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Abstract

Neonatal Abstinence Syndrome is a set of symptoms that result from prenatal exposure to addictive drugs. This syndrome is often attributed to opiate withdrawal; yet, there is a controversy within the literature as to whether cocaine, an addictive stimulant, leads to a variant, which I term "cocaine-based Neonatal Abstinence Syndrome." In this paper, I contrast the evidence that supports the presence of cocaine withdrawal in neonates with the opposing evidence that supports its absence. I offer an intermediary explanation through the "Adaptationist View," which attributes the supposed symptoms of cocaine infant withdrawal to the neonate adapting to extreme changes in its environment. Moreover, I introduce the Addictiveness of Cocaine Conclusion to serve as a logical means to bridge the addiction cycle with the Adaptationist view.

1. Introduction

Neonatal Abstinence Syndrome (NAS), historically known as "infant addiction" and "congenital addiction," describes a body of symptoms experienced by an infant as a result of maternal drug abuse over the course of a pregnancy (Jones & Fielder 2015). The symptoms that arise are the result of defects in the central nervous system (CNS), autonomic nervous system (ANS), gastrointestinal (GI) system, and respiratory system. Specifically what symptoms arise and their severity are dependent on the drugs used and when the pregnant mother uses them. Historically, NAS has been diagnosed in the context of opiates, yet it is controversial as to whether infants experience withdrawal when they have been exposed to cocaine prenatally (Jones & Fielder 2015). In pursuing the possible existence of infant cocaine withdrawal, I will refer to cocaine-based neonatal abstinence syndrome as "cNAS."

While the focus of this paper is to discuss the relationship between neonates and cocaine withdrawal, it is important to describe the effect of cocaine on neurotransmitters and the placenta; understanding the physiological effects of cocaine will provide context for symptoms. Cocaine is a CNS stimulant that inhibits norepinephrine transporters, serotonin transporters and dopamine transporters, preventing the reuptake of synaptic norepinephrine, serotonin, and dopamine respectively (Cain, Bornick, and Whiteman 2013). As these neurotransmitters are not removed in a timely manner, they remain in excess in the synaptic cleft and elicit a signal upon binding to their corresponding receptors on post-synaptic neurons. This signal, known as an action potential, ultimately leads to effects that are dependent on the neurotransmitter. The high concentration of neurotransmitters lead to the overstimulation of post-synaptic neurons; hence cocaine's classification as

a stimulant.

Every neurotransmitter has a corresponding effect. Due to the inhibition of mechanisms that reuptake norepinephrine, serotonin, and dopamine, cocaine creates an imbalance in these neurotransmitters. This dysregulation leads to the symptoms of cocaine-use. Norepinephrine is responsible for activating the sympathetic nervous system. The activation of the sympathetic nervous system increases blood flow that is directed from the GI tract and reproductive system to the heart, brain, and skeletal muscles (Buckley 2015). Serotonin is the prominent neurotransmitter that affects mood. Like cocaine, selective serotonin reuptake inhibitors (SSRIs) keep serotonin in the synaptic cleft. Due to its function in maintaining high serotonin levels within the synaptic cleft, there are similar arguments as to whether SSRIs lead to neonate withdrawal when used over the course of a pregnancy (Jones & Fielder 2015). Dopamine is attributed to the feeling of euphoria, colloquially known as a "high" (Cain, Bornick & Whiteman 2013; Kuczkowski 2003, 2004, 2005). Excess dopamine in the nucleus accumbens is the biologically evident site of addiction. Cocaine increases the production of enzymes that decrease dopamine levels. This increase in enzymes is a response to the abnormally high concentration of dopamine in the synaptic cleft. The body adapts and synthesizes more enzymes in order to counteract future imbalances. Thus, the body becomes less sensitive to dopamine; more precisely, it now takes more dopamine to experience euphoria. In the context of cocaine addiction, the user now requires more cocaine in order to attain a high enough dopamine concentration to experience euphoria.

As an extension to neurotransmitters, cocaine directly affects the placenta. The placenta is the site of maternal-fetal exchange. Within this exchange, the placenta transfers nutrients from mother to fetus, eliminates fetal metabolic waste, mediates fetal gas exchange, and produces steroid hormones. Effectively, the placenta serves as the fetal equivalent to the kidneys, the liver, and the lungs (De Giovanni & Marchetti 2012). Considering its wide-ranging utility, the placenta is the medium through which the mother prenatally provides the neonate with the necessary nutrients to support its growth and development (Coyle, et al. 2018).

