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Analysis of movement quality in preterm infants

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Preterm birth carries an increased risk for an impaired neurodevelopmental outcome. Preterm infants, especially those born before 30 to 32 weeks' gestation, often have serious medical complications that might lead to brain damage. The assessment of the quality of spontaneous motility proved to be a valuable and sensitive method for investigating the integrity of the neonatal brain. The quality of the general movements (GMs), easily recognized and frequently present in preterm infants, proved particularly valuable for assessing neonatal brain function. Normal GMs are characterized by a large variability in speed, amplitude, force and intensity. The sequence of arm, leg, head and trunk movements is complex, with rotations superimposed on flexion and extension, making the normal general movement look fluent. Abnormal GMs lack this complexity, variability and fluency. At about the end of the second month post-term, during the so-called age of transformation, the GMs acquire a fidgety character. Fidgety GMs are circular movements of small amplitude and moderate speed and variable acceleration of neck, trunk and limbs in all directions. In preterm infants, this change in the characteristics of spontaneous movements can be observed at about the same time provided the infant's age is corrected for preterm birth.

This thesis deals with spontaneous motility in preterm infants. Both qualitative and quantitative aspects of spontaneous motility were studied, from videotape recordings, with the emphasis on the quality of GMs. In **chapter 1**, after a brief historical overview, a literature review is given on the present knowledge on spontaneous motility. Several questions and unresolved problems are stated. The aims of the study are introduced. These were:

- to determine whether the qualitative assessment of GMs is a sufficiently sensitive diagnostic tool to discriminate between brain lesions and systemic disease;
- to determine the relationship between the developmental course of spontaneous motility, brain ultrasound findings and the neurological outcome in three distinct groups of preterm infants whose developmental course of spontaneous motility has not yet been elucidated.

The study groups consisted of:

- preterm infants with transient periventricular echodensities on ultrasound scans;

- preterm, small-for-gestational age infants;
- preterm infants at risk for chronic lung disease, requiring dexamethasone therapy.

The recording and assessment methods are described in detail in **chapter 2**. The inter-observer reliability of the assessment of spontaneous motility is reported. Considering the quantitative aspects of spontaneous motility, a good inter-observer reliability was found for the occurrence of different movement patterns and the duration of GMs. Inter-observer agreement on the assessment of the quality of GMs was even better: 95%, using *kappa* 0.89 (95% confidence interval 0.86-0.93).

Chapter 3 describes observations on spontaneous motility in preterm infants with septicaemia, providing some answers to the question whether the assessment method is sufficiently sensitive to differentiate between brain dysfunction and severe illnesses unaccompanied by brain dysfunction. Our study demonstrated that severe infections such as septicaemia have a limited influence on the quality of GMs in preterm infants. The GMs may have a transient sluggish character. At first notice, this can be mistaken for 'poor repertoire' GMs. However, the richness in complexity and variability, particularly the sequencing of moving parts, including superimposed rotations, is strikingly different from true 'poor repertoire' GMs. Therefore, the global assessment of the quality of GMs is normal. This indicates that it is possible to discriminate between abnormal GMs due to cerebral lesions and sluggish GMs due to severe systemic infections, provided complexity of the GMs is considered as the main characteristic when judging normality of GM quality.

Chapter 4 deals with the significance of localization and duration of transient periventricular echodensities for the quality of GMs. This was studied from birth until the 20th week post-term in a group of appropriate-for-gestational age infants. The relationship between ultrasound findings and GM quality and the neurological outcome was also established. Echodensities in the frontal white matter, which resolved before the 14th day of life, did not seem to have any impact on the individual developmental trajectories of GM quality. Echodensities, especially in the parieto-occipital white matter, lasting for more than 14 days, were found to be related to abnormal developmental trajectories of the quality of GMs. Parieto-occipital echodensities with a duration of up to

14 days resulted in abnormal GMs in some infants, but led to normal GMs in others. This indicates the difficulty of establishing the severity of echodensities on the ultrasound appearance alone. The assessment of GM quality helped to identify those infants who were at risk for developmental problems and those who were not. Normal GMs in infants with transient echodensities indicate that there is no brain dysfunction; these infants had a good prognosis. The persistent presence of abnormal GMs are predictive of an impaired neurological outcome. The quality of fidgety GMs is of great value to establish the prognosis for the outcome in infants with transiently abnormal GMs.

