

# Early identification and intervention in cerebral palsy

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## ABBREVIATIONS

COPCA	Coping with and Caring for Infants with Special Needs
GMA	General Movements Assessment
IMP	Infant Motor Profile
IVH	Intraventricular haemorrhage
PEDI	Pediatric Evaluation of Disability Inventory
PVL	Periventricular leukomalacia
TIP	Traditional infant physiotherapy

Infants with possible cerebral palsy (CP) are commonly assumed to benefit from early diagnosis and early intervention, but substantial evidence for this is lacking. There is no consensus in the literature on a definition of 'early', but this review focuses on interventions initiated within the first 6 months after term age. We cover basic neuroscience, arguing for a beneficial effect of early intervention, and discuss why clinical research to support this convincingly is lacking. We argue that infants offered early intervention in future clinical studies must be identified carefully, and that the intervention should be focused on infants showing early signs of CP to determine an effect of treatment. Such signs may be efficiently detected by a combination of neuroimaging and the General Movements Assessment. We propose a research agenda directed at large-scale identification of infants showing early signs of CP and testing of high-intensity, early interventions.

Cerebral palsy (CP) is the most common motor disorder among children, affecting approximately 2 to 2.5 per 1000 live births.<sup>1–3</sup> The term CP covers several disorders of movement, all attributed to non-progressive disturbances to the developing fetal or infant brain. The physical impairment is often accompanied by disturbances in cognition and perception.<sup>4</sup> Among others, genetic predispositions, maternal disease, preterm birth, low birthweight and birth asphyxia are associated with an increased risk of CP.<sup>5,6</sup> Most often, the pathology of CP in preterm infants can be ascribed to periventricular leukomalacia (PVL) or peri- or intraventricular haemorrhage (IVH), and in general, the risk of CP increases as gestational age decreases.<sup>6</sup> Some cases of CP in infants born at term are caused by birth asphyxia or neonatal arterial infarction,<sup>7</sup> but often a clear underlying pathology is not found. The incidence and prevalence of CP has fluctuated over time because of changes in prenatal and paediatric care, and advances such as avoiding kernicterus have contributed to preventing the subtype of athetoid CP. Improved care has led to an increasing number of surviving preterm and low birthweight infants at high risk of CP in Western industrialized countries.<sup>3,8</sup>

Severe CP can be predicted with high probability shortly after birth by cranial ultrasonography, magnetic resonance imaging (MRI) and other imaging techniques. This is not the case for mild to moderate CP. As the child develops,

early warning signs include delay in meeting motor milestones, seizures, poor sucking ability, a persistently fistled hand, and decreased rate of head growth.<sup>9</sup> However, the majority of cases do not present unequivocal symptoms early on and in current practice, most children with CP are diagnosed around the age of 1 to 2 years.<sup>1,2</sup> A fundamental question is whether these children would benefit from being identified earlier and receiving specific, early intervention.

In this review, we summarize the existing knowledge regarding the significance of environmental stimuli on early, neuronal development and use this to argue that early intervention ought to facilitate functional development in early childhood. In the literature, 'early intervention' encompasses approaches initiated before term age, when the infant is a few months old and at approximately 1 year of age. A clear consensus on a definition of 'early' is lacking. There is no unequivocal, scientific basis arguing in favour of a better effect of intervention initiated at, for instance, 3 months of age as compared with 12 months, and clinical studies documenting an age dependency of intervention are absent.<sup>10</sup> We have decided to focus on interventions aimed at infant motor development in which the infant shows active exploratory motor behaviour that can be externally facilitated through intervention. While the lower age limit of 'early' intervention in this context may be set at term equivalent age, the upper limit is more

difficult to delineate. We have somewhat arbitrarily limited the review to studies in which intervention was initiated before 6 months of age. Methods to identify infants with early signs of CP are discussed with a focus on the General Movements assessment (GMA) and neuroimaging. We subsequently review the existing literature on early intervention, pointing out that only a few studies have been performed on a selected population of infants with a high probability of developing CP. This may explain the overall lack of significant, long-term effects of intervention, since a large number of the infants included in the studies may be assumed not to have required the intervention. We end up by arguing that intervention should be initiated as early as possible and directed specifically towards infants selected on the basis of an effective neurodevelopmental evaluation. Thus, this review argues for a research agenda combining better identification and specific early intervention.

