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Proprioceptive cross stroking exercises: a preliminary retrospective chart review of its developmental impact

Laura Elaine Sisk
wtj269@vols.utk.edu

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Laura Sisk
Chancellor's Honors Program
University of Tennessee
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Between 2000 and 2012, the national rate of Neonatal Abstinence Syndrome (NAS) has increased over 400 percent, from 1.2 to 5.8 per 1,000 live births.[1] A region hard-hit by the opioid epidemic, some Appalachian counties in East Tennessee report NAS rates more than 10 times the national average, "with rates exceeding 60 per 1,000 live births."[2] Knox County's NAS incidence peaked in 2014, at 22.6 per 1,000 live births and has since held steady at just over 20 per 1,000 live births.*[3] As concern over the opioid epidemic increases, so have community efforts to combat it. As evidenced by the opioid epidemic, drug use pervades race, socioeconomic status, geography, and age; even neonates are not immune to drug addiction.

Dr. Loretta Finnegan first described Neonatal Abstinence Syndrome in the 1970's. She developed the first scoring system for babies who exhibited symptoms of withdrawal after birth to provide a more objective evaluation of the infant's withdrawal status. Providers still use the Finnegan scoring system today before, during, and after treatment to monitor progress and adjust pharmacologic treatment according to its uniform criteria. The Finnegan system assigns scores to specific symptoms in an itemized list that include central nervous system disturbances such as high pitched cry and tremors, metabolic and respiratory disturbances including hyperthermia, and gastrointestinal disturbances like poor feeding and regurgitation. NAS symptoms and criteria are listed in Table 1.[4,5] Providers initially attempt to treat these symptoms with non-pharmacological such as breast-feeding, low-stimulus environments, and swaddling. If these interventions do not sufficiently manage symptoms, then providers

* Most recent annual report available is for 2017

Table 1. Neonatal Abstinence Syndrome Symptomology.[4,5]		
Central Nervous System Disturbances	**Metabolic, Vasomotor, and Respiratory Disturbances**	**Gastrointestinal Disturbances**
High pitched crying	Sweating	Excessive sucking
Sleep disturbances	Frequent yawning	Poor feeding
Myoclonic jerks	Mottling	Regurgitation
Hyperactive Moro reflex	Nasal stuffiness	Projectile vomiting
Tremors	Sneezing	Loose or watery stools
Increased muscle tone	Nasal flaring	Weight Loss
Excoriation	Increased respiratory rate (> 60/ min), with or without retractions	
Convulsions/seizures	Hyperthermia	

use pharmacological treatments such as diluted morphine tinctures and phenobarbital. Research has shown prolonged exposure to opiates poses adverse neural, cognitive, and behavioral outcomes in the developing brain. Investigating how we can minimize pharmacotherapy treatment when possible, and promote favorable developmental outcomes is of great importance as hospitals see increased numbers of NAS patients.

While the health outcomes of babies in the Neonatal Intensive Care Unit (NICU) prove more than important finances, the financial strain on both families and healthcare systems due to increased length of stay should not be ignored. Since building a new NICU wing in 2012 specifically for neonates born with NAS, East Tennessee Children's Hospital (ETCH) spent over seventy five million dollars to expand it to sixty six private rooms. Babies born with NAS "experience withdrawal just like adults," ETCH writes on their site, describing the new NICU wing. "They have a screech-like cry, claw their faces, and squirm." This wing is built to limit stimulation; it has dark lighting, quiet rooms, and special volunteers to comfort the babies.[6] In a

similar attempt to create a less stimulating environment, the University of Tennessee Medical Center (UTMC) has a NICU wing for NAS babies with a noise level of about 25-30 decibels, much lower than the noise levels in the open bay, which range from 80-100 decibels. Less than two miles from ETCH, UTMC has also expanded its NICU in recent years to accommodate increasing numbers of NAS patients. Just this year, at the end of March, UTMC opened "The Firefly Cove" to accommodate NAS babies; the previously described, $60 million, new 30-bed NICU wing. Last year, UTMC admitted 860 babies, and for the past ten years or so, babies with NAS account for roughly 20 percent of NICU admissions.[7] In 2009, hospital charges for NAS patients' course of treatment averaged over $50,000.[8]

Prematurity and in-utero drug exposure

One study of preterm drug-exposed infants shows these infants frequently exhibit lower Finnegan scores than term infants do on several criteria, suggesting the need for an NAS scoring system specific for preterm infants' symptomology.[9] Despite consistent drug exposure during gestation, preterm infants develop NAS less often than term infants. This difference could be attributed to the NAS scoring system, which is symptom-based and is not optimized for preterm infants; or possibly because preterm infants lack a more developed CNS.[10] Premature infants, however, are born during a critical window of gestation – a period of rapid brain development. Dr. Allocco writes that "the combination of preterm birth and in-utero opioid exposure puts the infant at particularly high risk for poor neurodevelopmental outcomes." Currently, no standardized treatment guidelines exist for preterm drug-exposed neonates. Although these babies do not experience withdrawal in the same way, this does not necessarily indicate decreased severity of NAS.[11] The experience of in-utero drug exposure lays the foundation for

these infants' neurodevelopment, even if not apparent in the first few days of life. Premature neonates are rarely studied in the context of NAS. NAS scoring requirements would exclude nearly all of these patients from the study. The inclusion of drug-exposed premature neonates allows us to examine what developmental impact, if any, that in-utero drug exposure has on these infants' development.

The role of proprioceptive input

Integration of sensory input allows the sensory systems like vestibular, proprioceptive, and tactile systems to guide the body's movement.[12] Proprioceptors tell the body its location in space relative to environmental features and the body itself. Kathleen Cullen writes: "The ability to distinguish self-generated sensory events from those that arise externally is … essential for perceptual stability and accurate motor control."[13] Proprioception plays two critical roles in motor control. One function of proprioception is that it provides the quickest and most accurate input with respect to detecting unexpected changes in the external environment that necessitate alteration in movement. Secondly, proprioception provides periodic information about movement and position during motor movements. This input influences "planning and modification of internally generated motor commands."[14] Adequate functioning of proprioceptors is necessary for locomotion, and proprioceptive exercises that strengthen neural connections can aid in development of these motor control systems.

