REVIEW ARTICLE

4D in Functional Studies of the Fetus

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ABSTRACT

Assessing fetal neurobehavior has been a great challenge since the first steps of fetal medicine. The introduction of three-dimensional (3D) and four-dimensional (4D) ultrasound technology offered the opportunity to not only examine the fetus anatomically with explicit detail but also to observe the fetus directly and examine its behavior in real time, as one would examine a neonate. The development of the fetal central nervous system (CNS) follows a very structured path and these developmental steps are reflected by the behavior of the fetus *in utero* for each corresponding week or trimester. Which fetal movements develop during each month and which fetal behavioral patterns are normal or abnormal have been identified. In the same way that a neonatologist can understand by its motoric function if a neonate is premature or not. Similarly, we can now understand which fetal movements-behavioral pattern corresponds to each trimester of pregnancy. Structural and functional impairment of the brain can develop at any time during pregnancy. The structural anomaly of the brain is much easier to detect than functional. Delayed diagnosis of a neurological problem will make the possibility of timely treatment is rather doubtful. It is clear that the assessment of fetal neurological status is of utmost importance, and should be practiced both as a screening test for low- and high-risk pregnancies. The most complete method so far for the assessment of fetal neurobehavior, that relays on real time observation of the fetal behavior with 4D ultrasound and its efficacy has been tested through many multicentric studies is Kurjak's antenatal neurodevelopmental test (KANET). KANET has been introduced in everyday clinical practice and aims to assess the fetal behavior in a similar way that a neonate is assessed postnatally, through 4D ultrasound technology. The KANET has been introduced into systematic training and already ultrasound specialists have been certified to perform this test. Hopefully, application of KANET on larger populations, both high and low risk, will give more knowledge regarding early detection of fetuses at risk for neurological impairment, to allow accurate diagnosis prenatally, and as a consequence prompt intervention that could improve the outcome of some of these neonates postnatally.

Keywords: Fetal behavior, Four-dimensional ultrasonography, KANET test, Neurodevelopmental impairment.

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INTRODUCTION

Assessing fetal neurobehavior has been a great challenge since the first steps of fetal medicine. The introduction of 3D and 4D ultrasound technology offered the opportunity to not only examine the fetus anatomically with explicit detail but also to observe directly the fetus and examine its behavior in real time, as one would examine a neonate.[1-3] The development of the fetal CNS follows a very structured path and these developmental steps are reflected by the behavior of the fetus in utero for each corresponding week or trimester. Which fetal movements develop during each month and which fetal behavioral patterns are normal or abnormal have been identified. In the same way that a neonatologist can understand by its motoric function if a neonate is premature or not. Similarly, we can now understand which fetal movements-behavioral pattern corresponds to each trimester of pregnancy.[4] On the other hand, pregnancy is a long period and there is always a possibility that different factors or incidents can affect this very sensitive and delicate course of fetal brain development. And if this incidence causes an anatomical abnormality to the fetal CNS which can be detected prenatally by ultrasound then a neurological impairment may be suspected, but if an anatomical abnormality is not seen, then a neurological impairment of the fetus will not be suspected and of course will be only diagnosed sometime after birth, and possibly wrongly attributed to intrapartum or even postpartum events.

What is more, a delayed diagnosis of a neurological problem will make the possibility of treating it rather impossible. So what is needed for such cases is a timely diagnosis which will also offer the chance of early treatment–intervention which would aim to a better outcome of these fetuses. It is clear that the assessment of fetal neurological status is of outmost importance, and should be practiced both as a screening test for low-risk pregnancies, but also cases that there is suspicion of neurological impairment prenatally.[4-6] The most complete method so far for the assessment of fetal neurobehavior, that relays on real-time observation of the fetal behavior with 4D ultrasound and its efficacy

has been tested through many multicentric studies is Kurjak's antenatal neurodevelopmental test (KANET). KANET has been introduced in everyday clinical practice and aims to assess the fetal behavior in a similar way that a neonate is assessed postnatally, through 4D ultrasound technology.

