Fetal Behaviour Assessment as a Predictor of Future Neurological Development in Children: A Review

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Abstract

The development and implementation of three- and four-dimensional ultrasound in clinical practice have enabled both qualitative and quantitative assessment of fetal movements, including analysis of the fetal face. Ultrasound studies of fetal behaviour, compared with morphological assessments, have demonstrated that fetal behavioural patterns directly reflect the developmental and maturational processes of the fetal brain. This suggests that changes in fetal movements may allow the prenatal identification of neurological impairment.

Recently, a four-dimensional ultrasound-based prenatal screening approach for assessing fetal behaviour has been introduced. In this context, the Kurjak Antenatal Neurodevelopmental Test (KANET) has emerged as a 4D ultrasound-based scoring system for evaluating fetal neurobehavior and identifying fetuses at risk of later neurodevelopmental impairment.

This study presents a narrative review of the literature, based on a structured literature search, on fetal behaviour in normal and high-risk pregnancies, with particular emphasis on the potential for prenatal prediction of neurological development using this screening approach. The findings suggest that four-dimensional ultrasound-based prenatal assessment may be associated with postnatal neurodevelopment. However, scoring systems such as KANET should be interpreted with caution, as they remain promising but not yet definitive predictive tools.

Keywords: fetal behaviour; three-/four-dimensional ultrasound; KANET

Introduction

Although moderate or severe neonatal brain damage has traditionally been considered the result of intrapartum hypoxic-ischemic insult, it is now clear that antenatal factors such as prematurity and infections play a major role in its aetiology (1). Neonatal brain damage may subsequently result in cerebral palsy, which is one of the most common congenital chronic motor disorders of childhood, affecting 2 per 1000 live-born children (2). Contrary to prior beliefs that the global increase of caesarean sections would decrease the incidence of cerebral palsy, the number of affected children remains relatively high (3). Moreover, advances in neonatal and obstetric care and the increasing survival of the very preterm and very low birth weight infants may contribute to the increasing incidence of cerebral palsy in developed countries (4). Perinatal brain injury and cerebral palsy are among the most litigated conditions in modern medicine, resulting in substantial compensation claims mostly based on the belief that these disorders are related exclusively to intrapartum events, such as the use of forceps and vacuum deliveries, or failure to perform a caesarean delivery, while antenatal factors are often neglected. Taking all of the above into consideration, it is clear that investigations into fetal and neonatal neurological development are essential in both the scientific and legal fields (2).

Since basic neurodevelopmental studies have concluded that fetal movements reflect developmental and maturational processes within the fetal central nervous system, it may be speculated that studying fetal behaviour allows for the assessment of the optimality of fetal brain development (5). Furthermore, these findings supported the hypothesis that changes in fetal movements and behaviour could be used for the prenatal diagnosis of fetal neurological impairment (6-9). The first scientific studies of fetal behaviour were conducted centuries ago, with the first report published at the end of the 18th century (10). Later, in 1885, Preyer drew the attention of the scientific community by publishing an entire chapter about fetal behaviour in his book *Specielle Physiologie des Embryo* (11).

Throughout history, maternal registration of fetal movements and obstetric auscultation of fetal heartbeats were the only methods for assessing fetal well-being in utero. Maternal registration of fetal movements can be considered a direct assessment of fetal behaviour, recorded by the mother and subsequently analysed by her healthcare professional. This method is well accepted and widely used in clinical practice as a first indicator of fetal health due to its simplicity. Nevertheless, the technique of maternal counting of fetal movements has several limitations: the optimal number of movements and the ideal duration of counting have not yet been established. Another disadvantage is its limited sensitivity, since maternal awareness of fetal movements is influenced by placental position and fetal presentation.

A major advancement in the assessment of fetal behaviour was achieved with the development of two-dimensional ultrasound (2D US), which enabled direct visualisation of fetal anatomy and activity. With the implementation of ultrasound into clinical obstetric practice, a new window into the intrauterine environment was opened, which enabled the observation of fetal behaviour within its natural environment. This possibility encouraged many investigators to study fetal behaviour. Their findings, when compared with morphological studies, demonstrated that fetal behavioural patterns are direct reflections of developmental and maturational processes within the fetal central nervous system.