### Postnatal human brain development

Human brain development is characterized by a significant extension into postnatal life and lasts much longer than in other mammals, including our closest relatives, chimpanzee, gorilla, and orangutan. In humans synaptic density in the prefrontal cortex peaks at 3 years 6 months to 10 years of age,<sup>11,12</sup> in the auditory cortex at 5 months to 3 years 6 months,<sup>13</sup> and in the primary visual cortex around 3 months of age.<sup>14</sup> Analysis of gene expression has supported that synaptic growth and plasticity continues to increase in humans during at least the first decade.<sup>11,15,16</sup> Following an initial increase in the expression of synaptic genes and other molecules involved in synapse formation and plasticity, a decline is seen late in childhood and early adulthood, but with a sustained abundance far above that seen in other species.<sup>11,12,16</sup> It seems reasonable to relate this continued postnatal synapse formation and plastic moulding of neural circuitries in the brain to the protracted motor and cognitive development in human infants, children and young adults as compared with other species. Even basic motor abilities such as gait and hand function have been shown to develop and mature up to the age of 14 to 15 years<sup>17–19</sup> and most cognitive abilities continue to develop for much longer. This is most likely to be related to continued maturation of the corticospinal tract throughout childhood and adolescence.<sup>20,21</sup> In monkeys, the corticospinal tract establishes direct synaptic contacts with spinal motor neurons between birth and 8 months of age, which coincides with development of the ability of fractionated finger movements and precision grip.<sup>22–24</sup> Human infants develop this ability towards the end of the first year of life, consistent with the generally protracted development of the nervous system in humans as compared with monkeys. Physiological observations suggesting establishment of connections between corticospinal fibres and spinal motor neurons before birth in humans are at variance with this and require independent confirmation.<sup>25</sup>

### What this paper adds

- Demonstration of an effect of early intervention requires early identification of infants with possible CP.
- The term 'early intervention' is used in many different ways, which impedes comparison of published studies.

### Higher potential for recovery following neural lesions in infants than adults

It also seems reasonable to assume that the continued development of the brain well into adulthood creates a favourable environment for reorganization of internal connections and functional networks following lesions, whereas in adults reduced plasticity creates a somewhat less favourable environment.<sup>26</sup> People who were born blind thus show significant reorganization of their visual areas, which may process tactile and other sensory information, whereas such reorganization is not seen spontaneously in people who have become blind as adults.<sup>27</sup> It is also a general observation that surgical ablation of one hemisphere (in order to control epileptic seizures) leaves relatively mild impairments when performed before the age of 10 to 11 years of age.<sup>28</sup> This is well in line with original observations on the increasing functional severity of lesions in monkeys of increasing age, known as Kennard's principle.<sup>29,30</sup> The observation that early brain lesions may cause more severe effects than later lesions<sup>31</sup> does not necessarily challenge the idea that the plastic potential decreases with maturation. Such observations may as well be explained by the limited size and immature state of the nervous system at the time of lesion.

