REVIEW ARTICLE

Four-dimensional Ultrasound Evaluation of Fetal Neurobehavioral Development

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Abstract

The introduction of four-dimensional (4D) ultrasound techniques would facilitate fetal behavioral assessment in three-dimensions in real-time during pregnancy. We describe the latest 4D sonographic studies on fetal behavior, especially fetal whole-body movements and facial expressions in all three trimesters of pregnancy and the continuation of behavior from the fetal to neonatal period. Moreover, we introduce a new scoring system (KANET, Kurjak Antenatal Neurological Test) for assessment of the fetal neurological status using 4D ultrasound. 4D ultrasound also facilitated the evaluation of inter-human contact in twin pregnancies *in utero*. This novel technique may assist in the evaluation of fetal behavior and inter-twin contact, and offer potential advantages relative to conventional two-dimensional ultrasound. 4D ultrasound should become an important modality in future research on fetal neurobehavioral development and the prenatal identification of severely brain-damaged infants. Further studies involving a larger sample size are needed to ascertain the role of 4D ultrasound in the evaluation of fetal neurobehavioral development.

Keywords: 4D ultrasound, Fetal neurobehavioral development, KANET score, Inter-twin contact, Singleton pregnancy, Twin pregnancy, Maternal-fetal bonding.

INTRODUCTION

Fetal behavioral patterns have been considered as indicators of fetal brain and central nervous system development.[1, 2] Numerous studies employing conventional two-dimensional (2D) ultrasound have shown that normally developing fetuses and fetuses at risk exhibit different patterns of behavior.[3-14] “Analysis of fetal behavior in comparison with morphological studies had led to a conclusion that fetal behavior patterns directly reflect developmental and maturational processes of the fetal central nervous system”.[15] Fetal facial expressions are controlled by the nuclei of facial nerves in the brain, and have also been investigated using 2D ultrasound.[16-19]

Three-dimensional (3D) ultrasound has the potential to provide improved visualization of fetal anatomic morphology compared with conventional 2D ultrasound imaging. The imaging capabilities of 3D ultrasound mean that it is superior to 2D ultrasound in assessing fetal movements.[20] With the appearance and development of four-dimensional (4D) ultrasound, fetal behavioral movements and the full range of facial expressions can be observed.[15, 21-31] The ease with which 4D ultrasound can be used to evaluate fetal movements might well promote a resurgence of interest in fetal behavior and responsiveness.[32]

“Fetal behavior, defined as any observable action or reaction to an external stimulus by the fetus, reflects the activity of the fetal central nervous system”.[2,11] “It is assumed that endogeneous motility and reactions towards stimuli are expressions of early neuromuscular development and act on the differentiation of the neuromuscular system”.[33] The existence of intra-pair stimulation *per se* in twin pregnancies could provide important clues regarding the functioning of tactile and proprioceptive sensitivity, which are impossible to ascertain with an intact single fetus.[34] Fetal behavior in twins is an interesting topic and a challenge for both anthropological and medical researchers.[33] However, fetal behavior in twin pregnancies has been insufficiently studied.[34] To the best of our knowledge, only five studies have investigated inter-twin contact in twin pregnancies using conventional 2D ultrasound during pregnancy.[33-37] However, 2D ultrasound requires frequent changes of the transducer to visualize both twins simultaneously; even then, complex contacts are not always fully demonstrated, and fetal movements outside the scanning plane cannot be displayed on the monitor because of the 2D character of real-time scanning.[38]

The present paper reviews 4D ultrasonographic studies on fetal behavior, inter-twin contact, and the impact of 3D/4D images on maternal-fetal bonding, and, on this basis, makes recommendations for future research on fetal neurobehavioral development.

FETAL NEUROBEHAVIORAL DEVELOPMENT

Local reflexes following the "total pattern" type of movements begin to appear at 7.5 weeks of gestation, and the ratio of axosomatic synapses increases rapidly between 11 and 13.5 weeks.[39] By 11.5 weeks of gestation, reflexes are elicited only at the proximal part of the body in the presence of simultaneous stimuli applied to differentiate reflexogenic sites, whereas, in fetuses older than 12.5 weeks, reflexes can be elicited at both distal and proximal sites.[40]

The reflex response changed from simple lateral head flexion to the progressive inclusion of movements of the upper limbs, trunk, rump, and lower limbs as the fetus advanced in age.[41] Opening of the mouth was seen from 10 weeks of gestation, reflex swallowing from 12 weeks, and the gag reflex from 18 weeks.[42] Humphrey.[43] assumed that reflex activities demonstrable before 20 weeks of gestation are executed through the mesencephalon, lower brain stem, and spinal cord.

Shawker et al,[3] employing conventional 2D ultrasound, showed an orderly developmental progression of fetal activity beginning with the beating of the fetal heart (7 weeks), progressing to fetal trunk movement (8 weeks), and culminating in individual fetal limb movement (9 weeks). Reinold[44] characterized the fetal movements between 9 and 12 weeks as involving rapid changes of position and posture; from 13 to 16 weeks there were more prolonged episodes of changes in position, as well as flexion and extension of the limbs; and fetuses from 17 to 20 weeks made jerky or slow flexion and extension movements of the trunk; sometimes accompanied by movement of a single limb. Boue et al[45] reported that healthy fetuses at 18 to 20 weeks performed slow, supple, and harmonious movements with isolated leg movements, in contrast to synchronized movements of the whole body with twitches and kicking, as frequently noted at 12 to 13 weeks. Moreover, some movement patterns occurred more frequently than others at 7 through 19 weeks of gestation.

"The quantitative and qualitative spectra of behavioral patterns expand rapidly as the pregnancy progresses, and the random movements of the fetal body, which are the earliest signs of fetal activity, change into the well-organized behavioral patterns, observed later in gestation".[15] Based on the investigation of typical spontaneous human movements by de Vries et al,[5] variations in "general movements" were evident. General movements were shown as "gross movements" involving the whole body, and lasted from a few seconds to a minute. These movements are fluent and elegant, and create an impression of complexity and variability.[46] General movements in sick preterm infants are reduced in elegance and fluency, as well as in the variability and fluctuation of the intensity and speed of motor performances, rather than a change in the incidence of distinct motor patterns.[46] Today, "it is becoming more and more evident that the qualitative changes in motor patterns of both the fetus and the preterm infant precede quantitative changes when the integrity of the central nervous system is damaged".[15,47]

With respect to fetal facial movements employing conventional 2D ultrasound, blinking is a normal fetal activity.[19] "The increased frequency of blinking activity associated with vibroacoustic stimulation may be considered a part of the normal startle reflex".[19] "In both normal and high-risk fetuses, yawning was represented by isolated mouthing movements, and considered to be slow opening of the mouth with simultaneous downward movements of the tongue".[17] Growth-restricted fetuses demonstrated yawning patterns consisting of isolated yawns similar to those seen in normal fetuses, and unusual bursts of fetal yawning activity were noted in anemic fetuses.[17]

