Ann Ist Super Sanità 2020 | Vol. 56, No. 3: 390-396
DOI: 10.4415/ANN_20_03_18

BRIEF NOTE

Neurophysiological monitoring in neonatal abstinence syndrome from cocaine

Raffaele Falsaperla[1], Simona Zaami[2], Maria Giovanna Aguglia[1], Catia Romano[3], Agnese Suppiej[4] and Luigi Memo[1]

[1]*UOC Neonatologia e Terapia Intensiva, PO San Marco Azienda O-U Policlinico Vittorio Emanuele, Catania, Italy*
[2]*Dipartimento di Scienze Anatomiche, Istologiche, Medico-Legali e dell'Apparato Locomotore, Sapienza Università di Roma, Rome, Italy*
[3]*Sezione di Neuropsichiatria dell'Infanzia e Adolescenza, Dipartimento di Medicina Clinica e sperimentale, Università degli Studi di Catania, Catania, Italy*
[4]*Dipartimento di Scienze Mediche, Sezione di Pediatria, Università degli Studi di Ferrara, Ferrara, Italy*

Abstract

Introduction. Neonatal abstinence syndrome (NAS) in a newborn is a result of the sudden discontinuation of exposure to psychotropic drugs abused by the mother during pregnancy. Since forty decades, the standardized Finnegan Neonatal Abstinence Scoring Tool (FNAST) documents the infant withdrawal, and initiate the appropriate treatment regimen, when elevated scored are reported. Whereas FNAST is successfully applied for opioids NAS, in case of other psychotropic drugs and especially cocaine, the tool is not always efficacious or predictive.

Methods. Continuous v-Electroencephalography (vEEG) provides particularly useful information about brain cortical functioning and evaluation of background activity in normal newborns. vEEG allows to properly study and identify clinical manifestations as physiological motor paroxysms, that disappear from birth to infant age in correlation with the neurological development. Due to its feature to be a non-invasive tool continuous vEEG monitoring could be used to describe some clinical manifestations and assess if they can be correlated to possible injuries in critical neonates as those exposed in utero to psychoactive drugs presenting NAS.

Results. An example for the potential use of such methodology is discussed in a case of NAS due to prenatal exposure to cocaine as a complementary tool for the evaluation of behavioural state and clinical and neurological signs in newborns in utero exposed to psychoactive drugs, excluding epileptic phenomena.

Discussion. Video-EEG recording could be considered an important and objective tool that allows the evaluation of behavioural state and clinical and neurological signs in newborns in utero exposed to psychoactive drugs and the neurophysiological definition of signs and symptoms, which cannot be evaluated by FNAST such as startles and its variability during subsequent days after birth, subclinical seizures or brain injuries.

Key words

- intrauterine exposure to cocaine
- neonatal abstinence syndrome
- video-EEG

INTRODUCTION

Prenatal exposure to drugs abuse during pregnancy is a worldwide rising phenomenon with a great variability among different countries. In 2017, the American National Survey on Drug Use and Health (NSDUH) estimated that 194 thousand pregnant women had been used illicit drugs during pregnancy and in particular cocaine and methamphetamine in the previous year [1]. Similarly, in Europe, it is estimated that there may be as many as 30 000 pregnant women using opioids each year and the number of pregnant women using drugs other than opioids may be equally high [2]. More precisely, a significantly non negligible rate of illicit drug abuse and prescription psychoactive drugs consumption has been reported in cohorts of Spanish (3.9%), Danish (3.6%), and Italian (0.4%) pregnant women [3, 4].

Address for correspondence: Simona Zaami, Dipartimento di Scienze Anatomiche, Istologiche, Medico-Legali e dell'Apparato Locomotore, Sapienza Università di Roma, Viale Regina Elena 366, 00161 Italy. E-mail: simona.zaami@uniroma1.it.

Since gestational psychotropic drug consumption can be a serious hazard to the fetus, a careful monitoring of drug use during pregnancy is crucial to assess and eventually prevent prenatal exposure and provide high quality obstetrical health care. Drug consumption screening is essential to achieve identification of pregnant abusers and the most used screening method is the use of questionnaires. However, the use of standardized questionnaires presents some drawbacks, especially in pregnancy period. Pregnant women may underestimate their consumption and/or are unwilling to disclose their habits during pregnancy due to fear of legal repercussions, guilt, memory biases. All these reasons, demonstrated in several studies often render questionnaires unreliable to predict fetal drug exposure [5].