### Critical periods and sensitive periods

It is unclear to what extent this also signifies that the development of neural circuitries undergoes a critical period, where the maturation of the circuitries and their function in the adult brain depends crucially on the presence of specific environmental influences at a certain time in development. Since the original demonstrations of a critical period in the development of ocular dominance columns in the visual cortex of kittens by Wiesel and Hubel<sup>32,33</sup> critical periods have been demonstrated in a number of different species, in different cortical areas, and for a number of different functions.<sup>34</sup> For the motor system, Martin et al. have demonstrated that the development of the corticospinal system is impaired with severe functional deficits in adult cats when kittens are prevented from using their paw during a 1-week period, 2 to 3 weeks postnatal.<sup>35</sup> For obvious reasons it is difficult to determine whether similar critical periods exist in humans. Significant controversy surrounds this issue, but most authors agree that critical periods may exist for the establishment of binocular vision between 3 to 8 months and for language acquisition in the first few years of life.<sup>34</sup> In these cases it appears crucial to ensure the appropriate sensory stimulation very early, similar to what has been found in other species.

Considerably less controversy surrounds the existence of sensitive periods during human development. Sensitive periods are extended periods of time where children are more receptive to environmental stimuli than later in life. Accordingly there is every reason to assume that perceptual, motor and cognitive functions are more sensitive to environmental influences (i.e. training and other forms of stimulation) during childhood than later in life.<sup>36,37</sup> However, we know little of the magnitude and time course of this higher sensitivity for individual functions, what determines its variability among children, and how it may be utilized in training and learning. Based on the findings from kittens,<sup>35,38</sup> it may be speculated that the period where the corticospinal tract is in the process of refining its functional connections with the spinal motor neurons during development would constitute a sensitive period, where interventions would be especially efficient. In this case, the first year of life might be considered a sensitive period for motor development, but we have insufficient information to be able to conclude this with any certainty.

### **Enriched environments**

This also relates to observations on the significance of an enriched environment during development.<sup>39–41</sup> The concept of enriched environments was initiated with Hebb's anecdotal observations in the 1940s of larger behavioural improvements in rats he brought home as pets as compared with their litter mates kept in the laboratory.<sup>42</sup> In the 1960s, Rosenzweig et al. developed the concept into a testable scientific theory<sup>43</sup> and subsequent work has demonstrated the stimulating effect of an enriched environment during development in experimental animals on a range of parameters related to plastic changes in the brain,<sup>41</sup> and a meta-analysis recently concluded that interventions involving enriched environments are a promising tool for infants with or at high risk of CP.<sup>44</sup> It is generally accepted that no single factor is responsible for the stimulating effect of an enriched environment but that it is the combination of complex inanimate and social stimuli which is important (i.e. larger cages with more litter mates and possibility of interaction with toys).

Although controlled experiments are unavailable for obvious reasons, irrational human behaviour has occasionally provided evidence of the significance of an enriched environment during human development. The most publicized case is probably that of Genie, who was locked alone in a room during her first 13 years and showed severely arrested motor and cognitive development, including failure to develop any significant language skills, when she was discovered in 1970.<sup>45</sup> Although sad cases like that of Genie do not tell us anything about the amount of enriched environment necessary to guarantee normal human development, they do illustrate the significance of adequate stimulation during development. Most likely the relationship between stimulation and development follows the general law of decreasing returns: if a child is very deprived, a little stimulation will make a large difference,

whereas if the child is well stimulated it will take a lot more to make a significant difference. It should also be mentioned that reduced environmental stimulation, as implemented by the Newborn Individualized Developmental Care and Assessment Program in preterm infants in the neonatal period, has been proposed to prevent childhood attention disorders, however, a recent systematic review did not find evidence of long-term neurodevelopmental effects of NIDCAP.<sup>46</sup>

