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The tonic response to the infant knee jerk as an early sign of cerebral palsy

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ABSTRACT

Background: Early identification of infants at risk of cerebral palsy (CP) is desirable in order to provide early intervention. We previously demonstrated differences in knee jerk responses between 3-month-old high risk and typically developing infants.
Aims: To improve early identification by investigating whether the presence of tonic responses (continuous muscle activity occurring after the typical phasic response), clonus or contralateral responses to the knee jerk during infancy is associated with CP.
Study design: Longitudinal EMG-study.
Subjects: We included 34 high-risk infants (median gestational age 31.9 weeks) who participated in the LEARN2MOVE 0–2 years trial.
Outcome measures: Video-recorded knee jerk EMG-assessments were performed during infancy (1–4 times). Developmental outcome was assessed at 21 months corrected age (CA). Binomial generalized estimating equations models with repeated measurements were fitted using predictor variables.
Results: Infants who later were diagnosed with CP (n = 18) showed more often than infants who were not diagnosed with CP i) tonic responses – from 4 months CA onwards, ii) clonus - from 13 months CA onwards, and iii) contralateral responses - from 15 months CA onwards.
Limitations: The main limitation is the relatively small sample size.
Conclusions: The assessment of tonic responses to the knee jerk using EMG may be a valuable add-on tool to appraise a high risk of CP.

1. Introduction

Cerebral Palsy (CP) is the most common cause of physical disability in childhood. The diagnosis of CP indicates a permanent disorder of the development of movement and posture, attributed to disturbances in the fetal or infant brain [1]. The majority of children with CP are diagnosed with a spastic form [2]; they often exhibit pathological reflexes, including exaggerated patellar tendon reflexes [3].

Early identification of infants at risk of CP is desirable in order to provide early intervention, in a phase when the brain is most plastic [4]. However, the characteristics of the young nervous system hamper prediction. For instance, hyperexcitability of spinal circuitries, e.g., expressed by low thresholds for eliciting tendon reflexes and the occurrence of reflex irradiation, is a physiological phenomenon in early infancy [5,6]. In addition, spasticity is rarely present at early age in infants who develop CP [7]. Recently, we noticed that some high-risk infants showed a tonic reaction in response to the knee jerk. We therefore studied knee jerk responses with the help of surface electromyography (EMG) in infants aged three months corrected age (CA). We were able to demonstrate that EMG responses in infants at very high risk of CP differ from those in typically developing infants [8]. For example, the three-month-old high-risk infants more often showed tonic responses (TRs), i.e. continuous muscle activity occurring after the typical phasic response, and more often clonus and contralateral phasic responses than typically developing peers.

The aim of the present, longitudinal study was to evaluate the

Abbreviations: CA, corrected age; CP, cerebral palsy; CPG, central pattern generator; EMG, electromyography; GMs, general movements; L2M, Learn2Move; TINE, Touwen Infant Neurological Examination; TR, tonic response

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Table 1
Child characteristics.

Baseline characteristics	*n* = 34
Gestational age, weeks (median + range)	31.9 (25.9–41.3)
Birth weight, grams (median + range)	1794 (720–5400)
Sex, n (boys/girls)	19/15
Type of brain lesion, n	
Basal ganglia and/or thalamus lesion	5
Cortical infarction	2
Cystic periventricular leukomalacia	10
Periventricular leukomalacia (without cysts)	2
Posthemorrhagic porencephaly	8
Non-specific or no significant lesions	7
Corrected age at 21 months assessment, months (median + range)	21.3 (19.1–22.5)
Outcome at 21 months	
No cerebral palsy	16
GMFCS level I	3
GMFCS level II	5
GMFCS level III	4
GMFCS level VI	3
GMFCS level V	3

