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Two-year motor outcomes associated with the dose of NICU based physical therapy: The Noppi RCT

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ABSTRACT

Background: Interventions involving both the parent and the preterm infant have demonstrated lasting effects on cognitive outcomes, but motor effects are less salient. It remains unclear when to commence early intervention and if dosages have impact on motor outcomes.

Aims: To examine the effect on motor performance at 24-months corrected age following a parent-administered intervention performed with infants born preterm in the NICU. Intervention dosing and longitudinal motor performance were also analyzed.

Study design: Single-blinded randomized multicenter clinical trial.

Subjects: 153 infants born, gestational age \leq 32 weeks at birth, were randomized into intervention or control group.

Outcome measures: Infant Motor Performance Screening Test, Test of Infant Motor Performance, Peabody Developmental Motor Scales-2.

Results: No significant difference was found between the intervention and the control group assessed with the PDMS-2 at 24-months CA. However, a significant positive association was found between dosing and the Gross Motor and Total Motor PDMS-2 scores. Analysis of longitudinal motor performance showed a decreasing motor performance between 6- and 24-months corrected age in both groups.

Conclusions: There was no difference in motor performance between groups at 24-months corrected age. However, increased intervention dosage was positively associated with improved motor outcome.

1. Introduction

Preterm infants born before 32 weeks gestational age $(GA)^1$ are at risk for poor motor, cognitive and/or behavioral outcomes [1,2]. Therefore, early intervention $(EI)^2$ programs implemented in the Neonatal Intensive Care Unit $(NICU)^3$ or shortly after discharge are

designed to optimize one or more of these developmental outcomes. Experience-dependent neuroplasticity research serves as the rationale underpinning many of these EI paradigms [3,4], but the design and delivery of intervention varies considerably [3]. A Cochrane Review [5] of the cognitive and motor benefits of NICU-based and post-discharge interventions showed positive influences on both of these behaviors,

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¹ GA: Gestational Age

² EI: Early Intervention

³ NICU: Neonatal Intensive Care Unit

but the long term outcomes are stronger for cognition. Few of these studies reported on longitudinal changes in motor development over the first two years.

Recently EI studies have been designed to educate, coach, and support parent participation in the delivery of EI [5]. This study reports on the twenty-four-month motor outcomes from the Norwegian Physiotherapy study in Preterm Infants (NOPPI). The Noppi study was designed to investigate the impact of a parent administered, 3-week NICU based exercise program to improve motor development in high risk infants born preterm [6]. At discharge, motor outcomes favored the intervention group with an effect size of 0.4 [7]. At three months corrected age (CA), the difference in motor performance was no longer present, however, exploratory data-analyses indicated that infants who received at least 50 % of the recommended intervention dosage, independent of medical complexity, demonstrated significantly better motor outcomes [8].

The primary aim of this paper is to describe the 24-month motor outcomes associated with the Noppi intervention for infants born preterm. We aimed to investigate whether the three-week parent delivered NICU intervention would contribute to long term motor outcomes at 24 months CA. This was important to evaluate as reviews of the longitudinal effects of early motor interventions provided to infants born preterm show there may be performance gaps at younger ages and significant differences at older ages [9,10]. Therefore, it seems important to assess the potential long term effects of the Noppi study despite the lack of significant results between NICU discharge and the 3 month assessments. A secondary aim of the study was to investigate whether the dosing effects identified at three-months CA [8] would continue to explain motor outcomes at 24 months. Another secondary aim was to analyze the motor developmental trajectory of the infants during the first two years.

2. Methods

2.1. Trial design

This is a pragmatic, single-blinded randomized multicenter clinical trial (RCT), embedded in routine clinical practice. The study was approved by the Regional Committee for Medical and Health Research Ethics in Northern Norway (REC North: 2009/916-7) and registered at Clinical Trials.gov (NCT01089296). Three Norwegian hospitals with Level III NICUs were invited to participate. Infants were recruited for the study when they reached 33 weeks postmenstrual age (PMA), and informed consent was signed by their parents. Following the baseline assessment, infants were randomized into the intervention or the control group.

