10.5005/jp-journals-10009-1394

REVIEW ARTICLE

Is *in utero* Fetal Neurological Assessment Comparable to Postnatal Neurological Assessment?

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ABSTRACT

The traditional concept that brain damage is caused during birth or early neonatal period has been challenged. This is supported by the fact that the incidence of cerebral palsy stayed unchanged despite the global increase of cesarean sections. Consequently, the medicolegal importance of fetal neurological research is essential and needed. Years of research have provided us with important knowledge about association of fetal movements with brain development. The basic studies were done by two-dimensional ultrasound. The implementation of four-dimensional ultrasound in evaluation of fetal behavior has opened new and unexplored possibilities of evaluating the quality of fetal movements and a detailed assessment of fetal facial expressions. It is known that early postnatal neurological assessment, regarding future prediction of neurological optimality, has great limitations do to wonderful brain plasticity. Taking this very important limitation in to the account we could conclude that the preliminary studies comparing prenatal and postnatal neurological assessment are comparable. More importantly they emphasize the fact that the study of fetal behavior is most probably the right path in the study of fetal neurological development.

Keywords: Ultrasound, Four-dimensional ultrasound, Fetal behavior, Kurjak antenatal neurodevelopmental test, Neurodevelopment, Prenatal assessment, Postnatal assessment.

How to cite this article: Vasilj O. Is *in utero* Fetal Neurological Assessment Comparable to Postnatal Neurological Assessment? Donald School J Ultrasound Obstet Gynecol 2015; 9(1):91-95.

Source of support: Nil

Conflict of interest: None

INTRODUCTION

The traditional concept that brain damage is caused during birth or early neonatal period has been challenged, antenatal and unclassifiable factors are now considered as the most important etiological factors.[1] The best example is cerebral palsy the most common chronic motor disability of childhood. The worldwide prevalence ranges from 2 to 2.5 per 1000 live births and the incidence has not changed since mid-20th century.[2] The fact that the incidence of cerebral palsy stayed unchanged despite the global increase of cesarean sections supports the previously mentioned remarks.[3] This uncertainty regarding causation vitalizes plaintiff's attorneys throughout the world who attempt to relate these neurological abnormalities exclusively to intrapartum events, such as use of forceps deliveries or failure to perform a cesarean delivery. Consequently, the medicolegal importance of fetal neurological research is essential and needed.[2]

As basic neurodevelopmental studies have undoubtedly concluded that fetal behavior is a reflection of morphological brain development, therefore it can be speculated that by studding the fetal behavior we can study the optimality of fetal brain development.[4] The study of fetal behavior started long time ago, first scientific papers were written at the end of 18th century.[5] From today's standpoint it is hard to believe that in 1985. Preyer wrote a whole chapter about fetal behavior in the book 'Physiologie des Embrio'.[6]

With the implementation of ultrasound in to daily obstetrical practice a new window in to intrauterine environment was opened. We could finally see the behavior of a fetus in its natural environment. First studies of fetal behavior using two-dimensional ultrasound described the fetal movements from the very first trimester to the end of the third trimester.[7-9] All the movements were described in detail, their first occurrence a detailed description of how they are performed and how to recognize them.[7-9] It was amazing to discover that almost all of the movements were present in the first trimester with first spontaneous movements appearing at about 7.5 gestational weeks.[7-9] These are slow flexion and extension movements of fetal trunk accompanied by passive change in position of fetal extremities. They appear in unregularly time intervals and their ultrasonic impression is that of 'worm like movements'.[10] Between eighth and ninth week these movements are replaced by more energetic movements called 'startle movements'.[10] At this gestational age a very important and a specific movement called General movements (GM) start to appear as well.[10] These movements were first described by an Austrian neuroscientist Prechtl.[10] The importance of these movements will be discussed later.