The use of biomarkers in maternal and fetal matrices (e.g. drugs and/or metabolites detection in maternal blood, urine, neonatal hair, meconium and breast milk) and clinical assessment by instrumental tools are fundamental to objectively assess gestational drug abuse and consequent prenatal exposure to them. Thus, biomarkers measurement and instrumental tools use should always complement questionnaires, as it has been shown that self-report may underestimate prenatal consumption of substances of abuse [6-8].

It has to be said that the valuable assessment of in utero exposure to drugs of abuse can prevent its hazardous consequences such as premature rupture of membranes, placental abruption, preterm birth, low birthweight, small-for-gestational age, and admission to the neonatal intensive care unit. Prenatal exposure to drugs abuse may also result in neurodevelopmental problems as impairments of the growth and development of the brain and/or central nervous system and finally neonatal abstinences syndromes with related neurological and physiological consequences [9].

Neonatal abstinence syndrome (NAS) in a newborn is a result of the sudden discontinuation of fetal exposure to substances that have been used or abused by the mother during pregnancy [10].

NAS has been described as a complex disorder that primarily involves central nervous system, autonomic nervous systems and gastrointestinal system [11]. Clinical signs typically develop within the first few days after birth, although the timing of their onset, as well as their severity, can vary as a function of the drug abused by the pregnant woman [10]. In particular, NAS have been most frequently reported in case of maternal use of opioids and cocaine [11, 12].

The standardized Finnegan Neonatal Abstinence Scoring Tool (FNAST), ideated in 1975 by Loretta Finnegan and subsequently modified, is used identify the withdrawal symptoms, document the infant's withdrawal, and initiate the appropriate treatment regimen, when elevated scored are reported [13, 14]. Although this scoring system has been extensively used for all the psychoactive drugs, Finnegan test was validated only for NAS from opiates and up to now there are no validation studies for other drugs of abuse such as cocaine. For this reason, the investigation of cocaine and metabolites in maternal and neonatal biological matrices and specific instrumental and clinical tests on the newborn can improve an eventual diagnosis of cocaine NAS. In this regard, it has to be said that, differently from what happens with opioids, cocaine NAS presents a late onset and cannot be immediately recognized and treated [5].

In FNAST an important clinical sign to evaluate is the motor paroxysmal that vary to tremor from seizures. In this concern, electroencephalography (EEG) was firstly used in 1988 to examine neurologic and electroencephalographic abnormalities in newborns prenatally exposed to cocaine [15]. Indeed, the EEG monitoring in neonates is actually the unique diagnostic tool to well characterize the motor phenomenon differentiating the onset of startles from seizures and behavioural states anomalies.

Recently, Italian media highlighted several cases of neonates presenting cocaine NAS in different cities [16, 17], evidencing an epidemics of fetal exposure to cocaine in the national territory, already evidenced in several other western countries [1, 18-20].

In this concern, local health professionals involved in these upcoming cases may require updated information and tools for differential diagnosis.

Continuous video-electroencephalography (vEEG) provides particularly useful information about brain cortical functioning and evaluation of background activity in normal newborns, allowing to properly study and identify clinical manifestations as physiological motor paroxysms, that disappear from birth to infant age in correlation with the neurological development [21]. Continuous vEEG is also a useful tool in the intensive care unit to define neurologic status and brain functioning in critically ill neonates at high risk for adverse neurologic injuries as hypoxic ischaemic encephalopathy, cerebral infections, to diagnose electroencephalographic seizures and monitoring the responsiveness to anticonvulsivant treatment. Due to its feature to be a non- invasive tool, continuous vEEG monitoring could be used to describe some clinical manifestations and assess if they can be correlated to possible injuries in critical neonates as those exposed in utero to psychoactive drugs, such as cocaine, studying modified behavioural state and clinical neurological signs that onset in case of neonatal cocaine abstinence syndrome in newborns, with the aim to exclude onset of epileptic phenomena and seizures in these babies. Neurological signs as tremors and numerous startles, constant irritability and anomalies in behavioural states and sleep and wake cycle characterize the onset of neonatal abstinence syndrome during subsequent days after birth.

Fetal exposure to cocaine can be the cause, among other signs, the onset of neurological signs as tremors, startles and irritability after birth. Tremors are motor symptoms with muscular but not electroclinical correlate in vEEG monitoring. They could be very frequent during days after birth and have many extra cerebral causes.