Methodology

This study presents a narrative review based on a structured literature search, evaluating fetal neurobehavioral development using prenatal assessment techniques and examining their association with neonatal neurological outcomes. A literature search was performed using PubMed, Scopus, and Web of Science. Publications from 1837 to 2024 were included, encompassing various assessment methods and insights into fetal neurodevelopment throughout history.

Studies were considered eligible if they investigated fetal spontaneous movements, neurobehavioral states, and patterns, assessed by different ultrasound techniques (2D, 3D, and 4D), magnetic resonance imaging, and various neonatal neurological examinations. This review synthesizes publications analysing continuity from prenatal to postnatal neurobehaviour. Both physiological and high-risk pregnancies were included. This review primarily included systematic reviews, original research articles, and observational studies. Case reports were generally excluded due to their limited evidential value, although exceptional cases documenting rare neurobehavioral patterns were cited for illustrative purposes. We also excluded studies that were unavailable in full text or lacked sufficient methodological details.

Since this is a review of previously published data, there was no patient involvement, and formal ethical approval was not required.

Fetal behaviour in normal pregnancies

The first two-dimensional ultrasound studies of fetal behaviour described the onset and patterns of fetal movements from the first trimester to the end of the third trimester (12-14). All the assessed movements were described in detail regarding their quantity, quality, and first appearance (12-14). Although early embryonic development is characterized by embryonic immobility, the first spontaneous movements appear at around 7.5 gestational weeks, with most other movements emerging by the end of the first trimester (12-14). These first spontaneous movements can be described as slow flexion and extension movements of the fetal trunk accompanied by passive change in position of fetal extremities, which is why they have been described as "worm-like movements'' (15). By the end of the 9th week of gestation, these movements are replaced by more energetic movements called ''startle movements'' (15). General movements, which are of great importance in fetal behaviour assessments, start to appear in the first trimester and are the most frequent movement pattern between 9 and 14 weeks of gestation (15, 16).

In the second trimester, all the fetal movements, except startle movements, increase in frequency and become more complex and consolidated, especially with the beginning of the third trimester (15-17). The periods of fetal quiescence begin to increase, and the rest-activity cycles become recognizable. These changes in fetal behaviour coincide with the basic neurodevelopmental studies, which indicate that this period is crucial for the primary motor cortex to begin controlling fetal behaviour and voluntary movements. The frequency of general body movements, which tend to increase from the 9th week onwards, gradually declines during the last trimester (18). Simultaneously, with the decrease in the number of general movements, an increase in all types of facial movement occurs, along with increased complexity of each (18). The consolidation and organization of fetal movements in the third trimester were primarily recognized by Nijhuis, who clearly stated that from the 36th gestational week onwards, normal fetuses develop clearly defined fetal behavioural states (Fetal states 1 through 4) (15).

As mentioned in the introduction, the first extensive study on fetal behaviour started with the introduction of two-dimensional ultrasound, which enabled the visualisation of the fetus and its movements. Since then, fetal movements have been studied longitudinally in both low and high-risk pregnancies (12-14). Since two-dimensional ultrasound has some technical limitations regarding the assessment of movement quality, the mentioned studies were based mainly on the quantification of specific movements. Although the parameters of normality were set for all individual movements, this was not enough to conclude fetal neurobehavioral development, since the technical limitations of the available technology could not be surpassed.

The introduction of new ultrasound techniques, three- and four-dimensional ultrasound (3D/4D US), opened a new perspective for the study of fetal behaviour by providing the capability of simultaneous spatial imaging of the entire fetus and its movements. 3D/4D US added the possibility of further qualitative assessment of fetal and even embryonic movements, including their complexity and variability. Initially, they were primarily used to describe normal fetal movements and behaviour, their continuity into postnatal life, as well as aspects of fetal awareness (19-28). Three- and four-dimensional ultrasound enabled the observation of fetal face in three dimensions, which is important for the assessment of fetal facial expressions in near real time, indicative of the maturational processes of the primary motor cortex. Facial expressions such as smiling, pouting, or scowling can also be observed during the third trimester by 4D ultrasound. Fetal eye movements can also be detected, including nystagmoid eye movements between 15 and 17 weeks (29). The fetus shows blinking by opening and closing the eyelids at 23 to 26 weeks, and from 30 weeks onwards, clusters of rapid eye movements are observed (30).