Cocaine acts on the placenta due to the presence of surface norepinephrine and serotonin receptors. The surface norepinephrine receptors act in tandem with the mother's sympathetic nervous system. This connection is one of the reasons that cocaine-use during pregnancy has an increased risk for preterm rupturing of the membranes—colloquially known as "the water breaking early." This risk is due to the overstimulation of norepinephrine receptors that line the face of the placenta. As cocaine activates the sympathetic nervous system and there is an increase in norepinephrine, uterine contractions occur as the pregnant mother enters preterm labor (De Giovanni & Marchetti 2012). The constant stimulation of the sympathetic nervous system effectively pushes the neonate into delivery. The increase in norepinephrine is characteristic of a "catecholamine [1] surge" that occurs during birth and is speculated to be the mechanism in which the infant adapts to hypoxia during delivery (Buckley 2015). Additionally, there are higher levels of catecholamines in umbilical arterial blood during vaginal delivery than in caesarean sections, indicative of its use during stressful environments (Faxelius, et al. 1983). Regarding the use of serotonin, this neurotransmitter is transported to the fetus to regulate brain development, namely thalamocortical wiring in the forebrain, cortical development, and long-term behavior (Velasquez, et al. 2013).

Considering the potent effects of cocaine in both the placenta and the fetus, the presence of withdrawal from prenatal maternal cocaine use,

[1] The term catecholamine describes a class of structurally similar monoamine neurotransmitters. Among these neurotransmitters, norepinephrine and dopamine are a part of this class. Serotonin is not.

i.e. cNAS, is a point of controversy within the literature (Jones & Fielder 2015). It is logical to deduce that infants that were prenatally exposed to cocaine experience withdrawal. A deductive argument that aptly represents this view can structured such that:

1. Some drugs are addictive.
2. Users of addictive drugs become addicted after repeated use.
3. Removal of addictive drugs from an addicted user leads to withdrawal.
4. Cocaine is an addictive drug.
5. Therefore, the removal of cocaine from an addicted user leads to withdrawal.

I will label this argument the **Addictiveness of Cocaine Conclusion (ACC)**. This argument is commonsensical; if an addictive substance is removed from its timely abuser, then withdrawal follows. The ACC is described in part from the addiction cycle, which considers three interconnected phases: intoxication, withdrawal, and preoccupation (Herman & Roberto 2015). In intoxication, the addictive substance is consumed, prompting psychological and physiological effects, e.g. pleasure that stimulates the reward circuit in the brain. In withdrawal, an unpleasurable state is sustained after the addictive substance is removed for a period of time. Preoccupation is the state in which an addicted user craves the addictive substance after a period of abstinence. While addiction has been heavily researched in both human and non-human subjects (Koob & Le Moal 1997), there still remains a discrepancy as to whether cocaine-exposed neonates experience withdrawal. I will consider the ACC in response to whether withdrawal exists in cocaine-exposed infants.

In this paper, I will present two viewpoints, labeled "Study A" and Study "B". In Study A, I discuss evidence derived from a retrospective case-control study that concludes that withdrawal occurs in infants prenatally exposed to cocaine; their conclusion is derived through a symptom-based definition of withdrawal (Ogunyemi & Hernández-Loera 2004). In Study B, I discuss evidence derived from a cross-sectional case-control study that concludes that withdrawal does not occur in infants prenatally exposed to cocaine; their conclusion is derived through a standardized scale (Eyler, et al 2001). The purpose of defining each view as "Study A" and "Study B" is to utilize a representative argument in favor of each perspective. Among the different articles supporting either side of the argument, the article by Ogunyemi & Hernández-Loera in 2004 and Eyler, et al in 2001 were used as exemplars to support the presence and absence of cocaine neonate withdrawal respectively. Figure 2 under Conclusion and Discussion provides explicit differences between the two representative studies. Additionally, other supporting articles were considered in order to supplement both arguments provided in Studies A and B. In light of these opposing views, I conclude with the "Adaptationist View" to unite both views while responding to the ACC.

