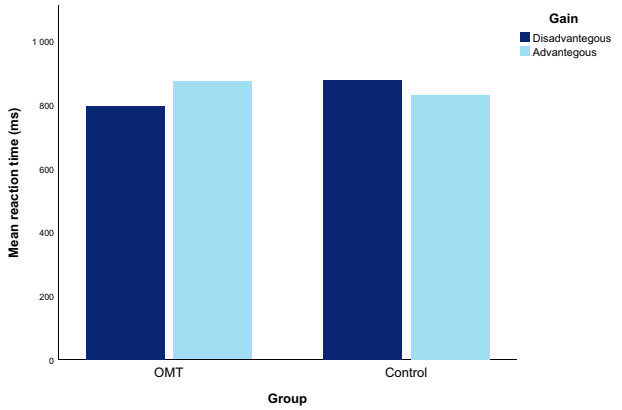

Fig. 4. Mean reaction times for the advantageous and disadvantageous decks for the OMT and control group. [Colour figure can be viewed at wileyonlinelibrary.com]

$\eta^2 = 0.005$, demonstrating that children selected doors associated with infrequent, but high punishment faster than doors associated with frequent, but low punishment. No other main effects were found, all $p > 0.05$. A significant interaction effect was found between group and gain, $F(1, 8{,}194) = 4.09$, $p = 0.04$, $\eta^2 = 0.001$, which is depicted in Fig. 4. As shown, children in the control group selected advantageous doors faster than disadvantageous doors, while an opposite result was found for children in the OMT group, who selected advantageous doors slower than disadvantageous doors. No other main effects involving group, gain, or frequency were found.

DISCUSSION

The main goals of the present study were to investigate affective decision making in children prenatally exposed to methadone or buprenorphine. Based on previous findings on the relationship between prenatal opioid exposure and frontal functioning, we hypothesized that children prenatally exposed to opioids would have poorer decision-making performance, were more sensitive to punishment, and would have reduced decision-making speed on a gambling task compared to non-exposed controls.

In contrast with our predictions, we did not find that children born to women in OMT had poorer decision-making skills compared to a group of non-exposed controls. Children in the OMT group performed as well overall as the control group (as evidenced by similar total net scores). In contrast, the children in the OMT group performed better over time throughout the task (as indicated by higher block net scores during block 4) compared to the control group (see Fig. 2). While children in the OMT group learned to take advantageous doors in the last part of the task, children in the control group kept choosing the disadvantageous doors. These results suggest that children prenatally exposed to opioids are able to consider future consequences when making decisions.

Previous findings have shown that with advancing age, children make increasingly more advantageous choices during the IGT, with a particularly marked improvement between the ages of 10 and 17 years (Crone & van der Molen, 2004; Hooper *et al.*, 2004). However, others have found that affective decision-making abilities progress in a J-shape, with younger children performing better on the IGT than early adolescents (Smith, Xiao & Bechara, 2012). A possible reason for this is that the ventral tegmental area and nucleus accumbens (NAcc), involved in reward-related processes, are more developed in early adolescents compared to younger children. Increased activity in the NAcc in early adolescence can cause an increased sensitivity to the large payoffs of the disadvantageous doors, which causes children in early

adolescence to continue to choose these doors even though they are disadvantageous in the long run (Smith *et al*., 2012). In this case, reduced performance actually suggests more advanced development of the NAcc, which tends to develop during early adolescence (Ernst, Nelson, Jazbec *et al*., 2005; Galvan, Hare, Parra *et al*., 2006). The finding that the OMT group performed better on the affective-decision making task compared to the control group and was not tempted by the large payoffs of the disadvantageous doors, may be a sign that their NAcc is less developed compared to the control group, who were more tempted by immediate high rewards.

Previously, Goff *et al*., (2013) found that children who experience early life stress, such as institutionalized care, do not have a typical increase in NAcc reactivity during adolescence. Instead, these children showed NAcc hypoactivation during adolescence. As more than one third of the children in the OMT group had been placed in foster care, it is possible that early life stress in the OMT group decreased activity in the NAcc, causing these children to be less sensitive to the large payoffs of the disadvantageous doors. However, as we did not use direct brain imaging in the current study, this hypothesis still needs to be verified with imaging studies.

Similar to previous reports, both children in the OMT and control group preferred choices associated with infrequent but high losses compared to choices associated with frequent but lower losses (Carlson, Zayas & Guthormsen, 2009; Crone & van der Molen, 2004; Geurts *et al*., 2006). This would suggest that both groups opted for immediate rewards and tried to avoid punishment. However, as can be seen in Fig. 3, the control group more often choose the infrequent but high loss option compared to the OMT group, particularly in the second half of the task. Seemingly, the children in the OMT group reacted more strongly to the high losses compared to the control group and shifted their choices accordingly.

The RT analysis indicated that both groups selected doors associated with infrequent punishment faster than doors associated with frequent punishment and that children in the control group made advantageous choices faster than disadvantageous choices (Crone & van der Molen, 2004). These findings have previously been interpreted using the decision-field theory, which states that previous choices in a task such as the IGT affect preference states which in turn affect decision making (Busemeyer & Townsend, 1993; Crone & van der Molen, 2004). This bias in decision making causes a faster selection of favorable choices and might be influenced by somatic markers (Busemeyer & Townsend, 1993). The finding that children in the OMT group did not select advantageous doors faster than disadvantageous doors may suggest that they experienced fewer or were less guided by somatic markers, such as a raised heart rate and increased skin conductance response. Future studies will need to include autonomic measures in order to confirm this hypothesis.

Several limitations should be noted when interpreting these results. The study had a limited amount of participants, which affects statistical power and generalizability. A recent meta-analysis investigating the cognitive development of children prenatally exposed to methadone or buprenorphine found effect sizes of $d = 0.56$ for results on tests of cognitive functioning (Andersen, Høiseth & Nygaard, 2020). Consequently, as our study was only able to detect effects of $d = 0.69$ or higher with a power of 0.80, we may not have had enough power to detect effects of the expected size based on previous studies. Future studies will, therefore, need to include more participants or draw their conclusions based on the combination of multiple studies, for example, meta studies. In addition, this study did not include physiological measures such as heart rate in order to measure children's arousal levels during the task. Including physiological measures in the future may help explain present findings and variability in task performance. Finally, we did not measure children's motivation to perform well on the task. As individual differences in motivation may effect task performance, children's motivation should be taken into account in future studies.

In sum, the results of this first study to investigate decision making in children prenatally exposed to opioids demonstrates that children prenatally exposed to opioids have normal risk-taking performance on an affective decision-making task. They effectively used previous experiences to guide future decisions and were able to select options that ensured long-term gain over immediate gratification. Compared to non-exposed children, they were less affected by immediate rewards. Future studies will need to investigate whether this could be a result of less activation in the NAcc, lower autonomic nervous system activity, or both.

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CONFLICT OF INTEREST

The authors have no conflict of interest to declare.

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DATA AVAILABILITY STATEMENT

Data available on request due to privacy/ethical restrictions.

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