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Review articles

Neurosonography in the second half of fetal life: a neonatologist's point of view

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Abstract

This article reviews the interpretation of the fetal motor repertoire in the light of neurophysiology and clinical neurology. The continuity of the maturative process from the fetus to the neonate allows us to speculate on the predictive value of optimal and non-optimal neurological function as observed in the fetus and their morphological consequences. Neonatologists know that early prediction concerning outcome is reliable only at the two ends of the spectrum, e.g., optimal and very abnormal situations. However, in intermediate situations the quality of observations achieved by 3D–4D ultrasonography already allows to demonstrate the prenatal onset of brain damage, based on morphologic and functional signs. Their identification during the second half of pregnancy may serve as a retrospective marker of a prenatal insult.

Keywords: Cerebral function; four-dimensional ultrasound; neurological assessment; prenatal.

Introduction

Fetal neurosonography begun more than 20 years ago when Prechtl and coworkers [13] described a large variety of specific movement patterns starting at 8–15 gestational weeks (GW) based on 2D sonographic observations. Since then, the qualitative assessment of spontaneous movements, named general movements (GMs), has been integrated in various fetal and neonatal neurological evaluations [16, 17]. The advent of 3- and 4-dimensional ultrasounds (3D/4D-US) allowed exploration of two new domains of fetal motor activity: fetal finger movements and facial expressions [26, 30, 32]. This new technology has obviously sharpened our level of evaluation of the fetus.

The goal of this review is first to consider the interpretation of the fetal motor repertoire in the light of neurophysiology and clinical neurology. A basic understanding of motor pathways organization and maturation [45, 46] allows the clinician to better interpret each observation and maneuver in the fetus as well as in the neonate. The experience acquired with the Amiel-Tison Neurological Assessment at Term (ATNAT) [3, 4, 19] will serve as a guide to complement and interpret fetal observations. Then, speculation on the predictive value of fetal motor behavior will be discussed in the light of those anatomical and physiological correlates [9, 20, 42, 44].

The scope of fetal neurology is too extensive to be fully described in such a review. Therefore, the discussion focuses on two domains which have been documented more recently by 3D/4D-US, i.e., cranial morphology and neuromotor function. Moreover, the description is limited to the second half of pregnancy, despite the fact that spontaneous fetal motility begins much earlier [13]. This means that we will only consider the period for 20–40 GWs, a period covering the end of the neuronal migration and the post-migratory phase and corresponding to the development of the neocortex.

Neonatal neurological assessment as a framework for fetal assessment

General Movements Assessment (GMA)

Prechtl and his coworkers [16, 43] have explored spontaneous motility during human development. They introduced the concept of ontogenic adaptation, meaning that during each developmental stage, the functional organization has to take into account internal and external requirements [16]. Any fetal brain damage will interfere with endogenous motor activity. Therefore, spontaneous movements, as an expression of neural activity, could be used as a marker for fetal brain status [16, 43]. Consequently, the observation of the unstimulated fetus or infant should contribute significantly to the assessment of central nervous system (CNS) function. All endogenously generated movement patterns from unstimulated CNS can be observed as early as the 7–8 GWs, with a rich repertoire of movements developing over the next 2–3 weeks and continuing to be present

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for 5–6 months postnatally [12, 25]. This remarkable continuity of endogenously generated activity from prenatal to postnatal life may allow identifying those fetuses and infants with emerging neurological impairment. GMA includes the consideration of body movements (arms, legs, neck and trunk) spreading in variable sequences with gradual beginning and end. They wax and wane in intensity, force and speed, being fluent and elegant, revealing the complexity and variability of motor activity already present at this early stage. In postnatal life, two specific patterns of movements emerge: writhing movements (36–47 weeks of GWs) and fidgety movements (48–57 GWs) [16, 21, 22]. GMA has to be videotaped and then analyzed based on visual "Gestalt perception", which provides an overall impression of GMs with standardized procedures [16]. Subsequently, movement patterns will be described in terms of complexity, variability and fluency [16, 22]. GMs will finally be classified as normal-optimal, normal-suboptimal, mildly abnormal and definitely abnormal [22]. While the application of GMA in postnatal life is standardized, it still has to be established in fetal life with the use of high-tech resources. Moreover, the debate is still open concerning the predictive value of postnatal GMA in regards to neurodevelopmental outcome in comparison to other methods [10, 21, 38].