Startles are physiological motor manifestations that can be defined as "brainstem reflex originated in the bulbopontine reticular formation that gradually undergoes the inhibitory control of the corticospinal motor pathway"; we can consider as a basic alerting reaction in response to stress stimuli [22]. In NAS, tremors, irritability and startles represent the excessive alerting reac-

tion due to the effect of exposure to psycoactive drugs. However, these neurological manifestations could hide electroclinical seizure as brain injuries and need adequate treatments. Clinically, it is not possible to differentiate electroclinical manifestations from motor signs. Video-EEG allows neurophysiological definition excluding an abnormal seizure pattern and to quantify the anomalies in behavioural states and sleep and wake cycle related to alerting reaction that characterize the onset of neonatal abstinence syndrome. The rapid and continuous transition from quiet sleep to active sleep and wake can be define and objectively quantify with neurophysiological study.

We here describe, just as an example, the case of a neonate with prenatal exposure to cocaine monitored by polygraphy/vEEG from the onset of neonatal abstinence syndrome to the time of hospital discharge and sought to correlate the obtained observations with the clinical signs evaluated with FNAST.

METHODS

Continuous vEEG monitoring allows to record electrical signals of cortical cells, providing particularly useful information about electrical brain function. Cortical electrical activity is defined background activity and it is related to EEG patterns typical for gestational age and behavioural state of newborns. Through vEEG normal or abnormal electrical patterns changes that characterize the background activity in healthy or critical newborns can be identified. Indeed, vEEG monitoring

Table 1
Comparative report of video-electroencephalography findings, Finnegan Neonatal Abstinence Scoring Tool and clinical manifestations

Timing	Finnegan Score	Finnegan signs and symptoms	EEG correlate to FCS	EEG no correlate to FCS	AS/QS
At birth	0	- no symptoms or signs			
At 1 hour	5	- spontaneous mild tremors - high pitched cry			
At 4 hours	0				
At 8 hours	0				
At 12 hours	3	- spontaneous mild tremors			
At 16 hours	0				
At 20 hours	2	- difficult feeding			
At 24 hours	6	- spontaneous mild tremors, - high pitched cry - excoriation			
At 48 hours	15	- sweeting - spontaneous mild tremors - polipnoic breath (FR > 60 b/min) - sleep < 2 hours after feeding - high pitched cry - hyperactive Moro reflex - excessive sucking - sneezing, regurgitation - regurgitation	- EDG - tremors without cortical correlate - PMG (polipnoic breath) - no other correlate - suction artefacts	- startles (AS/QS) - hiccups - grimacing - tongue movements - chewing - frequent arousal	normal AS/QS
At 52 hours	5	- mild tremors disturbed - excoriation			
At 72 hours	14	- sweeting - mild tremors disturbed - excessive sucking - sleep < 1 hours after feeding - excessive suction - increased muscle tone high pitched cry - excoriation - frequent yawning	- EDG - motor artefacts without cortical activity - suction artefacts	- startles (QS/AS) - oral movements	normal AS/QS
At 76 hours	10	- sleep after feeding < 1 h - increased muscle tone - excoriation - regurgitation			
At 80 hours	4	- excoriation - regurgitation - sleep after 3 h feeding			
Two weeks after birth	1	- sleep after 3 h feeding	- no motor artefacts	- reduced - startles (QS/AS) - motor sucking artefact	normal AS/QS

with associated polysomnographic data (breath, muscle activity, heart rate, eyes movements) allows to define behavioural state, distinguishing sleep from awake and different phases of sleep (quiet or active) in relation to electrical patterns changes.

Through vEEG electrical function showing normal or abnormal graphoelements (or named neonatal EEG features), electrical seizures with or without clinical correlate, rhythmic or periodic patterns can be defined.

The newborn, born with surgical delivery at 37 weeks of PMA, with regular adaptation (Apgar index 9/10), weight 2870 g (50° centile), cranial circumference 33.5 cm (50° centile), length 48 cm (50° centile) has been admitted to Neonatal Intensive Care Unit (NICU) and placed in continuous cardiac and respiratory monitoring. FNAST has been acquired because of the referred maternal cocaine abuse during pregnancy. From the first hour of life, the baby begun to show tremors and marked irritability, jitteriness and difficult consolability, so that wrapping, close feeding and reduction of sensorial stimulation was performed.

Newborn was evaluated through clinical examination and FNAST from birth every 4 hours to the disappearance of symptoms and signs. Cardiac and respiratory monitoring with continuous pulse oximetry was also started. At 48 hours of life video-EEG with polygraphy, EMG, ECG study lasting 90 min was initiated and we have revaluated at 72 hours and after two weeks, according American Clinical Neurophysiology Society.

At 48 hours after birth FNAST confirmed the onset of abstinence syndrome because of tremors, sweating, excessive sucking. Toxicological urine test on the newborn at 48 hours from birth confirmed the presence of high levels of cocaine metabolite as resulting of chronic maternal intake during gestation. Unfortunately, this result cannot be confirmed in maternal biological matrices (mother hair or urine), since baby mother did not give consent to any toxicological tests and once interviewed, denied the use of cocaine or any other drug of abuse.