Assessment of Fetal Behavior through the Years

When 2D ultrasound was introduced into clinical practice the fetal movements were observed to draw conclusions regarding the fetal well being and the fetal behavior.[7-10] Of course, this method is very subjective and inadequate to assess fetal behavior as a whole. The method that offered a complete and real time assessment of the fetus and not just information on isolated limb movements was 4D ultrasonography.[11-14] 4D gives the opportunity to examine not only gross fetal movements but also small details such as finger movements, facial expressions, eye blinking, etc. details that are not visible by applying 2D ultrasound.[15-17]

KANET used the advantages of 4D technology and succeeded to assess the fetus in the same way that neonates are assessed neurologically after birth by neonatologists.[18-21] Apart from the classical fetal movements, KANET through 4D ultrasound introduced all the markers that are used for postnatal neurological assessment according to the Amiel-Tison neurological assessment at term (ATNAT) test.[19,22] So it also includes the cranial sutures, head circumference and finger movements, detection of neurological thumb (adducted thumb in the clenched feast) and more specifically it includes: isolated head anteflexion, overlapping cranial sutures, head circumference, isolated eye blinking, facial alterations, mouth opening (yawning or mouthing), isolated hand and leg movements and thumb position, gestalt perception of general movements (overall perception of the body and limb movements with their qualitative assessment) (Figs 1 to 3). KANET consists of eight parameters, and its aim is to evaluate fetal motoric

Figs 1A to C: Mouthing as part of the assessment of fetal neurobehavior
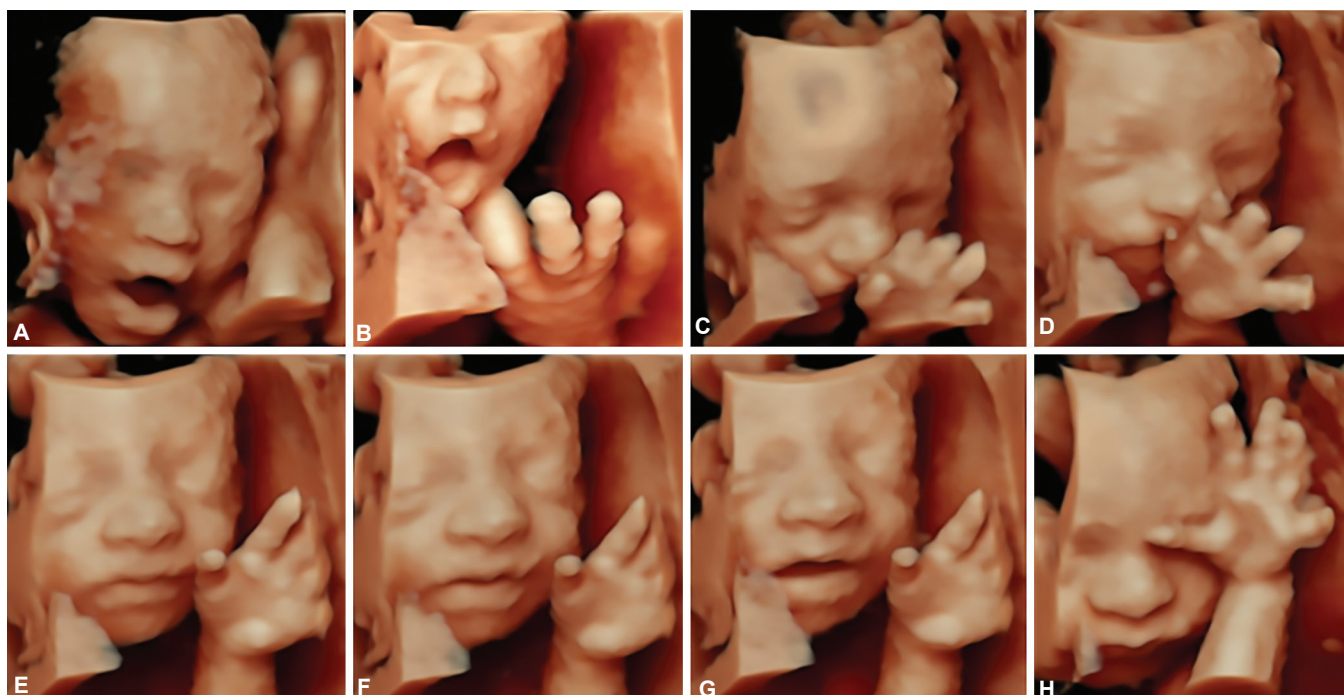
Figs 2A to H: Parameters of KANET test: mouthing, yawning, hand movements
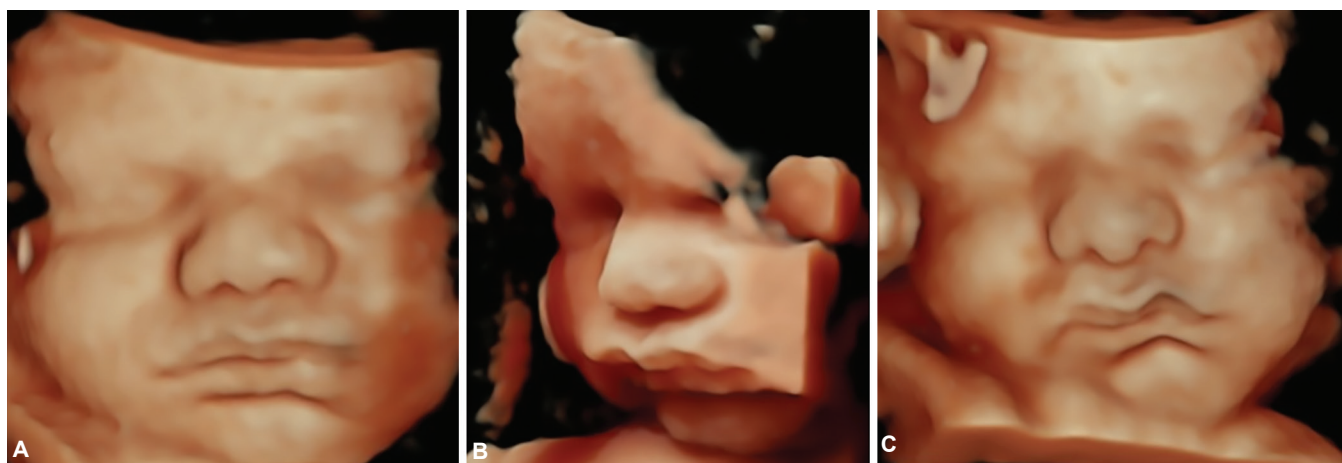
Fig. 3: Facial alterations and grimacing

