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Review article

Paroxysmal nonepileptic motor phenomena in newborn

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Abstract

Introduction: Understanding the pathophysiological meaning of paroxysmal nonepileptic motor phenomena in newborns represents a challenge for the clinicians of the Neonatal Intensive Care Unit.

Methods: This paper provides an extensive review of the most frequent paroxysmal nonepileptic motor phenomena in newborns, in order to improve the knowledge about this sub-topic of the neonatal pathology and to guide the diagnostic-therapeutic approach.

Results: The correct identification of an epileptic form, among different motor phenomena, which may clinically mimic seizures, is essential for a correct management, avoiding overtreatment. However, it is likewise important to know and to be able to identify other rare neurological conditions, such as hyperekplexia, spinal muscular atrophy, acute bilirubin encephalopathy, that could make a first appearance with paroxysmal motor manifestations, needing specific diagnostic work-up and treatment.

Conclusions: These clinical events should not be underestimated because, even if many times they are physiological and age-related, sometimes they could be the visible signs of an underlying epileptic or nonepileptic neurological disease.

Keywords: Tremor; Myoclonus; Hyperekplexia; Motor automatisms; Neonatal seizures

1. Introduction

In the newborns different types of paroxysmal motor phenomena, that stand out in the background motor repertoire, can be observed. The nature of these movements may be either physiological or pathological, therefore the distinction is important for a correct management, treatment and prognosis. Among pathological motor phenomena displayed by neonates, epileptic seizures represent the most recurring entity, thus differential diagnosis between neonatal seizures and paroxysmal non-epileptic motor phenomena is a frequent problem for clinicians in the Neonatal Intensive Care Unit. Paroxysmal motor phenomena during neonatal period are a frequent finding and this might be explained considering the peculiarities of the central nervous system (CNS) structures' maturation process, in particular concerning the myelination process. In the neonatal period, indeed, the maturation of two main axonal pathways implicated in the genesis of movements, the corticospinal tract (CST) and the corticobulbar tract (CBT), is not yet complete [1]. Specifically, the presence of still immature CST and therefore unable to mediate an efficient inhibitory control on the motor system, might make clear the newborn propensity to show paroxysmal motor phenomena of brainstem origin. In this review we provide a detailed description of paroxysmal nonepileptic motor phenomena, occurring during the first 28 days of life, in order to give to the clinicians useful information for a correct diagnosis.

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2. Tremor and jitteriness

Tremor is involuntary, rhythmical oscillatory movement of equal amplitude around a fixed axis, produced by reciprocally innervated antagonists. It can be defined as fine (high frequency, greater than 6 Hz, and low amplitude, lower than 3 cm) or coarse (low frequency, less than 6 Hz, and high amplitude, 3 cm or more). Jitteriness is the term used to describe recurrent tremors [2,3]. Tremor is the most common paroxysmal motor phenomenon in newborns and can be the clinical sign of both a physiological and a pathological condition. Physiological tremors are frequently an isolated finding in healthy neonates without a history of perinatal complications and seem to be related to a maturational process within the central nervous system. One theory attributes the tremor to an excessive muscle stretch reflex, due to a transient immaturity of spinal inhibitory interneurons [4]. A second hypothesis refers to elevated norepinephrine level in the jittery newborn as part of a process of adaptation to extrauterine life [5]. This condition interests two thirds of healthy infants during the first 3 days of life [3], with a prevalence in low gestational age neonates. Jitteriness was seen in 44% of a sample of 936 healthy full-term neonates, most commonly in low birth-weight infants and mainly during sleep, active wakeful and crying or stressful conditions [6]. Pathological tremors are related to different underlying conditions, including hypoxic ischemic encephalopathy, intracranial hemorrhage, electrolyte and metabolic disorders (hypoglycemia, hypocalcemia), sepsis, hypothermia, hyperthyroid state and drug withdrawal [2,3]. An association between tremor and maternal use of drugs (opiates, serotonin reuptake inhibitors) or toxic substances (marijuana, cocaine, inhaled volatile substances) is described, whereas it is not observed with alcohol or nicotine maternal use [2,6]. An autosomal dominant form of tremor, that involves the perioral muscles, is also reported. It can be observed especially during crying and it is known as familial trembling of the chin [2,7]. Differential diagnosis between benign and pathological forms of tremor is influenced by the quality of the movement. Fine tremor can be benign or secondary to hypoglycemia, while coarse tremor is usually pathological and associated with hypoxic ischemic encephalopathy, in particular in the context of "neonatal hyperexcitability syndrome" due to a mild asphyxia, or with intracranial hemorrhage [2,3]. Furthermore, physiological tremors are stopped by suckling stimulation test, consisting in introducing the examiner's middle finger into the mouth of the infant that lies supine with the head on the midline position and with the hands free [8]. In case of fine tremor associated with normal clinical assessment and absence of risk factors, only observation and serum glucose level are suggested. If a pathological form is suspected, considering the perinatal history, the clinical conditions of the newborn and the characteristics of the tremor, further investigations are necessary. Laboratory studies (serum glucose level; electrolytes; urine drug, thyroid or metabolic screening; septic workup) and neuroimaging can be performed [2,3]. There are some characteristics of the paroxysmal movement that should be strictly observed to differentiate tremor from epileptic seizure. First of all, tremor can be induced by stimuli, while epileptic seizures occur spontaneously and are relatively unpredictable events. Furthermore, ocular phenomena and autonomic signs are often present during neonatal seizures but are not associated with tremor. Another distinctive feature that should be always considered by clinicians is that a tremor can be stopped with a gentle passive flexion and restraint of the affected limb while the seizure activity is not suppressed by restraint or repositioning of the limb [9]. If tremor does not satisfy the above-mentioned criteria an electroencephalographic (EEG) recording is suggested. When an underlying disorder is discovered in a jittery newborn, a specific treatment is required in order to correct the cause. Particular attention is needed in establishing a good care givers-newborn interaction because jittery infants are inclined to be visually inattentive and difficult to console [6]. The outcome is related to the presence of perinatal complications. If tremor, both fine and coarse, is not associated to an underlying brain damage the prognosis is usually good. Jittery newborns with perinatal complications should be strictly monitored because they are at risk of adverse neurodevelopmental outcome [2,10–12].

3. Myoclonus

Myoclonus is a sudden, shock-like, involuntary movement due to muscle contraction [2,13]. It is brief (<500 ms), arrhythmic and irregular, with higher amplitude than tremor [2]. It is caused by an asynchronous contraction of a muscle or a group of muscles and can have either an asymmetric [14,15] or a symmetric distribution. It can be parcellar, segmental or generalized, can be located in the limb or in the axis [15] and can be isolated or repetitive. Some authors discern between "positive myoclonus", which presents the above-mentioned features, and "negative myoclonus", which is the type of myoclonus caused by lapses of muscles contraction [16]. In some circumstances, myoclonus can be provoked by visual, auditory or somatesthetic stimuli, appearing as a reflex phenomenon [16]. Neurophysiologically, the myoclonus can come into being from any level of the central nervous system (cortex, brainstem, spinal cord, nerve) [2,15,16]. Differential diagnosis between epileptic and nonepileptic myoclonus is a topic open to debate [2,9,17], given that myoclonus rarely has an EEG expression [2]. The epileptic myoclonus is however not triggered by stimuli and is not suppressed [2,17]