### **Passive stimulation is insufficient—learning requires active participation**

Since Donald Hebb put forward his theory of the neural basis of learning, popularized as 'what fires together—wires together', it has been a fundamental idea that learning requires coordinated activity in neural circuitries.<sup>42</sup> From a developmental perspective, this also relates to the notion that 'successful' neural circuitries, which produce an adequate model of the environment or an adequate behaviour, survive, whereas less successful circuitries are removed.<sup>47,48</sup> This pruning of neural circuitries probably explains the gradual decrease in the thickness of the cerebral cortex throughout late childhood and adolescence.<sup>49</sup> Essential to this idea is that the selection during development is based on a continuous testing of the efficiency of the neuronal circuitries' ability to produce a given sensory feedback when interacting with the environment. In other words, the establishment of valid internal models and representations of the external world in the nervous system is based on continuous testing of the validity of these models. This is done by monitoring the success of the models in producing sensory feedback corresponding to that expected by the model.<sup>50</sup> According to this idea, learning (i.e. alteration or selection of neural circuitries) happens when the internal model produces a behaviour that has sensory consequences different from what the model expects.<sup>50</sup> In this case, the sensory information from the environment acts as an error signal which updates and alters the internal model.<sup>50</sup> This is similar to the idea that learning only takes place in an action–reaction situation, or put differently, when the child actively explores the environment or participates actively (takes an interest) in the training. Therefore, an enriched environment, learning, and training do not involve passive stimulation, but rather require that the child plays an active part.

### **Early identification of infants with signs of cerebral palsy is important**

As previously mentioned, CP is on average diagnosed when the child is approximately 1 to 2 years old. This is too late for early intervention as defined here to be initiated and therefore, early intervention requires early identification of infants that may develop CP. Additionally, the time from suspicion is raised and until diagnosis is made can be very stressful for the parents and should be minimized if possible.<sup>6</sup> For the time being, techniques that can easily identify infants with early signs of CP are lacking. Infants with severe brain lesions are usually detected soon after birth on the

basis of neuroimaging such as ultrasonography and MRI and therefore they may benefit from intervention instigated very early. However, infants with severe lesions may require more intensive and long-lasting treatment efforts to achieve developmental effects. Age limits differ, but infants born after 28 to 30 weeks of gestation are not routinely examined with ultrasonography or MRI. This is partly due to the relatively low sensitivity of the modalities; ultrasonography: 66–79%<sup>51</sup> and MRI: 71–88%,<sup>52</sup> and partly to restricted time and financial resources. Thus, a brain injury that does not present clear clinical signs can go undetected for a long period of time, resulting in an intervention being initiated late. Additional methods for early identification are necessary, and the General Movements assessment may be one such system. It consists of an observation of the quality of spontaneous movement patterns, where abnormal general movements indicate a high risk of developmental disorders such as CP. General movements are present during the neonatal period and disappear at around 5 months corrected age. From 8 to 9 weeks corrected age, a pattern termed ‘fidgety movements’<sup>53</sup> is normally present, and absent or abnormal fidgety movements are associated with a high risk of later CP.<sup>54–57</sup>

Since not all children with abnormal findings at neurological examination or on neuroimaging go on to develop CP<sup>58</sup> several authors recommend combining MRI and GMA.<sup>59–61</sup> Skiold et al. recently found definitely abnormal general movements to be significantly associated with CP at 30 months corrected age and that moderate-severe white matter abnormalities on MRI had an even stronger association with CP than the general movements. When combining the GMA and MRI findings, sensitivity and specificity of 100% was achieved.<sup>61</sup> However, as the diagnostic value of MRI at term may not be much better than consecutive ultrasonography, and since MRI is demanding, routine MRI at term is unlikely to become standard practice. To our knowledge, studies combining ultrasonography and the GMA have yet to be performed.

Choice of imaging modality aside, a joint method seems appealing. However, the GMA requires ample training, upkeep of analytic skills and time for video analyses. The clinician must use the GMA regularly and considering the relatively low number of infants suspected of CP this may be challenging. One option is to computerize the GMA to identify infants who need a second opinion from a team of clinicians.<sup>62–64</sup> Computerizing the analysis may even allow screening of infants at risk. As the high specificity and sensitivity of the GMA is deducted from groups of high-risk infants, more research on the validity of the GMA in low-risk populations of infants is needed. Thus, one caveat for the use of the GMA as a screening tool is that it appears to have low predictive value in a general population of new-born infants.<sup>65</sup>