activity and through that to assess the development and integrity of the fetal nervous system (Table 1).

The maturation of fetal CNS and the transition from fetal to neonatal behavior is a very smooth process, with all movements that are present in postnatal life have been documented with 4D ultrasound in fetal life (with the exception of Moro's reflex, which is not present in fetuses) and that is exactly what KANET has managed to demonstrate and succeed.[23]

KANET is already a standardized method, with good reproducibility as proved by many multicentric studies. Training modules on KANET have been formed, and the training centers show that the learning curve is very reasonable for physicians and medical staff with a good ultrasound background.[24] Regarding the gestational age at which KANET should be performed, it has been decided that the best period is the 3rd trimester of pregnancy, and particularly after 28 weeks. The duration of KANET should be around 15–20 minutes and should be preferably performed at periods that the fetus is awake. If this is not possible, as it is not always easy to predict when a fetus will be active-awake, and the fetus is quiet for a prolonged period f time KANET should be repeated within 30 minutes or the following day, at a minimum interval of 14–16 hours.

When KANET is abnormal, or the score is borderline, it is proposed that the test is repeated every two weeks until delivery. Very important features are facial movements and eye blinking—"the face is the mirror of the brain". The overall number of movements must be documented in all cases.[22,25]

Examiners who apply KANET should have proper training, and adequate experience in low and high-risk pregnancies. Interobserver and intraobserver variability have to be documented. The suggestion regarding the ultrasonographic machines used is to have a frame rate of at least 24 volumes/second. The results of KANET are divided into 3 groups:

- Abnormal, when the score is 0–5,
- Borderline for a score from 6 to 13 and finally
- Normal for a score 14–20 (Table 2).