Video-EEG with polygraphy, electrocardiogram (ECG), electromyography (EMG) and associated cardiac and respiratory monitoring was started and acquired to define a complete sleep cycle, to study behavioural states and define motor paroxysmal excluding onset of subclinical seizures.

A comparative report of video-EEG findings, FNAST and clinical manifestations is shown in *Table 1*. The EEG tracing shows regular pattern characterized in active sleep (AS) by continuous low-medium voltage (25-50 mcV pp) mixed frequency activity, theta waves and slow delta activity in frontal and central regions, anterior dysrhythmia, frontal sharp transients and rolandic activity in central regions *(Figure 1a)*. The corresponding polygraphic pattern was characterized by irregular respiration and variable respiratory rate > 20 breaths/min, typical of AS, wakefulness and transition sleep. In quite sleep (QS), the background EEG activity was characterized by alternating activity, with slow delta waves (50-50 mcV pp) alternate with periods of lower voltage (25-50 mcV pp), lasting about 4-5 sec in frontal and central regions, theta activity in temporal regions, delta brushes in occipital regions *(Figure 1b)*. Polygraphic pattern showed regular respiratory pattern. Regular respiration typical of QS is characterized by a variability between the slowest and fastest breaths is less than 20 breaths/min. AS phase was about 62%, QS phase resulted about 34%, undetermined sleep phase was about 4%. And the first week after birth, sleep pattern resulted unchanged (AS 59% *vs* QS 32%).

At the onset of NAS, at 48 hours of life, we recorded in an half hour of EEG study at the onset of NAS (at 48 hours of life) in active sleep phase and mainly in quiet sleep 12 episodes of motor startles, some of them associated to grimacing, not correlated with cortical ictal activity, but with motor artifacts *(Figure 1c and 1d)*. Specifically, startles have been defined as physiological clinical motor manifestations in quiet sleep phase in healthy infant as "brainstem reflex that originates in the bulbopontine reticular formation and that gradually undergoes the inhibitory control of the corticospinal motor pathway"; and hence they could be considered a basic alerting reaction in response to stress stimuli [22]. We observed several episodes of startles *(Figure 1a* and *1c)* during first days after birth, respect following weeks from birth, with the continuous and sudden transition from quiet to active sleep (figure active and quiet sleep) that could define a sleep waking cycle disorder. These motor manifestations do not correlate to electroclinical abnormal pattern.

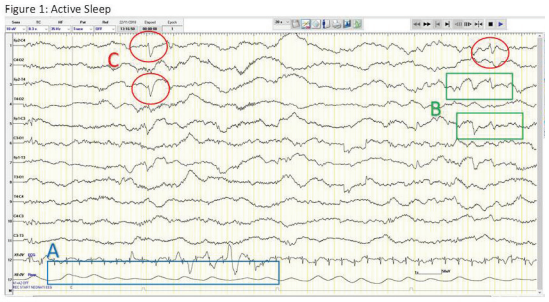
Tremors and irritability have not a pathologic electric correlate on cortical side; they are shown only as motor artefact caused by movements and associated with the onset of a regular rapid rhythm on electromyography. The lack of cortical parossistic manifestations can exclude seizures and then the need of anticonvulsant treatment.Moreover the frenetic suction, as described in Finnegan Score, is valuable in polygraphy/vEEG through the related electroclinical artefact. As demonstrated in *Figure 1e* suction reflex is shown as a motor artefact associated to the electrical manifestation due to repetitive tongue movements *(Figure 1e)*, without an electric correlate of seizures.

One week after, toxicological urine test and FNAST resulted negative. The newborn showed only difficulties in feeding, normal sucking reflex. Motor phenomena, previously defined as startles, disappeared. The vEEG recording in sleep and wakefulness was repeated and showed a background characterized by continuous low voltage activity with interbursts of < 2sec and voltage of 25 mcV in active sleep and alternating activity in quiet sleep phase. The background appeared to be compatible with the correct chronological age of the newborn and motor artefacts and electrodermogram described in previous EEG are decreased, sucking reflex was correlated with motor suction artefact *(Figure 1e)*.