Despite novel methods for identifying infants who may develop CP, the diagnosis of CP is still made from clinical observations. The commonly accepted definition of CP from 2005 by Bax et al.<sup>4</sup> reads: ‘Cerebral palsy (CP) describes a group of disorders of the development of movement and posture, causing activity limitation, that are attributed

to non-progressive disturbances that occurred in the developing fetal or infant brain. The motor disorders of cerebral palsy are often accompanied by disturbances of sensation, cognition, communication, perception, and/or behaviour, and/or by a seizure disorder.’ Finding a large IVH on neuroimaging or finding absent fidgety movements predicts the development of CP but does not allow the diagnosis. Even with perfect prediction of the final outcome of a developmental process, the clinical condition at the beginning of that process is different from that at the end. Strictly speaking, if the condition at the beginning and at the end were perfectly linked, then intervention could have no effect.

### **Unconvincing evidence of the efficacy of early intervention**

Based on our knowledge of neuroplasticity and sensitive periods it seems apparent that early intervention ought to benefit infants with brain damage during development. However, from the vast amount of literature on the subject it is difficult to determine whether early intervention is effective or not. Several reasons for this may be proposed. As already mentioned, one is the matter of defining ‘early’. Another problem is that it is difficult to compare studies since a countless number of diverse ‘early interventions’ have been applied. This is a challenge for meta-analyses. Researchers have tried everything from teaching parents how to handle their preterm infant, improving the parent-infant relationship,<sup>66,67</sup> specially educated staff,<sup>68</sup> different physiotherapeutic approaches<sup>69–71</sup> to acupuncture.<sup>72</sup> Furthermore, the methods of measuring the effects are numerous, not all have been validated and some may not be adequate to measure the outcome in question.

Early intervention studies also face the challenge of actually achieving a genuine comparison of the intervention to no treatment, as it is difficult not to offer infants in a control group any treatment. Usually the solution is to provide training for the control group as well, although less frequently than the intervention group. Yet, the training of the control children is likely to mask the effect of the intervention. Additionally, it is well known that people may be disappointed when allocated to the control group,<sup>73</sup> and if randomized to the control group some parents will presumably attempt to train the child themselves. Finally, the physician responsible for the children in the study may feel compelled to prescribe intervention for children showing early signs of CP during the period of intervention. To avoid this, a cross-over design, in which all participants are included in both the intervention and the control group and switch places halfway, is commonly used.

The effect of early intervention has been investigated in a range of randomized controlled studies, which have been reviewed in a number of previous reviews.<sup>54,74–76</sup> An overall conclusion from these reviews has been that there is no convincing evidence to support early intervention. We will only discuss two of the more recent reviews here. In 2005, Blauw-Hospers et al. systematically reviewed 34 studies with a total of 3255 infants to evaluate the effect of early intervention

on motor development.<sup>10</sup> As a reflection of the problems mentioned in the previous section, the interventions, outcome measures and the age at initiation of intervention were too variable to permit a formal meta-analysis. The authors divided the included studies into groups depending on the onset of intervention and evaluated the quality of the studies according to the level of evidence and internal and external validity. Of the 17 studies initiated after dispatch from the neonatal unit, 12 had a high methodological quality. Only four of these showed a beneficial effect on motor development. Eight of the 12 studies evaluated neurodevelopmental treatment, otherwise referred to as the Bobath concept, which mainly involved passive handling techniques. By and large, these studies found no significant effect on motor development. In contrast, a generally positive effect was found in the remaining high-quality studies, which evaluated interventions that required active participation from the child.<sup>10</sup> Of these, one had an attrition rate of greater than 25%,<sup>77</sup> one investigated children with Down syndrome,<sup>78</sup> one compared conductive education to passive handling<sup>79</sup> and the last study considered a physiotherapeutic intervention.<sup>71</sup> This study by Lekskulchai and Cole is discussed later in this review.

