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Early Gait Development in Human Infants: Plasticity and Clinical Applications

ABSTRACT: *In this paper we focus on how a developmental perspective on plasticity in the control of human movement can promote early therapy and improve gait acquisition in infants with developmental disabilities. Current knowledge about stepping development in healthy infants across the first year of life highlights strong plasticity, both in behavioral outcome and in underlying neuro-muscular activation. These data show that stepping, like other motor skills, emerges from the interaction between infant's maturation and the environment. This view is reinforced by showing that infants with different internal resources (like genetic disorder or neural tube defect) show unique developmental trajectories when supported on a treadmill, yet do respond. Moreover, we will show that their behavior can be improved by context manipulations (mostly sensory stimulation) or practice. Overall, plasticity in the neural, skeletal, and muscle tissues create new opportunities for optimizing early intervention by creatively tapping into the same developmental processes experienced by healthy infants.* *© 2015 Wiley Periodicals, Inc.* Dev Psychobiol. 57:447–458, 2015.

Keywords: *plasticity; infant stepping; early intervention*

INTRODUCTION

A growing body of work argues for reconsidering the process by which infants develop patterns of behavior (Johnston, 2009; Karmiloff-Smith, 2009; Spencer et al., 2009; Stiles, 2009) positing that the interaction between nature and nurture is ubiquitous across behaviors and from conception while evidence for innate programs or core knowledge is sparce. The continuous and cascading interactions among many subsystems, from individuals' intrinsic characteristics (e.g., genetics, neural integrity, skeletal structures) and their environment (from the cellular environment to the outside world) shape infant development and acquisition of skills. In fact, the property of neurons referred to as plasticity is a prominent feature of the central nervous system (Johnson, 2004). This enables small modifications in the brain environment and history of activation to shape neural networks, to lead to strengthened connections and specializations of function within the brain, reducing, evolutionarily, the need for pre-specified networks. The beauty of this highly evolved system is that it is adaptive- capable of finding solutions to goals with the available resources. While these ideas are well accepted for studies of the development of perception, intelligence, social skills and most motor skills, we could wonder why some scientists still argue that a different explanation exists for the development of walking.

The first expression of behavior that resembles gait is produced at birth, when neonates react to tactile stimulation by producing alternating flexion and extension of the legs when supported by an adult on a table and moved forward slowly over the support surface (Shirley, 1931). This behavior, supposedly highly stereotyped, is used to test neurological integrity in neonates. It can be observed up to two or three months of age, then disappears before re-emerging close to the age of autonomous walking. This unique U-shaped developmental trajectory tended to set gait development apart from other motor skills. Hence, the significance

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of this transient neonatal response has been discussed for a long time, as scholars tried to understand its role in regard to later voluntary movement (Andre-Thomas & Autgearden, 1966; Forssberg, 1985; McGraw, 1932; Thelen, Bradshaw, & Ward, 1981; Zelazo, Zelazo, & Kolb, 1972). The earliest hypotheses were about the need for cortical inhibition of reflexes followed by further cortical maturation to allow the development of self-initiated stepping (Andre-Thomas & Autgearden, 1966). But empirical work changed this conception by showing that if newborn stepping was trained every day from birth on, then "newborn" stepping did not disappear and led to earlier onset of walking (Zelazo et al., 1972) and that when put in different contexts (like water or on a treadmill) infants could produce this pattern even after 3 months of age (Thelen, Fischer, & Ridley-Johnson, 1984). Based on those results, new hypotheses were proposed, suggesting alternatively that this reflex was a precursor to bipedal walking that could be maintained by intentional practice (cognitive override of inhibition) (Zelazo et al., 1972) or that stepping was an emergent phenomenon that could contribute to walking but that walking was a skill to be learned just like other motor skills (Thelen & Ulrich, 1991).

The precursor hypothesis followed the seminal work of Grillner (Grillner & Zangger, 1979) proposing a parallel between the human stereotypic response and quadruped gait, arguing that stepping in infants could be produced by an innate central pattern generator (CPG) at the spinal cord level (Forssberg, 1985; Yang and Gorassini, 2006). Current data (Dominici et al., 2011) tend to show that rhythmical structures in electromyographic activity at birth are very basic and far from the stable timing of muscular activation found in adults. This variability makes it hard to conclude if this response is only due to an immature CPG or if it is a basic adaptation of the motor system to the specific stimulation of the infant's foot contacting the floor that creates a muscular contraction forcing the leg to flex, followed by a release of the muscle activation when the foot is in the air. Stepping as an emergent phenomenon is supported by numerous studies showing the appearance/disappearance/improvements in the behavior via changes in context, intrinsic non-neural contributions (e.g., arousal, joint compliance, strength), practice, and so on (Pantall, Teulier, Smith, Moerchen, & Ulrich, 2011; Thelen et al., 1984; Ulrich, Ulrich, Collier, & Cole, 1995; Ulrich, Ulrich, & Angulo-Kinzler, 1998; Ulrich, Ulrich, Angulo-Kinzler, & Yun, 2001). We will argue in favour of this dynamic systems point of view (Spencer et al., 2009; Thelen & Ulrich, 1991; Ulrich & Kubo, 2012), where coordinations like stepping patterns are not pre-set but softly assembled in response to task demands and the maturation of relevant interacting subsystems. We will show that these processes explain the real-time emergence of changes in stepping patterns over time, resulting in a non-linear trajectory of behavior during ontogeny, similar to that observed in other motor milestones.