A 2-year follow-up should be available and documented for all fetuses that KANET has been applied, to draw safe conclusions.
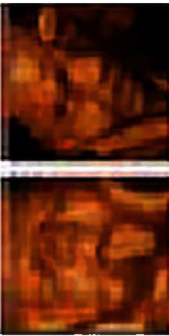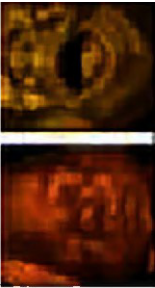
KANET has been introduced in training and has been calculated that the number of KANET needed to be performed by an experienced ultrasound specialist to be familiar to assess a fetus with the 4D US in 20 minutes is 80. The success rate of the test ranges from 91 to 95% and further study of each parameter reviled a success rate for the assessment of particular signs of 88% for isolated eye blinking and 100% for mouth opening and isolated leg movement. KANET has almost 100% negative predictive value, interobserver variability was satisfactory with the lowest being for the facial expression (K = 0.68) and highest for the finger movements (K = 0.84).

Clinical Results of KANET (Table 3)

The first application of KANET was on growth-restricted fetuses,[26] where mainly facial expressions and body movements were studied and what was noticed was a decreased behavioral activity in the IUGR fetuses compared to normal growth cases. The study that followed was the first with complete neurologic postnatal assessment for all studied fetuses, and according to the criteria, they used neonates were divided into three groups: normal, mildly or moderately abnormal and abnormal. According to these groups the formation of the first KANET scoring system was decided which was as follows: 14–20 (normal), 5–13 (mildly or moderately abnormal) and 0–5 (abnormal) and based on this scoring system were all the following studies designed.[12,27]

The first study with a large number of high-risk pregnancies identified 32 fetuses at neurological risk: they identified 7 cases with the abnormal score and 25 with a borderline KANET score. There were also 11 cases which

Table 1: Parameters of standardized KANET[24]

Sign	Score			Sign score
	0	1	2	
Isolated head anteflexion	Abrupt	Small range (0–3 times of movements)	Variable in full range, many alternation(>3 times of movements)	
Cranial sutures and head circumference	Overlapping of cranial sutures	Normal cranial sutures with measurement of HC according to GA	Normal cranial sutures with normal measurement of HC below or above the normal limit (-2 SD) according to GA	
Isolated eye blinking	Not present		Fluency (>5 times of blinking)	
Facial alteration (grimace or tongue expulsion)	Not fluent (1–5 times of blinking)			
Mouth opening (yawning or mouthing)	Not present	Not fluent (1–5 times of alteration)		

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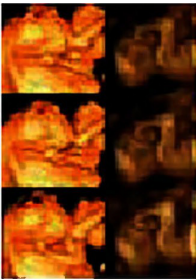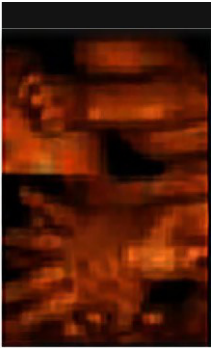
Sign	Score			Sign score
	0	1	2	
Isolated leg movement	Cramped	Poor repertoire or small in range (0–5 times of movement)	Variable in full range, many alternation (> 5 times of movements)	
Isolated hand movement	Cramped or abrupt	Poor repertoire or small in range (0–5 times of movement)	Variable in full range, many alternation (> 5 times of movements)	
or				
Hand to face movements				
Fingers movements	Unilateral or bilateral clenched fist, (neurological thumb)	Cramped invariable finger movements	Smooth and complex, variable finger movements	
Gestalt perception of GMs	Definitely abnormal	Borderline	Normal	
			Total score	

Table 2: KANET scoring system[24]