Over the past twenty or so years, Dr. Miriam Weinstein has implemented proprioceptive cross-stroking exercises in the UTMC NICU to aid in neurodevelopment. In the plastic neonate brain, proprioceptive input can have maximal impact. This technique can be taught to and utilized by nurses and caregivers, so babies can receive this treatment both in and out of clinical

settings. This paper presents a universally-available neurodevelopmental treatment for at-risk neonates. The data used in this study comes from a larger ongoing study led by Dr. Weinstein, a pediatric physiatrist at the University of Tennessee Medical Center (UTMC) in Knoxville, Tennessee. The patients in this study were all seen by Dr. Weinstein in the UTMC NICU, and all received the cross-stroking exercise intervention.

This study initially began researching the impact of these exercises on motor development. Upon data analysis, intriguing differences in length of stay became apparent. We discuss how the intervention has played a role in the early postnatal stage and its implications for later in development. NAS' potential indication for proprioceptive cross stroking exercises is promising. We describe the role of proprioception in two of the three clusters of NAS symptoms, Central Nervous System (CNS) and respiratory disturbances.

Methods

Dr. Weinstein, a pediatric physiatrist (PM&R), implemented cross stroking (CS) exercises during rounds in the University of Tennessee Medical Center's Level III NICU. Nurses performed CS by gently holding the infant's right hand to the left cheek, then with the back of the right hand, stroke down the left arm all the way to the fingertips. Then the left hand repeated this same exercise. Nurses repeated this sequence on each side three times before bringing one hand to rest on top of the other on the chest. In addition to having sensorimotor and segmental spinal cord components, this exercise gives afferent proprioceptive input to the motor cortex. This free and simple hands-on technique taught to all nurses did not place undue burden on them in the busy NICU. Besides creating an instructional video, this intervention was implemented

with no extra equipment. Families and caregivers were also taught the intervention to encourage involvement and maximize opportunity for the neonates to receive the exercises. Because the NICU is very busy, the intervention's simplicity and minimal demand of nurses' time was of great importance. Other therapists who rounded once a week also performed the exercises. Following NICU discharge, PM&R monitored these patients, instructed mothers on CS and other exercises, and coordinated care with therapists.

For this study, I reviewed all of the charts in Dr. Weinstein's office for patients that were exposed to drugs in-utero. These patients were divided into two categories, *NAS* and *Drug-Exposed Premature*. This study categorizes prematurity as infants born at 32 weeks' gestational age or less. Inclusion criteria eliminated some patients from the study whose charts were originally included. UTMC uses the Finnegan scoring system to diagnose NAS. If the patients did not have a diagnosis of "NAS" on their NICU summary, "in utero poly-substance exposure" had to be listed as a diagnosis for inclusion; in order to analyze effects of drug-exposure in premature patients, this was particularly important for inclusion.* For the patients who had in-utero poly-substance exposure, some were not included in the study because they were not clearly affected by the exposure; babies excluded from the study who had "in-utero poly-substance exposure" were AGA/normal-to-high birth weight, had high Apgar scores, spent limited time in the NICU (<10 days), or only admitted to the NICU for reasons unrelated to drug exposure. "In utero drug exposure" or "poly substance exposure" is characterized by 1) consistent drug use self-reported by mother during pregnancy, and supported by positive urine or

* Premature infants are rarely diagnosed with NAS, see References: 9

Table 2. Patient demographics.	*Drug-Exposed Premature*		*NAS*	
	n	**Mean ± SD**	***n***	**Mean ± SD**
N	12		36	
Gestational age (weeks)	12	28 3/7 ± 1.9	35	37 4/7 ± 2.4
Birth weight (grams)	12	1121.3 ± 301.9	36	2697 ± 532
1-minute Apgar score (points)	12	4.2 ± 2.2	35	7.8 ± 1.1
5-minute Apgar score (points)	12	6.6 ± 1.5	35	8.7 ± 0.9
SGA (small for gest. age)	1 (8.3%)		9 (25%)	
AGA (average for gest. age)	12 (91.7%)		27 (75%)	
IUGR	1 (8.3%)		6 (16.7%)	
NICU LOS (days)	12	97.8 ± 38.6	34	20.91 ± 9.69
Walking age (months)	8	18.09 ± 4.17	23	11.7 ± 1.72
Received PT	11 (91.7%)		13 (36.1%)	
Received OT	8 (66.7%)		10 (27.8%)	
Received Orthodics	3 (25%)		5 (13.9%)	

other samples, when available 2) neonate with positive meconium or urine sample. Another inclusion factor required patients stay in Dr. Weinstein's practice after discharge from the NICU, for at least one year or until they reached developmental milestones, such as cruising and walking (whichever occurred earliest.) Table 2 shows demographics of patients in the study.*

This study uses walking age as a measurement of development because it serves as an important motor milestone and convenient identifier of development: Dr. Weinstein frequently recorded walking ages in patient charts that were not initially intended for research. "Walking" is defined as taking six or more steps independently. Because of the manner which the data was recorded, gaps exist in available data for each patient. Of the twelve patients in the *Drug-*

* table excludes outliers, explained in results

Exposed Premature category, one left the practice before acquiring ambulation and one other had inconclusive data in the file about their walking age. Of the thirty six *NAS* patients, two left the practice before acquiring ambulation, and nine had inconclusive data about walking age described in their charts.* In most cases walking ages were well documented, with office notes that corroborated parent reports; some charts had a lapse of visits and in which, parent reports were the only certain evidence of at the exact age a patient first walked independently. Altogether, definitive walking ages have been established for 34 patients, 9 in *Drug-Exposed Premature* and 25 from *NAS*. The length of stay in the NICU was determined for all but two patients, one in each category. All data was obtained from patient charts. No identifying information was recorded in data sets.