Fetal behaviour in high-risk pregnancies

As we have mentioned previously, the whole idea of prenatal assessment of fetal behaviour was first based on the presumption that differences in fetal motility could be found between normal and abnormal pregnancies and that changes in fetal behaviour could lead to conclusions about the impaired prenatal neurological development and even postnatal sequelae. Abnormal motor behaviour was first prenatally assessed and described using 3D and 4D US in a case of an anencephalic fetus (31). This is a cephalic disorder that results from a neural tube defect and is usually diagnosed in the first trimester, with the termination of the pregnancy in most cases. In certain circumstances, these pregnancies continue due to religious or personal reasons, providing a good model for the study of fetal behaviour. When longitudinal studies were performed, the findings unexpectedly revealed how abundant fetal behaviour was in the first and early second trimester, coinciding with the time when the control of fetal behaviour is mainly under lower control centres (31, 32). As the pregnancy continues, at the end of the second and especially in the third trimester, the ontogenetic shift of motor control from lower to upper control centres occurs, which is reflected in fetal behaviour (31, 32). The fetal movement repertoire changed; the movements became jerky and simple, and facial movements were rare or absent (31, 32).

Intrigued by fetal motility, researchers studied fetal behaviour in various pathological conditions. The first study of fetal behaviour using 4D US showed that the median value of all movement patterns differed between normal fetuses and those with intrauterine growth restriction (IUGR). Statistical evaluation revealed significant differences in the distribution of movements between these groups. A tendency for IUGR fetuses to exhibit less behavioural activity than normal fetuses was noted in all observed movement patterns, with statistical correlation for hand-to-head and head retroflexion movements in the third trimester (33). On the other hand, with the use of 3D/4D US, it became possible to determine the fetal behaviour as normal even in cases of unfavourable intrauterine conditions, such as intrauterine growth restriction, fetal hypoxaemia, and preterm labour (34).

Earlier studies investigating diabetes-related influences on fetal movement patterns revealed delayed emergence of fetal motor activity, with a delay of 1 to 2 weeks in almost all observed movement patterns emerging in the first 12 weeks of gestation. Only fetal breathing-like movements were observed for the first time at the same gestational age as in normal fetuses (35). Moreover, compared with normal pregnancies, fetal breathing-like movements in late diabetic pregnancy were not influenced by Braxton Hicks contractions and did not show a clear-cut state-dependency, supporting the conclusion that the neural mechanism underlying fetal breathing-like movements differs from that in normal pregnancy (36).

Furthermore, maternal exposure to certain environmental factors can impact short-term intrauterine development and overall infant health. These factors can cause modifications and "reprogramming" of organ structure, particularly in organs with greater plasticity, such as the brain, leading to neurodevelopmental alterations. Some studies have investigated the impact of air pollution, smoke, stress, depression, anxiety, and obesity that increase the state of maternal inflammation and therefore play a role in neurodevelopment (37). Additionally, even modest maternal alcohol intake has been shown to reduce fetal eye movements, disorganize behavioural state organization (rapid eye movement sleep being affected in particular), and suppress fetal breathing activity almost completely (38). Maternal smoking is another parameter with a negative influence on fetal behaviour. It has been shown that fetuses less than 37 weeks of gestation whose mothers smoke throughout pregnancy have a delayed onset of behavioural response to the maternal voice (39).

Collectively, these studies provided a promising basis for the development of the 3D/4D ultrasound investigations of fetal behaviour in high-risk pregnancies to predict neurobehavioral postnatal development.

