

Clinical Study of Fetal Neurobehavior by the Kurjak Antenatal Neurodevelopmental Test

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ABSTRACT

Fetal neurology is an evolving field in prenatal diagnosis and fetal medicine with great interest. The identification and diagnosis of brain damage prenatally has been a great challenge in obstetrics for many years. Investigations of the fetal behavior in comparison with morphological studies led to the conclusion that fetal behavioral patterns directly reflect developmental and maturational processes of fetal central nervous system (CNS). Four-dimensional ultrasound (4D US) has remarkably improved the assessment of the quality of fetal spontaneous movements, and enabled a better evaluation of fetal behavior. The assessment of normal neurobehavioral development by 4D US provided the opportunity to investigate functional characteristics of the fetus that could predict neurological developmental dysfunction. Some studies have already been carried out to evaluate this new methodology in the observation of the fetal behavior during different stages of gestation, in an attempt to better understand the relationships between the maturation of the CNS of the fetus and its implications on its behavior pattern. We present a review of literature on fetal behavior by 4D US.

Keywords: Fetal behavior, Fetal neurologic screening, Fetal neurology, Four-dimensional ultrasound, Prenatal brain impairment.

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INTRODUCTION

Fetal behavior can be described as any fetal action or reaction seen by US.¹ This fetal activity has been observed by

two-dimensional ultrasound (2D US) and many papers on fetal behavior assessed by 2D US have been published up to now.²⁻⁴ This method of investigation of fetal behavior has limitations, mainly because only the number of movements can be visualized, while the quality of fetal movements could not be assessed. More than this, complex facial movements could not be depicted by using only 2D US, which has been considered as a great disadvantage of 2D US.^{5,6} The development of 4D US has significantly increased the assessment of the quality of fetal movements and permitted better evaluation of fetal behavior compared with 2D US, especially in assessment of facial movements like sucking, yawning, blinking, smiling, and even crying.⁷⁻¹⁰ As a result, spontaneous fetal movements, as an expression of neural activity, could be used as a marker for assessment of fetal neurological status.¹¹⁻¹³ The evaluation of fetal behavior could give the opportunity to recognize the difference between normal and abnormal neurological development, and even an early diagnosis of different structural or functional CNS abnormalities.¹¹ It has been proven by many studies that most of the neurological disorders like cerebral palsy (CP) develop prenatally, while postnatal and intrapartum factors are not that important.^{14,15} Analysis of fetal behavior by 4D US should be standardized as any other clinical test.^{13,16} Kurjak et al¹⁷ in the field of perinatal neurology have proposed a prenatal screening test for assessment of motor activity called Kurjak antenatal neurodevelopmental test (KANET). This test is a continuation of 2D US assessment of fetal behavior using new 4D US technique and introduces some postnatal signs which have been part of postnatal neurological assessment developed by Amiel-Tison neurological assessment at term (ATNAT).¹⁸⁻²⁰ This was a new approach to the assessment of fetal neurological status enabling longitudinal follow-up of fetal behavior throughout gestation, making the clear distinction between neurologically normal, borderline, and abnormal fetuses.¹⁹⁻²³

The aim of this review is to evaluate the contribution of 4D US in the assessment of fetal neurobehavior.

FOUR-DIMENSIONAL ULTRASOUND US EVALUATION OF FETAL BEHAVIOR

For a long time, the only approach for the follow-up of fetal well-being was the maternal sensation of fetal movements and obstetric auscultation of their heartbeats. After the appearance of real-time US, there was

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Fig. 1: Three-dimensional image in frontal view



Fig. 2: Two-dimensional image in frontal view



Fig. 3: Three-dimensional image in profile view



Fig. 4: Two-dimensional image in profile view

a revolutionary change in the assessment of fetal well-being.²⁴ Undoubtedly, one of the most amazing advancements in ultrasonography was the 4D technology.^{25,26} During the last decade, 4D sonography has encouraged studies on fetal behavior with more persuasive imaging data than those obtained by 2D conventional US and even other nonultrasonic methods.⁹

The first embryonic movements begin at the seventh to eighth week of gestation. Motor activity is clearly recognizable, consisting of several movement patterns between the 8th and 9th week and can be observable by 2D US.^{23,25,27-29} Prechtl¹¹ stated that these are gross movements, involving the whole body. But 4D US has enhanced the investigation of the quality of spontaneous fetal movements and implementing a better evaluation of fetal behavior in comparison with 2D US.^{7,9,10,28,30-34}

The majority of sequences of extension and flexion of the legs and arms are complex and may be better assessed with the 4D US (Figs 1 to 4). From 10 weeks onward, head anteflexion, retroflexion, and rotation could easily be observed by this new method,^{4,17} as well as facial



Fig. 5: Mouth opening

movements, swallowing, mouth opening, and yawning (Figs 5 and 6). Moreover, 4D US seems to be the preferred approach for detecting sophisticated movements, such as overlapped rotations and changes in direction. These components make the movements fluent and elegant and