An interdisciplinary approach to medical treatments proves beneficial to patient outcomes. Proprioceptive cross stroking constitutes just one of the interventions for NAS treatment. Because of Knoxville's unique geographical relation to the opioid epidemic, we also examined some of the social history of the patients, such as type of drug exposure and post-discharge placement. This information is valuable when assessing developmental interventions in the context of gestational drug use, maternal and prenatal care, and NAS treatment.

Results

The average gestational age of the *NAS* neonates was 37 weeks and 4 days (*SD*=2.4 days). The average birth weight for *NAS* was 2697 grams ± 532 grams; seventeen of the thirty-six neonates delivered were Low Birth Weight (LBW < 2500g). *Drug-Exposed Premature*'s

* Inconclusiveness can be attributed to gaps in visits that overlapped the age at which they began walking, or ambiguous notation in files from which a definitive walking age could not be established

average gestational age was 28 weeks and 3 days (*SD*=1.9 days). The average birth weight for Drug-Exposed Premature was 1121.3 grams (*SD*=301.9 g). With the exception of one, all of the *Drug-Exposed Premature* patients were classified Very Low Birth Weight (VLBW < 1500g).* Twenty nine of the *NAS* patients were formally diagnosed with NAS.† Only one of the twelve *Drug-Exposed Premature* patients was diagnosed with NAS. Six of the 36 *NAS* patients suffered intrauterine growth restriction while again, only 1 of the 12 Drug-Exposed Premature patients did. Twenty seven (75 percent) of *NAS* patients received pharmacologic treatment, and eight (22.2 percent) did not receive pharmacologic treatment.‡ The difference in percentage of Small for Gestational Age (SGA) births between non-premature and premature categories, 25 percent vs. 8 percent, suggests a lesser effect of gestational drug-use in premature neonates.

Drug Use

Between 60 and 80 percent of newborns exposed to heroin or methadone in utero show NAS symptoms.[15] While Neonatal Abstinence Syndrome presents most frequently in the context of gestational opiate use, other drugs are also of concern.[16-18] Figure 1 shows antepartum drug use by mothers of patients in the study. Many mothers used several drugs concurrently; percentages are not mutually exclusive.

Of the 48 moms of babies in the study, 41 used narcotic pain relievers (including illicit drugs, opiates/opioids, and opiate replacements.) The seven who did not use narcotic pain relievers during pregnancy used at least one of the following drug types: benzodiazepines,

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* The one VLBW exception was LBW

† Inclusion of non-NAS patients in *NAS* is explained in Length of Stay — *NAS* results

‡ One chart of patient (diagnosed as NAS) was missing a NICU summary so whether they received pharmacologic intervention is inconclusive

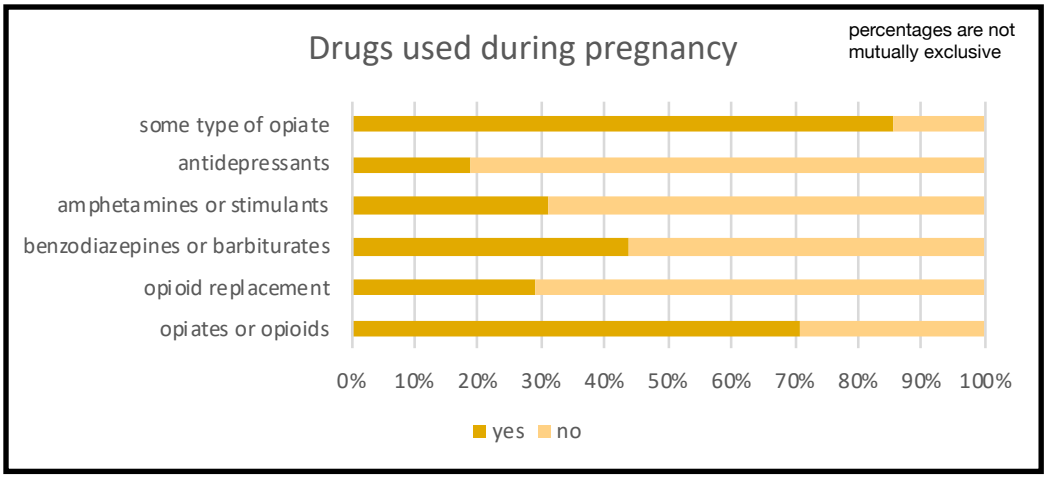
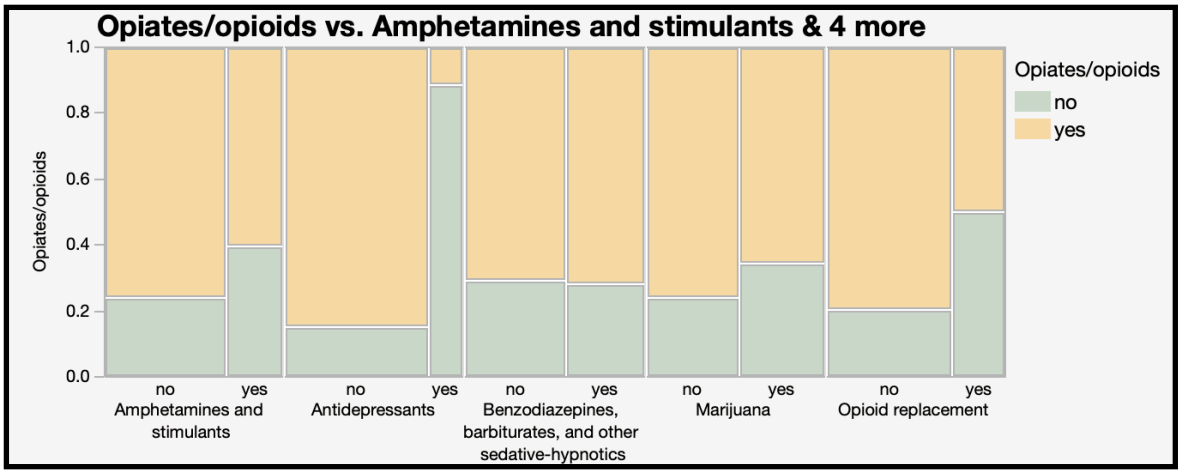