Neurological Assessment at Term (ATNAT)

Prior to this observational approach that has found its utility mainly in the assessment of extremely premature and sick infants not tolerating any handling, the classical approach was relying on responses to specific maneuvers. The Amiel-Tison Neurological Assessment belongs to this trend with a specific contribution in the exploration of passive and active tone according to neurological maturation [3, 4, 19]. The clinical significance of this type of assessment was more fully understood when Sarnat [45, 46] reviewed anatomical and physiological correlates of early neurological development. In fact, it became possible to clinically dissociate the development of upper and lower motor systems: (1) the lower system, consisting of the brainstem and cerebellum, matures early (beginning at 24 GW) in an ascending wave; its essential role is to maintain posture against gravity and flexor tone in the limbs; (2) the upper system, consisting of the cerebral hemispheres and basal ganglia, matures later (beginning at 32 GW) and rapidly for the first 2 years in a descending wave; its essential role is to control the lower system, with relaxation of the limbs and control of the antigravity forces, finally allowing erect posture, walking and fine motor skills (Figure 1).

This distinction became even more relevant for clinicians after pathological and radiological data had shown that brain damage is mainly located in cerebral hemispheres, in the full term infant with hypoxic-ischemic encephalopathy or in the preterm infant with periventricular leukomalacia (PVL).

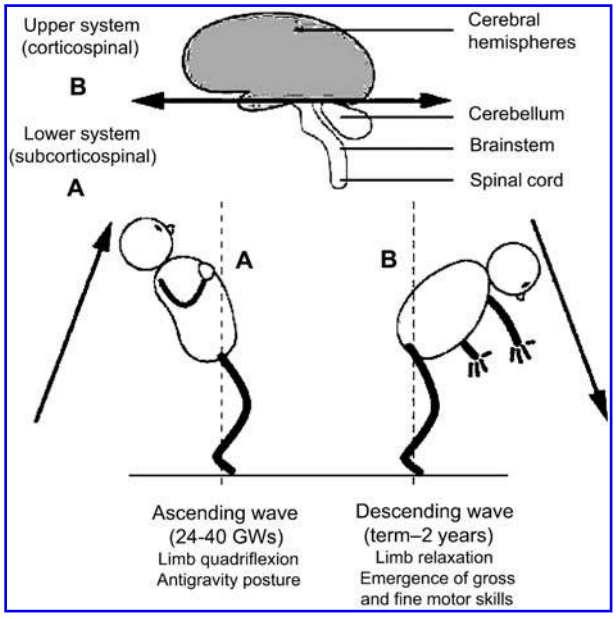

Figure 1 Schematic representation of the developmental patterns of both upper and lower motor systems [adapted from reference 4].

Based on this revisited framework, signs depending on the integrity of the upper structures, such as axial tone and alertness, as well as cranial signs linked to the volumetric increase of the cerebral hemispheres, have been emphasized. The signs depending on brainstem function, such as primary reflexes and passive tone in limb flexor muscles, have been de-emphasized at the neonatal period as they do not provide direct information about the cerebral hemispheres.

Fetal assessment with 3D/4D sonography

Quantitative assessment of fetal movements and facial expressions

Physics and technology of 3D/4D-US have been described in detail elsewhere [25–34]. By enabling synchronized spatial imaging of the whole fetus and movements, 4D-US offers new prospects for quantitative assessment of GMs [1, 7, 8, 25–29, 31–34]. Recently, multicentric studies on fetal brain function have been carried out [25, 33] with the aim of establishing standards of fetal limbs and body movements as well as for facial expressions. Such standardization is required prior to evaluate their criterion-related validity in cases of prenatal brain impairment (Figure 2).