Fig. 6: Yawning



Fig. 7: Crying



Fig. 8: Tongue expulsion



Fig. 9: Smiling

create the impression of complexity and variability, which can be depicted only by 4D US.³⁵

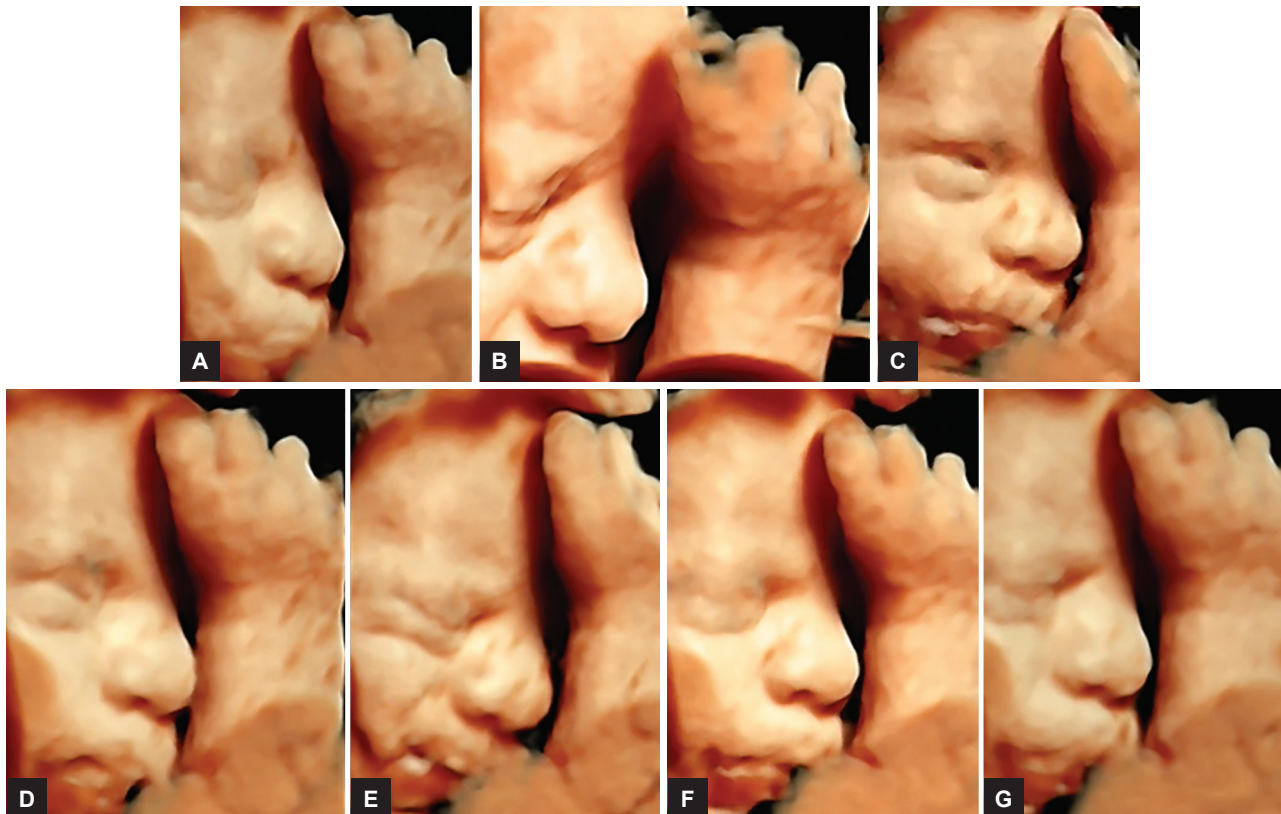
The second half of pregnancy is characterized by the organization of fetal movement patterns and increase in complexity of movements.¹³ Not only the movements but the periods of rest–activity cycles become recognizable.³⁶

Besides, the surface rendering mode, seen only in 4D US, improves the visualization of fetal face and opens the possibility of assessment of a full range of facial expressions, including smiling, crying, scowling, and eyelid movements (Figs 7 to 9).^{37–39} It is not possible to see these complex facial movements using real-time 2D US. Furthermore, 4D US combines the advantage of the spatial imaging of the fetal face with the addition of time, allowing detailed imaging of each fetal facial movement. Now we know that the observation of facial expression may be of scientific and diagnostic value (Fig. 10).⁴⁰