2. Comparison of Methods between Parent Studies

Study A: Source of Data, Definition of Withdrawal, and Methodology

Study A utilizes a retrospective case-control study. In this study, cNAS was defined as "neurobehavioral abnormalities, including greater irritability, hypertonicity, tremulousness, mood alterations and inconsolability" (Ogunyemi & Hernández-Loera 2004). Thus, the presence of cocaine neonate withdrawal is determined on the basis of observed symptoms.

Study A's cases included 253 pregnant women with neonates that were diagnosed with prenatal cocaine exposure and selected from the study's Division of Obstetrics database. The control group was determined through a random selection of 237 pregnancies with neonates that have no his-

tory of prenatal cocaine exposure from the same database. Of the selected, 53 cocaine-exposed and 37 non-exposed maternal-neonatal charts were excluded from the analysis as a result of incomplete records. Each chart of the selected maternal-neonate pair was then reviewed for the following pieces of information: maternal age, gravidity, parity, race, onset of prenatal care, medical history, obstetric and gynecological history, educational level, employment, marital status, legal problems, living conditions, urine toxicology results, routine prenatal laboratory data, obstetric complications, delivery records and neonatal complications. If the maternal-neonatal chart did not possess these variables, they were excluded from the analysis and were considered incomplete (Ogunyemi & Hernández-Loera 2004).

Data analysis was undertaken through an SPSS statistical program with categorical variable relationships being tested for significance through chi squared analysis. T-tests, variance, and linear regression were used as needed. Multiple logistic regression was also used for multivariable analysis. A p-value less than 0.05 and a 95% confidence interval was considered statistically significant (Ogunyemi & Hernández-Loera 2004).

Study B: Source of Data, Definition of Withdrawal, and Methodology

Study B was a cross sectional case-control study. In this study, cNAS was defined as the lack of improvement or the worsening of cocaine metabolite-positive infants following the removal of cocaine (Eyler, et al 2001). Thus, the presence of cocaine neonate withdrawal is determined from significantly lower scores for varying qualitative data of cocaine metabolite-positive neonates contrasted with the data from an exposed cocaine metabolite-negative group and non-exposed control group.

Study B selected 74 cocaine-exposed neonates and 81 nonexposed neonates. The selectivity of the study is described in Table 1.

	Matched controls	Cocaine-exposed	Totals
Total enrolled (parent study)	154	154	308
Who survived	151	150	301
Were born at term	140	125	265
By vaginal delivery	114	102	216
Were well and stable	110	95	205
Behaviorally tested within 24 h	92	79	171
And first day urine known	81	74	155

Table 1. Study B's selection of controls and cocaine exposed infants.

Urine toxicology was used to differentiate cocaine exposed neonates at birth. Infants testing "cocaine–" for cocaine metabolites was indicative of the fact that cocaine was not found in the infant's system. Infants testing "cocaine+" for cocaine metabolites was indicative of the fact that cocaine was found in the infant's system. The reason why urine toxicology is nominally used is because cocaine, after consumption, is eventually broken down in the body and removed through the infant's excretory system. Of the cocaine exposed neonates, 47 tested cocaine– and 27 tested cocaine+ at birth. Neonates that were born preterm or by cesarean section were disqualified to avoid confounding factors (Table from Eyler, et al 2001).

Data analysis was undertaken to compare categorical variable relationships for significance through chi squared analysis and t-tests. In particular, these variables were graded using the Brazelton Neonate Behavior Assessment Scale (NBAS). Significant differences in correlative studies among mean levels by group or by time were determined through ANOVA (Eyler, et al 2001).

3. Results

Study A indicated that cocaine-users, on average, delivered their infants earlier than the controls, i.e. at 36 weeks versus 39 weeks, with

birth weights significantly lower than their control counterparts, i.e. 2660 grams versus 3305 grams. Fetal death had only occurred in the cocaine-using sample. 131 cocaine-exposed infants tested cocaine+ in the womb with 75 of these infants fitting the criteria to be diagnosed with neonatal abstinence syndrome after birth. The average time that cocaine metabolites remained in the urine toxicology tests was 3.16 days after birth (Ogunyemi & Hernández-Loera 2004).