Total Score	Interpretation
0–5	Abnormal
6–9	Bordeline
10–16	Normal

either died in utero or had a termination of pregnancy and all of these cases had an abnormal KANET score. The seven remaining neonates with abnormal KANET were followed up postnatally at 10 weeks of neonatal life and 3 had confirmed pathological ATNAT score. These 3 cases included a neonate with arthrogryposis, a neonate with cerebellar vermian complete aplasia and 1 case with a history of cerebral palsy in a previous pregnancy. Out of the parameters that KANET uses, facial expressions appeared to be most pathological–the fetal faces were characterized as "masks" by the authors, due to lack of expressions on 4D ultrasound. The remaining 4 pathological KANET cases had a normal postnatal assessment. These 4 cases, however, had complications of pregnancy: 1 case with ventriculomegaly, 1 case with preeclampsia, 1 case with maternal thrombophilia and 1 case with oligohydramnios. From the 25 cases diagnosed with borderline KANET result, 22 neonates showed a borderline ATNAT score and were followed up, while the 3 remaining cases showed normal ATNAT result. An interesting paper was the one that studied a case of a fetus with prenatally diagnosed acrania. The authors studied the fetal behavior and managed to document how it altered from 20 weeks of gestation onward. It was noticed that as the pregnancy progressed and the control center of motoric activity shifted from the lower to the upper part, KANET score was decreasing respectively, suggesting that neurological damage in later pregnancy is possible.[28]

A study with[29] 226 cases, including different study populations, identified 3 cases with pathological KANET score. All 3 cases had chromosomal abnormalities and all 3 of them postnatally also had an abnormal ATNAT score. Scores from antenatal KANET and postnatal ATNAT were compared between low and high-risk groups, and showed differences between them, for 8 out of the 10 parameters. These included: head anteflexion, eye blinking, facial expressions–grimacing, tongue expulsion, mouth movements such as yawning, jawing, swallowing– isolated hand movements, hand to face movements, fist and finger movements, and general movements.

The comparison of the two tests revealed a correlation between them, proving that the neonatal exam (ATNAT) was a satisfactory confirmation of the prenatal ultrasound examination (KANET), stating that KANET could offer useful information about the neurological status of the fetus and can be applied in clinical practice.

One of the largest studies regarding KANET,[30] including 620 cases, of both low and high-risk populations (100 low risk and 520 high risk cases) showed differences in the scores between the two groups. What was interesting in this study was that most abnormal cases were noted from pregnancies with the previous history of CP (23.8%) and that most borderline scores were noted in cases with possible chorioamnionitis (56.4%). The parameters of KANET that were more notably different between the two groups were: overlapping cranial sutures, head circumference, isolated eye blinking, facial expressions, mouth movements, isolated hand movements, isolated leg movements, hand to face movements, finger movements, and general movements. This study confirmed the relationship of pathological KANET with an increased risk of perinatal mortality and neurological impairment and showed that the results can be confirmed and are reproducible postnatally.

A recent study with a complete follow-up[31] postnatally up to 3 months of life, with complete postnatal documentation in all cases and showed that a normal KANET score is very reassuring of a good neonatal outcome, confirming the consistency of prenatal and postnatal assessment. Understanding the evolution of fetal movements by 4D ultrasound throughout pregnancy, and how these movements reflect the development and integrity of the fetal nervous system was a great challenge. What was shown was that during the first weeks of pregnancy the development of the frequency and the complexity of fetal movements is more important, while during the second trimester the variation of fetal movements develop, with more detailed movements (facial expressions and eye blinking) appearing at the end of this trimester. Finally, at the end of the third trimester, the number of fetal movements decline as a result of the increase of fetal rest periods, due to fetal cerebral maturation, and this is something that most pregnant women notice near term.[12-14] A very interesting study which tried to shed some light on the clinical dilemmas caused by the prenatal diagnosis of ventriculomegaly, compared fetuses with ventriculomegaly[32] with apparently low-risk fetuses (normal CNS appearance on ultrasound examination). A significant difference was noted between the two groups, with the KANET score decreasing as the degree of ventriculomegaly was increasing. For isolated cases of mild or moderate ventriculomegaly, no pathological KANET scores were noted, and postnatal evaluation confirmed the prenatal KANET, offering valuable information for the more complete assessment of these fetuses and better counseling regarding their prognosis.