FIRST AND EARLY SECOND TRIMESTERS

Visualization of the entire fetal body by 4D ultrasound is limited before 20 weeks of gestation (although it depends on the defined region of interest), because the viewing area is limited to that of the 4D probe (Figs 1 to 7). Kurjak et al[48] used 4D ultrasound to study 98 normal embryos and fetuses aged from 6 to 12 weeks, and found that body and limb movements can be visualized a week earlier than with 2D ultrasound. Three types of movement could be visualized in the first trimester: gross body movements between seven and eight weeks, limb movements after ten weeks, and complex limb movements after 11 weeks of gestation. In the recent study by these authors, 100 women with normal singleton pregnancies were recruited for longitudinal 4D ultrasonographic examination to evaluate fetal neuro-developmental parameters from the 7th to 14th week.[49] The measurements of 7 parameters (general movements, stretching, isolated arm movements, isolated leg movements, head retroflexion, head rotation, and head anteflexion) were correlated with the gestational age, and these parameters showed an increasing frequency of fetal movement during the first trimester (Fig. 8). However, the frequency of a startle pattern did not correlate with gestation in the first trimester

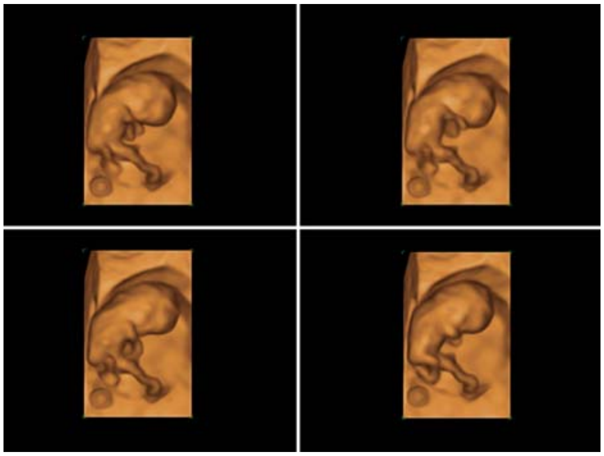


Fig. 1: Consecutive 4D sonographic observations of subtle fetal movements of the upper and lower extremities at 9 weeks and 5 days of gestation

Fig. 2: Trunk movements in a 10-week fetus

Fig. 3: Jumping movements in a 10-week fetus

Fig. 4: Consecutive 4D sonographic observations of fetal movements of the head and upper extremities at 11 weeks' gestation

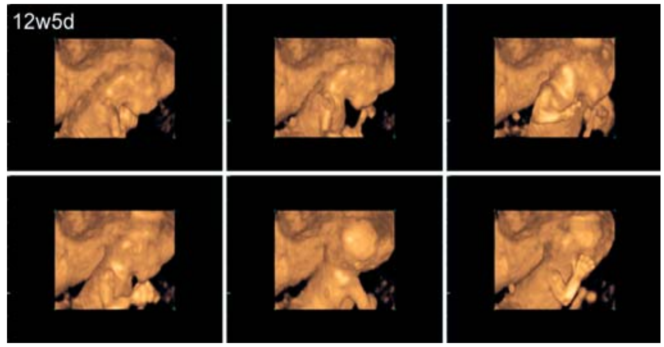


Fig. 5: Consecutive 4D sonographic observations of fetal movements of the head and upper extremities at 12 weeks' gestation

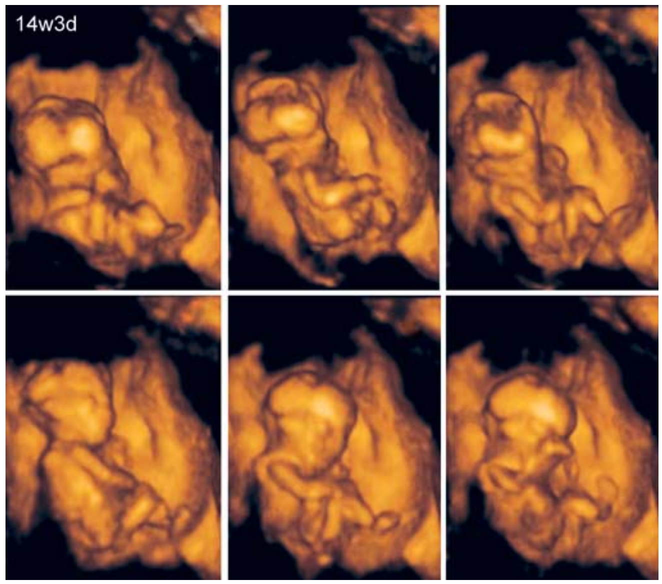


Fig. 6: General movements in a 14-week fetus

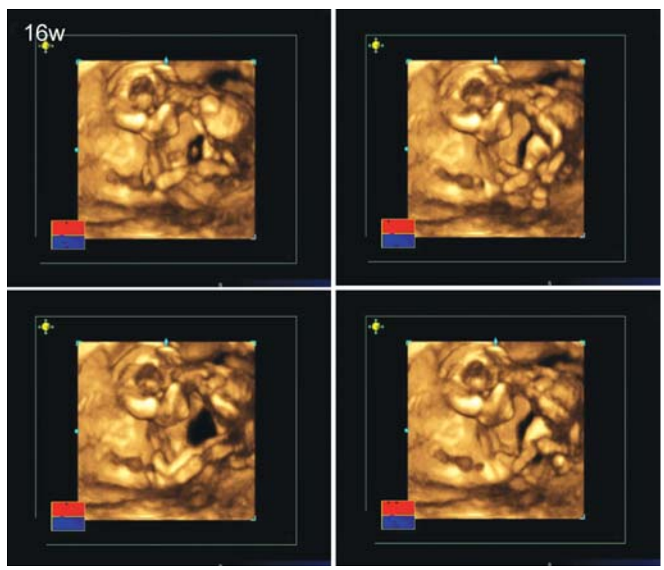


Fig. 7: Leg movements in a 16-week fetus

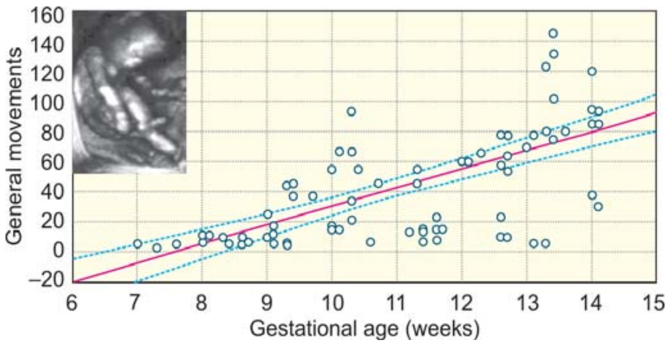


Fig. 8: Scatterplot and multiple regression analysis of the first trimester frequency of general movement versus the gestational age. Reprinted with permission from Kurjak A, et al. J Perinat Med 2006;34:56-65[49]