Introduction of the Kurjak Antenatal Neurodevelopmental Test (KANET)

Since fetal behavior reflects fetal well-being and brain development, authors highlighted its clinical and research importance, but these ideas have not been widely adopted in clinical practice for fetal neurological assessment (40, 41). Although several different tests for assessing fetal behavior were suggested, they were not used routinely due to their complexity, observer variability, and time consumption. Among these methods, general movements (GM) were preferred because they show continuity from prenatal to postnatal life (42). General movements can be described as holokinetic movements, which are periodic bursts involving the entire fetal body in the first trimester. The potential prognostic value of evaluating GM for predicting fetal neurobehavioral state has been extensively studied both before and postnatally (42-43). GM assessment relies solely on recognizing global patterns of qualitatively different motor behaviors and has shown predictive value comparable to magnetic resonance imaging, with sensitivity for consistently abnormal GMs around 98–100%, although specificity is lower, especially in preterm infants (42). Conversely, De Vries emphasized the importance of GM and proposed including their assessment as part of routine antenatal sonographic care. In cases of abnormal GM findings, she recommends advanced sonographic examinations, focusing on head movements, including the eyes and jaw, as well as the torso and limbs (44). The author also noted the advantages of four-dimensional ultrasound over two-dimensional ultrasound for future fetal behavior research (44).

Ultrasound evaluation of fetal body movements has previously been integrated into a test of fetal well-being for assessing the fetal biophysical profile (BPP). This test combines prenatal quantitative ultrasound evaluation and fetal heart rate monitoring, using a scoring system commonly referred to as Manning's score (45). Although BPP can be sufficiently used as a method of fetal surveillance for predicting acute or chronic fetal hypoxia, its utility in assessing fetal neurobehavioral conditions is quite limited. Neonatal neurological evaluation can be performed using the Amiel-Tison neurologic assessment at term, which has a scoring system and a complete procedure that takes approximately 5 minutes (46). The Amiel-Tison Neurological Assessment at term age (ATNAT) focuses on infant responses that depend on the corticospinal control system, a stage of maturation that can be clinically explored. This test, which is helpful in the recognition of prenatal brain damage, was used as a model for creating a new prenatal neurologic assessment test due to its utility, effectiveness, and simplicity of performance. As previously mentioned, there is continuity from fetal to neonatal behaviour, in terms of all facial and hand movements directed toward the head, except the Moro reflex, which is present only in neonates (23). In addition, multiple studies using 3D/4D US have shown that fetal and embryonic movements constantly expand in their repertoire and frequency, whereas the second and third trimesters are characterized by the progressive organization of fetal activities into complex and clearly distinct behavioural patterns (47-51). Following the ultrasound studies in normal pregnancies, several investigations using the same ultrasound methodology confirmed differences in fetal movements and behaviour in normal pregnancies as compared to high-risk pregnancies with respect to cerebral palsy (34, 52-54). All these findings were used to create a platform for the new ultrasound evaluation test of fetal neurobehavior. Kurjak and his group developed a new scoring system for the fetal neurobehavioral state based on prenatal assessment of fetal movements by 3D/4D sonography to enable more objective evaluation of fetal movements and comparison among professionals and across different centres (55, 56). The test was named the Kurjak Antenatal Neurodevelopmental Test (KANET), and it is the first structured and systematic test that uses 4D US technology to assess the functional development of the central nervous system of the fetus in a similar way that neonates are examined postnatally for brain damage by neonatal neurological tests. The selection of parameters to be included in the test was very extensive, with GM being added based on a developmental approach to the neurological assessment and on the theory of emergence of GM from central pattern generators (42). Other parameters included in KANET are those that have already been shown to be sufficient in ATNAT, such as overlapping sutures and the neurological thumb (55).

The two main advantages of the 4D US incorporated in KANET, compared with 2D US, are the detailed evaluation of fetal facial movements and improved assessment of the quality of all other fetal movements (55). For example, a hand does not just move or flex as in a two-dimensional image; now we can assess simultaneously its rotation, supination, pronation, individual finger movements, direction of the movement, and, most importantly, the overall impression of quality and complexity of the movement.