The Zagreb studies on fetal 4D-US assessment which included dynamic observations of the fetus in the first and second trimester [7, 8, 26] as well as neonatal clinical examination [32], also allowed dynamic 3D observations of fetal behavior (Figure 3). Confirming the

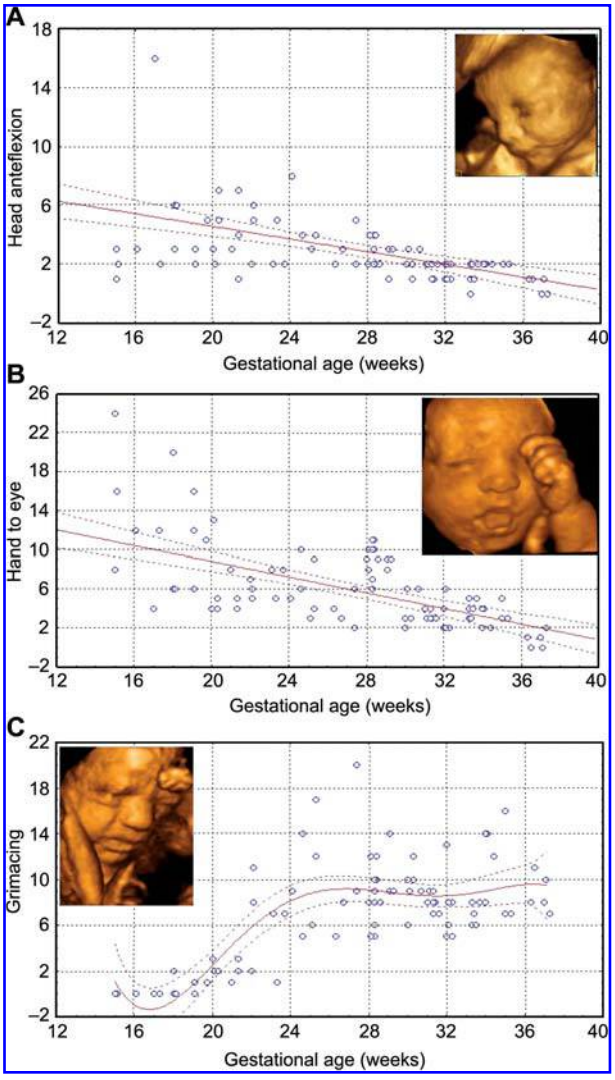

Figure 2 Quantitative analysis of normal fetal behavior patterns using 4D-US (A) Head anteflexion; (B) Hand to eye movement; (C) Grimacing expression.

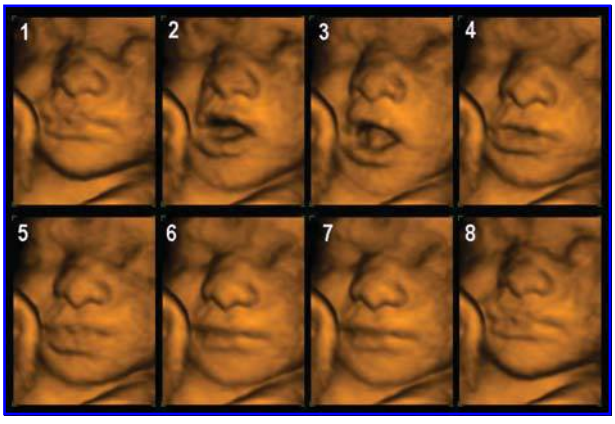

Figure 3 Four-D image sequences of facial expression characterized by stereotyped mouth opening.

feasibility of early dynamic observations in pregnancy, these studies also showed our capacity to obtain much better defined images as the whole fetus could be visualized [30, 31, 34].

New domains explored

One crucial question often posed to neonatologists is to determine the exact timing of brain damage, prenatal or *intrapartum*, in the context of neonatal encephalopathy. In this perspective, repeated neurological assessments over the first days of life allow identification of two profiles. The first, a dynamic profile, is associated with signs of CNS depression increasing within the first 3 days and then decreasing gradually with obvious improvement in alertness, motor activity, and sucking [19]. This profile is typical of recent insult, most often *intrapartum*. The second one, a static profile, is disclosed by lack of changes along repeated assessments in the first week of life. This latter profile is typical of a prenatal insult that occurred *in utero* at least several weeks earlier and therefore, already stable at the time of birth. In addition, the identification of three signs already present at birth offers a precious clue to fetal brain damage, when observed in a cluster:

1. high-arched palate (due to insufficient molding forces of a hypoactive tongue)
2. non reducible adduction of the thumb in a clenched fist (due to absence of spontaneous motor activity)
3. cranial ridges over each suture or restricted to the squamous suture (due to severe or moderate impairment of hemispheric growth).