Abo-Yaqoub et al.[33] aimed to study how practical is to apply 4D ultrasonography for the assessment of fetal neurobehavior and also how useful it is for the prediction of

Table 3: Application of KANET for the detection of neurological impairment

Author	Year	Study	Study design	Study population	Indication	No	GA (weeks)	Time (minutes)	Result	Summary
Kurjak et al.[27]	2008	Cohort	Retrospective	High risk	Multiple	220	20–36	30	Positive	Introduction of scoring system for antenatal assessment of fetal neurobehavior
Kurjak et al.[28]	2010	Multi-center	Prospective	High risk	Multiple	288	20–38	30	Positive	First proof of prognostic value of KANET for detection of neurological impairment in fetuses. Correlated severe fetal anatomical anomalies, with neurological damage.
Miskovic et al.[29]	2010	Cohort	Prospective	High risk	Multiple	226	20–36	30	Positive	Comparison of prenatal (KANET) and postnatal (ATNAT) findings. KANET differences when applied to high and low risk populations
Talic et al.[30]	2011	Multi-center Cohort	Prospective	High risk	Multiple	620	26–38	15–20	Positive	KANET's significance was proved in distinguishing normal from borderline and abnormal cases. Abnormal KANET was predictive of both intrauterine and neonatal death.
Talic et al.[14]	2011	Multi-center Cohort	Prospective	High risk	Ventriculo-megaly	240	32–36	10–15	Positive	KANET was applied to cases with ventriculomegaly and compared to low risk cases. KANET score was worse as the degree of ventriculomegaly increased, particularly when combined with other anomalies
Honemeyer et al.[31]	2011	Cohort	Prospective	Unselected	Unselected	100	28–38	N/A	Positive	KANET showed a very good negative predictive value, reassuring of a good neurological outcome
Lebit et al.[27]	2011	Cohort	Prospective	Low risk	Normal 2D examination	144	7–38	15–20	Positive	Specific neurobehavioral patterns were described for each stage of pregnancy was.
Abo-Yaqoub et al.[33]	2012	Cohort	Prospective	High risk	Multiple	80	20–38	15–20	Positive	Differences in KANET scores between high and low-risk cases were shown. All abnormal KANET scores had postnatal confirmation with an abnormal neurological assessment.
Vladareanu et al.[34]	2012	Cohort	Prospective	High risk	Multiple	196	24–38	N/A	Positive	Most fetuses with normal KANET → low-risk, those with borderline → IUGR fetuses with increased MCA RI and most fetuses with abnormal KANET → threatened PTD with PPROM. Differences in fetal movements were identified between the 2 groups. For normal pregnancies → 93,4% of fetuses had normal score, for high risk pregnancies → 78,5% of fetuses had a normal score.
Honemeyer et al.[35]	2012	Cohort	Prospective	High and low risk	Multiple	56	28–38	30 Max	Positive	Introduction of the average KANET score (combination of the mean value of KANET scores throughout pregnancy). Relationship of fetal diurnal rhythm with the KANET score.