Figure 1. Antepartum drugs used by mothers of patients in the study.

barbiturates, sedative-hypnotics, anxiolytics, amphetamines, or stimulants. Though tobacco does not cause Neonatal Abstinence Syndrome, it mediates increased NAS peak scores, and impacts the timing of the course of NAS, when used in conjunction with methadone.[19] Roughly 91 percent of mothers of babies in this study used tobacco or nicotine patches regularly. Forty seven percent used marijuana during pregnancy. Studies have shown mixed outcomes of gestational marijuana exposure, with no certain fetal abnormalities; some long-term behavioral and emotional outcomes have been described, but no major withdrawal symptoms have been observed.[20]

From this data, we also found that opioid replacement medication use was not the strongest predictor of whether moms used other opiates/opioids. Antidepressant use was most highly correlated with no maternal opiate use. Of the nine women using antepartum antidepressants, only one used opiates/opioids; this woman did not use opiate replacement medication. Twenty seven of the women in the study used opiates or opioid medications with no opiate replacement treatment. Fourteen of the mothers used antepartum opiate replacement medications, half of whom used in conjunction with opiate/opioid drugs. Figures 2 and 3 show proportions of antepartum drug use compared with use of narcotic pain relievers.



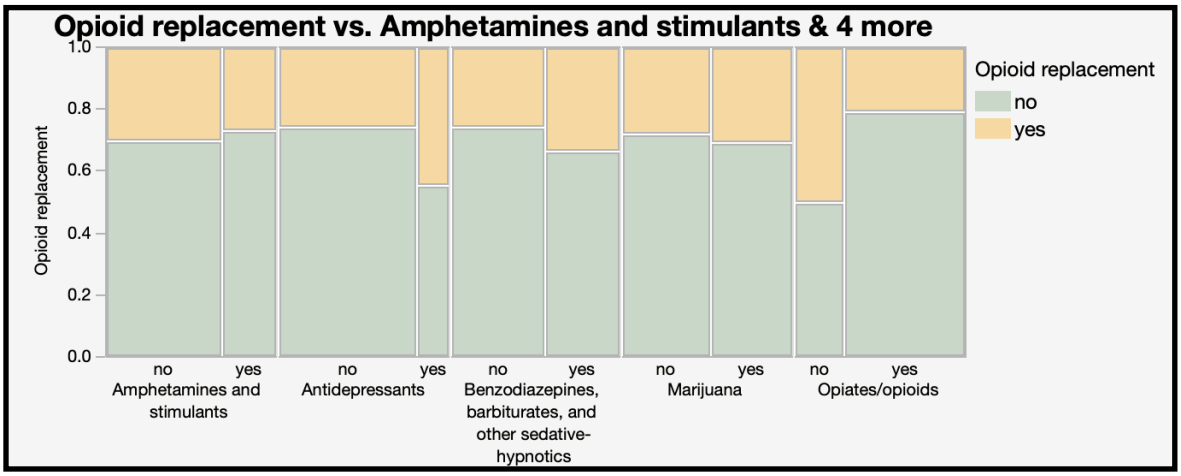


Figure 2 (top). Antepartum drugs vs opiates/opioid use.

Figure 3 (bottom). Antepartum drugs vs opioid replacement use.

Walking Age

Distribution of the age that patients began walking independently shown in Figure 4*; *Drug-Exposed Premature* (left), *NAS* (right.) Tables 3 and 4 show summaries of *Drug-Exposed Premature* and *NAS* data, respectively.

* Outliers removed

Figure 4. Distribution of walking age (months). *Drug-Exposed Premature* shown left. *NAS* shown right.