Using 3D-US, only two of these three signs can be diagnosed *in utero* (Figure 4). As for now, it remains impossible to visualize the high-arched palate with 3D surface imaging since this technique does not permit visualization of deep structure in the oral cavity. However, detection of the two other signs as a specific expression of brain impairment appears promising.

Criteria of fetal CNS optimality

The ATNAT, extensively described elsewhere [3, 6, 16], may be used to determine the neurological status during the first days of life for full term infants or at 40 GWs (corrected age) for premature neonates. In terms of physiological correlates, it is satisfactory to cluster the different items into four subgroups according to their conceptual meaning (Table 1): adequate hemispheric growth, absence of CNS depression, integrity of the upper motor control, stability of autonomic nervous system (ANS). When result for each item is normal, it seems reasonable to conclude to CNS optimality.

The methodological adaptation of the assessment from the neonate to the fetus can be summarized as follows (Table 1):

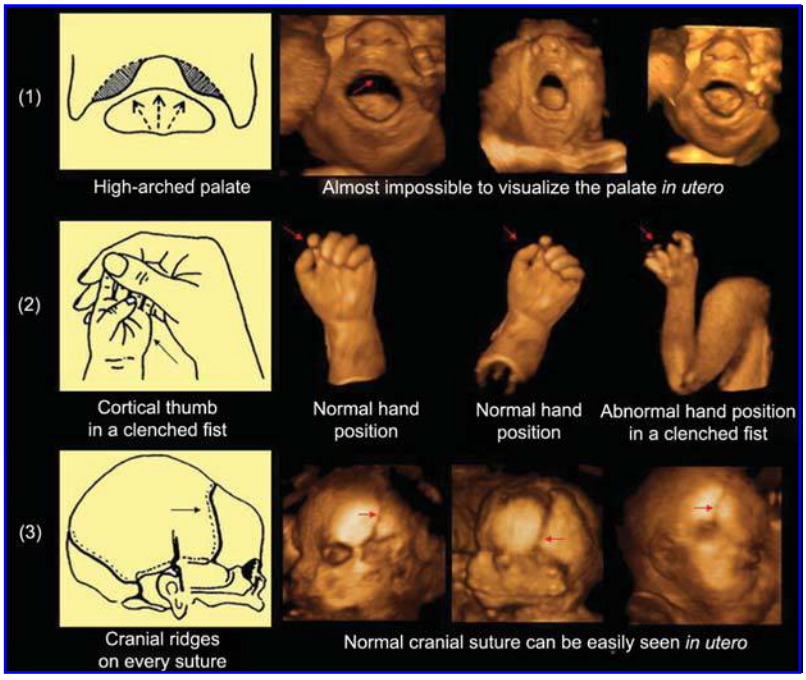

Figure 4 Neonatal signs indicating a prenatal insult (sketch pictures) and comparison with 3D-US imaging *in utero*. (1) High-arched palate (left) and 3D-US imaging of the entire oral cavity (right); (2) Cortical thumb in a clenched fist (left) and 3D-US imaging of the normal and abnormal hand position. (3) Cranial ridges on every suture (left) and 3D-US imaging of the normal cranial suture *in utero.*

1. *Some criteria are similar in fetal and neonatal assessments:* head growth parameters including sutures' status, primary reflexes, (restricted to sucking behavior), fingers' movements and abduction of thumbs (shaded boxes in Table 1).
2. *Some criteria observed in the fetus are only prerequisites for ex utero functional achievements:* opening of the eyes for visual pursuit, facial expressions for social interaction. Their identification by 4D imaging, in addition to efficient and rhythmic sucking supports the absence of CNS depression.
3. *Analytical criteria of typical passive and active tone in the neonate cannot be elicited in the fetus*: head anteflexion versus retroflexion, ventral versus dorsal incurvations in the axis, both being of the utmost importance postnatally to confirm CNS optimality. However, optimality in the fetus should be reflected in typical GMS.
4. *Criteria aiming to check autoregulation are slightly different:* typical non stress test (NST) in the fetus and absence of reactions in the neonate.