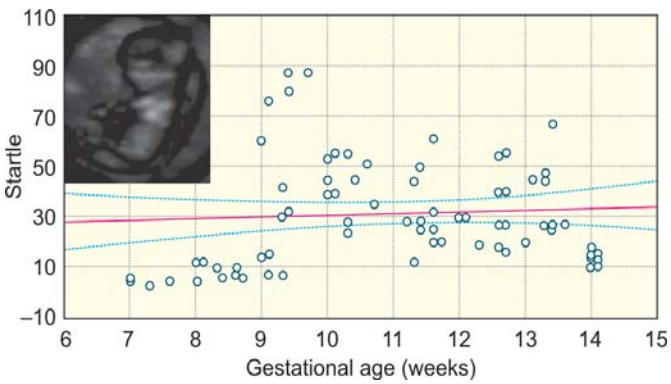
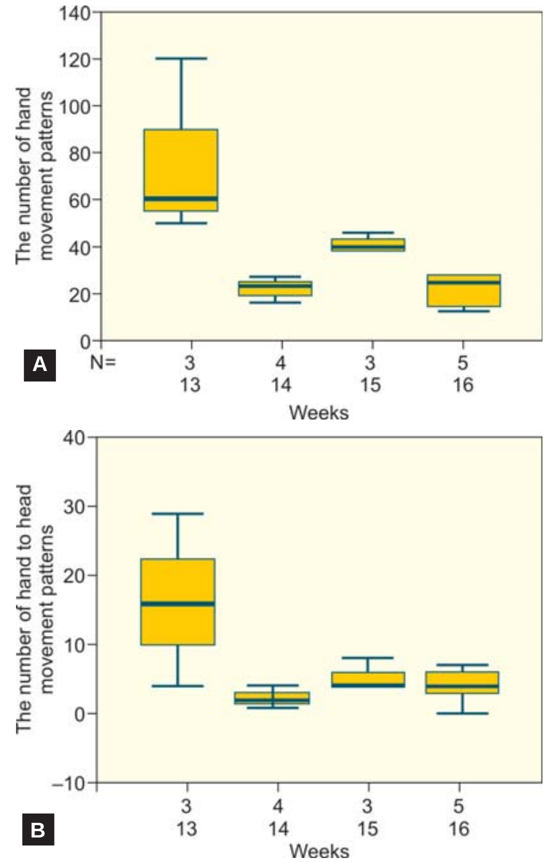


Fig. 9: Scatterplot and multiple regression analysis of the first trimester frequency of startle movement versus the gestational age. Reprinted with permission from Kurjak A, et al. J Perinat Med 2006;34:56-65[49]



Figs 10A and B: The incidence of isolated hand (A) and hand to head (B) movements from 13 to 16 weeks' gestation by 4D ultrasound. Reprinted with permission from Kurjak A, et al. J Perinat Med 2003;31:496-508[52]

(Fig. 9). Yigiter and Kavak[50] also employed 4D ultrasound to investigate 13 normal fetuses at 11 and 14 weeks of gestation, and noted a tendency towards an increased frequency of fetal movement patterns with advancing gestational age. Only the startle movement pattern frequency seemed to remain unchanged during the first trimester. Moreover, the frequency of fetal movement patterns tended to increase at the beginning of the second trimester. Hata et al[51] evaluated the frequencies of 5 fetal movements (isolated arm, isolated leg, short trunk, long trunk, and jumping movements) in normal singleton pregnancies for 10 minutes at 10-11 and 12-13 weeks of gestation using 4D ultrasound. In the 17 pregnancies studied, the most frequent fetal movements were isolated arm movement at 10-11 weeks and jumping movement at 12-13 weeks. There was a significant difference in the frequency of jumping movement between 10-11 and 12-13 weeks. These authors suggested that the difference in the frequency of the 5 fetal movements at 10-11 and 12-13 weeks of gestation may be caused by early neuromuscular development and differentiation of the neuromuscular system. Kurjak et al[52] studied a total of 15 fetuses at 13 to 16 weeks of gestation with abdominal 4D ultrasound for 15 minutes. Isolated hand and subtypes of hand movement (hand to head, hand to mouth, hand near mouth, hand to face, hand near face, hand to eye, and hand to ear) were easily identified. All subtypes of hand to head movement could be seen from 13 weeks of gestation, with a fluctuating incidence (Figs 10A and B). These authors suggested that 4D ultrasound is superior to conventional 2D ultrasound for the qualitative, but inferior for the quantitative analysis of fetal hand movements during the early second trimester of pregnancy. Kuno et al[20] performed 4D ultrasonographic examinations involving 11 healthy pregnant women at 14 to 18 weeks of gestation. The active phase (time period showing fetal movements) comprised 59.4% of the time, and the resting phase 40.6%. The most active fetal behavior pattern was arm movement, whereas the least was mouth movement. Moreover, each fetal movement was synchronized and harmonized with other movements (a few movement patterns were found to be generated simultaneously). "Here, it is important to bear in mind that more short-duration isolated movements might constitute more pronounced fetal movement in early gestation, whereas whole-body movements that are characteristic of the mature fetus may constitute greater movements in late gestation. However, whole-body movements are actually a composite of the isolated body movements".[31]

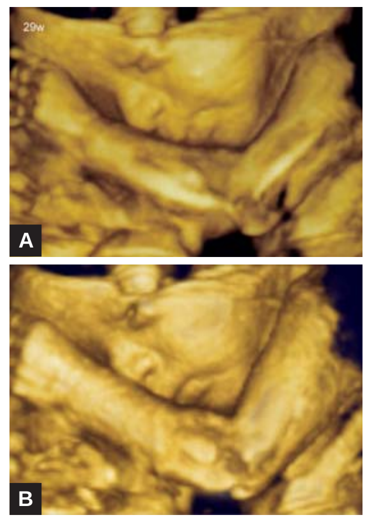
Only one study determined the accuracy of 4D ultrasound in the assessment of embryonic and early fetal motor activity, in comparison with conventional 2D ultrasound.[53] General body, head, and limb movements recorded by 2D ultrasound were notable by 4D ultrasound between 6-14 weeks of gestation, and there were significant correlations in the frequencies of all observed movement patterns assessed by the two different techniques. However, several movement patterns, such as side-way bending, hiccup, breathing movement, mouth opening, and facial movement, could be observed only by the 2D ultrasonographic technique, and not by 4D ultrasound. This study shows that 2D and 4D ultrasound could be used as complementary methods for the evaluation of fetal movement patterns in early gestation. Although the quantitative analysis of most movement patterns can be done using both techniques during this period, 2D ultrasound appears to be superior in terms of the evaluation of certain patterns.[53]