2.2. Participants and setting

2.2.1. Study population and sample size

Infants born prior to 32 weeks GA were recruited between March 2010 and October 2014. Neonatologists identified infants physiologically able to tolerate handling. Parents were required to understand and speak Norwegian and to agree to return to the hospital at 3-, 6-, 12- and 24-months for follow-up visits. Triplets, infants with malformations or syndromes and infants having major surgery were excluded from participation.

We calculated the sample size based on Peabody Developmental Motor Scales-2 (PDMS-2)⁶ scores at 2 years CA. A difference on gross motor and fine motor function of 0.5 SD between the intervention and control group was considered clinically significant. Sixty-three infants in

each group were needed to achieve a statistical power of 80 % at a 0.05 (α) significance level on two-sided tests. We planned to recruit 75 children in each group to account for the impact of twins and potential dropouts.

2.3. Randomization and intervention

We performed the randomization using a Web-based, computer-generated randomization system developed and administered by the Unit for Applied Clinical Research, Faculty of Medicine, Norwegian University of Science and Technology, Trondheim, Norway. Stratification was based on GA at birth (<28 weeks and ≥28 weeks) and recruitment site. Twins were assigned to the same group because it was impossible to withhold knowledge of group assignment from the parents and the physical therapists (PTs) teaching the parents.

The parent-administered exercise program, performed from 34 weeks through 36 weeks PMA for 10 min twice a day, was a modified version of Girolami's handling and motor stimulation program for infants born preterm [6,11]. The intervention was designed to improve postural and motor control of the head and trunk, and midline orientation of head, arms and legs in prone, supine, side-lying and supported sitting. In each position guided movements and intermittent manual compressions over relevant muscle groups and joints were performed.

The original protocol implemented by Girolami [11] included activities in prone, supine, side-lying and supported sitting. This was grounded in guided movements combined with visual, auditory, tactile, vestibular, and proprioceptive input, to improve body awareness, increase isometric coactivation, as well as the ability to initiate and sustain muscle activity for functional performance. In supine the activities were designed to improve head in midline and head turning to both the right and left sides, as well as hands to mouth and hands to chest. Activities in prone were directed toward head lifting and turning while weight bearing through the forearms. The goal of the side-lying activities was to assist the infant to initiate and sustain contraction of the abdominal and back muscles with the head in midline and visual gaze to the hands. In supported sitting the infant was guided to sustain the head in midline and the opportunity to practice vertical head control and head turning. The arms were free to explore the face and trunk and visual interaction with the caregiver was encouraged. The original program was modified to add transition activities from supine to side-lying and supine to upright sitting through side-lying [6]. The PTs individualized the intervention based on each infant's performance on the Test of Infant Motor Performance Screening Items (TIMPSI)⁷ [12] and tolerance for movement. At least one activity in each of the four positions and one transition activity was always included.

The protocol developed by Girolami [11] was further modified by changing it from a therapist- to a parent-delivered protocol. To ensure the parents were comfortable and able to carry out the intervention, experienced pediatric PTs trained the parents to skillfully perform the intervention strategies. Parents also received training in how to observe and interpret their infant's behaviors and physiological signs of pleasure and stress. The PTs discussed and emphasized the role of communication and social interaction between parent and infant. For example, the infant should be in States three (drowsy or semi-dozing) or four (alert with bright look) [13]. Parents were instructed to pause the intervention to calm the infant if signs of stress were observed (e.g., grimacing, changes in skin color, irregular respiration, or loss of muscle tone). Parents were given the autonomy to adjust the length of the treatment session based on their infant's behavior or physiological condition.

A minimum of three sessions with the PT were provided to teach, supervise, and support parent learning. In addition, parents were invited to contact the PT if they needed additional support or clarification regarding the exercises. Finally, the intervention protocol was printed in

⁴ CA: Corrected age

⁵ PMA: Postmenstrual age

⁶ PDMS-2: Peabody Developmental Motor Scales-2

⁷ TIMPSI: Test of Motor Performance Screening Items

a "Play-Book" with photos and written instructions. This was provided to each parent in the treatment group [6,8].