In this paper we describe stepping responses from pre-natal life to autonomous walking and show that their development, characterized by plasticity at every level of observation, aligns well with current knowledge about brain development and skill acquisition. Collectively these points set the stage for scientists to design specific contexts to stimulate gait development and to test early therapies for infants with neuromotor problems, as we highlight in the second part of the paper.

PLASTICITY IN GAIT DEVELOPMENT

To understand the development of gait, we first need to describe changes in the production of leg coordination from the perinatal period to autonomous walking. The structure and construction of these coordinations evolve, reflecting neural and biomechanical constraints and their interactions with the environment that shape the emergence of specific coordinations. Because this process is highly complex yet essential, the patterned outcome needs to be studied from several levels of analysis and with full appreciation of individual differences observed across infants in real and developmental time and variability in responses across repetitions in the same infant. If data are simply averaged across trials and infants or only optimal outcomes are selected for analysis, one can lose sight of the complex set of factors involved that enable and challenge infants as they grow, experience their world, explore, and attempt new goals. In reality, typical development is messy!

Plasticity in the Stepping Responses of Newborns

If newborn stepping responses are mostly characterized by alternation of flexion extension of the legs, close examination of this pattern, either at a behavioural or at a more microscopic level, reveals only weak reproducibility. The literature shows that only 70–84% of healthy newborns respond to the tactile stimulation by producing step-like patterns (Dominici et al., 2011; Siekerman et al., 2015; Thelen & Fisher, 1982). This ratio reduces to 25% if only infants who produce consecutive right-left step sequences are included (Forssberg, 1985; Siekerman et al., 2015). Rather, newborns produce several types of interlimb coordinations in this context, moving either one leg only, or two legs at the same time, or alternating, hence reproducing movements that emerged in utero (deVries, Visser, & Prechtl, 1982). When frequency of stepping movements is low, researchers tend to attribute this to low levels of arousal (Okamoto, Okamoto, & Andrew, 2001; Thelen et al., 1984). Nevertheless, variability of step frequency is high even when arousal level is in the "optimal" range (Forssberg, 1985).

All together those data on newborn stepping responses show that this behavior is not elicited as automatically as other primitive reflexes like Moro (Futagi, Toribe, & Suzuki, 2012). Moreover, even when the response is observed, we can see variations in the form of the pattern produced and the impact of the environment, with responses being affected by changes in the neuron excitability (variation of arousal). Hence those data in newborns reinforce the idea that stepping behavior is not highly stereotypic or completely preset, but is, rather, quite plastic.

Plasticity in Stepping Response Across the First Year of Life

Newborn stepping, in the classic elicitation context, can be observed only up to 2–3 months of age. Hence if we want to map the developmental trajectory of stepping, specific contexts enabling infant stepping need to be used. In the 1980s Esther Thelen was the first to create a paediatric treadmill, which provides much more proprioceptive information than the table top context for stepping (mainly by stretching leg, muscle, and joint receptors). Inspired by the research of colleagues working on gait in quadrupeds she began to support babies upright and test their leg responses to the belt moving under their feet (Thelen, 1986a). Her goal was to test support for a systems approach to explaining the emergence of stepping and walking.

Through a series of studies Thelen and her colleagues mapped out both a developmental trajectory describing changes in step patterns of infants and experimentally tested the adaptability of their responses. First she showed that 7-month-olds, for whom the previously hypothesized spinal pattern generator for walking was supposed to be switched off by maturation of higher brain centers, readily responded to the treadmill context by producing alternating steps a high proportion of the time (Thelen, 1986a). Contributing to this behavior were many subsystems, including the neuromotor capacity to rhythmically alternate their legs, but also sufficient strength to lift their legs against gravity, the support of the holder, the dynamic sensory input of the belt moving under their feet and changing the relative location of their center of mass relative to their feet and the loading and unloading of joint and pressure receptors (Thelen, 1986b). In other words, their behavior was a function of the context, level of development of intrinsic subsystems, and perhaps the "goal" of the baby as well.