LATE SECOND AND THIRD TRIMESTERS

There have been numerous reports on fetal behavioral assessment using 4D ultrasound in the late second and third trimesters of pregnancy.[49,50,52,54-59] All studies focused on the assessment of fetal facial movements or expressions and fetal behavioral movements (mainly hand movements) (Figs 11 to 22), because the viewing area was limited to that of the transabdominal probe. "Clearly, the ability to image facial as well as hand movements and their co-occurrence is an advantage that may be related to the 4D technology. In addition, a possible advantage of this imaging feature is the implications it may have for the early coordination of hand to mouth activity, which is known to be relevant in the neonatal period, and possibly for the assessment of fetal emotion through the evaluation of facial expressions. Moreover, it is difficult to evaluate complex facial activity using conventional 2D ultrasound because of the anatomic features of the face and limitations of the 2D character of conventional 2D ultrasound. However, 4D ultrasound provides consecutive sculpture-like 3D images of the fetal face in real time".[31]

Kurjak et al[52] were the first to employ 4D ultrasound to study 10 healthy fetuses aged from 30 to 33 weeks, and they found that facial activities and different forms of

Fig. 11: 4D sonographic observation of fetal smiling at 32 weeks of gestation. The mouth is closed, with bilateral elevation of the mouth angles



Figs 12A and B: 4D sonographic observation of fetal blinking at 29 weeks of gestation (A) closed eyelid (B) open eyelid

Fig. 13: 4D sonographic observation of fetal crying at 32 weeks' gestation

Fig. 14: The fetus seems to show disappointment at 32 weeks' gestation

Fig. 15: 4D sonographic observation of fetal scowling at 34 weeks of gestation. There is a bilateral contraction of the eyebrows accompanied by a bilateral drop of the mouth angles, with curling of the upper or lower lip

Fig. 16: Consecutive 4D sonographic observations of fetal yawning at 31 weeks of gestation. Yawning is a slow, wide, prolonged opening of the jaws followed by rapid closure with simultaneous retroflexion of the head

Fig. 17: Consecutive 4D sonographic observations of fetal tongue expulsion at 29 weeks day of gestation

Fig. 18: Consecutive 4D sonographic observations of fetal tongue protrusion at 34 weeks and 6 days of gestation

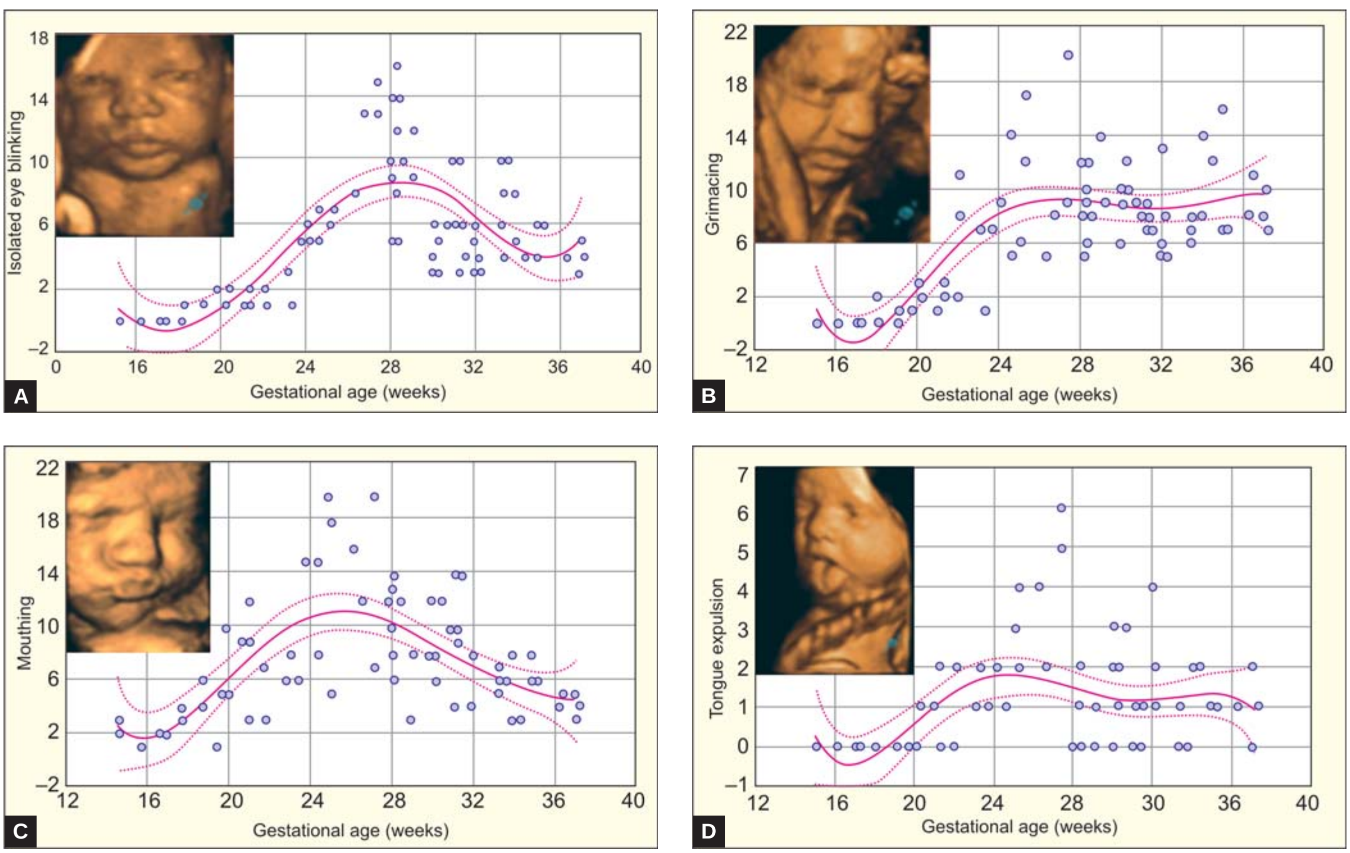
Fig. 19: Consecutive 4D sonographic observations of fetal sucking at 36 weeks and 2 days of gestation