In cases of early discharge, the parents were asked to continue the intervention at home until the end of the 36th postmenstrual week. The infants in the control group received no parental intervention, but parents were given general information about handling and positioning. In each NICU, standard nursing care was provided for both infant groups based on principles from the Newborn Individualized Developmental Care and Assessment Program [14]. A more complete description of the intervention was previously published [6].

2.4. Outcome measures

The primary outcome was the Peabody Development Motor Scale-2 (PDMS-2) Total Motor Quotient at 24 months CA.

Secondary outcomes were the Gross and the Fine Motor quotients of the PDMS-2. Changes in total motor performance over time and the impact of the intervention dosage were also analyzed.

The Test of Infant Motor Performance Screening Items (TIMPSI) was administered to measure baseline motor performance. The TIMPSI is a shortened version of the Test of Infant Motor Performance (TIMP),⁸ a norm-referenced standardized assessment that can identify changes in motor development in two-week increments from 34 weeks PMA to fivemonths CA [12,15,16]. The TIMP has high specificity and moderate sensitivity [17] and strong inter- and intra-rater reliability [18]. It is responsive to intervention in infants born preterm both prior to term age [7] and from term age to five-months CA [19,20]. Like the TIMP, the TIMPSI assesses movement and postural control in prone, supine, supported sitting and standing. The TIMPSI is reliable and valid for use within the same timeframe as the TIMP. TIMPSI test results were used to individualize the treatment protocol. The TIMP was used to assess shortterm outcomes. To establish inter-rater reliability, raters completed the researcher reliability protocol developed by the TIMP publisher. The protocol uses the Facets computer program for Rasch analysis of rater consistency and severity/leniency [21]. All testers achieved a reliability level of >0.90.

The PDMS-2, a standardized outcome measure for children from birth through five years of age [22], was administered to assess motor development at 6-, 12- and 24-months CA. It is a reliable and valid measure to assess fine and gross motor function using 3 gross motor and 2 fine motor subtests. The scores on the subtests are summed to calculate a Gross Motor Quotient (GMQ), Fine Motor Quotient (FMQ) and Total Motor Quotient (TMQ) [22]. High test-retest reliability and acceptable responsiveness to intervention effects have been shown based on these quotients [22,23]. The Noppi PT testers (n=7) met five times to view and discuss videotaped Peabody assessments. They independently scored 2 assessments demonstrating very good inter-rater reliability (ICC = 0.95).

2.4.1. Data collection

PTs blinded to group assignment performed the pre- and posttests. In rare cases, when the PT administering the post-intervention assessment was aware of the group assignment, the test was recorded and scored by a PT blind to group assignment. Parents of infants in the intervention group were asked to record the time spent on the intervention and report reasons for not performing or terminating a session.

2.5. Statistical analysis

All test scores were transformed to z-scores to allow a normalized

comparison of scores for all test outcomes from baseline to 24-months. TIMPSI and TIMP raw scores for adjusted age were converted to z-scores as described in the TIMP manual. [12] PDMS-2 scores were converted to z-scores based on tables in the PDMS-2 manual [22].

A linear mixed model (LMM) analysis was used to test for group differences between the intervention and control group. Twins in the sample create potential dependencies in motor development, so family ID was included in the analysis to account for this dependency when comparing motor scores at 24 months. Because risk variables may contribute to substantial increases in power [23], we incorporated known risk factors correlated with motor skills (including respiratory distress-syndrome, small for gestational age, sepsis, intraventricular hemorrhage (degree 2 or higher) and periventricular leukomalacia) [24,25] in our analysis. Group differences in total motor function were assessed longitudinally using LMM. Test scores at six points in time between 34 weeks PMA and 24 months CA are nested within children which in turn are nested within family. LMM is a robust method to handle nested data.

Because the mean total motor *Z*-scores in the two groups followed a non-linear curve we used two variables representing time: Time and Time squared. Including Time squared in a model predicting motor development gives a highly significant improved model fit. Group differences on longitudinal development were evaluated by testing the overall effect of the Time by Group and the Time squared by Group interaction. We used change in the $-2*\log$ likelihood for this purpose, comparing the full model (including the two interaction terms) with a reduced model (not containing these interactions). The time variable was treated as a continuous variable in the longitudinal analysis (baseline was coded 0, and the following measurement occasions were coded as the number of weeks since baseline).