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With the continuation of the pregnancy all the individual movements become more complex and consolidated especially with the beginning of the third trimester.[10,11] This change in fetal behavior coincides with the basic neurodevelopmental studies which indicate that this time period is precisely the starting point when the upper neurological control centers start to take control of the fetal behavior. This consolidation of fetal movements was recognized by Nijhuis and he clearly pointed out that from about 36th gestational week onward normal fetuses develop clearly defined fetal states (Fetal states 1 through 4).[10] He has shown that a disorganization of these fetal states coincides with disrupted fetal brain development.[12] Therefore we can see that the development of fetal behavior is a process that directly depends on the development of the central nervous system. If there is a change or a disruption in the development of central nervous system whether it is a morphological or a functional disruption it will reflect itself on the development of fetal behavior.[12] A very good and a practical example for this shift of neurological control from lower to upper control center and its effect on fetal behavior is excellently shown in the behavior of anencephalic fetuses.[13,14]

This condition is usually diagnosed in the first trimester and most of these fetuses are aborted but in some cases do to religious or personal reasons the parents have decided to continue the pregnancy. These instances were perfect for the study of fetal behavior. When longitudinal studies were performed it was a surprise to discover how abundant the fetal behavior was in the first and early second trimester, a time when the control of fetal behavior is mainly due to lower control centers.[13,14] As the pregnancy continued at the end of second and especially in the third trimester the ontological shift of motoric control from lower to upper control center happens and the same was reflected on the fetal behavior.[13,14] The fetal movement's repertoire changed, the movements become jerky and simple, facial movements rare or absent.[13,14]

This simple clinical and research setting clearly implies how complex the neurodevelopment is! The right path to study the neurodevelopment is most probably a combination of morphological and functional studies in both fetuses and infants.

Fig. 1: Fetal face with opened eyes

Fig. 2: Fetal face with opened mouth

Fig. 3: A fetus smiling

Study of Fetal Behavior

As mentioned in the introduction the study of fetal behavior started a long time ago but it gained a substantial momentum with the introduction of two-dimensional ultrasound. The fetal movements were studied longitudinally in both low- and high-risk pregnancies.[7-9,15] Due to technical limitations of two-dimensional ultrasound these studies were based mainly on quantification of specific movements. As parameters of normality were set for all individual movements, in time authors lost interest in the study of fetal behavior because a limit was reached and the technical limitations of available technology could not be surpassed.

With the advance of computer technology which in turn was implemented in to ultrasound technology the dawn of volume ultrasound started and a new perspective for study of fetal behavior was opened. Three- and four-dimensional ultrasound offered something that was not possible in the plain B-mod. For the first time we could observe fetal face in three-dimensions, first statically in three-dimensions and in just a lite while a new dimension of time was added and we could see fetal facial expressions in almost real time (Figs 1 to 3).[16] This technical possibility opened a completely new aspect in the study of fetal behavior the study of fetal awareness, and its value needs to be yet explored.[17]

Since, fetal behavior is considered a reflection of fetal brain development authors pointed out its clinical and research value but these study methods were never widely implemented for fetal neurological assessment.[18,19] Several different tests for evaluation of fetal neurobehavior were proposed but do to their concept, complexity and time consuming they were not practical for daily use.[20,21] General movements could be singled out as they show a continuity from prenatal to postnatal period and their prognostic value was studied extensively both prenatally and postnatally.[22-25] In a review article about postnatal assessment of GM during the fidgety movements' period they conclude that GM could be used as a prognostic tool to identify infants with neurodevelopmental disabilities.[26] Another author implies that impaired fidgety GMs could be used for detection of high-risk late preterm infants who need early intervention.[27] Similar conclusion was reached by De Vries in her review article about fetal behavior.[28] She notices the problems regarding studies of fetal behavior and emphasized the importance of GM and proposes their assessment as a part of routine sonographic care. In case of abnormal GM finding she advocates advanced sonographic examination where special attention should be focused on the head, including eyes and jaw, torso and limbs.[28] De Vries also noted the advantages of four-dimensional ultrasound for the future research of fetal behavior.[28]

Kurjak Antenatal Neurodevelopmental Test

The test is based on the evaluation of fetal behavior using four-dimensional ultrasound. Since, there were no studies of fetal behavior done by four-dimensional ultrasound, first the standards of normality for all individual movements had to be made.[29] The next in line was the selection of parameters to be included in the KANET. The choice was based on developmental approach to the neurological assessment and on the theory of emergence of GM from central pattern generators.[30] General movements are part of the spontaneous movement repertoire and are present from early fetal life onwards until about 5 month's postnataly.[26] These movements involve the whole body in a variable sequence of arm, leg, neck and trunk movements.[26] They wax and wane in intensity, force and speed and they have a gradual beginning and end. If the nervous system is impaired, GMs lose their complex and variable character and become monotonous and poor.[26]