Chapters 5 and 6 document the development of spontaneous motility in a group of preterm intrauterine growth-retarded infants from birth until approximately 20 weeks post-term. Almost all showed evidence of placental dysfunction. Data on the quantity of spontaneous movements are provided in **chapter 5**. The incidence of various frequently occurring movement patterns did not differ from normative data previously found in low-risk appropriate-for-gestational age preterm infants (the reference group). This indicates that intrauterine growth retardation does not influence the normal developmental course with respect to the rate of occurrence of movement patterns. We evaluated the quantitative aspects of spontaneous motility according to both postmenstrual age and postnatal age, because possible changes in the quantity of spontaneous motility due to the deterioration of the fetal condition just before birth might thus become evident. However, only an increased duration of GMs with increasing postnatal age was revealed, a tendency not found in the reference group. A possible explanation is a reduced duration of GMs in the first week after birth, after a period in which the fetal condition had been more or less severely compromised.

The developmental course of the quality of GMs for this group of preterm, small-for-gestational age infants is reported in **chapter 6**. Most infants showed abnormal GMs during their preterm period. The longitudinal approach of this study revealed that the quality of GMs normalized in the majority of the infants after term age. Furthermore, a clear relationship was demonstrated between specific developmental trajectories of GM quality and neurological outcome. The quality of fidgety GMs, in particular, was predictive for the final outcome. By contrast, the neurological outcomes were not correlated to brain ultrasound

findings, obstetrical variables indicative of fetal distress, the degree of growth retardation or the extent of brain sparing. A large proportion of infants with normal brain ultrasound scans appeared to have abnormal GMs. This finding suggests that the chronically reduced fetal supply of oxygen or nutrients or both may lead to longer lasting but often transient brain dysfunction, which is not necessarily caused by haemorrhagic or ischaemic lesions detectable on ultrasound scans. The assessment of the quality of GMs in preterm, small-for-gestational age infants is a sensitive method with a high predictive value for eventual outcome, similar to previous studies of preterm, appropriate-for-gestational age infants.

Chapter 7 describes the effects of dexamethasone treatment on spontaneous movements in preterm infants at risk for chronic lung disease. This longitudinal study demonstrated that dexamethasone had profound acute effects on the quantity and quality of GMs, as early as 24 hours after the first dose of dexamethasone had been given. The incidence and duration of GMs was substantially reduced and after detailed analysis of the quality of GMs, we found a reduction of speed and amplitude. In this group of high-risk preterm infants, we also found a clear relationship between the severity of brain ultrasound abnormalities and specific developmental trajectories of GM quality and the neurological outcome, confirming previous reports. It was impossible to discriminate between the effects of brain lesions and possible adverse long-term effects of dexamethasone on spontaneous motor activity. Nevertheless, the acute changes were such that cautious use of systemic dexamethasone therapy in preterm infants is recommended by us, until more is known about long-term neurological sequelae.

Chapter 8 reports a multi-centre study on the quality of fidgety GMs in a large group of normal and abnormal, preterm and term infants, in relation to the final neurological outcome and the quality of GMs prior to the age of transformation. The quality of fidgety GMs in young infants yielded information for making valid predictions about later neurological outcome long before the first signs of spasticity appeared. Not only are *abnormal* or *absent* fidgety GMs indicative of a poor outcome but *normal* fidgety GMs are an excellent marker for a normal neurological outcome. The assessment of the quality of GMs before the onset of fidgety movements had an equally high

sensitivity but its specificity was considerably lower. Many of the earlier GM abnormalities were transient phenomena and normalized before or at the appearance of fidgety movements. On the other hand, infants with abnormal or absent fidgety movements did not normalize, bar a few exceptions (5 %), but retained abnormal neurological signs after the age when fidgety movements normally disappear.

In **chapter 9** the studies are placed within general perspectives. Implications for future studies are discussed.

In conclusion, our studies have shown that assessment of the quality of GMs is a powerful diagnostic tool for evaluating brain function in preterm infants. It is non-intrusive, quick, and can be applied reliably in ill preterm infants. After the age of transformation, the quality of fidgety movements is an excellent marker for the eventual neurological outcome. The method is a valuable extension of other ways of assessing the central nervous system in young infants, in particular brain ultrasound imaging. The observation of general movements, preferably from videotape recordings, should be included in the standard neurological examination during the preterm and term period. Moreover, it is a useful tool for investigating the influences of disease and medication on the young central nervous system.