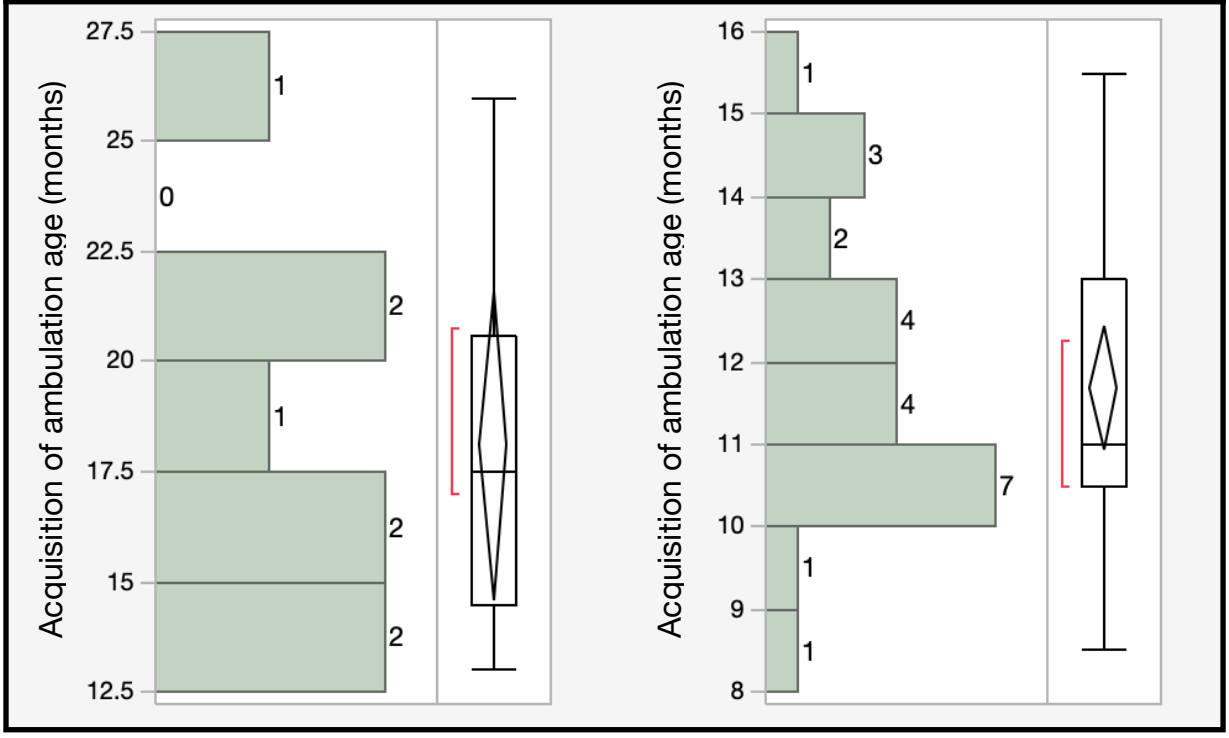


Table 3. *Drug-Exposed Premature* walking age (months) [*n*=8]
Mean = 18.1 ± 4.2 (SE=1.5) 95% Mean CI [14.6, 21.6] 95% SD CI [2.8, 8.5]
Median = 17.5 (IQR=6)

Table 4. *NAS* walking age (months) [*n*=23]
Mean = 11.7 ± 1.7 (SE=0.3) 95% Mean CI [11, 12.4] 95% SD CI [1.3, 2.4]
Median = 11 (IQR=2.5)

Drug-Exposed Premature

For *Drug-Exposed Premature*, [n=8] the mean walking age is 18.1 months ± 4.2. The median walking age is 17.5 months, with lower and upper quartiles being 14.5 and 20.5. One major outlier (x=54) was excluded from the *Drug-Exposed Premature* data. After the removal of the 54 months outlier, another data point (x=26 months) became a minor outlier. For consistency's sake, and because of the extremely small sample size, this outlier was left included in the set for analysis. When removed, however, the average walking age [n=8] becomes 16.96

months ± 2.89. The age at which these patients acquired independent ambulation exceeds the age for typical children but this can be attributed to compounded adverse conditions of birth and development. No developmental studies exist to which we can compare these patients. All but one of these patients received extra therapies (physical therapy, occupational therapy, orthotic devices) beyond the cross-stroking exercises and at-home exercises assigned by Dr. Weinstein.

NAS

The mean walking age of *NAS* patients [*n*=23] is 11.7 months ± 1.72, 95% Mean CI [10.95, 12.44]. The median walking age for *NAS* is 11 months, with the lower and upper quartile values being 10.5 and 13 months, respectively. We determined definitive walking ages for 25 patients but for this data set, two outliers were excluded, 18.5 months and 23.5 months. Before the data point with the value 23.5 was removed, the 18.5 month data point was only a minor outlier; after removal of 23.5 however, 18.5 months became a major outlier as well, so it was also removed. Receiving other therapies did not affect the age at which infants acquired independent ambulation (Table 5). Neonates discharged to their mothers showed greater compliance compared to those discharged to other family members or foster families.* Other patients less frequently had exact walking ages recorded in their charts, which indicate that they missed appointments more frequently or had large gaps in treatment during critical periods of development. Of the

Table 5. Walking ages — *NAS*	
Received other therapy treatments* [*n*=9]	Mean walking age (months) = 11.6875 SD = 1.41, SE=0.5 95% Mean CI [10.51, 12.86]
Did not receive other therapy treatments* [*n*=14]	Mean walking age (months) = 11.7 SD=1.91, SE=0.49 95% Mean CI [10.64, 12.76]
***PT, OT, orthotic devices**	

* This includes patients discharged to mothers under the supervision of other family members

twenty-three patients included in the walking data, fourteen patients were discharged from the NICU to their mothers, grandparents, or other family (occasionally through foster care.) Nine *NAS* patients were placed in foster care with non-family members upon discharge. These nine patients began independently walking slightly later, at 12 ± 1.3 months, than their family-placed counterparts who walked at 11.2 ± 1.6 months.

Length of Stay (LOS)

Drug-Exposed Premature

The average LOS for our *Drug-Exposed Premature* patients is 99.3 ± 40.2 days, 95% Mean CI [72.3, 126.3]. The median LOS is 100 days with the IQR parameters being 70 and 123. Length of stay for *Drug-Exposed Premature* patients was not correlated with birth weight. Drug-exposed premature Apgar scores for 1- and 5-minutes averaged 4 ± 2, and 6.5 ± 1.5, respectively. Figure 5 shows the LOS distribution and Table 6 shows corresponding summary statistics.

Figure 5. Length of stay (days) for *Drug-Exposed Premature*.

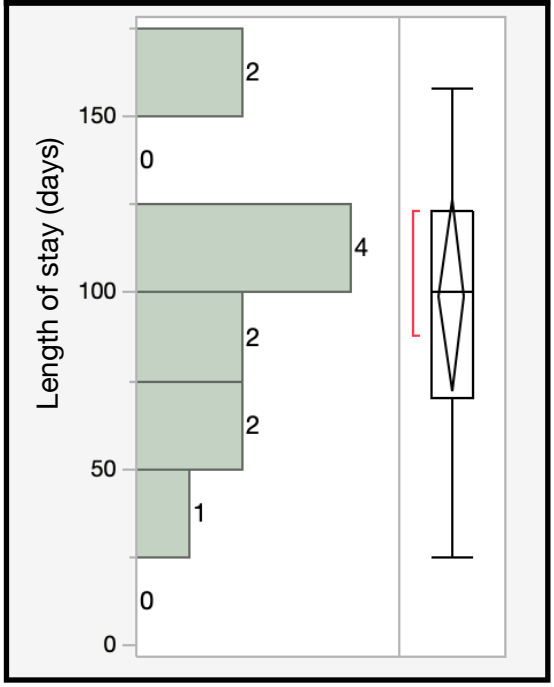


Table 6. Length of Stay (Days) for *Drug-Exposed Premature* [*n*=11]

Mean = 99.3 ± 40.2 (SE=12.1) 95% Mean CI [72.3, 126.3] 95% SD CI [28.1, 70.5]
Median = 100 (IQR=53)

Figure 6. Length of stay (days) of all *NAS* patients.