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Author	Year	Study	Study design	Study population	Indication	No	GA (weeks)	Time (minutes)	Result	Summary
Kurjak et al.[45]	2013	Cohort	Prospective	High and low risk	Multiple	869	28–38	20	Positive	Statistical differences regarding the distribution of normal, abnormal, and borderline results of KANET between low-risk and high-risk groups found. Fetal behavior was significantly different between the normal group and the high risk subgroups.
Predojevic et al.[46]	2014	Case study	Prospective	High risk	IUGR	5	31–39	30	Positive	KANET could recognize pathologic and borderline behavior in IUGR fetuses with or without blood flow redistribution. Combined assessment of hemodynamic and motoric parameters could enable in better diagnosis and consultation
Athanasiadis et al.[37]	2013	Cohort	Prospective	Unselected (High and low risk)	Multiple (IUGR, PET, GDM)	152	2nd and 3rd trimesters	N/A	Positive	The neurodevelopmental trimesterscore was higher in the low risk in comparison to that of high risk group (p <0.0004). The KANET results in the diabetes subgroup was higher when compared to that of the IUGR and the preeclampsia subgroup (p = 0.0001)
Neto et al.[38]	2014	Cohort	Prospective	High and low risk	Multiple	51	3rd trimester	20	Positive	Statistical significance between high- and low-risk cases. All abnormal results derived from high-risk cases
Hanaoka et al.[39]	2015	Cohort	Prospective	Mixed (Asian and Caucasian)	Multiple	167	3rd trimester	N/A	Positive	Differences in pattern movements in different racial groups, suggesting that ethnicity should be considered when performing KANET
Hata et al.[47]	2016	Cohort	Prospective	Mixed (male vs female)	Multiple	112	3rd trimester	20	NO	No difference in fetal behavior between male and female fetuses in the third trimester of pregnancy. These results suggest that 4D ultrasound study examining fetal behavior does not need to consider the factor of fetal sex.
Antsaklis et al.[48]	2017	Cohort	Prospective	High and Low Risk (diabetic vs non-diabetic)	Multiple	80	3rd trimester	20	Positive	Differences in the fetal behavior between diabetic and non-diabetic fetuses were shown, and also the specific parameters—movements that were different between the two groups were identified

Abbreviations: KANET: Kurjak's antenatal neurological test; No number of patients; IUGR, intrauterine growth restriction; MCA, middle cerebral artery; PTD, preterm delivery; PPROM, preterm premature rupture of membranes; PET, preeclampsia; GDM,,gestational diabetes mellitus)

neurological impairment. Their results showed the agreement of prenatal scores with the postnatal assessment. The parameters that were significantly different between the two groups were isolated head anteflexion, isolated eye blinking, facial expressions, mouth movements, isolated hand movements hand-to-face movements, finger movements, and general movements. Regarding isolated leg movements and cranial sutures, the difference was not statistically significant.

Vladareanu et al.[34] noted that the majority of normal KANET scores derived from low-risk populations that they studied, while the majority of cases with borderline or pathological KANET scores derived from the high-risk groups and in some cases were related to abnormal values of Doppler studies in IUGR fetuses. The authors concluded that KANET can be useful for the detection of neurological impairment which could become obvious during the antenatal or postnatal period.

The average KANET score was introduced for fetuses who had more than one assessments to have a more complete picture of the behavior of these fetuses. The average KANET score derived from the mean calculation of KANET scores for each fetus throughout pregnancy since these fetuses had more than one KANET assessments. What was new from this study was the association of KANET score with fetal diurnal rhythm. For the high-risk group, 89% of the borderline scores were recorded at times that the mothers characterized them as active periods, compared with 33.3% respectively in the low-risk pregnancies.[35]

Other studies[36,37] confirmed the feasibility of neurodevelopment assessment by 4D ultrasound and showed further evidence that KANET test is useful in early identification of fetuses prone to neurological impairment.

What was also important was to compare all parameters of KANET between high and low-risk pregnancies and observe differences in fetal behavior between them. For pathological KANET score 5 out of 8 parameters where significant different: isolated head anteflexion, cranial sutures, and head circumference, isolated hand movement or hand to face movements, isolated leg movement and fingers movements.[38] Further results showed that only high-risk patients had abnormal scores (8.5%) while comparing high and low-risk groups it was noticed that 80.6% of high-risk patients had borderline results while 85.3% of low-risk patients were normal, both being statistically significant. For abnormal KANET results (score between 0 and 5), some were related to pregnancy complications (preeclampsia, threatened preterm labor and drug abuse) and some were related to fetal condition (trisomies 13, 18 and 21 and intrauterine growth restriction).