Criteria for fetal CNS compromise

In the presence of neurological signs, the next step is to proceed to the clinical synthesis. In the full term neonate [3, 4, 19], the final categorization is based on the clustering of signs and symptoms observed within the first week of life; the non-optimal status can be graded into three categories:

- minor degree, without CNS depression
- moderate degree, with CNS depression
- severe degree, with deep CNS depression and repeated seizures

The categorization based on the different findings yielded a good inter-rater reliability with a Kappa coefficient of 0.76 [11].

As described above, the identification of "CNS depression" during fetal life is based on pre-competences (opening of the eyes, variety of facial expressions), primary reflexes (rhythmical bursts in the sucking pattern) and quality of GMs. The addition of cranial signs (such as insufficient head growth and overlapping sutures) to neurological signs could be a valuable complement. Moreover, the identification of dynamic and static patterns of the symptoms may be as helpful to date the insult as it is postnatally: the more stable the signs, the more precocious the insult [3, 6, 16]. Seizures are known to occur *in utero*, abnormally rhythmic movements having been occasionally perceived and reported by mothers. However, it is unlikely that such a brief and rare event should be seen with 4D-US.

Consequences of *in utero* environment

Favorable mechanical effects of fetal environment

Head stability passively maintained Grenier has demonstrated the essential role of head instability on motor behavior during the first two months of life [20]. In

Table 1 Optimality criteria assessed in the term neonate and comparable optimality criteria observed in the fetus in the second half of pregnancy with 3D-4D sonography.

	Neonate At 40 GWs	Fetus Between 20 - 40 GWs	
Optimality Criteria	**ATNAT**	**Prechtl GMA 3D/4D-US**	**Significance**
Head circumference Cranial sutures	Within normal limits Same range as other growth parameters Edge-to-edge, squamous included		**Adequate hemispheric growth**
Visual pursuit Social interaction Sucking reflex	Easily obtainable Eager Efficient, rhythmic	Opening of the eyes Facial expressions	**Absence of CNS depression**
Raise-to-sit and reverse Passive axial tone Passive tone in limbs	Active flexion of head Flexion ≥ Extension Within normal limits and symmetrical	Optimality should be reflected in typical GMs	**Integrity of the upper motor control**
Fingers and thumbs movements	Independent movements of fingers Active abduction of thumbs		
Autonomic control	No disturbance during the assessment	Typical NST	**Stability of SNA**

*Shaded boxes indicate criteria which are similar for the fetus and the neonate

experimental situation, manual support is given to the neck and spine while the infant's alertness and attention are solicited by the examiner: an amazing communication state is reached and facial expression becomes more diversified. The most spectacular part of the experiment follows with jerking movements disappearing (an event termed "debugging"), flexor tone in upper limbs decreasing, infant's hand opening and Moro and grasp reflexes disappearing for a while. This particular state, called "liberated state", allows the infant to intentionally reach and grasp an object. The significance attributed to this transiently obtained ability in an infant as young as two weeks, is of high predictive importance: a positive response brings an additional confirmation about the upper system integrity.

Why is the demonstration of this liberated state so contributory to our understanding of fetal motor behavior? This is because head stability passively maintained by the uterine wall during the second half of pregnancy obviously creates a permanent situation comparable to the head control transiently obtained postnatally during the experiment described above. Moreover, the facial expression during the experiment in the neonate, calm, concentrated, and totally involved in reaching the proposed object looks very much like the facial expression and attitude of fetuses manipulating with both hands their umbilical cord in front of them. In addition, the natural and permanent "liberated state" of the fetus contributes to the explanation of the absence of Moro and grasp reflex *in utero,* as routinely observed [32].

It is tempting to speculate on those observations:

1. The fetus is really well protected, even against himself: although the amount of Wharton's jelly is able to protect the umbilical vessels, it is more secure if the grasp reflex is somewhat inhibited by the head stability *in utero.* The same remark applies to the Moro reflex which could be a nuisance if repeatedly induced by postural changes.
2. The young infant will have a much less comfortable life from birth until the acquisition of head control around 2–3 months postnatally. Physiological hyperexcitability and very active primary reflexes are well-known transient characteristics during the first 3 months of life. When tested in the parent's presence, emotion peaks when the newborn begins to walk automatically, precompetence reminding the evolution since *homo erectus* [2], although this archaic performance cannot be considered useful neither for the newborn infant nor for the neonatologist. Prechtl already pointed out long ago that those minor deviations from typical aspects (bugs?) could be ignored when restricted to the first 3 months of life, as they are not predictive of later cerebral dysfunction [42].

