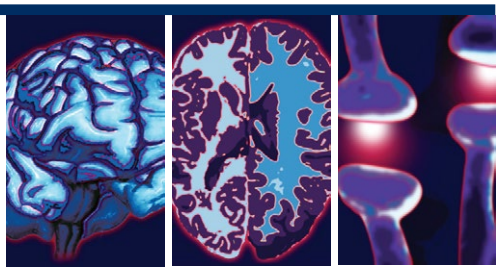
Commentary



Joint Hyperlaxity and Preterm Delivery: A Possible Genetic Correlation

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Abstract

In the last years, several epidemiological evidence indicates that genetic factors could play a significant role in the etiology of spontaneous preterm delivery (PTD), defined as delivery occurring before 37 weeks of gestation.

Keywords

Joint hyperlaxity; Preterm delivery; Genetic correlation; Cervical incompetence

In the last years, several epidemiological evidence indicates that genetic factors could play a significant role in the etiology of spontaneous preterm delivery (PTD), defined as delivery occurring before 37 weeks of gestation [1-6].

Clinicians and researchers have sought to better identify phenotype involving in PTD. Among the several etiologies involved in PTD, Preterm premature rupture of membranes (PPROM) and Cervical incompetence (CI) represent the leading identifiable cause, occurring in 1% of all pregnancies [2,3].

Several genes contributing to premature birth have been reported in the literature showing an association between the connective tissue disorders synthesis involving abnormal matrix metabolism and prematurity [6-9] increasing risk of PPROM and CI [10]. Furthermore, different gene variations both presented in the mother or inherited by the fetus have been found to predispose to preterm birth as a result PPROM, including COL5A1, COL5A2, COL3A1, COL1A1, COL1A2 [10,11]; furthermore, polymorphisms in the COL1A1 and TGFB1 genes have been associated with cervical incompetence [10,11]. These observations reveal the importance of the extracellular matrix in the maintenance of the integrity of the fetal membranes and reveal the propensity of those membranes with an abnormal fibrillar collagen to rupture prematurely [9].

Preterm birth is responsible for long-term morbidity with possible evolution in neurodevelopmental disability (intellectual disability, seizures, cerebral palsy) related to macroscopic lesions of the central nervous system [4]; on the other hand, a lot of longitudinal studies have shown that minor dysfunctions (as delay in motor competence and clumsiness) related to abnormalities in the phase of organization of the cerebral cortex [4] could be reported in preterm infants even in the absence of neurological deficit. Different studies have reported the presence of perceptual and motor abilities difficulties resulting in clumsiness in preterm infant improving with age, related to delayed maturation in preterm than term born children [12]. Our clinical experience in the follow-up of preterm infants led us to observe frequently joint hyperlaxity in these infants even at early infancy and these could be lead to fine and global motor skills difficulties resulting in clumsiness. Joint hypermobility is defined as a more than normal range of movement in a single joint or generalized; in the majority of cases, however, joint hypermobility is observed

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in clinic as an isolated phenomenon, defined as asymptomatic hypermobility [5].

The etiopathogenesis of hyperlaxity in preterm infants is not clearly known, and probably both genetic and environmental factors could be involved.

Bell et al. [13] reported genetic variants within the *COL1A1, COL5A1* and *COL12A1* genes, previously associated with anterior ligament injury and also associated with greater magnitudes of different joint laxity.

Based on these data of literature, we can suppose a possible common genetic basis relating prematurity and ligamentous laxity. The identification of genetic basis of hyperlaxity in preterms would be extremely useful in term of early diagnosis and prognosis to plan early intervention (physical therapy, occupational therapy).

Longitudinal studies on preterm infants are needed to confirm a high incidence of joint hyperlaxity in this population and to identify specific genes involved as *COL1A1, COL5A1.*

This issue is of great interest in term of prognosis and in the counselling of families for precocious and specific treatments.

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