DISCUSSION

NAS refers to the sequence of symptoms arising with the interruption of exposure to the substances of abuse taken by the mother during pregnancy. Initially valuated for abuse of opioids, the term has been extended to infants exposed to other drugs maternal abuse in prenatal age [11]. Finnegan scoring was introduced as "clinical" scoring systems to define neurological symp-

Figure 1: Active Sleep



A: Irregular respiration in pneumogram

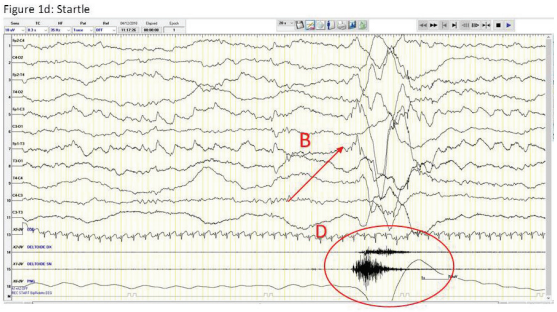
B: anterior dysrhythmia

C: Frontal sharp

Figure 1

Electroencephalography tracing in a cocaine neonatal abstinence syndrome. Nikon Kohden Neurofax EEG 1200 was used. EEG recording has been started with the application on scalp of 9 cerebral electrodes, according to International 10-20 System, modified for neonates. Extracerebral channels have been placed for analysis of polygraphic data. Electromyogram (EMG) has been recorded with electrode in right deltoid, respiration has been recorded through respiratory channel placed with sensor in the epigastric area. Electrocardiogram (ECG) has been recorded with sensor placed in left thorax side.
Active Sleep: behavioral state characterized in healthy term neonate because the closure of eyes, intermittent periods of rapid eye movements, irregular breath, small and large body movements. On vEEG by a continuous low to medium voltage (25-50 mcV peak-to-peak) mixed frequency activity with a predominance of theta and delta and overriding beta activity. This activity is indistinguishable from that of normal wakefulness.

Figure 1d: Startle



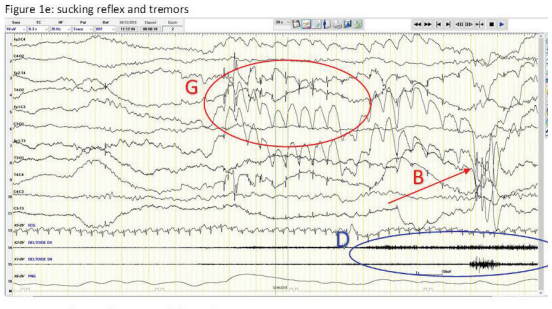
B: motor artifact in electroencephalography

D: motor paroxysm in electromiography

Figure 1d

Startle: Rapid sequence of movements: grimacing and blinking, flexion of neck, trunk, hips and knees, arms adduction and fists clenching, in response to unexpected stimuli [22].

Figure 1e: sucking reflex and tremors



B: motor artifact in electroencephalography

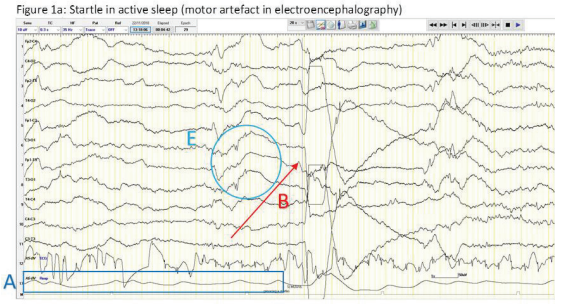
G Sucking artefact in anterior and central regions

D: Tremors and mild startle in electromiography

Figure 1e

Sucking reflex: automatic stereotypic oral and tongue movements caused by brainstem-mediated reflex; Tremor: an involuntary, rhythmic oscillatory movement of equal amplitude around a fixed axis. Jitteriness: recurrent tremors.

Figure 1a: Startle in active sleep (motor artefact in electroencephalography)



A: Irregular respiration in pneumogram

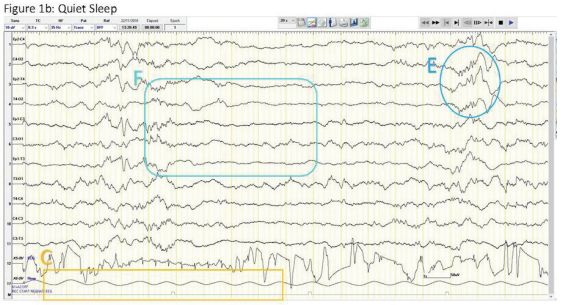
B: motor artefact in electroencephalography

E: delta brushes in occipital regions

Figure 1a

Startle in active sleep (motor artefact in electroencephalography).

