

Arguments for Daily Training of all Premature Infants on the Joey

Prematurity: a public health problem

The epidemic of prematurity is constantly increasing according to several recent reports in Europe and the United States (Ananth et al., 2005; Blondel et al., 2011). Currently, about 10 to 12% of births in the US and 5 to 7% in Europe occur before full term is reached, i.e., before 37 weeks of amenorrhea (SA) according to the definition of prematurity from the World Health Organization. In France, 61,000 children are born prematurely each year, including 35,000 between 35 and 36 weeks SA, 13,000 between 32 and 34 weeks SA and 13,000 classed as very premature with less than 32 weeks SA. In comparison, 11,300 very premature infants are born each year in England. In parallel with the steady increase in prematurity, the survival rate of these children has increased in recent years, particularly for very premature babies, thanks to advances in medical practices and the quality of neonatal services.

Paradoxically, this situation creates a real public health problem because the increase in the survival of very premature infants leads to an increase in children with handicaps during their development. According to the study EPIPAGE 1, carried out on more than 2000 very premature infants in France, 42% of the children born between 24-28 weeks and 32% of the children born between 29-32 weeks required a medical follow-up for a particular handicap up to the age of 5 compared to only 16% in the normal population born at term (Larroque et al. 2008). According to the same study, 9% (about 1000 children per year) developed cerebral palsy during the first two years, with disabilities ranging from motor disorders of posture and movement to the impossibility of walking independently. These disabilities are often associated with disorders of perception, cognition and communication. To these alarming percentages are added an increasing number of results showing that even if the general motor development of premature children seems normal, they often develop secondary motor disorders likely to impede their learning, especially at school level. However, these dyspraxias are often revealed far too late, during tests in which the child must perform a fine motor action towards a specific goal (Mazeau, 2000). It should be noted that these dyspraxias affect not only the very premature infants but also the populations born between 33 and 36 weeks.

The importance of early training of infants at risks for cerebral palsy and motor delay

Movement is the sole means available to the child for expressing its life activity. Movement is integral to activities of daily living as well as to communication, socialization, and self-expression. Consequently, motor development is at the center of all the changes that occur across the multiple domains of development, and it constrains all of the interactions the child will have with its environment. Without a stable posture of the head and body, symmetry and coordination of movements, and the ability to freely move all or part of one's body into one's environment, the infant's ability to interact with and operate on its environment will drastically diminish. The acquisition of motor skill is even more crucial for the premature child, who is already deprived of typical interactions in neonatal care. Early control over movement enables the premature child to engage with her environment, especially with her parents, and to establish the links essential for optimal development. It is therefore essential to prevent in this population, as early as possible, the manifestation of any postural anomaly of the head or trunk, atypical movements of the legs and arms, imbalances between flexion-extension forces at the joints, and asymmetries in flexor-extensor muscular tonus. In summary, it is crucial to implement, as early as possible, a suitable **remediation-prevention** strategy **before anomalies emerge**.

Why should intervention be as early as possible in premature infants?

We have already argued that earlier is better in order for premature infants to begin appropriate interactions with their environment as soon as possible. Another critical argument is the growing evidence that active practice is: 1) necessary for the learning of motor skills, 2) crucial for brain plasticity, and 3) more effective for learning if initiated during sensitive periods early in development.

Active practice increases performance in postural stability and locomotion

For a longtime, postural stability and locomotion were considered as phylogenetic skills that would expectably be acquired by all members of the species without the need for intervention. This mindset was related to the old idea that postural stability and locomotion were relatively immune to the effects of practice and experience because their emergence was largely under genetic/maturational control. However, a wealth of evidence since that time has dispelled this myth.

Two recent studies in typically developing infants are particularly telling. The first study reveals that training the standing position in 3-5-month-old infants during 12 weeks of a swimming program considerably improves the emergence of their upright postural stability. The trained infants were able to stand up in the hand of the experimenter or on a corkboard for 15 sec or more at around 4 months of age, while untrained infants typically don't develop this skill until after at least 9 months of age! (Sigmundsson et al., 2017: <https://www.youtube.com/watch?v=BR5ZA5mxBFk>)

Another example of the tremendous effect of practice on motor skills comes from a study by Karen Adolph's group (2012) on the acquisition of walking. In this study, the authors reported that the quality of walking was significantly correlated with the number of steps, the travelled distances and falls per hour performed by the infant. Both step length and step width were improved as experience increased. If active practice is central to the acquisition of skilled locomotion and postural stability in typically developing infants, is it also the case in atypical populations?