When comparing Caucasian to Asian populations to check for ethnic differences, the total KANET score was normal in both populations, but there was a difference noted in total KANET scores between these two populations. When individual KANET parameters were compared, significant differences were observed in four fetal movements (isolated head anteflexion, isolated eye blinking, facial alteration or mouth opening, and isolated leg movement). No significant differences were noted in the four other parameters (cranial suture and head circumference, isolated hand movement or hand to face movements, fingers movements, and gestalt of general movements), showing that ethnicity is a parameter that should be considered when evaluating fetal behavior, especially during the assessment of fetal facial expressions. The authors concluded that although there was a difference in the total KANET score between Asian and Caucasian populations, all the scores in both groups were within normal range proving that ethnical differences in fetal behavior do not affect the total KANET score, but close follow-up should be continued in some borderline cases.[39]

Unpublished data from Greece, from 655 singleton pregnancies, showed that KANET is a method which is feasible in everyday clinical practice, with a success rate of 95% and a very low negative predictive value. For the cases that KANET could not be completed, the reason was severe oligohydramnios, fibroid uterus (difficult imaging), very increased BMI and a case that due to vasovagal reaction-supine hypotensive syndrome ultrasound examination could not be completed. From the 655 cases, 1712 KANET were performed from only two operators, and the interobserver variability was calculated showing adequate results for all parameters, with the lowest being for facial alterations (k-value = 0.68) and the highest for finger movements (k-value = 0.84). This study was primarily designed to compare the neurological status of pregnancies complicated by diabetes, compared to low-risk pregnancies and it did show that there was a difference between the fetal neurobehavior of these two groups, with the diabetic pregnancies having lower scores.[40]

DISCUSSION

One of the greatest challenges in perinatal medicine is the assessment of fetal neurobehavior and detection of fetal neurological impairment in utero. KANET is the first method that applied 4D ultrasound for the assessment of the fetus in the same way that a neonate is assessed neurologically after birth by neonatologists and it appears to be a strong diagnostic method for the detection of neurological impairment and for the assessment of fetal neurobehavior, conditions that were inaccessible with the traditional prenatal diagnostic methods used so far.[23] Studies have proved the validity of this method,[13,41,42] its applicability in everyday clinical practice, especially for

high-risk cases, how and by whom it should be performed and what is the value of the result of KANET and how it should be managed. Diagnosis of neurological impairment prenatally is very difficult and usually, all these diagnoses are made postnatally, even months or years after delivery.

What is more neurological conditions, such as cerebral palsy are not adequately understood and falsely attributed to incidents during labor, although it has been proven that the majority of CP cases originate sometime during in utero life and are not related to intrapartum events. All these things lead to delayed diagnosis of neurological conditions. The later a neurological impairment is diagnosed the less the possibility of an effective intervention. It would be extremely challenging to have a timely diagnosis of such conditions, even during in utero life, to increase the possibility of an effective intervention or even treatment. KANET offers the possibility of prenatal detection of fetuses at risk for neurological problems, offering the possibility of even an in the utero intervention or at least an early postpartum intervention.[43] The earliest physiotherapy is commenced and intervention programs are applied in neonates that are born prematurely or with neurological problems the better the neurodevelopmental outcome of these neonates, with the cognitive benefits persisting into preschool age. KANET appears to be able to offer this advantage of early identification of these fetuses with neurological problems, so that they could be put under treatment as early as possible, aiming to a better outcome.[43,44]

What is more, the explicitly detailed pictures obtained by the new ultrasound machines but also the advanced techniques of molecular genetics, many times brings us, as ultrasound specialists, across findings (anatomical and chromosomal) of uncertain clinical significance and prognosis, especially regarding the neurological integrity of the fetus.[45-47] A method like KANET offers a more comprehensive diagnostic approach to such dilemmas and hopefully in the near future with more data, we could form a complete neurosonobehavioral assessment of the fetus and more complete counseling of these couples.[48]

KANET has currently been introduced in everyday clinical practice by many centers for the assessment of fetal neurobehavior of not only high-risk cases, but also low-risk pregnancies. Studies show that the sensitivity and specificity of the test are satisfactory, as are the positive and negative predictive values and the inter- and intraobserver variability of this method. The KANET has been introduced into systematical training and already ultrasound specialists have been certified to perform this examination. Hopefully, application of KANET on larger populations, both high and low risk, will give more knowledge regarding early detection of fetuses at risk for neurological impairment, to allow accurate diagnosis prenatally, and as a consequence prompt intervention that could possibly improve the outcome of some of these neonates.

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