Freedom from gravity Long before the availability of ultrasonography, Liley [36] commented about the differences between fetal and postnatal motor behaviors. For example, he suggested an explanation to the fact that an infant does not roll over until 14–20 weeks of postnatal life although he was able to do so very early during fetal life "… a trick which is simple in a state of neutral buoyancy becomes difficult under the new-found tyranny of gravity".

At the first minute of postnatal life, the most spectacular response ready to counteract gravity is the full righting reaction observed when the neonate is placed in the upright position: tactile stimulation of the sole of the feet evokes an active response in the extensor muscles; body weight is then actively sustained for a few seconds; this response depends on the brainstem (lower motor system), and so evolves with the subcortical structures in a caudocephalic wave (with a response restricted to the lower limbs around 28 GWs and reaching the head by 38–40 GWs) [3]. During fetal life, verticality is not at all necessary to elicit the activity of antigravity muscles: the contact of the soles with the uterine wall stimulates *in utero* the extensor muscles of the axis, whatever the fetal position is. Motility *in utero* around mid-pregnancy is very free indeed, under the control of brainstem reflex activity, righting reactions, automatic walk, trunk rotations. At birth, the infant is powerless against gravity. Later, with maturation of the upper motor system, the infant will acquire head control, independent sitting and independent walking, in a descending maturative wave. It is remarkable to observe how the motor system is already well prepared for protection of the infant at each new victory on the "tyranny of gravity". New postural reactions occur, such as lateral propping reaction to maintain sitting position and later 'parachute' reaction, ready to attenuate bad falls when learning to walk [5].

Frustrating limitations of hands-off observation

Haptonomists have developed the ability to "play" with fetuses through the abdominal wall of the mother, perceiving and provoking fetal movements. Until now, most researchers do not practice haptonomy during their assessment; they privilege the natural observation, without external interferences. In this line, researchers in Zagreb restrict their fetal assessment to the observation of spontaneous behavior and do not study responsiveness to extra-uterine stimuli. Other types of assessment, however, take into account fetal responsiveness, such as the Fetal Neurobehavioral Coding System (FENS) derived from Brazelton's work in the neonate [44].

The essential limitation in assessing fetal CNS status is due to the impossibility of hands on assessment on the fetus. For instance, the most frustrating deprivation for a pediatrician is not to be able to compare passive ventral and dorsal incurvations of the axis or to evoke the activity of flexor muscles of the neck by the raise-to-sit maneuver. Despite those limitations, our conviction is that for both optimal status and severe degree of CNS compromise, which are the two extremes of a same continuum, fetal assessment will prove to be as valid as the assessment in the neonatal period [3]. Mild to moderate degrees of CNS depression may be detectable as well during fetal life but probably cannot be influential on obstetrical management.

Early diagnosis of cerebral palsy (CP): state of the art

Definition of CP

CP is an "umbrella" term, for which each word has recently been meticulously discussed to produce this consensual statement [9]. Cerebral palsy describes a group of disorders of development of movement and posture, causing activity limitation, that are attributed to non-progressive disturbances that occurred in the developing fetal or infant brain. The motor disorders in cerebral palsy are often accompanied by disturbances of sensation, cognition, communication, perception, and/or behavior, and/or by a seizure disorder. "Attributed to" is purposely vague because our understanding of developmental neurobiology is evolving rapidly. "Disturbances" is used as a comprehensive term referring "to events or processes that in some way interrupt damage or otherwise influence the expected pattern of brain maturation…" [9]. Those events or processes are many, with

consequences varying from very conspicuous to very subtle.

Our goal in this review is to improve obstetrical management. Due to the recent advances in fetal MRI, it seems reasonable to consider separately, on the one hand, the situations with abnormal brain imaging showing destructive lesions or structural anomalies and, on the other hand, the situations with typical brain imaging.