In their seminal work on training atypical infants at risk of locomotor delay, Beverly Ulrich and Dale Ulrich have shown convincingly that early training of treadmill stepping dramatically improves the emergence and quality of walking in children with disabilities like Down syndrome, myelomeningocele and cerebral palsy (see Ulrich, 2010 for a review). As B. Ulrich (2010) and Mijna Hadders-Algra (Blauw-Hospers & Hadders-Algra, 2005; Hadders-Algra, 2007) highlight in their reviews, training should be initiated as early and intensively as possible in order to get the best outcomes in a still-young brain and body in a stage of high plasticity.

Brain plasticity and physical activity

It is well established that early intervention allows dramatic recoveries from serious brain and spinal cord damage in adults (see Norman Doidge's books 2007, 2015). Moreover, recent studies have also yielded some truly groundbreaking discoveries about adult brain plasticity even in non-disabled adults. This is the case for example of the recent discovery that myelin can regenerate even in the adult central nervous system as soon as the adult *actively engages in motor learning* (see the excellent review by Mount & Monje, 2017). Discoveries have also been made concerning infant brain plasticity. For example, Beverly Ulrich and her group have conducted a study in which they explored the correlation between the training of two motor tasks (reaching and stepping) and the activity of the primary motor cortex in typically developing infants between 6 and 12 months of age. Their findings strongly suggest that when new skills emerge, the brain recruits large numbers of redundant neural circuits generating a more-diffuse-motor cortex activity than when the skill is mature, thus allowing motor cortex activity to be refined (Nishiyori et al., 2016).

Atypical experience has more pronounced effects during sensitive periods in development

Sensitive periods are well established phenomena in embryological development, where the period of most rapid growth of a tissue, organ, or system is the period when it is most susceptible to a lack of environmental input or noxious or atypical input (e.g., Moore & Persuad, 1998). Sensitive periods beyond the embryological period are now considered pervasive in human development (Maurer, 2005; Werker & Hensch, 2015). Though much of the work on sensitive periods in human development has been focused on neurological development, particularly of the perceptual systems, animal research suggests that all mammals might have early sensitive periods for the development of the muscular system, which in turn impacts motor development. For example, Walton et al. (1992) showed that using tail suspension to unload the weight bearing limbs in young rats led to permanent disruptions in swimming and walking. Subsequently, Jamon and Serradj (2009) reported that disruptions to the normal forces on the limbs during early postnatal development had pronounced effects on the morphological and contractile properties of the muscles. Because experience (or environmental input) is often the trigger that opens a sensitive period in development, young infants who are unable to self-generate the requisite motor experiences upon which typical motor development depends, are at heightened risk for permanently compromised motor outcomes.

However, research has also shown that mutant mice who were missing a specific signaling cue that guides the wiring of neuromotor circuits during embryonic development and permanently impairs motor functioning, could be remediated if raised in an enriched environment immediately after birth but not if placed in the enriched environment 4 weeks after birth (Helmbrecht et al., 2015). The authors proposed that during early postnatal development, when perineuronal nets had not yet formed around spinal motor neurons, enrichment induces adaptive plasticity in the motor system to compensate for coordination deficits. The demonstration of this early sensitive period for adaptive plasticity in neuromuscular circuitry, even though the evidence is drawn from an animal model, provides one more reason interventions for infants at risk for developmental delay should be initiated as early as possible.

Taken together, all of these discoveries described above open a totally new way to reconsider training strategies in atypical and typical populations.

Why do we propose intervention for ALL premature infants and why should interventions be performed every day?

Despite the existence of brain imaging techniques, such as MRI or transfontanellar ultrasound, and the existence of numerous pediatric assessment scales and motion-observation techniques, such as those developed by the Prechtl school (Prechtl, 1990, 2001), it is often necessary to wait for 1 year to be certain of a clinical diagnosis and to include a child in a training protocol. In addition, when these protocols are monitored by clinicians in clinical settings, the child is typically permitted to get a maximum of two visits per month. These visits are time consuming and burdensome for parents living far away or who must care for other children, but more importantly, two interventions per month are insufficient to boost the motor development of the premature infants at risk of developing motor anomalies.