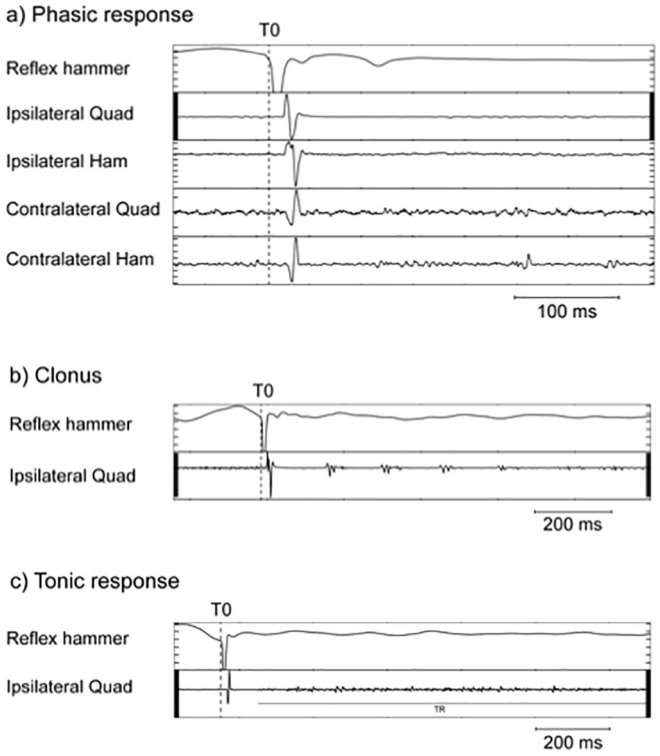

Fig. 1. EMG responses to the knee jerk
Responses were considered a phasic response if they a) occurred within 40 ms after T0, b) lasted maximally 15 ms, c) were bi- or triphasic, and d) significantly differed from background activity and muscle activity prior to tap application (Fig. 1A). The presence and the number of repeats of repetitive phasic responses (clonus) were recorded (Fig. 1B). Reponses were considered as tonic response if they a) started within 150 ms after a phasic response, b) lasted at least 500 ms, and c) visual inspection indicated continued activity of a similar intensity (Fig. 1C). Adapted from Hamer et al. [8].

development of knee jerk responses in high-risk infants during the first two years of life. We investigated whether the presence of TRs, clonus or contralateral responses during infancy is related to the diagnosis of CP.

We hypothesized that in particular the persistence of tonic responses is associated with CP, as the occurrence of tonic responses in early infancy is related to an abnormal quality of the infant's general movements (GMs) [8], and abnormal GMs are associated with CP [9,10]. In addition, we hypothesized that contralateral reflex irradiation of phasic responses may be a typically transient phenomenon of early ontogeny that persists in children with CP [11,12].

2. Materials and methods

2.1. Participants

Out of the 43 infants who had participated in the LEARN2MOVE (L2M) 0–2 years project, 34 infants had underwent at least one proper knee jerk EMG assessment and had participated in the assessment around 21 months CA and were therefore included in this study (Table 1). The L2M 0–2 years project was primarily designed as a randomized controlled trial to study the effect of early intervention [13]. Inclusion criteria of the L2M 0–2 years project were maximally nine months CA at enrolment and the presence of at least one of the following conditions: (1) cystic periventricular leukomalacia, (2) parenchymal lesion of the brain, (3) severe neonatal hypoxic-ischaemic encephalopathy with brain lesions on MRI and (4) neurological dysfunctions suggestive of the development of CP [13]. Children with severe congenital disorders or with caregivers having insufficient understanding of the Dutch language were excluded. The project was approved by the Ethics Committee of the University Medical Centre Groningen and registered under trial number NTR1428. Parents gave informed consent.

2.2. Knee jerk assessment

We aimed to perform a videotaped knee jerk EMG assessment at baseline, i.e., between 0 and 9 months of age, at 6 and 12 months after baseline, and around 21 months CA, as part of the L2M research protocol. Bipolar surface electrodes (inter-electrode distance 14 mm) were placed over the bellies of the right and left quadriceps and right and left hamstrings. Surface EMG signals were continuously recorded by means of an electro-physiological front-end amplifier (Twente Medical Systems International, Enschede, The Netherlands) at a sampling rate of 2000 Hz. The EMG amplifier simultaneously recorded accelerations of the connected reflex hammer to allow for precise determination of tap application. In each infant, the knee jerk was elicited approximately ten times on each side.

2.3. Video and EMG analysis

The PedEMG software (Developmental Neurology, University Medical Center Groningen, The Netherlands [14]) allows for analyses of synchronized signals, such as surface EMGs, reflex hammer and video recordings. The videos were analysed to include only trials in which a clear kick of the leg was observed in response to the tendon tap. The EMGs were subsequently analysed in random order and without video to allow for blinded analysis. First, the tap-signal from the reflex hammer was used to define T0 of the knee jerk latency (Fig. 1). Next, onset times of phasic and tonic responses (PRs and TRs, respectively) were determined with the use of the model-based algorithm of Staude and Wolf, which detects significant changes in muscle activity [8,14].

For each child at each assessment, the percentages of occurrence of ipsilateral and contralateral PRs as well as TRs and clonus were calculated. Parameters were only computed if at least five suitable trials were available for analysis.

2.4. Developmental assessments

At the last assessment, i.e., around 21 months CA, we performed the Touwen Infant Neurological Examination (TINE) [15] to specify whether or not the child had CP, in accordance with the criteria of the Surveillance of Cerebral Palsy in Europe [3]. The diagnosis of CP implies the presence of abnormalities in movement and posture,