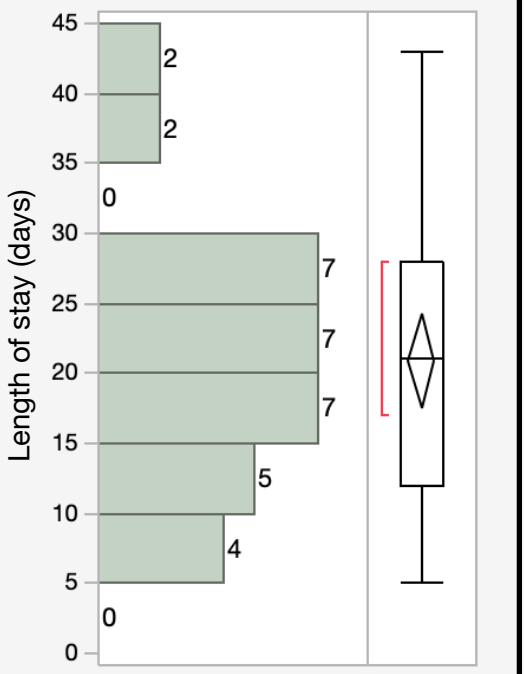


Figure 7. LOS of *NAS* patients diagnosed as NAS in the NICU.

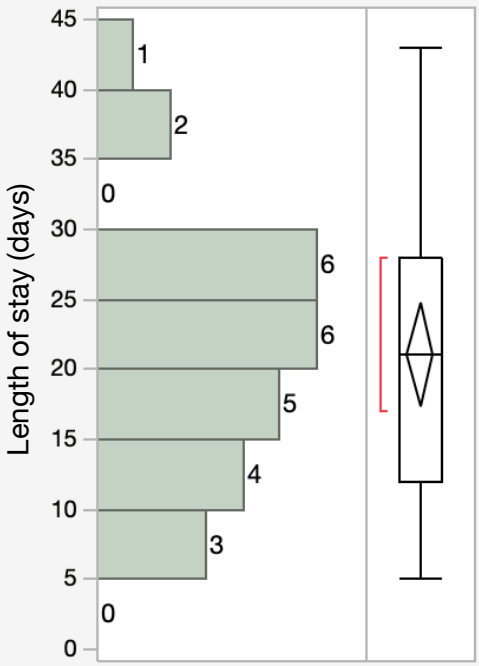


Table 7. Length of Stay (Days) of all *NAS* patients [*n*=34]
Mean = 20.9 ± 9.7 (SE=1.7) 95% Mean CI [17.5, 24.3] 95% SD CI [7.8, 12.8]
Median = 21 (IQR=16)

Table 8. Length of Stay (Days) of all *NAS* patients diagnosed NAS [*n*=27]
Mean = 21 ± 9.4 (SE=1.8) 95% Mean CI [17.3, 24.7] 95% SD CI [7.4, 12.8]
Median = 21 (IQR=16)

NAS

Data was only available for 34 of the 36 *NAS* patients due to NICU summaries missing in two of the charts. Distribution shown in Figure 6, and summary statistics in Table 7**.** Neonates stayed in the NICU, on average, for 20.9 days ± 9.4. The median LOS was 21 days, with the upper and lower interquartile values being 12 and 28 days, respectively. Birth weight did not significantly influence LOS; LBW neonates and non-LBW neonates average length of stays were 20.6 and 21.2, respectively. Twenty-nine of the patients in this category were diagnosed as

"NAS." Only one patient who was diagnosed as NAS did not receive pharmacologic treatment; this patient stayed in the NICU for only 5 days - the shortest length of stay of all patients in the study.* Seven of the thirty six patients in the *NAS* category were not diagnosed NAS in the NICU, but were diagnosed with "in-utero poly substance exposure" and included in the study. Figure 7 shows distribution of the patients in the study who did receive NAS diagnosis; summary statistics shown in Table 8**.** These patients' average length of stay was 21 days ± 9.7. The length of stay for patients who did receive NAS diagnosis was not significantly different than from the whole of patients in the category. For patients that did not receive NAS diagnosis, the average LOS was 20.6 days ± 11.7. There was only one patient who did receive NAS diagnosis that did not receive pharmacological treatment. Creating a sample of all patients who were diagnosed as NAS and received pharmacologic treatment involves removal of only a single data point, and thus, had negligible impact on the LOS.

Discussion

The *Drug-Exposed Premature* category is a very small sample size of all drug-exposed premature neonates. These statistics should be interpreted as insights into the condition of drug exposed neonates, rather than statistics that are descriptive of all drug-exposed neonates. The differences between drug-exposed premature patients and non-drug-exposed premature patients highlights the need for continued research of this patient population.

* The two patients whose NICU summaries I could not find (thus, LOS = unknown) were both diagnosed NAS

Drug use

Because the sample size is extremely small, further studies should assess the validity of the claim that antidepressant use is correlated with less opiate use.* Another possible explanation for this correlation is that a therapeutic regimen for depression may indicate better access to medical professionals, and these women are more likely to be using replacement therapy than illicitly using drugs. Additional evidence supporting this possibility is that women who took antidepressants while pregnant were much more likely to use benzodiazepines - indicating they potentially received psychiatric treatment. Lapses in documentation of the medication/drug sources pose limitations to this study; it is possible that women using opiate replacement medications obtained them illicitly, used them unmonitored by providers, or abused them by using them at unprescribed frequencies or dosages. Meanwhile, some women claimed they used prescription pain relievers, but prescriptions were not always confirmed.