We used SPSS 26 for all analyses. Significance was evaluated using 95 % confidence intervals, or a significance level of 0.05.

3. Results

Fig. 1 shows a flow chart of the 217 invited participants. Consent to participate was obtained for 153 (71 %) children. After baseline assessment, 74 were randomized to the intervention group and 79 to the control group. Based on withdrawals and logistical issues 62 intervention group infants and 65 control group infants were assessed at 24-month CA. Parents of 59 (95 %) of the intervention group infants maintained a record of the number and total time of each session. There were no significant differences between groups with respect to birth weight, perinatal medical or social factors [7,8]. We did however find a significant difference between the number of infants small for gestational age (SGA) with more infants SGA in the control group ($X^2(1) = 5.5$; p = 0.02) (Table 1).

3.1. Group differences at 24-months

Table 2 shows estimated marginal means for the intervention and control groups, all of which were below average.

Controlling for gender and risk factors no significant treatment effect for Gross Motor, Fine Motor or Total Motor function was found at 24-months CA.

3.2. Effect of the number of sessions

Families were asked to complete two 10-min sessions per day for 3 weeks (42 sessions). The data were analyzed to determine if dosing, the number of treatment sessions received, had an impact on gross or fine motor outcomes.

We found that families in the intervention group (n=59) completed a mean of 25.3 sessions (SD = 11.1). Controlling for the number of risk conditions and gender, we evaluated whether there was an association between the number of sessions and motor function at 24-months for

⁸ TIMP: Test of Infant Motor Performance

⁹ GMQ: Gross Motor Quotient

¹⁰ FMQ: Fine Motor Quotient

¹¹ TMQ: Total Motor Quotient

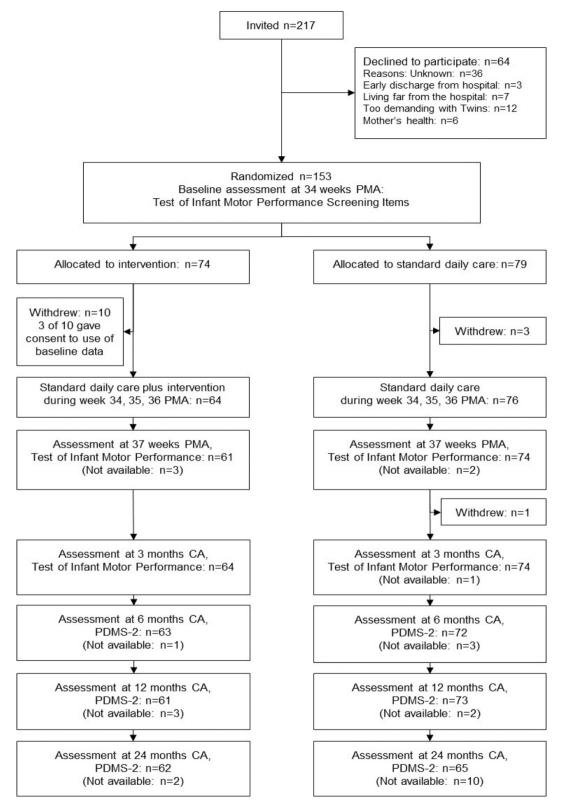


Fig. 1. Flow of the participants through the study.

those receiving intervention. With respect to gross motor function, this association was significant with an estimated increase in the gross motor *Z*-score of 0.019 per session unit increase (b = 0.019; p = 0.017; 95 % confidence interval: (0.004; 0.034)). For fine motor function, the effect was not significant (b = 0.012; p = 0.10; 95 % confidence interval: (-0.002; 0.026)).

For total motor function the effect was also significant (b = 0.017; p = 0.025; 95 % confidence interval: (0.002; 0.032)). Fig. 2 illustrates this effect using quartiles of the number of sessions.