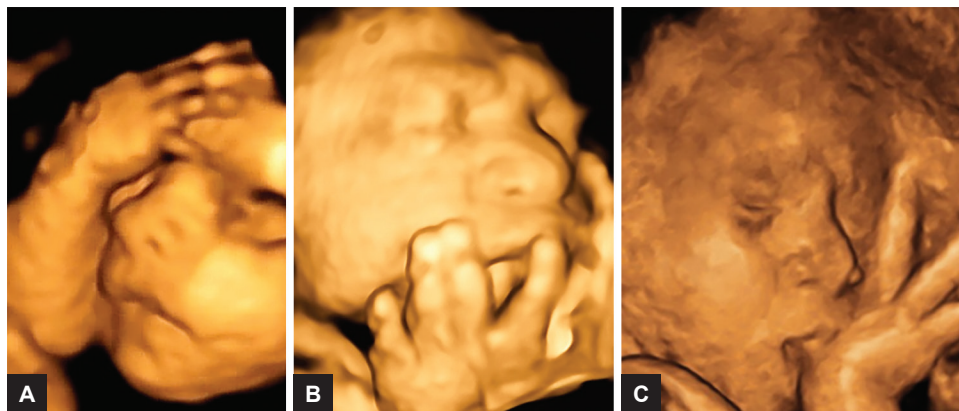
For many years, obstetricians were concentrated mostly on the number of fetal movements which was considered as an indicator of fetal well-being. Later studies

have shown that a count of movements is a unsatisfactory indicator of brain activity, mainly due to the great intra- and inter-individual variability and the large variations between normal and abnormal, which makes this method clinically useless.⁴¹ Instead, changes of the elegance and fluency, as well as the variability and fluctuation of intensity and speed of general movements (GMs) were shown to be the best indicator of impaired brain activity, and they are considered to be the first sign of a supra-spinal control of the motor activity.⁴² It became unmistakable that the qualitative changes in GMs of both the fetus and the neonate anticipate quantitative changes when the integrity of the nervous system is damaged (Fig. 11).⁴³

Four-dimensional ultrasound emerged as a practical way for the evaluation of both brain function and structure. The analysis of fetal activity *in utero* by 4D US may allow early diagnosis of fetal neurological impairment.^{9,44,45} A group of researchers from Zagreb, Croatia, led by Asim Kurjak, has had a great experience using 4D US in the assessment of fetal behavior.^{17,29,46,47} Relying on their own



Figs 10A to G: Sequences of different facial expressions by 4D US



Figs 11A to C: Complex and sophisticated fetal movements

experiences in the field of fetal and neonatal neurology, they suggested a new scoring system for evaluation of fetal behavior based on the prenatal assessment of fetal motor activity and called it KANET.¹⁷ This new test shows a relationship between fetal behavior and neurodevelopmental processes in different periods of pregnancy, making it possible to distinguish between normal and abnormal brain development.¹⁸ The KANET has a great potential because is the first test that evaluates the functional development of the fetal CNS using 4D US in a structured and systematic way.¹⁷ This test used a pioneering idea by using 4D US to assess fetal movements and facial expressions, similar to postnatal neonatal neurological tests, such as ATNAT and Prechtl's GMs.^{17,21,48-52} The KANET has the capacity to

detect and differentiate normal, borderline, and abnormal fetal behavior in high- and low-risk pregnancies and it can, consequently, become a relevant diagnostic tool for fetal neurological assessment. In order to make the test reproducible and easy to apply for fetal medicine specialists, its standardization was proposed in 2010 during the International Symposium on Fetal Neurology in Osaka, Japan, since then this has been widely accepted.⁵³ In 2014, a new consensus statement on the KANET was created in Bucharest during the 4th International Fetal Neurology Conference, with the conclusion that KANET is ready for use in everyday clinical practice for normal and high-risk fetuses.⁵⁴

So far, KANET has proven its usefulness in standardization of neurobehavioral assessment, with the potential

for prenatal detection of fetuses with severe neurological dysfunction. Many studies using this method on fetal behavior have been conducted and published from different centers proving that conclusions about the use of KANET in everyday clinical practice have been accurately stated.^{27,43,52-71} However, more research is needed in order to introduce the KANET as a screening test. Components of KANET and its resulting scores are shown elsewhere.⁷²

CONCLUSION

As can be understood from this review, the development of US, especially the 4D technology, has enabled a unique insight into the neurological development of the fetus with the purpose of determining whether this tool could serve as a prenatal diagnostic method to detect prenatal neurological disorders which may result in development of CP. In addition, 4D US may become a method to assess fetal well-being.^{9,17} In the last three decades, there were several attempts to create a diagnostic test for evaluation of fetal behavior. The tests were different, but none of them were implemented into daily clinical use.^{2-4,73} With a multidisciplinary approach, a prenatal neurologic screening test based on neurological 4D technology was proposed. KANET is the first prenatal neurological test based on the 4D US technique, whose preliminary results are encouraging.^{17,70,74-76} Results of numerous studies using KANET are promising and stimulating. However, all researchers involved in the estimation of fetal behavior using KANET agree that further studies in a large population with long-term follow-up are required and it is of utmost importance to continue the long-term follow-up of newborns who obtained borderline or abnormal scores after prenatal KANET assessment.

The development of 4D US has significantly improved the assessment of the quality of fetal movements and enabled a better evaluation of fetal behavior in comparison with 2D US. It is our belief that recent data obtained by 4D sonography are stimulating and might result in a more effective strategy to assess neurodevelopment before birth.

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