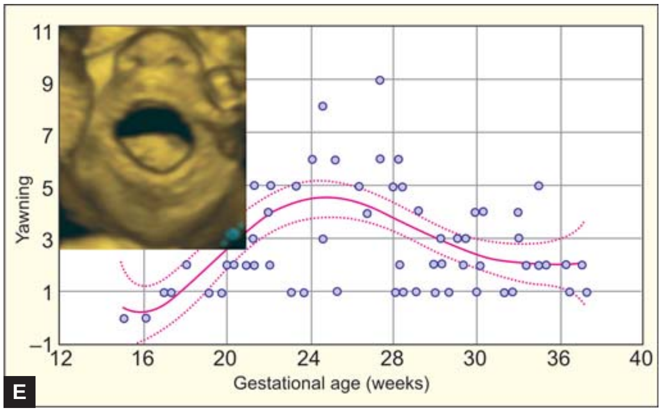
Fig. 20: Consecutive 4D sonographic observations of an 'embarrased' pose by a fetus at 26 weeks and 5 days of gestation

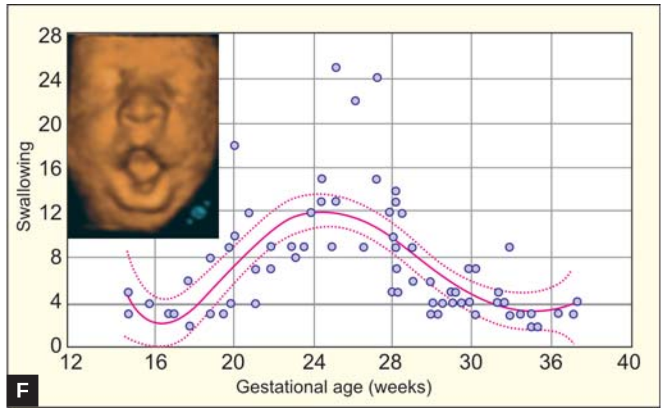
Fig. 21: Hand to nose movement at 32 weeks and 2 days of gestation. This fetus seems be wiping his nose

Fig. 22: Hand to face movement at 25 weeks of gestation. This fetus is showing an OK sign using his fingers

expression could be easily recognized, and eyelid and mouthing movements dominated this gestational age. In the recent study by these authors, 100 women with normal singleton pregnancies were recruited for longitudinal 4D ultrasonographic examinations to evaluate fetal neuro-developmental parameters from the 15th to 40th week.[49] All types of facial expression were noted as displaying a peak frequency at the end of the second trimester, except for isolated eye blinking, whose frequency increased at the beginning of the 24th week (Figs 23A to F). This observation appears to be very important, especially since the 2D technique does not appear capable or comparable to the 4D technique in terms of evaluating early facial expression. A tendency towards a decreasing frequency of facial expression with increasing gestational age needs to be demonstrated. Yigiter and Kavak[50] also used 4D ultrasound to investigate 50 normal fetuses in the second and third trimesters, and found that multiple and polynominal regression revealed significant changes in tongue expulsion, smiling, grimacing, swallowing, and eye blinking, whereas there were no significant changes in mouthing, yawning, and sucking. In the middle of the third trimester, the fetuses displayed a decreasing or unchanging incidence of fetal facial expressions except for eye blinking, which showed an increased frequency with advancing gestational age. In a recent study by Yan et al[59] the full range of fetal facial expressions early in the third trimester (from 28 to 34 gestational weeks) were studied using 4D ultrasonographic techniques. As in previous reports,[52,57] mouthing was found to be the most active facial expression during this gestational period. However, the frequency of eye blinking, which in other studies was thought to be similar to that of mouthing, was lower. Differences in the characteristics of the samples recruited and in interpreting the definition of each facial expression may be reasons for the contradictory results. "The question raised here is whether or not facial expressions represent a reliable behavior or emotional state, or constitute reflexive behavior on the part of the fetus".[31] Kurjak et al[49] observed that an increase in facial movement is simultaneously associated with a decrease in the number of general movements. This observation is considered to reflect the normal neurological development of the fetus.[1,46,60] The application of 4D ultrasound to the examination of fetal facial movements reveals the existence of a full range of facial expressions similar to emotional expression in adults.[21, 22, 49] Moreover, different facial expressions and movements depicted by 4D ultrasound might represent fetal awareness. In addition, although the same 15-minute period







Figs 23A to F: Frequency of observed facial expressions versus gestational age. Reprinted with permission from Kurjak A, et al. J Perinat Med 2006;34:56-65[49]

of observation was employed in all studies, the limitations of such a short period have been pointed out.[57] Extending the observation time and recruiting large sample sizes are needed in future studies.

Andonotopo and Kurjak[56] compared the frequency of all types of fetal facial expression between 50 normal and 50 growth-restricted fetuses in the third trimester, and noted that there were significant differences in isolated eye blinking, mouthing, yawning, tongue expulsion, grimacing, and swallowing. Moreover, the correlation reached significance between normal and growth-restricted fetuses in the third trimester for head rotation, head anteflexion, and head retroflexion. Significant differences were also noted in the distribution of the median values based on observation over five qualitative categories of head and hand movement (hand to head, hand to mouth, hand to eye, hand to face, and hand to ear movement). They encouraged the future use of 4D ultrasound for the quantitative and qualitative assessment of fetal behavior as possible indicators of the neurological condition in growth-restricted fetuses.

"For the 4D ultrasound device, the frame rate in most studies was 0.5 frames per second, being 4-6 frames per second in one investigation. Therefore, rapid fetal facial activities including rapid blinking, subtle lip movement, and dynamic lingual movement could not be depicted using these 4D ultrasound devices because of the relatively slow repetition time for data acquisition to obtain a satisfactory image. The ontogeny of fetal behavior develops from rapid, somewhat isolated fetal movements, to a greater proportion of less jerky and smooth whole-body movements later in gestation. The inability of the 4D technique to assess the subtle and rapid movements means that assessing the developmental level throughout gestation may be compromised in the absence of available evidence related to short-duration fetal movements. These short-duration movements, sometimes referred to as isolated fetal movements and isolated spikes, represent the immature development of the nervous system and a lack of coordinated behavior. Subsequent to approximately thirty weeks of gestation, there is an increase in long-duration fetal movements, referred to as epochs and episodes".[31] There have been no studies on the comparison of 2D and 4D techniques to assess fetal facial expression or behavior in the late second and third trimesters of pregnancy, in which the neurobehavioral regulations of fetal movement are the most important.

FETAL TO NEONATAL PERIODS

There have been two reports on the 4D ultrasonographic assessment of behavioral pattern continuity from the fetal to early neonatal periods.[57,61] Continuity was shown from fetal to neonatal behavior, especially in terms of isolated eye blinking movements, mouth and eyelid opening, yawning, tongue expulsion, smiling, scowling, and hand movements directed to other parts of the face[61] (Figs 24 and 25). There were no movements observed in fetal life that were not present in neonatal life, while the Moro reflex was present only in neonates.