When fetal brain imaging is abnormal

An elegant atlas on fetal CNS diseases recently reviewed fetal brain imaging; one chapter covers any visible congenital brain anomalies [39], while acquired brain abnormalities *in utero* including destructive lesions due to hypoxic-ischemic events, intracranial hemorrhage, porencephalic cysts and pseudocysts, are reviewed in another chapter [40]. The probable outcome may be estimated according to fetal age at the time of diagnosis, size and location of clastic lesions or structural abnormalities as well as to the degree of severity of functional consequences evaluated by 4D US. How to use that information still remains litigious in many cases, depending not only on ethical positions (personal or national) but also on expectations concerning the degree of cerebral plasticity at this early stage. We understand morphologists and neurosurgeons who often refer to a few personal cases with a favorable motor outcome despite very destructive brain lesions: they optimistically conclude that morphology does not always correlate with neurodevelopmental outcome. On the contrary, pediatricians and neuropsychologists involved in long term follow-up studies certainly are less optimistic. For example, an infant born with a massive destruction of the whole Sylvian artery territory in the left cerebral hemisphere may look fine when he sits independently at 7 months or walks independently at 18 months. However, at age 7 years with a confirmed diagnosis of hemiplegic CP, severe motor disorders are accompanied by disturbances of sensation, cognition, perception, behavior and a seizure disorder. As a conclusion, it is wise to check down the road: for each specific type of fetal brain damage, appropriate decisions for a conservative management have to rely on series including long term outcome measurements.

When fetal brain imaging is typical

Neuropathologists know very well that the best radiological techniques are not microscopes: many changes are below the limits of resolution of neuroimaging [35, 46]. Reviewing fetal and perinatal brain damages in 1998 [6], we stressed the point that the group of children with normal imaging but non-optimal cerebral function presents an exciting opportunity to hypothesize correlations between neurocognitive disabilities and subtle diffuse brain abnormalities. However, we must refine every method of fetal assessment (fetal neurology included) before we can provide obstetricians with safe guidelines for the optimal management of fetuses at risk of neurodevelopmental disabilities. The 3D/4D-US gives hope for better future fetal management.

As far as subtle brain lesions are concerned, pathological gliosis [6] has to be distinguished from PVL as a diffuse lesion of white matter associated with an increase of hypertrophic astrocytes (positive with glial fibrillary acidic protein staining). When using routinely this staining, similar lesions are also detected based on the presence of reactive astrocytes in the germinal matrix; the de-population of this transient structure that can follow a hypoxic-ischemic event may influence the later capacity to produce neuroblasts and glial cells. In the post-migratory phase during the second half of gestation, another transient structure, the subplate, appears to be the site of selective vulnerability [24] with consequences on neocortex formation. The subplate is located between the cortical plate and the intermediate zone, reaching its maximal thickness between 22 and 36 GW. Each neuron will migrate into the subplate which plays several important roles up to term [37]. Programmed cell death, wiring, and synaptogenesis are active processes during the second half of pregnancy, “processes that in some way interrupt, damage or otherwise influence the expected pattern of brain maturation” [9].

Those damages can occur *in utero* but they probably occur as well in postnatal life in many extremely low birth weight (ELBW) infants. We know that in this risk group the incidence of PVL is not higher than in the LBW group. However, we are aware of the high incidence of learning disabilities in the ELBW group (nearly half of them when tested from 7–9 years). It is obviously tempting to correlate those developmental sequellae to those subtle damages, as a result of early cerebral disorganization without macroscopic tissue destruction, and without detectable imaging.

Finally, it appears that when we consider not only CP, the tip of the iceberg, but the full spectrum of motor disorders, the moderate and mild clinical aspects are much more frequent than the severe ones [18]. It is probably the same proportion for the pathologist between the clastic forms of brain damage and the more subtle and diffuse tissue impairment. However, we cannot equate clastic damage-positive imaging and CP on the one hand, and diffuse damage and negative imaging with milder disabilities on the other hand. Those categories overlap, i.e., some cases of the CP are not associated with clastic imaging and some cases with subtle motor disability (non-disabling CP) are associated with, for instance, obvious scars of PVL. In conclusion, clinico-pathological correlations are established statistically but have to be applied with caution for each individual case.