In the first version of KANET the following ten parameters were incorporated: isolated head flexion, overlapping cranial sutures and head circumference, isolated eye blinking, facial alteration, mouth opening (yawning or mouthing), isolated hand and leg movements, hand-to- face movements, finger movements and thumb position, and Gestalt perception of general movements (overall perception of the body and limb movements with their qualitative assessment) (55). The KANET was standardized in Osaka, Japan, on the 24th of October 2010 to make it more reliable, reproducible, and practical for fetal medicine specialists (56). According to the Osaka Consensus Statement, the KANET should be performed in the third trimester of pregnancy, between 28 and 38 weeks, and fetuses should be examined while they are awake. If the fetus is asleep, the assessment should be postponed by 30 minutes or until the following day, with a minimum interval of 14-16 hours. The newly modified KANET test should include 8 instead of 10 quantitatively and qualitatively assessed parameters: facial and mouth movements are combined in one category, and isolated hand movements and hands-to-face movements are combined in another (56). First studies on the use of KANET in normal pregnancies have shown that a normal prenatal KANET score is significantly predictive of a normal postnatal neurological outcome (57), while newborns with abnormal or borderline KANET scores should undergo postnatal follow-up (58-62). Infants should be followed until at least 24 months of age, when a diagnosis of disabling or non-disabling cerebral palsy can ultimately be established (62).

Could assessment of fetal behaviour predict the future neurological development of children?

There is substantial evidence showing that many neurological problems in infants and children, from minor cerebral dysfunction to cerebral palsy, originate from the prenatal, rather than the perinatal or postnatal periods, raising the question of whether the prenatal assessment of fetal behaviour could predict the future neurological development of children. If we could answer this complex question, we could not only prepare parents and professionals for the delivery of a child with some form of disability but also provide information regarding the gestational age at which brain injury occurred, which could be important in medico-legal circumstances. In addition, findings on normal or abnormal fetal behaviour could also serve as a basis for investigations into possible future therapies.

With the introduction of KANET, we might believe that we are on the right path in fetal neurobehavioral assessment, but we cannot - and should not - be so bold at the moment as to say we can diagnose neurological disorders prenatally. The complexity of this problem is illustrated by the fact that the brain continues to develop intensively in the postnatal period as well, and we should not forget that the fetus grows in a different environment than an infant, mainly due to the lack of gravity (63).

We must be realistic and consider that even the clinical assessment of muscle tone, strength, and control of voluntary movements for early detection of infants at risk for cerebral palsy has been frustrating, because as many as 43% of 7-year-old children with cerebral palsy had a normal newborn neurological examination (64).

In addition to 3D and 4D ultrasound, MR imaging has also been investigated by various researchers as a diagnostic tool for assessing fetal behaviour. A study conducted at the Robert Steiner MRI Unit, Hammersmith Hospital, analysed the correlation between fetal motor behaviour, brain MR imaging, and postnatal outcome. Cine MR imaging was used to record sequences of fetal behaviour from 18 weeks of gestation until term in fetuses divided into two groups based on their normal and abnormal findings on standard brain MR imaging. The infants were monitored for four years to determine whether MR imaging of fetal motor function could predict postnatal neurodevelopment. This study showed that fetal behaviour observed by cine MR imaging correlated with the neuropathology identified by standard brain MR imaging and was predictive of future postnatal neurodevelopmental outcomes (65).

Some pathological fetal conditions, such as fetal growth restriction (FGR) caused by suboptimal placental function, are associated with altered brain development. During the third trimester, from 28 weeks of gestation onward, neurogenesis is completed, and at this stage, neuronal complexity increases primarily through axonal and dendritic growth accompanied by synaptogenesis. If placental function is reduced during this period, it can lead to the disturbance of the cerebral cortex morphology, affecting both white and grey matter, with the latter being affected more significantly (66). Considering this, we suggest that specific algorithms for fetuses at higher risk of neurodevelopmental disturbance should include more detailed in utero fetal behaviour monitoring and imaging to improve the prediction of adverse neurodevelopmental outcomes to which these fetuses are more susceptible. Another important point to keep in mind is that neuropaediatricians can directly evaluate the neonate, while obstetricians have only an indirect view inside the uterus when evaluating the fetus that is free from gravity and therefore able to perform more complex motor tasks than the neonate.

Conclusion

In conclusion, our preliminary work on the prenatal ultrasound evaluation of fetal neurobehavior, in correlation with long-term neuropediatric follow-up, appears promising in addressing whether 4D ultrasound-based prenatal assessment can predict postnatal neuromotor development in both low- and high-risk pregnancies. However, a scoring system such as KANET, although promising as a screening tool, should be interpreted with caution, as it is not yet a definitive predictor of future neurodevelopmental outcomes. Therefore, postnatal monitoring and close follow-up remain essential.

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