Kurjak Antenatal Neurological Test (KANET)

Kurjak et al[62] proposed a new scoring system (KANET, Kurjak Antenatal Neurological Test) for assessment of the neurological status for antenatal application using 4D ultrasound for a 30-minute examination (Table 1), and identified severely brain-damaged infants and those with optimal neurological findings (Table 2). KANET for the

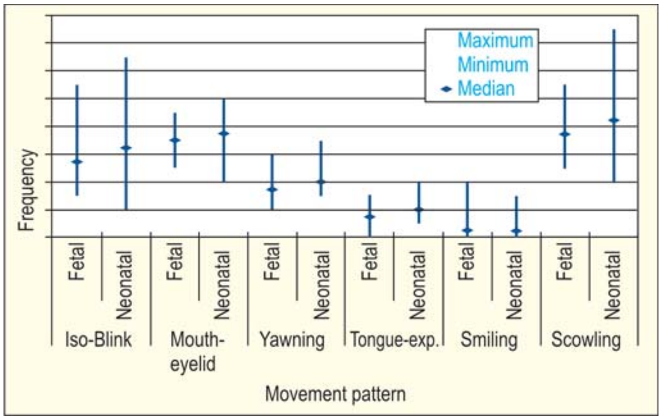


Fig. 24: Frequency of facial movements in the fetal and neonatal period. Reprinted with permission from Kurjak A, et al. J Perinat Med 2004;32:346-353[61]

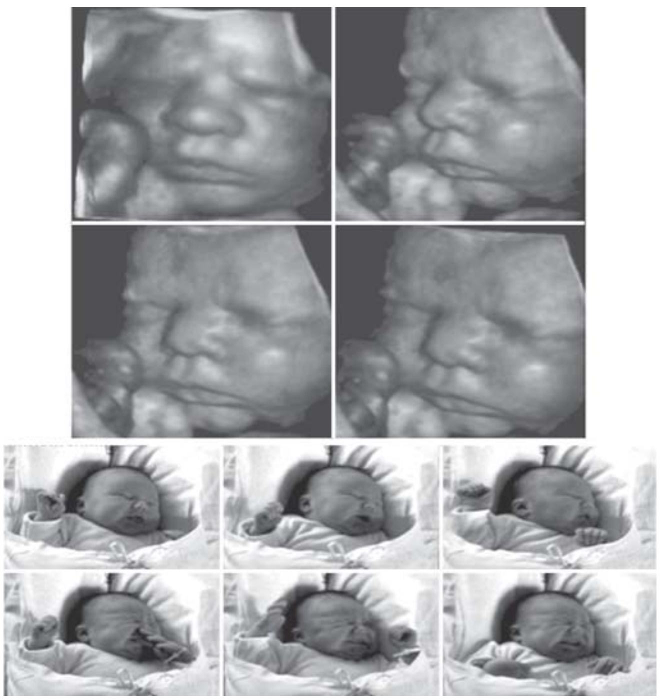


Fig. 25: 4D fetal and neonatal facial expression. Reprinted with permission from Kurjak A, et al. J Perinat Med 2004;32:346-353[61]

assessment of the neurological status for antenatal application is similar to the neonatal optimality test of Amiel-Tison.[63-68] In a group of 120 high-risk pregnancies, three subgroups of newborns were identified: normal, mildly or moderately abnormal, and markedly abnormal. Normal neonates showed a prenatal score between 14 and 20, mildly or moderately abnormal neonates had a prenatal score of 5-13, whereas infants designated as neurologically abnormal had a prenatal score from 0-5. This scoring system may help in detecting fetal brain and neurodevelopmental alterations due to *in utero* brain impairment. “However, there are some criticisms of KANET. The most important problem is the reproducibility of this antenatal test, because neither inter- nor intra-observer reliability was evaluated. Another problem arises from the fact that KANET is a very complicated procedure, and very time-consuming”.[31] Kurjak et al[62] stated that they do not yet know the conceptual and neurological strengths and weaknesses of KANET.

Kurjak et al[69] studied prenatal neurological assessment in high-risk fetuses using 4D ultrasound applying KANET. Postnatal neurological assessment was performed using Amiel-Tison’s neurological assessment at term (ATNAT) for all live-borns and general movement (GM) assessment for those with borderline and abnormal ATNAT. Out of 32 borderline and abnormal fetuses by KANET, ATNAT was normal in 7, borderline in 22, and abnormal in 3; GM assessment was normal in 24, borderline in 6, and abnormal in 2 (Table 3). These authors suggested that KANET requires further studies before being recommended for wider clinical application.

Miskovic et al[70] compared fetal behavior in high-risk (N=116) and normal pregnancies (N=110) using 4D ultrasound applying KANET. The newborns were assessed by ATNAT. There was a significant difference between the high-risk and normal pregnancy groups, for 8 out of 10 parameters in KANET: isolated anteflection of the head, eye blinking, facial expression, mouth movement, isolated hand movement, hand to face movement, fist and finger movement, and general movements. There was no difference for cranial sutures and isolated leg movement. Comparison of KANET and ATNAT showed significant, moderate correlation between the two tests, which means that ATNAT confirmed KANET. However, these authors also suggested that their results are promising but further studies have to be conducted before KANET can be recommended for wider clinical application.

INTER-TWIN CONTACT

Baba et al[71] were the first to publish a 3D ultrasonographic image of a twin pregnancy at 15 weeks’ gestation. Hata et al[72] demonstrated various types of inter-twin contact and interrelationships in 13 twin pregnancies at 9-36 weeks’ gestation using 3D ultrasound. However, all 3D pictures in both investigations were static images. Only with the appearance of 4D sonography has the full range of fetal movements been observed.[8] Sasaki et al[73] evaluated the total number of inter-twin contacts between monochorionic diamniotic (MD) and dichorionic diamniotic (DD) twins using 4D ultrasound late in the first trimester of pregnancy.