Correlations between the number of risk conditions and the number of sessions and time used were low and not significant: Pearson correlation =0.04 (Risk with #sessions: p=0.74) and r=0.06 (Risk with

Table 1Baseline characteristics at baseline and medical conditions at birth.

| Baseline characteristics | Intervention group (<i>n</i> = 71) | Control group (<i>n</i> = 79) | p ^a |
|--|-------------------------------------|--------------------------------|----------------|
| $\begin{array}{c} \text{Gestational age} < 28 \text{ wk., n} \\ \text{(\%)} \end{array}$ | 19 (14) | 15 (19) | n.s. |
| Boys, n (%) | 36 (51) | 44 (56) | n.s. |
| Twins, n (%) | 12 (17) | 23 (29) | n.s. |
| Birth weight, g, mean (SD) | 1417 (417) | 1385 (368) | n.s. |
| Mother's age, y, mean (SD) | 32.1 (5.5) | 30.5 (4.9) | n.s. |
| Mother's education, y, mean (SD) | 15.6 (2.7) | 14.9 (2.8) | n.s. |
| Father's education, y, mean (SD) | 14.5 (3.0) | 14.6 (2.7) | n.s. |
| Has no older siblings, n (%) | 41 (58) | 54 (68) | n.s. |
| Medical conditions at birth | | | |
| RDS ^b , n (%) | 39 (56) | 51 (65) | n.s. |
| SGA ^c , n (%) | 6 (9) | 18 (23) | 0.02 |
| Sepsis, n (%) | 6 (9) | 11 (14) | n.s. |
| PVL ^d , n (%) | 4 (6) | 3 (4) | n.s. |

^a *p*-Value (n.s. = non-significant).

Table 2Estimated marginal means, standard errors and group differences for motor functioning at 24 months.

| Variable | Intervention mean (SE) | Control mean (SE) | Group effect T | 95 % CI for difference |
|----------------|---------------------------|----------------------|-------------------|---------------------------|
| Gross motor | -1.08 (0.09) | -1.04 (0.08) | 0.27 | (-0.21, 0.28) |
| Fine motor | -0.29 (0.08) | -0.49 (0.08) | -1.69 | (-0.42, 0.03) |
| Total motor | -0.83 (0.08) | -0.88 (0.08) | -0.45 | (-0.28, 0.18) |

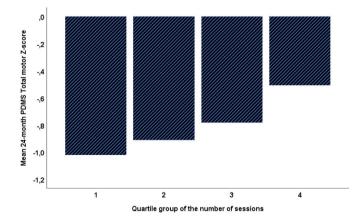


Fig. 2. Bar chart: 1: The approx. 25 % with the lowest number of sessions (1–16 sessions), 2: The next 25 % (17–25 sessions), 3: 26–32 sessions, 4: The 25 % with the highest number of sessions (33 or more sessions). Negative mean z-scores made the bar chart look upside down. Quartile group 1 differs significantly from quartile group 4 (estimated mean difference = -0.53; p = 0.03).

Time used; p = 0.64); n = 59.

3.3. Longitudinal development

Fig. 3 shows the mean standardized total motor scores on the six measurement occasions. Both groups follow a non-linear curve with some initial improvement followed by a decrease in motor function

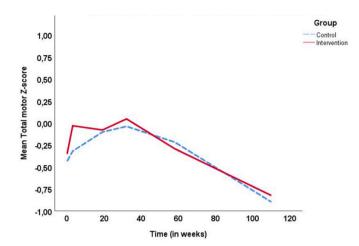


Fig. 3. Mean total motor z-scores for the two treatment groups.

relative to age norms.

We tested whether a linear model for development would be sufficient or whether the model could be improved by adding the square of time. A linear model with Time showed a $-2^* log$ likelihood =1545.66, and when Time squared was added to the model the $-2^* log$ likelihood =1445.08. The change in $-2^* log$ likelihood was highly significant $(\chi^2(1)=1545.66-1445.08=100.58, p<0.0005)$. Therefore, adding the square of time improves prediction of total motor score over time. We therefore included Time squared in models evaluating group differences on motor development.

3.4. Group difference on motor development

When testing group differences in motor development, we included gender and the number of birth risk factors as covariates. We tested whether the inclusion of Time by Group and Time squared by Group interactions improved the model fit. The change in $-2\ast log$ likelihood was $\chi^2(2)=1434.24-1431.07=3.17; p>0.05. This indicates we do not have sufficient evidence to claim motor development differs over time between groups. From the end of the intervention to testing at 24-months CA, the overall z-scores of both groups decreased, resulting in similar performance at 24-months.$

No adverse effects of the intervention were reported.