Limitations due to immaturity of the fetal brain

The main obstacle to early prediction of CP based on a functional observation of the fetus such as visual obser-

vation by 3D–4D US is due to the "precompetent" stage of most of the motor abilities observed *in utero*. In other words, can we predict the presence or absence of hemispheric brain damage, based on the observation of motor and reflex activity under the control of lower structures? This dilemma can be illustrated by a few examples:

1. *Automatic walking is a precompetent stage*, present very early in fetal life and still at birth. Then it is diminishing in the first 3 months postnatal, apparently disappearing but later involved in the automatization of independent walk for the rest of life. This is a typical example of "change of power" from a lower (brainstem) to a higher (cortical) command. As a didactic joke, one can say that fetuses and neonates walk with their feet (tactile primary reflex) while young children walk with their head (upper control).
2. *Global straightening in the standing position* shows the same evolutional pattern: antigravity straightening initially depends on a tactile reflex, then disappears completely for a few months (between 4–7 months of life), and then re-appears in a self-initiated pattern when the infant is able to stand on his own. This profile is a precious clue for the clinician (delighted to check the absence of straightening in a 5 months old infant at risk), illustrating the typical process of inhibition of the upper on the lower motor system.
3. *Finger and thumbs movements* are visible very early in fetal life [41], long before the maturation of the upper system. Fetuses start to clench and unclench their fists from 12 GWs and independent movements of each finger are occasionally seen from 13–14 GWs. Therefore, this motor activity depends on the lower system up to 30–32 GWs and switches later on to the upper control. An illustration is to be found in severely damaged children who cannot open their hands spontaneously but do so automatically in the "facial limb" as a result of the asymmetric tonic neck reflex.
4. *Head forward flexion* which is visible very early in fetal life is another example [13]. However, the activity of flexor muscles will depend on the upper system from 34 weeks or so. The absence of active head flexion explored by the raise-to-sit maneuver is one of the major neurological signs at 40 GWs [3, 4, 19].
5. *Visual function* itself has to be considered as still another example, as indicated in this title [15]: *Visual function in the newborn infant: is it cortically mediated?* "A few infants with cystic leucomalacia who later become cortically blind seem to retain their ability to track and show pattern preference until around 48 weeks postmenstrual age. This observation suggests that until two months these functions are not dependent on cortical integrity, but are mediated through subcortical pathways".

Those few examples are sufficient to illustrate how the clinician is able to follow the switch in neural circuitry observed for each motor acquisition according to a specific chronology. As most of the hypoxic-ischemic damages of minor and moderate degrees are located in the cerebral hemispheres, it seems unwise to expect reassurance about the integrity of upper structures based on precompetent functional stages. Nevertheless, it remains important to test the integrity of the lower system as a prerequisite for a favorable outcome. This dilemma is not specific to neuromotor function. For example, fetal habituation which has attracted a lot of attention as a potential means of assessing fetal neural integrity, may just be a prerequisite depending on the lower system [23]. More long-term data are necessary to establish its predictive value for later development.

Conclusion

We agree with DiPietro that a consensus recognizing the fact that fetal neurobehavior reflects the developing nervous system is emerging [14]. However, we do not know yet the conceptual and methodological strengths and weaknesses of the currently available fetal assessments. Consequently, we are not yet ready to predict the neurodevelopmental outcome for the whole spectrum based on these methods. The predictive value for a favorable outcome of a complete neurobehavioral repertoire in a fetus as young as 20 GWs has to be demonstrated; this is the goal of an on-going collaborative project by the Kurjak's group using 3D/4D-US technology. Pediatricians know that they need to wait until the age of 6 months postnatally to diagnose a severe CP, 12 months for a moderate CP and 24 months for a minor non-disabling CP [5]. This delay for the full clinical expression of functional consequences of a brain damage strictly depends on brain maturation. Nevertheless, the possibility with 3D/4D-US to demonstrate the prenatal onset of brain damage, based on morphologic and functional signs, will be of invaluable help in cases of litigation. Any deviant observation recorded during fetal life will serve retrospectively as a unique clue to a prenatal insult.

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