Table 1: Neurological scoring test for the fetus (KANET, Kurjak Antenatal Neurological Test). Reprinted with permission from Kurjak et al. J Perinat Med 2008;36:73-81[62]

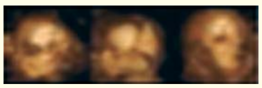
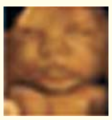
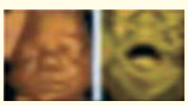
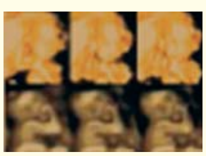
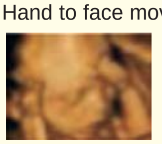
Sign	*Score*			*Sign Score*
	0	1	2	
Isolated headanteflexion 	Abrupt	Small range (0-3 times of movements)	Variable in full range, many alternation (> 3 times of movements)	
Cranial sutures and head circumference 	Overlapping of cranial sutures	Normal cranial sutures with measurement of HC below or above the normal limit (-2SD) according to GA	Normal cranial sutures with normal measurement of HC according to GA	
Isolated eye blinking 	Not present	Not fluent (1-5 times of blinking)	Fluency (> 5 times of blinking)	
Facial alteration(grimace or tongue expulsion) 	Not present	Not fluent (1-5 times of alteration)	Fluency (> 5 times of alteration)	
Mouth opening (yawning or mouthing) 	Not present	Not fluent (1-3 times of alteration)	Fluency (> 3 times of alteration)	
Isolated hand movement 	Cramped	Poor repertoire	Variable and complex	
Isolated leg movement 	Cramped	Poor repertoire	Variable and complex	
Hand to face movements 	Abrupt	Small range (0-5 times of movement)	Variable in full range, many alternation (> 6 times of 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: Interpretation of the total KANET score. Reprinted with permission from Kurjak, et al. J Perinat Med 2008;36:73-81[62]

Total score	*Interpretation*
0-5	Abnormal
6-13	Borderline
14-20	Normal

Table 3: Combined results from the KANET, ATNAT and general movement assessment. Reprinted with permission from Kurjak et al. J Perinat Med 2010;38:77-82.

Results of postnatal general movements (GMs)		*Postnatal neonatal neurological assessment (ATNAT)*			*Prenatal assessment (KANET)*	
		Normal	*Borderline*	*Abnormal*	*Borderline*	*Abnormal*
Normal optimal	4	3	1	0	4	0
Normal suboptimal	20	4	16	0	20	0
Abnormal	6	0	5	1	1	5
Definitely abnormal	2	0	0	2	0	2
Total	32	7	22	3	25	7

KANET = Kurjak antenatal neurodevelopmental test, ATNAT = Amiel Tison's neurological assessment at term.

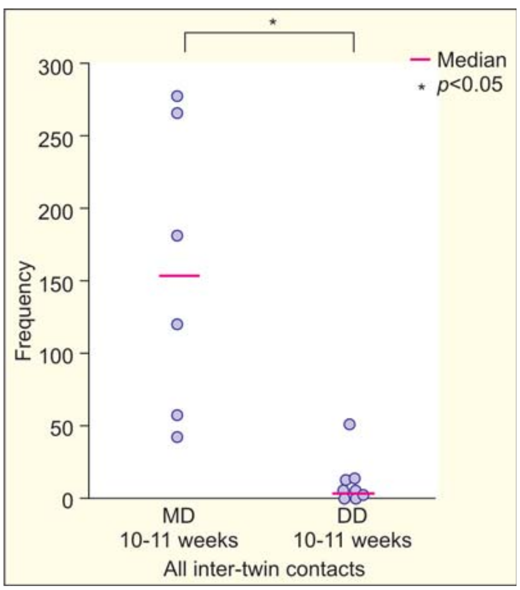


Fig. 26: Total frequencies of all inter-twin contacts between monochorionic diamniotic (MD) and dichorionic diamniotic (DD) twins at 10-11 weeks

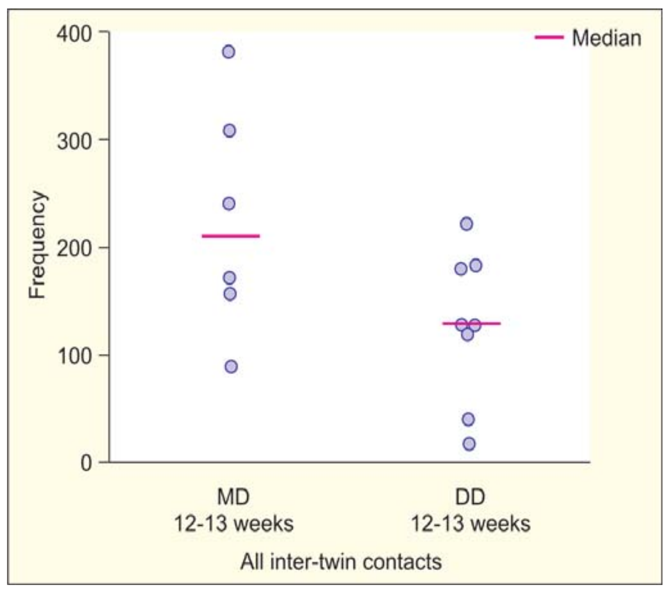


Fig. 27: Total frequencies of all inter-twin contacts between monochorionic diamniotic (MD) and dichorionic diamniotic (DD) twins at 12-13 weeks

Six MD and eight DD pregnancies were studied for 30 minutes with 4D ultrasound at 10-11 and 12-13 weeks' gestation, and a total of 10 inter-twin contacts (head to head, head to arm, head to trunk, head to leg, arm to arm, arm to trunk, arm to leg, trunk to trunk, trunk to leg, and leg to leg contact) was evaluated. There was a significant difference in the total number of all contacts between MD and DD twins at 10-11 weeks' gestation (Fig. 26). However, no significant difference in the total number of all contacts was found between MD and DD twins at the 12-13 weeks' gestation (Fig. 27). There was a significant difference in the total number of all contacts between 10-11 and 12-13 weeks' gestation in DD twins (Fig. 28). However, no significant difference in the total number of all contacts was noted between 10-11 and 12-13 weeks' gestation in MD twins (Fig. 29).

Degani et al[74] studied inter-twin differences in activity during early pregnancy and examined their relationship to

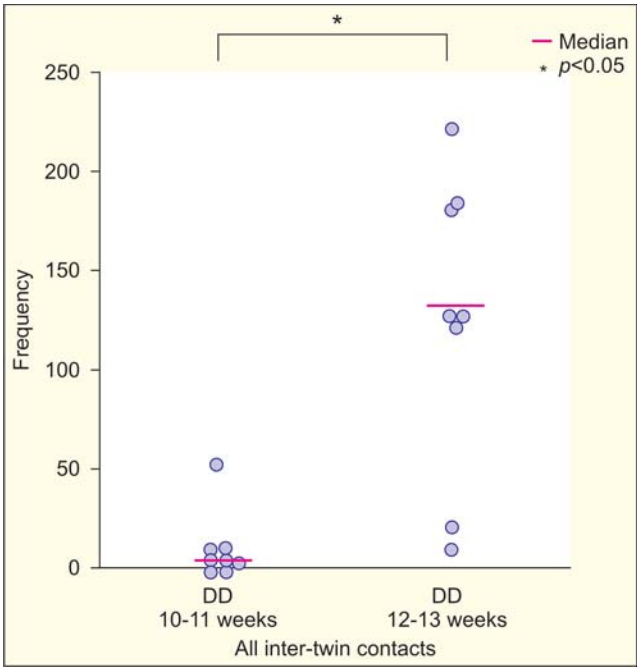


Fig. 28: Total frequencies of all inter-twin contacts between 10-11 and 12-13 weeks in dichorionic diamniotic (DD) twins