Study B revealed that only autonomic regulation scores differed significantly between the groups at birth. The data that was not controlled for the effects of other drugs—i.e. marijuana, alcohol, and tobacco—indicated that there were significant differences in alert responsiveness, regulatory capacity, state regulation, and reinforcement value as shown in Table 2.

Toxicity: simple comparisons (uncontrolled for the effects of other drugs) for mean NBAS scores of the three cocaine exposure groups

	Unexposed controls $N=81$	Cocaine exposed urine-negative $N=47$	Cocaine exposed urine-positive $N=27$	P values $<.10$
Cluster scores				
Habituation	6.8	6.8	6.7	ns
Orientation	6.0	6.3	5.1	ns
Motor performance	5.0	4.9	5.0	ns
Range of state	3.1	3.2	3.1	ns
Regulation of state	5.0	5.0	5.0	ns
Autonomic regulation	6.0	6.2	5.8	ns
No. of abnormal reflexes[a]	4.5	3.9	4.6	ns
Summary scores				
Excitable[a]	1.3	1.2	1.4	ns
Depressed[a]	2.2	2.0	2.5	ns
Qualifier scores				
Alert responsiveness	4.6[b]	3.7	3.0[c]	$P=.009$
Cost of attention	5.5	5.3	5.0	ns
Examiner persistence	4.9	4.5	4.3	$P=.095$
General irritability	6.8	6.3	6.6	ns
Robustness and endurance	5.5	5.1	5.2	ns
Regulatory capacity	5.5[b]	4.8	4.6[c]	$P=.027$
State regulation	6.1	5.1	5.4	$P=.022$
Balance of motor tone	5.8	6.2	5.9	ns
Reinforcement value of infant's behavior	6.3[b]	6.1	5.6[c]	$P=.055$

[a] Higher scores represent better scores with these exceptions.
[b] Values were significantly different than values in planned comparisons.
[c] Values in planned comparisons.

Table 2. The results of Study B that did not control for the effects of other drugs. In controlling their effects, the data reveals that autonomic regulation was the only source of significant difference from one another. (Table from Eyler, et al. 2001)

Of the 27 cocaine+ infants, 79% remained positive between Days 2–4 with none testing positive between Days 5–7. In analyzing NBAS scores over time, the regulation state was the only statistically significant change over time when contrasted between the cocaine-exposed groups and the control group. Figure 1 depicts the actual NBAS scores and a pictorial representation of tested regulation state scores of the groups over time.

Within the data depicted in Figure 1, it is important to note that on Day 1, there was no significant difference among the three groups. From Days 2 to 4, the cocaine+ group had a significantly higher regulation state score than both the control group and cocaine– group. For the data between Days 5 to 7, the cocaine+ group was significantly lower than the control group but not significantly different than the cocaine– group.

Mean regulation of state scores for each exposure group (n) at each NBAS test time

NBAS test times			
Exposure group	1 day	2–4 days	5–7 days
Unexposed controls (81)	5.03	5.38	5.22
Cocaine exposed, urine-negative (47)	4.98	5.10	5.01
Cocaine exposed, urine-positive (27)	5.03	5.76	4.74

Overall group effect was not significant.
Overall time effect, day 1 < days 2–4 ($P=.0007$), days 2–4 > days 5–7 ($P=.0006$).
Interaction effect was significant ($P=.0413$).

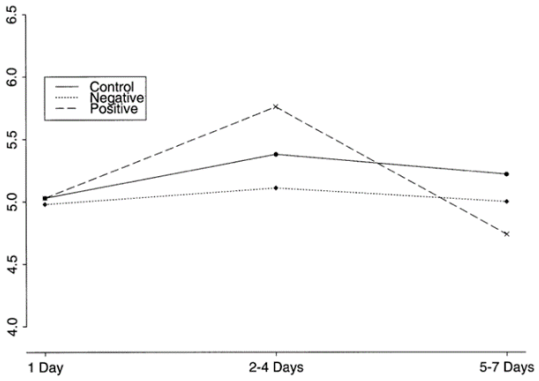

Table 3. Chart depicting the mean regulation state scores for each of the three groups over time. State regulation score is also given as a function of time in a graphical representation. (Figures from Eyler, et al. 2001)