Figure 1b: Quiet Sleep



C: regular respiration in pneumogram

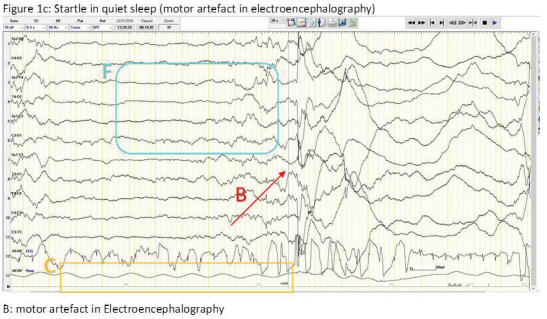
E: delta brushes in occipital region

F: alternating activity

Figure 1b

Quiet Sleep: clinically characterized by eye closure, absence of rapid eye movements, occasional sucking activity or generalized myoclonic "startles." EEG background, defined alternant, is characterized because of higher voltage bursts (50-150 mV pp), predominantly of delta activity and lasting roughly 4 to 10 seconds, alternate with briefer, lower voltage (25-50 mV pp) interburst periods composed mostly of mixed theta and delta activity.

Figure 1c: Startle in quiet sleep (motor artefact in electroencephalography)



B: motor artefact in Electroencephalography

C: regular respiration in pneumogram

F: alternating activity

Figure 1c

Startle in quiet sleep. startle has probably the meaning of a basic alerting reaction and appears during the quiet sleep phase; the EEG-trace shows motor artefact not associated to electric pathologic activity.

toms and signs and represents a rather subjective and variable evaluation method that depends on the infant's general conditions and usually correlates to course of NAS [13].

Several studies suggested that the development of the central nervous system could be affected by exposure to cocaine in prenatal period and correlate with long-term neurodevelopmental effects in this cohort of infants [15]. Already in 1985, Chasnoff *et al*., noted increased tremulousness, more startle responses and deficient interactive behavioural state organization in cocaine exposed infants evaluated with Brazelton Neonatal Behavioral Assessment [12].

The study of the background and neurophysiological patterns actually allows to define normal cerebral function in healthy infants. Numerous studies demonstrated the usefulness of EEG monitoring in cocaine exposed newborns for the characterization of neurophysiological anomalies and abnormal behavioural states. Indeed, in these infants, the reduced bioavailability of drug for increased placenta catabolism near term or exposure cessation after delivery could determine altered behavioral state in postnatal EEG [23]. EEG sleep patterns could be used to assess cerebral maturation and neurophysiologic organization of the developing CNS this cohort of neonates. Clinical seizures in first days from birth, unrelated to structural brain damage have been reported as an important complication in newborns exposed to cocaine. [23].

Moreover, neonates with suspected NAS due to in utero exposure to drugs show seizure-like clinical activity. The aim and the usefulness of FNAST is to describe the onset of SAN and define the severity of these overexpressed motor manifestations (myoclonus during sleep, tremors), physiological reflexes, seizure-like manifestation as jerking or rhythmic movement of extremities, apnoea, anomalies related to the involvement of autonomic and central nervous system with a clinical score.

However, excluding major neurological anomalies due to hypoxic ischemic encephalopathy, metabolic disorders that cause seizures, the electrical abnormal activity related to these manifestations can be excluded or define only with vEEG monitoring [24].

Video-EEG monitoring can be a valid tool for identification of seizures-like episodes that can appear in a baby exposed to drugs or to define activity as motor phenomena evaluated in FNAST. Video-EEG also allows to define motor manifestation that FNAST does not analyze, always with the aim to exclude onset of neonatal subclinical seizures or brain injuries in exposed cocaine newborns.

In fact, prenatal cocaine exposure is also associated with increased risk of neonatal seizures and anomalies in brain wave activity in newborns [25].

In agreement with this, early in 1990 Kramer *et al.*, observed that all the infants prenatally exposed to cocaine experienced seizures within 36 hr of delivery with 50% of these infants showing repetitive seizures during their neonatal hospitalization stay, but did not have recurrences during a follow-up period of 4 to 12 months. The other 50% continued to experience neonatal seizures after their initial month of life and a smaller subset continued even after 6 months of life, suggesting long-term neurodevelopmental effects of early cocaine exposure [26].

Even earlier, in 1988, Doberczak *et al*., focused on EEG patterns and evaluated that 90% of infants that prenatally exposed to cocaine displayed deficits in neurophysiological behaviour, such as increased CNS irritability, and over 50% had abnormal EEGs. These effects were transient for some of them, so that only 20% of infants displayed abnormal EEGs by the second week, while only one of neonates identified in this study displayed abnormal EEG patterns by 3 to 12 months of age. In particular EEG have shown multifocal anomalies, lateralized anomalies and an asymmetric background [15]. As a confirmation, in 2002 Scher *et al.*, reported that prenatal cocaine exposure affected reflexes, motor maturity and autonomic stability in the newborn, underlining the importance of electroencephalographic (EEG) sleep patterns that can be used to assess cerebral maturation and neurophysiologic organization of the developing CNS [27].