4. Discussion

The main finding of this study shows motor development reported on PDMS-2 at 24-months was not significantly different between groups. However, when dosing was considered, we found the PDMS-2 scores for gross motor function and total motor function were significantly associated with the number of intervention-sessions received in the NICU.

Recent systematic reviews and meta-analyses investigating NICU-based intervention programs on motor outcomes show continued effects up to 24-months [9,26]. Further, parent-delivered interventions are reported to be the most beneficial [9]. However, the results of our parent-administered intervention are not consistent with those reported in the literature. One difference between our study and others is the duration of the intervention. Studies having positive long-term outcomes continued the intervention protocols after hospital discharge [3,9]. The Noppi intervention was implemented solely in the NICU. Therefore, the shorter intervention period of our study may have contributed to the diminishing effect on performance over time. We hypothesize that a prolonged intervention period, with a protocol adapted to support changes in motor performance/development over time, would be needed to produce a sustained developmental impact at 24 months.

 $^{^{\}rm b}$ RDS = Respiratory distress syndrome.

^c SGA = Small for gestational age.

 $^{^{\}rm d}$ PVL = Periventricular leukomalacia.

However, we did find that dosage, that is infants who received a greater number of parents administered sessions had significantly higher scores on the PDMS-2. Therefore, we hypothesize underdosing may reduce the effectiveness of the intervention. In this study, and in our previous study [8], our analysis of dosing controlling for medical complexity demonstrated a significant positive relationship between intervention dose and motor outcome. This effect was shown based on two different outcome measures. At three-months CA, the infants were tested using the TIMP, while the PDMS-2 was used for infants tested at 24-months CA. We speculate the significant association between dosing and motor outcomes supports the need to more thoroughly study both the dosing and the duration of the intervention to find the optimal balance that will yield the most effective outcomes [8].

The decision to train parents to administer the intervention may have also contributed to the improved scores of infants. Research indicates maternal interventions, which, for example, baby massage and/or skinto-skin care in the NICU, also have positive effects on developmental outcomes [27-29]. It has been proposed that optimizing parent-child interactions and the environment of the infant are protective and supportive to development and competence of the infant [28,30,31]. Development is understood to be experience-dependent and characterized by the continuous interplay between genetic, biological, parenting and physical environmental factors [32]. Touching, targeted handling and facilitation during play exercises while the infants were in the NICU may have offered the parents' additional opportunities to create closer bonds with their infants, allowing them an enhanced understanding of the amount of physical stimulation and play their infant could tolerate. Ultimately, this may have enabled the parents to give their child a more stimulating home-environment after discharge, perhaps continuing to pursue developmental activities throughout the first two years of their child's life. This aligns with evidence that parents educated about child development show improved parental competency and empowerment in caring for their preterm infant [33,34].

On the other hand, over the 3-week intervention, only 3 parents completed the requested dosage of 42 treatments. For parent's unable to complete the required dosing protocol, infant behavioral state, increased fussiness, or decreased wakefulness, were cited as the primary reasons for not implementing the full protocol or for stopping the intervention early. We explored the possibility that less healthy infants received fewer treatments. However, the data do not support this hypothesis. Additionally, we do not know if the reduced number of intervention sessions might be attributed to the infant. We did not collect physiological data during the parent intervention sessions that might indicate the infant was unable to tolerate the movement and/or guided handling.

The study of Girolami and Campbell [11] reported no negative impact on weight gain, nor an increase in apnea or heart rate changes during the intervention. In addition, that intervention program was implemented with a higher dose than requested in the Noppi study. We therefore hypothesize that perhaps parents did not have the emotional and physical reserves to comply with the requested number of sessions. This hypothesis rests on data indicating parents frequently report reduced self-confidence when caring for their preterm infant, both in the NICU and post-discharge [3,35]. In hindsight, we feel that monitoring physiological variables of the infant during the intervention periods may have reduced caregiver stress and strengthened the study by providing a broader understanding of why parents made the decision to reduce the duration or dosage of the intervention. Additionally, incorporating a questionnaire to assess parental factors such as personal and financial well-being, stress and anxiety might provide information to explain parental decisions to decrease the number of planned intervention sessions. We may find a relationship between enhanced personal or financial resources and/or decreased stress and improved adherence to the intervention protocol. For future studies using a parent administered intervention, we recommend parents receive expanded education regarding the identification of infant states. This would ensure they

understand the difference between mild fussing that might be resolved with a pacifier or consoling and crying and signs that indicate the infant can no longer participate in the intervention.