Walking Age

Drug-Exposed Premature

All but one of the patients in our study received other therapies, including physical therapy, occupational therapy, and orthotic devices. Even after receiving these therapies and the cross-stroking exercises, these patients began walking independently at around 18 months. When for controlling for gestational age, studies have shown that premature infants attain independent ambulation at a later age than term infants. Our patients independently walked later than other premature infants. *Drug-Exposed Premature* patients walked much later (M=18.1 months, SD=4.2) than the non-premature *NAS* patients (M=11.7, SD=1.72.) The Apgar scores for our

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* *n(women who used antidepressants)* = 9

patients (1-Minute *M*=4.2, 5-Minute *M*=6.6) averaged about two points lower than Apgar scores for other premature patients.[21] These lower Apgar scores support the theory that effects of prematurity and drug-exposure likely compound to result in greater adverse outcomes.

NAS

The *NAS* group's walking age (*M*=11.7 months, *SD*=1.72.) is typical for children, with documented average age being around 12 months.[22] Limited research exists on NAS' long-term developmental impact, but data from this study shows these babies reach the "walking independently" motor milestone slightly before the average. These "slightly before the average" ages can most likely be attributed to a smaller sample size, as well as the fact that these children received the cross-stroking therapy both in the NICU and at home, as well as at-home exercise plans Dr. Weinstein gave. The thirteen patients* discharged from the NICU to family members (including mothers) walked earlier (*M*=11.2 months, *SD*=1.6) than the nine patients placed with non-family foster care (*M*=12 months, *SD*=1.3). This difference is small, but likely attributed to family members being more familiar with the condition of the patient and exercise plans than foster parents. Patients discharged to non-familial foster care had more gaps in treatment than those discharged to family. Foster parents were instructed on the exercises before discharge but family who spent more time in the NICU with the patients likely performed the exercises more frequently and were more familiar with them post-discharge.

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* NICU discharged fourteen patients with family, but one outlier (15.5 months) was excluded from this data set

Length of Stay

Drug-Exposed Premature

The length of stay in the *Drug-Exposed Premature* category did not shorten; in fact, the length of stay for these patients was longer than the average premature neonates' stay. One study of thousands of newborns' NICU stays found the neonates born at 28 weeks' gestation resided in the NICU for 66 days on average; for 30 weeks the stay averaged 48 days.[23] There is very little data on NAS and prematurity but our data suggests that drug exposure necessitates a much longer stay than for non-exposed premature neonates. Because the Finnegan scoring system is symptom-based, many drug-exposed premature neonates may not qualify for an NAS diagnosis, and thus elude NAS care. This lapse in treatment could explain longer NICU stays for these patients. Though limited (N=12), this data indicates a need for greater research on the impact of in-utero drug exposure in the context of prematurity.

NAS

The similar lengths of stay between NAS and non-NAS neonates justifies the inclusion of these neonates who were drug-exposed but not formally diagnosed as NAS in the study. Non-NAS neonates in the *NAS* category stayed in the NICU an inappreciably less length of time; one that is not statistically significant. This suggests a discrepancy in diagnoses rather than actual conditions of the infant, likely caused by providers coding diagnoses differently and non-uniform Finnegan scoring usage. This inclusion does not, however, extend to all drug-exposed neonates. Including these patients shows disparities in diagnosis and treatment of NAS. Rather than assert drug exposure warrants NAS diagnosis, this data demonstrates the possibility that not all

neonates are evaluated in the same fashion. Of course there are always exceptional cases; the one patient who was diagnosed NAS and did not receive pharmacologic treatment was sent home after just 5 days.

Proprioceptive cross-stroking points to decreased length of stay for babies with NAS cases that warranted NICU stay. Though we have not explored what symptomology has been specifically impacted by proprioceptio, we have identified proprioception's role in two of the three main foci of NAS pathology, the CNS and respiratory disturbances. Both hospitals and families have a vested interested in reducing length of stay; longer length of stay places both under financial strain, and also results in psychosocial strain on families and patients. One 2003 study found the average length of stay for NAS neonates to be 30 days.[24] Another study comparing pharmacologic treatments found the average length of stay of neonates treated with the most effective pharmacologic combination in the study to be 38 days.[25] Before a years-long NICU LOS reduction effort by a multidisciplinary task-force in Ohio, the NICU LOS in the hospital system for NAS neonates averaged 36 days.[26] A study comparing LOS associated with treatment by methadone and an oral morphine preparation found the average length of stays to be 40 and 36 days, respectively.[27]

Why the shorter length of stay?

The shorter LOS seen in *NAS* patients who received cross-stroking exercises could be attributed to the plasticity in the young neonate brain; providers and caregivers can utilize this plasticity to regulate CNS functioning in vulnerable neonates. Neonates, just as adults,

experience increased pain sensitivity and an exaggerated pain response during opiate withdrawal. The CNS processes afferent input received from proprioceptors.[28]

Interventions can reduce pain directly "by blocking nociceptive transduction or transmission or by activation of descending inhibitory pathways…" Opioids are the staple for pharmacotherapy for direct pain management in neonates, but these drugs can have adverse developmental effects.[29,30] Indirect non-pharmacological means of reducing pain in neonates include environmental measures, breastfeeding, and skin-to-skin contact.[31]

One animal study of acute opiate withdrawal shows evidence of neonatal rats experiencing allodynia* and hyperalgesia in this context.[32] In neonates, this confusion in afferent input is in part due to the plasticity of the brain. Peripheral proprioceptive neurons converge onto central nociceptive neurons in the dorsal horn, where they have the opportunity to activate nociceptors. In adults with normal afferent activity, and with no nerve or tissue damage, the synaptic locales of the neurons is inconsequential. Neural plasticity, however, can sensitize nociceptors to the proprioceptors' activity, which causes the neonate to perceive normal proprioceptive input as painful. Just as pain can be "learned" through neural plasticity, it can be unlearned through regular afferent input.[33,34] The early postnatal stage is critical for neural plasticity, specifically, dorsal horn plasticity.[35] Proprioceptive cross-stroking provides consistent peripheral afferent input that can mediate the fine-tuning of these connections in the dorsal horn.[36,37] In the short-term, could aid the neonate in self-regulatory soothing. In the long-term, this could help correct the maturation process of afferent input innervation. Proprioceptive input

* Allodynia is a conditioned in which a normal, non-painful stimulus, such as clothes touching the skin, causes an abnormal or painful sensation)

reduces length of stay by promoting CNS development and fine-tuning the CNS response to allodynia secondary to drug-withdrawal.[38]

Repetitive pain exposure can cause permanent changes to the immature pain system of the neonate.[39] Early repetitive pain exposure contributes to altered pain thresholds and physiological responses, as well as adverse neurodevelopmental outcomes.[40-42] All potential ways to reduce the risk of these unfavorable outcomes should be evaluated.