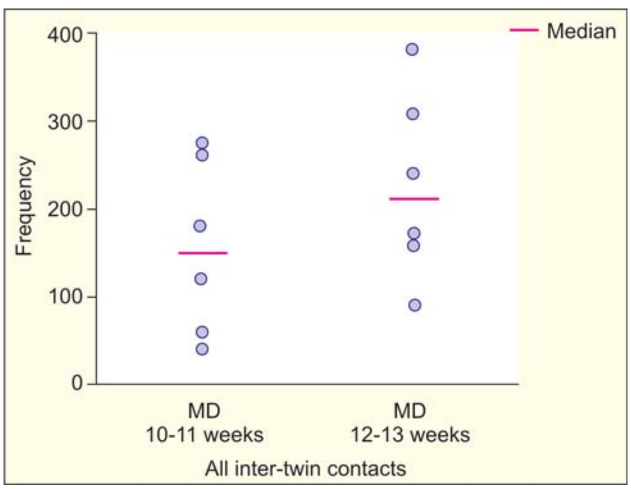


Fig. 29: Total frequencies of all inter-twin contacts between 10-11 and 12-13 weeks in monochorionic diamniotic (MD) twins

subsequent infant twins' temperament. Measures of fetal motor activity (frequency, duration, and number of movements) were collected from 26 twin pairs in the late first and early second trimester (11 to 14 weeks' gestation) using 4D ultrasound. After birth, maternal reports on infants' temperament and the more active twin in each pair showed a close correlation with prenatal inter-twin differences in activity. These authors suggested that differences in activity in each pregnancy even before the emergence of fetal behavioral patterns were followed by differences in temperament postnatally.

MATERNAL-FETAL BONDING

"Maternal-fetal attachment or bonding is a natural phenomenon that develops gradually throughout pregnancy and peaks in the few weeks after birth of the child".[75] "Conventional 2D ultrasound scans are believed to enable mothers to form an early affectionate bond to their child, to provide a reassuring image of the fetus, and to promote improvements in mothers' health behaviors on the behalf of the fetus".[76] The question raised here is whether the addition of 3D/4D ultrasound to a conventional 2D scan facilitates the maternal recognition of specific fetal structures and movements, has an emotional impact, and improves maternal-fetal bonding.

Manabe et al[77] evaluated whether or not 3D images of the fetus could improve maternal-fetal bonding, and suggested that 3D ultrasound has a positive effect on the maternal-fetal relationship. Ji et al[78] reported that 3D ultrasound appears to more positively influence the perceptions mothers have of their babies postbirth compared to 2D ultrasound. Specifically, mothers who underwent 3D ultrasound showed their ultrasound images to a greater number of people compared to mothers who had 2D ultrasound alone. Sedgmen et al[79] explored the impact of the timing and type of ultrasound, particularly 3D, exposure on maternal-fetal attachment and maternal health behavior during pregnancy. Ultrasound had a positive impact on maternal-fetal attachment, particularly in the first trimester. Alcohol consumption was the only behavior to show a significant change following ultrasound exposure, with a reduction in the reported average number of drinks per week. However, there was no significant difference in the patterns of change for 2D compared with 3D ultrasound exposure, and no effect of ultrasound exposure on maternal perception of the fetus. Lapaire et al[80] also reported that 3D images may facilitate recognition of the fetus, but 3D ultrasound did not have a more marked impact on maternal-fetal bonding compared to 2D ultrasound.

Rustico et al[81] assessed the effect of the addition of 4D ultrasound to a conventional 2D scan on maternal recognition of the specific fetal structures and movements and emotional impact, as subjectively perceived by the women. These authors indicated that the addition of 4D ultrasound did not significantly change the perception women have of their babies nor their antenatal emotional attachment compared with conventional 2D ultrasound. Leung et al[82] tested the hypothesis that the use of 2D with 3D/4D ultrasound can reduce anxiety to a greater extent in women at risk of having a fetus with congenital abnormalities than the use of 2D ultrasound alone. This randomized study indicated that the addition of 3D/4D ultrasound did not bring about a significant reduction in maternal anxiety in pregnancies at risk of fetal abnormalities compared with conventional 2D ultrasound alone. However, with the advent of the latest 4D ultrasound, "it is the visible humanity of the fetus in the third trimester, the baby-like facial expressions, and the sucking, grasping, and other movements that could trigger a surge in bonding in the last 16 weeks of pregnancy".[75] Further randomized studies are needed to assess the effect of 4D ultrasound on maternal-fetal bonding.

LIMITATIONS

The limitations of 4D ultrasound cannot be overlooked. Several fetal movement patterns cannot be observed primarily because of the frame rate of the machine used in most studies. "At these relatively slow frame rates, the ability to study fetal behavior in the surface rendered mode, especially long-duration fetal movements, such as gross body, limb, and complex limb movements, is satisfactory for research purposes. However, it appears that the inability of 4D ultrasound is restricted to short-duration fetal movements, which occur early in gestation".[31] Secondly, only the quantity, and not the quality, of fetal movements can be studied in fetuses, because criteria for quality have not yet been determined.[58] However, KANET includes some qualitative parameters for the assessment of fetal movements.[62]

It should also be borne in mind that the fetal movements studied in most investigations might represent subjective impressions of the examiner. This fact may raise some concern about inter-observer variability relating to the definition of each of the movements. Further studies are needed to establish an acceptable level of inter-observer agreement regarding fetal movements.[51] "Presently, studying fetal behavior is very time-consuming, and, therefore, limited to research. An easier way of analyzing fetal behavior should be developed for diagnostic and prognostic use (e.g. automated computer-based analysis for evaluating fetal movements). These limitations of 4D ultrasonographic fetal imaging will be resolved as further technical advances such as high-frame rate 4D ultrasound devices with automated objective recognition systems, etc. are made".[31]

CONCLUSIONS

This review focused on 4D ultrasonographic studies evaluating fetal behavior, inter-twin contact, and maternal-fetal bonding during pregnancy. "There are fetal behaviors that can be detected by the 4D assessment procedure in instances where the 2D technique cannot provide the same information. One aspect that appears to favor the 4D technique is in the evaluation of facial movement and expression. 4D ultrasound should be an important modality in future fetal behavioral research and in the evaluation of fetal well-being. If we can observe fetal behavior precisely using this technique, we can obtain new and/or additional information to facilitate improved diagnosis and understanding of fetal brain impairment *in utero*".[31] Moreover, we might uncover new fetal behavioral functions and inter-human contacts. Further studies are needed to ascertain the present and future application of this modality to fetal neurobehavioral assessment.

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