The fast-paced, technology laden NICU is a challenging and scary environment for families, which may lead to insecurity and a loss of autonomy for families [36]. The goal of the Noppi study was directed at improving the functional capacity of the infant, but it was also designed to empower parents by providing knowledge, training, and support. However, we also feel more rigorous follow-up on the part of the PT trainers may have led to greater adherence to the program by providing more opportunities to support the parents and clarify questions regarding the intervention.

Finally, we would like to address the trajectories of motor development reported over the duration of this study (Fig. 3). After six-months of age, motor performance relative to age norms decreased in both groups. Previous reports regarding the developmental trajectories of infants born preterm state that preterm and full term infants differ in gross motor abilities until about three years [37]. Further, very preterm infants achieve significantly lower scores than full term infants on gross and fine motor development tests with an increasing gap between 1 and 18 months CA [38]. Infants born preterm are known to be delayed in the acquisition of the postural control and movement components that support early motor development [39]. This aligns with our findings of suboptimal motor outcome for both groups indicating the need for continued and individualized intervention following NICU discharge and throughout the first year of life.

Major strengths of the Noppi study include a parent-administered intervention integrated within regular NICU practice, longitudinal assessment with tools that are valid and reliable for the study population, and an adequate sample size with the statistical power to ensure the validity of the study outcomes.

A limitation because of the lack of nursing-staff and parent blinding, is the potential spillover effect in favor of the control group. This effect was possibly reduced by instructing the nurses and the parents in the intervention group not to discuss the protocol with anyone. The failure to assess the fidelity of the intervention delivered by the caregivers and parental stress is another limitation of our study. Also, we do not know if any of the parents continued the intervention or if infants in either group received physical therapy after discharge which might have affected the long term study outcomes. Finally, the relationship between motor and cognitive development is well established [9], and it would have been interesting to investigate the cognitive effects of the Noppi intervention, in particular if there might have been a correlation with motor development and dosage. However, limited resources (financial and personal) did not allow for such elaboration.

5. Conclusions

No significant differences were found on PDMS-2 scores between the intervention group and the control group at 24-months CA. There was a significant positive relationship between the number of intervention sessions (dosing) and the Gross Motor and Total Motor scores. This may indicate that a parent administrated NICU intervention can provide a positive long-term effect on motor development in infants born preterm when adequately dosed. These findings call for hands on motor interventions that emphasize support and guidance to empower parents as well as large-scale prospective studies on the timing and dosing of early interventions for preterm infants.

CRediT authorship contribution statement

Gunn Kristin Øberg: Conceptualization, Methodology, Investigation, Data Curation, Writing-Original Draft, Writing - Review & Editing, Visualization, Funding acquisition.

Bjørn Helge Handegård: Formal analysis, Visualization, Writing-Original Draft, Writing - Review & Editing.

Suzann K. Campbell: Methodology, Writing - Review & Editing. Tordis Ustad: Methodology, Data Curation, Writing - Review & Editing, Funding acquisition.

Toril Fjørtoft: Data Curation, Writing - Review & Editing.

Per Ivar Kaaresen: Methodology, Writing - Review & Editing.

Gay L. **Girolami**: Conceptualization, Methodology, Investigation, Writing-Original Draft, Writing - Review & Editing, Visualization.

All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

Role of the funding source

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Declaration of competing interest

Dr. Girolami and Dr. Campbell are partners in Infant Motor Performance Scales, LLC and co-developers of the TIMP, the measurement tool used to assess the infants in this study at baseline, after the intervention and at 3 months corrected age. However, they did not participate in any of the pre- or post-testing. All other authors declare no conflicts of interest.

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