4. Conclusion and Discussion

Study A concluded that 75 of the 131 cocaine-exposed infants were afflicted with cNAS. Namely, this diagnosis of cNAS was undertaken through the observation of specific symptoms. These symptoms focused on neurobehavioral abnormalities such as hyperirritability, hypertonicity, tremulousness, mood alterations and inconsolability (Ogunyemi & Hernández-Loera 2004). Concurrent with these observations, Ogunyemi & Hernández-Loera found that cocaine– infants of-

ten did not meet the criteria to be diagnosed with cNAS. Instead, they proposed the idea of an "in utero withdrawal," i.e. the concept that cocaine– infants at birth did not display withdrawal symptoms because they had already experienced withdrawal in the womb. The authors came to this suggestion by analyzing both maternal urine toxicology and neonatal urine toxicology. In finding trends within neonatal toxicology, they found that if the urine sample had resulted in a positive test for only one day or outright negative for cocaine metabolites postnatally, withdrawal was unlikely to be observed. In contrast, if the urine sample had resulted in a positive test for two days or longer postnatally, neonatal withdrawal was more likely to be observed. The authors attribute this discrepancy to the time taken between the last administration of cocaine and delivery. If the infant was cocaine+ for one day or cocaine– at birth, it is suggested that the mother's last dose was one week or earlier prior to delivery. In this instance, withdrawal would have occurred in utero. If the infant was cocaine+ for greater than two days postnatally, it is suggested that the mother's last dose was two to seven days prior to delivery. Thus, the infant would exhibit symptoms that resemble withdrawal postnatally (Ogunyemi & Hernández-Loera 2004).

Study A is particularly convincing in that it provides an explanation as to why some cocaine-exposed neonates do not display withdrawal symptoms. The study draws a distinction between cocaine+ and cocaine– infants, where the former group is proposed to experience withdrawal in utero and the latter experiences withdrawal postnatally. The results of Study A are also supported by other studies that have diagnosed mild to moderate withdrawal based on observed behavior (Cherukuri, et al. 1988; va de Bor, et al. 1990; Mastrogianis, et al. 1990). Studies have also supported Study A's conclusion through a standardized scale, i.e. Finnegan's Neonatal Abstinence Scoring System (Fulroth, Phillips & Durand 1989; Terri, et al. 1995). It is important to recognize, however, that this system is nominally used to diagnose opioid NAS, which bears different symptoms than cocaine addiction and cocaine withdrawal (Eyler, et al. 2001). Thus, the reliability of these results are questionable as to whether the scores were the result of cNAS or simply an overall effect of cocaine.

Study B suggests otherwise. While Study A concludes with the presence of neonate withdrawal in utero and postnatally, Study B statistically concludes that cocaine– and cocaine+ infants are not significantly different from one another as denoted by their NBAS score; thus, the evidence supports the idea that the generally lower scores of cocaine-exposed infants relative to the nonexposed infants is an overall effect of cocaine. This approach is convincing because NBAS is a standardized evaluation that has the capacity to measure behaviors that are commonly attributed to cocaine exposure. Thus, the usage of this evaluation provides a standardized means for diagnosing cNAS. In analyzing the results, the lack of a statistical significance between cocaine+ and cocaine– symptoms leads to the conclusion that withdrawal does not occur within neonates exposed to cocaine. Instead, the results indicate that, when contrasted with the behavior of the control group, cocaine-exposed groups experience intransient defects due to the influence of cocaine on an infant's neurobehavioral pattern. This view is supported through observational studies (Chiriboga 1993; Hadeed & Siegel 1989) and through Finnegan's Neonatal Abstinence Scoring system (Ryan, Ehrlich, and Finnegan 1987). Again, it is important to note that Finnegan's system was primarily used to diagnose opiate NAS rather than cNAS. Moreover, it is also noteworthy that the creator-namesake of this system, Loretta Finnegan, also concluded the lack of cocaine withdrawal in infants (Ryan, Ehrlich, and Finnegan 1987). Both views are outlined and contrasted in Figure 2.