The transient neurological symptoms we have observed which decreased with the passing of the time and disappeared at the second week of life could be related to the manifestation of marked irritability and jitteriness due to altered catecholaminergic pathway associated to the toxic effect of cocaine in first days after birth, as also Mirochnick *et al*., have previously described [28].

In our case we also observed during active sleep phase other minor motor manifestations not described in FNAST as oral and tongue repetitive movements, grimacing, that correlate to motor artifacts in absence of cortical ictal activity. These motor phenomena are described as "the expression of brainstem release phenomena, correlated to immaturity of the inhibitory control" [18].

Sucking reflex that is valuated in FNAST, correlated in EEG recording with muscular activity of masseter in temporal leads and slowing waves in frontal derivations due to repetitive tongue movements as described. These motor automatic stereotypic and repetitive movements could hide misunderstood subtle seizures, underling the usefulness of vEEG analysis. Interpretation of neonatal EEG is still challenging and background activity is frequently intermixed with physiological artefacts, such as ocular, muscle and movement artifacts, as in NAS [27, 29].

In conclusion, whereas FNAST is essential to promptly define the clinical presentation of newborn exposure to drugs and the onset of NAS, vEEG recording could be considered an important and objective tool that allows the evaluation of behavioural state, clinical and neurological signs in newborns in utero exposed to psychoactive drugs, excluding epileptic phenomena and defining if exposure has determined EEG background disturbances, to establish also neurological outcome in these cohorts of neonates.

Disclosure

None declared

Conflict of interest statement
None declared

Received on 17 February 2020.
Accepted on 29 May 2020.