To solve these different problems, we propose a completely new strategy. As the active training of typically developing infants has only positive effects on the development of their future motor skills (see previous paragraphs), we believe it is unnecessary to wait until the diagnosis of a developmental anomaly around one year of age before starting an active training in premature infants. In contrast, we propose training all of them as soon as they leave the neonatal care unit. Moreover, we propose training them daily and at home under the oversight of a competent practitioner.

We are especially interested in stimulating the emergence of skilled postural stability of the head and body as well as independent locomotion in the premature population as these infants are often hypotonic and delayed in postural and locomotor skills. However, in order to adapt the training to this population, it is necessary to use a protocol that compensates for the hypotonicity and fatigue these infants experience, while allowing them to actively engage all brain and spinal cord neuromotor circuits, bones, muscles and joints important for postural stability and locomotion.

Our strategy is based on daily stimulation of the active motor capacity of the infant to propel itself in a quadrupedal position, stimulation that can be done at home by the parents thanks to the Joey.

Why stimulate neonatal quadrupedal mobility on a Joey?

We have shown recently that neonatal crawling is far from being a simple spinal reflex since it can also be controlled at a supra-spinal level by the visual environment. When 3-day-old infants are placed in a quadrupedal position, suspended in the air or in contact with a solid surface, and given

the illusion of moving forwards or backwards by the projection of optical flow traveling on the ground, they are able to adapt the number of their steps according to the direction of these flows (Barbu-Roth et al., 2009, 2014, Forma et al., 2018). In addition, the work of Katona and his collaborators suggests the existence of a link between this neonatal crawling and mature walking: the daily practice of quadrupedal propulsion from birth suppresses its disappearance in the infant and leads to the emergence of an earlier mature quadrupedal and then bipedal locomotion (Katona et al., 1988 and personal communication). Dominici et al. (2011) have also used sophisticated neural modeling to show that the basic patterns of lumbosacral motorneuron activity seen in neonatal stepping movements are retained in adult walking, even though new patterns are also evident. Finally, recent work by Kanasawa et al. (2014) on the premature and the term newborn shows that their leg movements are already correlated with brain activity in the primary motor cortex. This study has recently led Kuniyoshi's group to propose a model of brain development based on the sensory-motor interactions of infants with their environment, with this development taking place right from early fetal life (Yamada et al., 2016). These results suggest that the quadrupedal mobility of the newborn is already a complex activity, controllable at a supra-spinal level (including the primary motor cortex), that it is modifiable by various stimuli, and that it is connected with mature walking. These criteria therefore make early crawling an excellent candidate to stimulate the development of mature locomotion and postural stability.

Quadrupedal mobility stimulation has several advantages over stimulation of other motor activities such as isolated head movements, walking on a treadmill, or repetitive limb movements. The active practice of early crawling can lead the infant to engage in a complete and functional motor behavior that can promote the symmetrical coordination of several body segments and the sequencing of multiple motor patterns in the service of obtaining a measurable result: propulsion and orientation of the child in her environment. Thus, the active practice of crawling potentially facilitates the development of not only quadrupedal and bipedal locomotion, but also holding of the head, the sitting position (by strengthening the muscles of the neck and trunk), and standing.

However, in order to help the infant practice optimal crawling that minimizes stress on the spine, promotes a lengthening of the spine and a neutral position of the head, facilitates arm movements and independent propulsion, we designed the Joey. The results of a previous study on 60 typically developing newborns clearly showed the advantages of using the Joey to improve the crawling of these newborns (Forma et al., 2016 and article submitted). The newborns were able to propel themselves significantly further on the Joey and they demonstrated more mature crawling patterns, in terms of limb kinematics and interlimb coordination, than when observed crawling without the Joey.

Conclusion

We believe that Joey training could be used by all premature infants as soon as they leave the NICU (unless there is a medical contraindication). We strongly believe Joey training will be a great step in the future to avoid or considerably reduce potential delay at their base and thus reduce the need for additional postural equipment in later years.

Dr. Marianne BARBU-ROTH

Team leader of the Perception Action Cognition Development Group
- Integrative Neuroscience & Cognition Center - UMR 8002 CNRS,
Université de Paris.

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