In a recent Cochrane review, Spittle et al.<sup>80</sup> selected a homogenous group of quasi-randomized and randomized controlled trials (RCT) to review the effects of early developmental intervention programmes. The review encompassed 3133 preterm infants who all started some kind of intervention within the first 12 months of life, and at least part of the intervention took place after discharge. The conclusion was that early intervention had moderate effects on cognitive development, but only weak effects were found for motor development and the cognitive improvements did not last into the early school years. Similarly, RCTs not included in the Spittle et al. review have struggled to provide substantial evidence of a positive effect on motor and cognitive development by early interventions.<sup>66,81,82</sup>

We find it likely that a key reason for the lack of significant results in these studies is that only very few have investigated the effect of early intervention in children with a high probability of developing CP. According to a meta-analysis of 25 studies, the average prevalence of CP is 14.6% (95% confidence interval [CI] 12.5–17) among preterm infants born at 22 to 27 weeks' gestational age, 6.2% (CI 4.9–7.8) at 28–31 weeks, 0.7% (CI 0.6–0.9) at 32 to 36 weeks, and among infants born at term 0.1% (CI 0.093–0.014).<sup>83</sup> Thus, infants born preterm have a higher risk of CP than infants born at term. However, a large number of preterm infants will still develop normally. Therefore, when recruiting infants for a trial, relying solely on preterm birth as a risk factor of CP is somewhat insufficient. The cohort of preterm infants needs to undergo further selection using techniques such as brain ultrasound, MRI or the GMA in order to identify the infants who are in most need of intervention. If this is not done, major effects of early intervention cannot be expected, as a large proportion of the children included in the studies would not require the intervention and, therefore, would dilute

the treatment effect in those children who needed it. An early distinction between high-risk infants may help direct the treatment towards infants who are in definite need of the intervention and thereby help ensure stronger evidence of the effect of the intervention. In other words, a more targeted intervention could be pursued. However, it is to be kept in mind that by using targeted intervention there is a risk of excluding infants who may have needed the intervention and, thus, 'undertreating' children who do not fit very specific inclusion criteria.

An attempt at this type of early distinction was made almost 30 years ago when 80 preterm infants were divided into 'normal', 'at-risk' and 'neurologically impaired' groups by clinical neurological examination at 3 months corrected age. Subsequently, intervention was offered to randomly selected 'at-risk' and 'normal' infants, while the most severely affected children in the 'neurologically impaired' group were all offered intervention.<sup>84</sup> Unfortunately, the authors do not specify any details of the intervention and it is therefore unclear why they did not gain significant results. However, the notion of focusing on the children who would benefit the most from the intervention is of interest. Along these lines, we have been able to find only three more recent studies in which intervention has been directed specifically towards children with a high risk of CP. Lekskulchai et al.<sup>71</sup> enrolled 111 preterm infants with no congenital abnormalities or serious brain damage. At 40 weeks gestational age the infants were evaluated using the Test of Infant Motor Performance and infants with a score less than 66 were randomly assigned to either intervention or control. The intervention consisted of daily home-based activities, such as assisted kicking and weight bearing on forearms, provided by the primary caregiver, who had been trained by a physiotherapist beforehand and each month new tasks were added. There is no information on the regimen for the control infants. At 4 months corrected age the infants in the intervention group showed significantly better motor development than those in the control group.<sup>71</sup>

Weindling et al.<sup>85</sup> studied 105 preterm infants with major cranial ultrasound abnormalities such as PVL. All infants were included around term age and showed no clinical signs of motor or cognitive disability. The infants were randomized to early physiotherapy or to standard treatment, which was physiotherapy initiated when a paediatrician found it appropriate. Thus, the difference between the groups reflects the effect of the time of onset of physiotherapy rather than the effect of physiotherapy as such. The physiotherapists used neurodevelopmental therapy (a.m. Bobath) where parents of infants in the intervention group were given advice on handling and positioning of their child. A little more than half of the infants developed CP. There was no significant difference between the groups at neither 12 nor 30 months. There may be several reasons for this, including an insufficient difference between the physiotherapy administered for the intervention and control groups respectively, the choice of intervention (the passive manipulation mainly used is likely to

have little effect<sup>10,86,87</sup>), and that the study included several infants who did not develop CP regardless of intervention.