Therefore the KANET scoring system is a combination of some parameters from the fetal GM assessment and parameters from postnatal ATNAT assessment, which can be prenatally visualized by four-dimensional ultrasound.[30,31] On suggestion of Amiel Tison two very important neurological signs that are visible with four-dimensional ultrasound were included in the test: overlapping sutures and neurological thumb.[30,31]

The main two advantages of the four-dimensional ultrasound in comparison to two-dimensional ultrasound, incorporated in KANET, are the possibility of evaluation of fetal face movements and better evaluation of quality of fetal movements.[32] In a two-dimensional sonographic image the investigator can see the movement he can count the number of movements and just sometimes he can see the combination of several movements as well. What four-dimensional ultrasound adds is the assessment of quality of the movement. A hand does not just move or flex as in two-dimensional image now we can assess simultaneously the rotation, supination, pronation, individual finger movements and direction of the movement and as mentioned most importantly the impression of quality and complexity of the movement.

In the first version of KANET the following 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, Gestalt perception of general movements (overall perception of the body and limb movements with their qualitative assessment). In total ten different parameters.[30]

A revision of KANET was done in 2011 and was published as Osaka statement. It was concluded that KANET should be performed in the 3rd trimester from 28th to 38th week of gestation (a time period when upper neurological control centers take control of fetal behavior).[33] The assessment should last from 15 to 20 minutes, and the fetuses should be examined when awake. If the fetus is sleeping, the assessment should be postponed for 30 minutes or for the next day between 14 and 16 hours.[33] In cases of definitely abnormal or borderline score, the test should be repeated every 2 weeks till delivery. New modified KANET test should

be used with 8 instead of 10 parameters: Facial and mouth movements are combined in one category, isolated hand movements and hands to face movements are combined in one category.[33] After four-dimensional assessment of behavioral patterns in the fetuses from high-risk pregnancies, which were scored as borderline or abnormal, it is very important to continue with follow-up after delivery. Infants should be followed until the age of at least 24 months when diagnosis of disabling or nondisabling cerebral palsy could ultimately be made.[33]

Are Prenatal and Postnatal Neurological Assessments Comparable?

This is the most important question we could ask but the answer is not a simple one. We might just decide that we are on the right path with our research, but we cannot and should not be bold enough to say we will diagnose neurological disorders prenatally. The problem is a very complex one. The brain continues to develop intensively in the postnatal period as well and we cannot forget the fact that the fetus grows in a different environment than an infant, mainly due to the lack of gravity.[34]

The brain has a wonderful possibility of surprising us pleasantly. In cases where neurodevelopment is very disturbed it is possible to predict future neurological outcome but surprises do happen and in some individuals with severely affected neurodevelopment in infancy at the age of small child or young adolescent clinicians were surprised with encouraging outcome due to brain plasticity. This is the reason why definition of cerebral palsy has changed many times in the last several decades. When trying to predict the future of high-risk babies in terms of individual neurodevelopment, than one should always bear in mind that it is only a statistical category without possibility to predict neurodevelopment on individual basis.

We have to be realistic and take in to account that even clinical assessment of muscle tone, strength, and control of voluntary movements for early detection of infants with the risk for cerebral palsy has been frustrating as well, because 43% of 7-year-old children with cerebral palsy had a normal newborn neurological examination.[35] Things become even more complex when we take in to the account that neuropediatricans have the hands on possibility to evaluate the neonate and obstetricians have a passive look inside the uterus but on the other hand the fetus is free of gravity and is able to perform more complex motoric tasks than the neonate. In the end is there anything that we can or could conclude? To answer this question I will quote our previously published work.[36]

Personal Experience

We compared fetal behavior longitudinally in high-risk (N = 116) and in normal pregnancies (N = 110).[36] Individual KANET parameters were compared but more importantly the results of KANET from both groups were compared with postnatal neurological assessment according to Amiel-Tison neurological assessment at term (ATNAT). Comparison of KANET and ATNAT showed statistically significant, moderate correlation between the two tests, which means that the neuropediatric exam (ATNAT) confirmed the prenatal four-dimensional finding (KANET).[36] Even though these numbers were small they indicate that we are on the right path and that the study of fetal behavior could be the best tool that we have for diagnosing or maybe more precisely said placing a suspicion that there might be a neurological developmental problem. It will be crucial to design long lasting double blinded studies in order to prove clinical prognostic value of KANET test or any other method of prenatal neurological assessment. The final goal is to identify fetuses at risk for neurodevelopmental disorders follow them prospectively and introduce early intervention.

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