Considering both studies aptly describe different perspectives regarding the existence of cNAS,

Study	Claim?	Subjects used:	Definition of withdrawal	Other Drugs:	Argument against opposing view:	Conclusion
A	NAS	Cocaine+ at birth Cocaine- at birth Control	Patient exhibits greater irritability, hypertonicity tremulousness mood alterations, and inconsolability	Tobacco, Alcohol, Heroin, Marijuana	Withdrawal proposed to occur prenatally; thus symptoms would not arise postnatally in cocaine-patients	Withdrawal symptoms present prenatally and postnatally
B	No NAS	Cocaine+ at birth Cocaine- at birth Control	↑ regulation of state by days 2-4 followed by a statistically significant ↓ relative to control and other cocaine sample	Tobacco, Alcohol Marijuana	Symptoms resemble direct effects of cocaine in system	Lack of withdrawal; cocaine exposed scored worse than control due to direct effects of cocaine

Table 4. A Comparison of Study A (Ogunyemi & Hernández-Loera 2004) and Study B (Eyler, et al. 2001). Notice the conclusion column for a summary of both studies' main point.

the question arises as to whether both views can be united. Study A is reasonable when a symptom-centric perspective is considered, where specific defects are a result of cNAS. The downfall from this study, however, is the inability to distinguish the symptoms of withdrawal from the direct effects of cocaine. Likewise, Study B is reasonable when a scale-centric perspective relative to a control is considered, where lower NBAS scores compared to controls are the result of cocaine's direct effects rather than withdrawal. The concern for Study B, however, is that this conclusion is counterintuitive. Recall the logic behind the ACC: the removal of an addictive drug from a user leads to withdrawal. Neonates are exposed to cocaine with the substance flowing in and out of their system; how can the exposed infant seemingly be immune to withdrawal from cocaine, an addictive substance? The answer is that they are not immune to withdrawal and this question can be approached by uniting both perspectives through the "Adaptationist View".

The Adaptationist View begins with the maternal-fetal connection of the placenta. The effects of cocaine stimulate the sympathetic nervous system. As a result of the active sympathetic nervous system, less blood flows to the placenta. Thus, less oxygen, hormones, and nutrients arrive at the fetus (Messiah, et al. 2011; Nathanielsz & Hanson 2003). Due to this low supply, the exposed neonate does not possess comparative amounts of nutrients or oxygen in order to grow at a similar rate to unexposed neonates; this concept is evident in that cocaine exposed neonates, on average, weigh less than nonexposed neonates as birth (Ogunyemi & Hernández-Loera 2004; Chiriboga et al., 1999; Bandstra et al., 2001; Bada et al.,2002; Nordstrom-Klee et al., 2002). Thus, the fetus adapts to this state by growing accustomed to its low-resource environment. It is of interest to note that as hypoxia occurs during labor, norepinephrine is in high concentration as part of the catecholamine surge in order to adapt to this state (Buckley 2015). Though I am not claiming that cocaine-exposed infants become hypoxic per se, they do utilize a comparatively lower supply of oxygen; thus, neonates are forced into making necessary adjustments, i.e. less expenditure of energy and devoting less resources for growth. Norepinephrine is the principal hormone for long-term

adaptation. Moreover, dopamine has recently become a prominent treatment for neonate hypotension due to its capacity to increase blood pressure, circulating more oxygen (Bhayat, et al 2016). In this low-resource state, the neonate adapts to cocaine use at the expense of size and neurobehavioral development.

Upon birth, this adapted, maintained state is disturbed. In particular, the neonate is not reliant on the mother's blood supply and is thus exposed to an excess of environmental oxygen. With this significant amount of oxygen, the infant is overstimulated and ill-informed as to what he or she ought to do with this excess energy. Thus, the symptoms of hyperirritability, hypertonicity, and tremulousness arise. With an excess amount of oxygen, the body also must readjust to the higher concentrations of usable dopamine, readapting from its adapted cocaine-exposed state. This excess dopamine leads to the observed mood alterations and inconsolability described in Study A.

Upon the excretion of the cocaine metabolites, the Adaptationist View would posit that the body attempts to recalibrate a set point, indicative of the stark increase in state regulation followed by a stark decrease as shown in Eyler, et al.'s study (2001). As the infant seeks a set point for homeostatic function, the final result would, when compared to unexposed infants, be lower in NBAS scores. Due to the distressing environment in utero and the change of environment postnatally, a decrease in the state of regulation is an expected result of adaptation when contrasted with the unexposed controls. This result is in accordance with Eyler, et al.'s study (2001), indicative of an overall effect of cocaine rather than cocaine withdrawal.