Hielkema et al.<sup>68</sup> and Blauw-Hospers et al.<sup>88</sup> compared an intervention programme, Coping with and Caring for Infants with Special Needs (COPCA), to traditional infant physiotherapy (TIP,) mostly based on the principles of neurodevelopmental treatment. At a corrected age of 3 months, 46 infants, who at 10 weeks gestational age had definitely abnormal general movements, were included and randomized to either COPCA or TIP. The COPCA intervention ( $n=21$ ) was home-based and provided twice-weekly from 3 to 6 months corrected age by specially trained physical therapists. Frequency and location of TIP ( $n=25$ ) depended on a paediatrician's advice, the median frequency being once a week. After the intervention period, 36 infants continued receiving physical therapy until 18 months corrected age; 12 infants received COPCA, three had TIP as no COPCA coach was available, and 21 received TIP. All infants were assessed several times using the Infant Motor Profile (IMP), the Pediatric Evaluation of Disability Inventory (PEDI) and other neurodevelopmental examinations. At 18 months, the infants who received COPCA had significantly better functional PEDI skills compared with the infants who received TIP a.m. Bobath. There was no difference between motor outcomes in the two groups; however, some elements of COPCA were associated with a better IMP score. The lack of difference in motor outcome between the intervention and control group is likely to be due to an insufficient difference between the therapies offered to the two groups in combination with a relatively small number of infants.<sup>68</sup> Additionally, the authors found extensive heterogeneity in the intervention strategies applied within the two groups, especially in the TIP group.<sup>88</sup>

Thus, the evidence available regarding early intervention directed specifically at children with a high probability of developing CP is limited. There is clearly a need for additional randomized studies in which early, intensive training is offered to a group of infants showing early signs of CP. Recently, a pilot study on the effects of kicking and stepping exercises in a group of preterm infants with ultrasonography-confirmed severe IVH or PVL has provided promising results on motor development.<sup>89</sup>

**Matching neurodevelopmental evaluation and intervention**  
Even if identification of infants with early signs of CP is achieved, the ideal type of early intervention has yet to be

found. However, as mentioned earlier, interventions requiring active participation from the infant have shown promising effects. Furthermore, studies on older children with CP and adults with late onset brain damage may be of relevance.<sup>90,91</sup> These studies also argue that training must involve active participation. In addition, intervention must be of greater intensity and longer duration than what has been used previously<sup>90</sup> and improvement is more likely if tasks are motivating and practised at home for at least 20 minutes a day.<sup>91</sup> Thus, we suggest that the early intervention should be performed daily in the child's home and, considering the importance of the parent-infant relationship, the parents must be trained to administer the intervention. The intervention must stimulate active participation from the child and must, therefore, be both fun and easy to manage to keep parents and children motivated. Ideally, a therapist should be available to support and ensure the quality of the training. However, this will not be possible on a large scale because of costs. This leads us to consider if the vast number of devices available for telecommunication are useful. Professional guidance and encouragement is often necessary to gain sufficient compliance, and online, daily sessions with a physiotherapist may be a financially viable solution.

In conclusion, although systematic reviews of RCTs have struggled to show lasting benefits of early intervention, this evidence is not sufficient to exclude the value of early intervention. The main reasons for this are the lack of precision in identifying infants for intervention studies and insufficient difference between the interventions offered to the intervention and control group. Although we realize that early identification of all infants with CP in the general population will not be possible, we propose a research agenda directed at large-scale identification of infants with early signs of CP and testing of high-intensity, early interventions in which the infant actively participates.

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