Drug-exposed neonates often have signs of respiratory disturbances including increased respiratory rate, transient tachypnea, chest retractions, and nasal flaring. NAS patients frequently require cardiopulmonary assistance such as supplemental oxygen, ventilation, and intubation.[43] One study has shown that proprioceptive limb stimulation in premature neonates has reduced the number of breathing pauses and intermittent hypoxia. Proprioceptive interventions can increase breathing and synchronize breathing patterns with limb movement. Neuromodulation of proprioceptive afferents offers a non-invasive and low-cost method to reduce aberrant breathing episodes; these interventions promote neural and pulmonary development, rather than reliance on mechanical and pharmacologic agents, which pose risks to the development of these structures.[44]

Limitations and further research

Many length of stay studies disproportionately exclude many of the patients that inevitably have longer NICU stays. Some studies show NAS neonates with a shorter average NICU stay than our patients. A quarter of the NICU sites in paper that published results from a years-long task force were Level II NICUs; this study also excluded patients born <35 weeks' gestation.[45] UTMC's Level III NICU is equipped to handle more severe NAS cases; neonatal

teams at other hospitals in the area care for drug-dependent neonates who do not have severe enough symptoms to warrant NICU admission.[49] Another study with a shorter LOS than our paper excluded "not otherwise well newborns" and those born less than 35 weeks' gestation. It also included NAS patients who were placed in the pediatric unit; thus, it included many patients who exhibited less severe NAS cases.[46] The newborns in our study all resided in the NICU before the hospital created major initiatives to optimize the NICU environment for these babies. Other studies with similar shorter lengths of stay have excluded with mothers who engage in poly-drug uses.[47,48] Nearly all of the mothers in our study used multiple drugs during pregnancy so these factors could not be isolated in our patients. Across both categories, only 23 percent (seven) of our patients exposed to narcotic pain relievers were exposed to only opiate replacement medications; and of these seven patients, six were exposed to at least one of the other drugs listed in Table 1. Additionally, over 90 percent of the mothers in our study consistently used tobacco, which is known to prolong and increase NAS symptoms.[50] Patients born at less than 35 weeks' gestation comprised roughly 20 percent of our *NAS* patients. Unlike large and expensive multidisciplinary initiatives to reduce length of stay, our NICU implemented simple and free exercises in addition to the pharmacologic treatment which resulted in an average LOS of 21 days.

Some papers have shown increases in length of stay as the opioid epidemic unfolds in the United States.[51] Being in the foothills of Appalachia, the opioid epidemic's presence here outdates, and prevalence here exceeds other regions. In addition to types of drugs used, we believe geography may have a role in the length of stay in our patients as well.[52]

Based on this preliminary study, future research will focus on length of stay for NAS patients. In order to maximize the studies to which we can compare our data, we hope to control for factors, such as co-occurring drug use, prematurity, and severity as previously mentioned papers have done. We recognize the impact post-discharge placement has on length of stay as well, and plan to control for babies who were not discharged as soon as they were ready to leave.* The study's small sample size limits the extent to which we can examine differences between groups including post-discharge placement circumstances, type of drug exposure, pharmacologic treatment received and length of pharmacologic treatment, and more. Additional literature regarding nicotine from cigarettes and methadone maintenance therapy (and perhaps, all opiates) should be reviewed for the next study because our patients reported tobacco use at much higher rates than other studies. This was shown to increase peak NAS scores and alter the time course of NAS, which was not considered during data analysis. Because this preliminary study excluded all patients who did not stay in Dr. Weinstein's practice for at least one year or until the patient began walking (whichever occurred earliest), a future study of all NAS patients' NICU length of stays will include many more patients. The concept of proprioception's possible role in mediating respiration was previously only considered after data collection. We plan to examine the impact of proprioception on respiratory function and assistance in the NICU more closely than this study. Reduction in length of stay decreases the social and psychological strain on families and their babies; as well as the financial strain on hospitals and patients. Reduced length of stay could also indicate decreased pain exposure; pain exposure is associated with

* One study mentions that some patients spent 1-2 extra days in the NICU while DCS or foster care coordinated placement - something we did not consider

worse developmental outcomes. While still preliminary research, this paper shows promising future research directions in neonatology and PM&R.

Main ideas
• Proprioceptive cross stroking is a free developmental intervention that can be employed by anyone.
• Unlike mechanical and pharmacologic treatments that can have adverse neurodevelopmental outcomes and pulmonary development, CS exercises promote self-regulatory soothing and long-term development which can reduce hospital length of stay.
• Future research: possible role of antidepressants in reduced opiate/opioid use
• Proprioceptive input can fine-tunes plastic neural connections in the early postnatal stage to reduce pain.
• Proprioceptive input may contribute to increased pulmonary function.
• Drug-exposed premature neonates' NICU stay far exceeds the average premature neonates' stay, which displays the need for further research in this patient population and improved NAS diagnostic tools for premature drug-exposed neonates.
• Type of drug exposure can have very different impacts on NAS pathology, course, and timing. This should be considered when assessing NICU stay, NICU events and associated treatments, and proprioceptive input's specific role in these patients' development.
• Drug-Exposed Premature infants begin walking at a later age than their normal premature counterparts, indicating a possible compounding effect of adverse developmental conditions.

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