The Adaptationist View connects the data presented between Study A and Study B and also satisfies a logical basis through which symptoms arise from both studies. Yet, it formulates an important objection to Study A: the presence of in utero withdrawal. According to Ogunyemi & Hernández-Loera's study, their primary explanation was that cocaine– neonates tended to lack withdrawal symptoms due to the withdrawal phase occurring in utero (2004). When juxtaposing this view with the Adaptationist view, there does not leave much room as to when the neonate would experience withdrawal prenatally. Though it can be argued that in utero withdrawal occurs as the neonate is adapting to the low resource environment, this environment and subsequent adaptation is undertaken in the presence of cocaine; withdrawal, as considered in the addiction cycle, occurs when cocaine is absent (Herman & Roberto 2015; Eyler, et al. 2001). The unpleasurable state sustained is the result of cocaine affecting the mother's sympathetic system, hindering the optimal nutrients needed in neonate growth and development. Thus, in utero withdrawal is not compatible with the Adaptationist view.

When considering Study A, the argument in favor of withdrawal is supported as a pathophysiological function, where each neurobehavioral symptom can be derived when observing this view. When considering Study B, the Adaptationist View can explain how cocaine leads to an overall effect on the infants, i.e. lower amounts of oxygen and nutrients and rapid changes in environment, rather than withdrawal specifically. Thus, in application, the Adaptationist View very aptly connects the differences within Studies A and B and lines up with the conclusion made by Study B. Yet, by rejecting the presence of in utero cocaine withdrawal, there is no explanation as to why withdrawal-like symptoms are present in some cocaine-exposed neonates but not others. Moreover, if the symptoms that were present postnatally are the effects of neonate cocaine withdrawal, there must be an explanation as to why withdrawal is selective to one cocaine-exposed population but not the latter.

Though I united the results of both studies to support the notion of an overall effect of cocaine, the following scenario must be addressed: When neonates are exposed to cocaine repeatedly over the course of a pregnancy if cocaine is suddenly

removed, as is the case after birth, shouldn't the infant experience withdrawal symptoms, considering that cocaine is an addictive substance? This scenario falls in line with the ACC presented in the introduction. As commonsensical as the argument may be, I will offer a solution that may circumvent this discrepancy between cocaine addiction and neonate withdrawal. The infant may experience some variant of selective attention, where there is a stronger negative effect experienced directly from cocaine than there is from withdrawal. In essence, the negative stimuli attributed to the overall effects of cocaine are perceived stronger than the negative distractor stimuli attributed to withdrawal (Johansen-Berg & Lloyd 2000). If there is withdrawal within a cocaine-exposed neonate, its effects are secondary to the direct effects of cocaine and the body physiologically reacts to the stronger stimulant. Thus, the ACC may be accepted in this context. Note that this conclusion does not undermine the Adaptationist View but rather provides an explanation as to why some cocaine-exposed infants did not experience withdrawal symptoms. The complication that arises is that the scales used to diagnose cNAS are actually diagnosing the overall effects of cocaine. In effect, these scales are not sensitive enough to capture less stimulating cNAS. Without any data on borderline cases of NAS, i.e. cases where their score was minutely below the threshold for diagnosis, this concern may hold. More studies, however, need to be done to verify that this complication is present.

Both studies support the Adaptationist View by equating the symptoms commonly attributed to cNAS to the adaption of an infant to a new, higher oxygen environment. This view continues by attributing the extreme increases and decreases in NBAS scores for autonomic regulation to be the result of seeking a setpoint for homeostasis. Thus, withdrawal is not primarily evident and both studies would support the presence of an adaptation mechanism that points to the direct effects of cocaine. In introducing the ACC, the presence of withdrawal may be still be possible but secondary to the overall effects of cocaine, causing the lack of an identifiable physiological response for NAS. When considering NAS in the context of the Adaptationist View and ACC, the argument in favor of the direct effects of cocaine on the infant is strengthened but the presence of withdrawal remains logically possible.

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