REFERENCES

1. Carlier J, La Maida N, Di Trana AG, Huestis MA, Pichini S, Busardò FP. Testing unconventional matrices to monitor for prenatal exposure to heroin, cocaine, amphetamines, synthetic cathinones, and synthetic opioids. Ther Drug Monit. 2020;42(2):205-21 doi: 10.1097/FTD.0000000000000719
2. Gyarmathy VA, Giraudon I, Hedrich D, Montanari L, Guarita B, Wiessing L. Drug use and pregnancy – challenges for public health. Eur Surveill. 2009;14(9):33-6.
3. Cortes L, Almeida L, Sabra S, Muniesa M, Busardo FP, Garcia-Algar O, Gomez-Roig MD. Maternal hair and neonatal meconium to assess gestational consumption and prenatal exposure to drugs of abuse and psychoactive drugs. Curr Pharm Biotechnol. 2018;19(2):136-43. doi: 10.2174/1389201019666180405163612
4. Rausgaard NL, Ibsen IO, Jørgensen JS, Lamont RF, Ravn P. Prevalence of substance abuse in pregnancy among Danish women. Acta Obstet Gynecol Scand. 2015; 94(2):215-219. doi: 10.1111/aogs.12528
5. Chiandetti A, Hernandez G, Mercadal-Hally M, Alvarez A, Andreu-Fernandez V, Navarro-Tapia E, Bastons-Compta A, Garcia-Algar O. Prevalence of prenatal exposure to substances of abuse: questionnaire versus biomarkers. Reprod Health. 2017;14(1):137. doi: 10.1186/s12978-017-0385-3
6. Joya X, Marchei E, Salat-Batlle J, García-Algar O, Calvaresi V, Pacifici R, Pichini S. Drugs of abuse in maternal hair and paired neonatal meconium: an objective assessment of foetal exposure to gestational consumption. Drug Test Anal. 2016;8(8):864-8.
7. Joya X, Pacifici R, Salat-Batlle J, García-Algar O, Pichini S. Maternal and neonatal hair and breast milk in the assessment of perinatal exposure to drugs of abuse. Bioanalysis. 2015;7(10):1273-97. doi: 10.1002/dta.1921
8. Pichini S, Garcia-Algar O, Alvarez A, Gottardi M, Marchei E, Svaizer F, Pellegrini M, Rotolo MC, Pacifici R. Assessment of unsuspected exposure to drugs of abuse in children from a Mediterranean city by hair testing. Int J Environ Res Public Health. 2014;11(2):2288-98. doi: 10.3390/ijerph110202288
9. Dodge NC Jacobson JL, Jacobson SW Effects of Fetal Substance Exposure on Offspring Substance UsePediatr Clin North Am. 2019;66(6):1149-61. doi: 10.1016/j.pcl.2019.08.010
10. Kocherlakota P. Neonatal abstinence syndrome. Pediatrics 2014;134(2):e547-61. doi: 10.1542/peds.2013-3524
11. Stover MW, Davis JM. Opioids in pregnancy and neonatal abstinence syndrome. Semin Perinatol. 2015;39(7):561-5. doi: 10.1053/j.semperi.2015.08.013
12. Chasnoff IJ, Burns W, Schnoll SH, Burns K A. Cocaine Use in Pregnancy. New Engl J Med. 1985;313(11):666-9.
13. Finnegan LP, Kron RE, Connaughton JF, Emich JP. Assessment and treatment of abstinence in the infant of the drug-dependent mother. Int J Clin Pharmacol Biopharm. 1975;12(1-2):19-32.
14. Jansson LM, Velez M, Harrow C. The opioid exposed newborn: Assessment and pharmacologic management. J Opioid Manag. 2009;5(1):47-55.
15. Doberczak TM, Shanzer S, Senie RT, Kandall SR. Neonatal neurologic and electroencephalographic effects of intrauterine cocaine exposure. J Pediatr. 1988;13(2):354-8.
16. Mento M. Positività alla cocaina, succede in alcuni ospedali italiani e le vittime sono dei neonati. Available from: www.newnotizie.it/2019/11/03/positivita-alla-cocaina-neonati-coinvolti/.
17. Bocci M. I medici: "Emergenza neonati in crisi di astinenza". Available from: www.repubblica.it/cronaca/2019/11/03/news/i_medici_emergenza_neonati_in_crisi_di_astinenza_-240102649/.
18. Joya X, Gomez-Culebras M, Callejón A, Friguls B, Puig C, Ortigosa S, Morini L, Garcia-Algar O, Vall O. Cocaine use during pregnancy assessed by hair analysis in a Canary Islands cohort. BMC Pregnancy Childbirth. 2012;12:2. doi:10.1186/1471-2393-12-2
19. Joya X, Fríguls B, Simó M, Civit E, de la Torre R, Palomeque A, Vall O, Pichini S, Garcia-Algar O. Acute heroin intoxication in a baby chronically exposed to cocaine and heroin: a case report. J Med Case Rep. 2011;5:288. doi: 10.1186/1752-1947-5-288
20. García-Algar O, Felipe A, Puig C, Monleón T, Pacifici R, Pichini S. Fetal exposure to cocaine and infections during the first 18 months of life in infants from a Mediterranean city. Acta Paediatr. 2007;96(5):762-3.
21. The American Clinical Neurophysiology Society. Standardized EEG terminology and categorization for the description of continuous EEG monitoring in neonates: Report of the American Clinical Neurophysiology Society Critical Care Monitoring Committee. J Clin Neurophysiol. 2013;30:161-73.
22. Facini C, Spagnoli C, Pisani F. Epileptic and non-epileptic paroxysmal motor phenomena in newborns. J Matern Fetal Neonatal Med. 2016;29(22):3652-9. doi: 10.3109/14767058.2016.1140735
23. Legido A, Clancy R, Spitzer A, Finnegan L. Electroencephalographic and behavioral state studies in infants of cocaine-addicted mothers. AJDC. 1992;146:748-52.
24. Palla MR, Khan G, Haghighat ZM, Bada H. EEG findings in infants with neonatal abstinence syndrome presenting with clinical seizures. Front. Pediatr. 2019;7:111. doi: 10.3389/fped.2019.00111.
25. Martin M, Graham D, McCarthy D, Bhide P, Stanwood G. Cocaine-induced neurodevelopmental deficits and underlying mechanisms. Birth Defects Res C Embryo Today. 2016;108(2):147-73. doi: 10.1002/bdrc.21132
26. Kramer L, Locke G, Ogunyemi A, Nelson L. Neonatal cocaine-related seizures. J Child Neurol. 1990;5:60-4.
27. Scher M, Richardson G, Day N. Effects of prenatal cocaine/crack and other drug exposure on electroencephalographic sleep studies at birth and one year. Pediatrics. 2000;105(1 Pt 1):39-48. doi: 10.1542/peds.105.1.39
28. Mirochnick M, Meyer J, Cole J, Herren T, Zuckerman B. Circulating catecholamine concentrations in cocaine-exposed neonates: A pilot study. Pediatrics. 1991;88(3):481-5.
29. Falsaperla R, Marino SD, Aguglia MG, Cupitò G, Pisani F, Mailo J, Suppiej A. Developmental EEG hallmark or biological artifact? Glossokinetic artifact mimicking anterior slow dysrhythmia in two full term newborns. Neurophysiol Clin. 2019;49(5):377-80. doi: 10.1016/j.neucli.2019.07.015