In a longitudinal study, Thelen and Ulrich (1991) explored the impact of changes in the level of development of relevant intrinsic subsystems. A key discovery was that babies' responses changed over developmental time but similarly across infants. At ages one to two months step frequency was low and interlimb coordination patterns varied. Of the steps produced, the modal response was alternating but on average at least 40% consisted of single or parallel steps with some double or stutter steps observed as well. Thus, one contributing subsystem at least, neural communication between the limbs, may be less-well tuned and more disperse in its transmission, or inconsistent, at this point. Figure 1 shows a young infant taking a step with the right leg while being supported on a treadmill.

By three to four-months of age infants' step frequency and percent of steps that were alternating concurrently began a steady increase as infants grew stronger and heavier, making optimal contact with the support surface. This non-linear shift in responsiveness was correlated with infants' individual development of leg extensor and hip abductor strength. The timing varied from baby to baby but, as individuals accepted more weight on their legs and could maintain their legs aligned in the sagittal plane, treadmill steps followed more readily. By six to seven months infants were producing alternating steps during most of the time they were supported upright on the treadmill.

The fact that babies show varied interlimb coordinations and alternating stepping patterns at ages when maturationist approaches would argue they should not appear, and that they do so in a context evolution could not anticipate for babies, argues more strongly

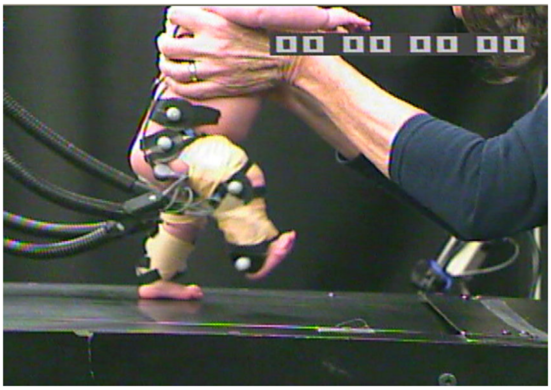

FIGURE 1 Infant with typical development stepping on pediatric treadmill.

in favor of a complex system that self-organizes behavior in an adaptive or plastic manner. Experimental variations on this basic context strengthen the latter argument. When researchers have provided extremes of belt speed, from fast to slow, or split the belt down the middle so one leg is moved faster than the other, babies adapt and continue to step (Thelen, Ulrich, & Niles, 1987; Thelen & Ulrich, 1991; Yang Lamont, & Pang, 2005). When the belt direction reverses, babies step "backward" and even respond with more sideward steps when we hold them sideways, though they do this less well (Lamb & Yang, 2000). Step characteristics suggest the behavior arises from a combination of active neural input and the passive dynamics- biomechanics of leg segment rotations influenced by gravity. For example, when speeds increase, like adults, the component of the stride cycle that changes most in terms of duration is the stance phase. This is the only part of the cycle for which the limb trajectory is controlled by active neural commands; the swing phase changes little because its motion is driven largely by leg length biomechanics and passive motion-dependent forces.

Plasticity in Muscle Activity Underlying Stepping Responses

To understand the development of neuro-muscular pathways underlying the stepping pattern, electromyographic (EMG) activity has been recorded on infants at different ages. Dominici et al. (2011) showed some very basic rhythmical muscular activity at birth evolving toward a more adult like stepping EMG activity by two years of age. Nevertheless, those cross-sectional data were averaged across infants, eliminating the ability to appreciate potential plasticity in neuro-muscular activation from one step to another. The only published data for individual babies' EMG activity (Teulier et al., 2011) shows very high variability at both intra- and inter-individual levels of response as well as high levels of co-activation, at one month of age. This strong plasticity is characteristic of other nascent infant motor behaviors, like reaching and sitting (Hadders-Algra, Brogen, & Forssberg, 1996; Thelen et al., 1993; Thelen, Corbetta, & Spencer, 1996). Initially, strong co-contractions are observed that decrease with practice (Forssberg, 1985; Okamoto, Okamoto, & Andrew, 2003; Teulier et al., 2011; Yang, Stephens, & Vishram, 1998). Rather than reflecting a gross pre-set program, we proposed that this co-contraction may reflect infant brain development in response to early attempts to achieve a goal, where large areas of the cortex are activated by sensory input early in life that becomes tuned and more specific in response to stimuli over developmental time (Karmiloff-Smith, 2009). This could explain some of the reduction in muscle response across the first year of life.

Second, infant stepping is characterized by random timing of muscle activations. That is, one step is never the same as the following one in terms of which muscles fired, how often, how long, and when they were activated during the cycle (Teulier et al., 2011). This variability persists throughout infancy, evident on a treadmill just before walking onset and after walk onset (Chang, Kubo, Buzzi, & Ulrich, 2006; Teulier et al., 2011). Variability, or wild fluctuations in muscle activity, coordination, movement trajectory etc., is characteristic of all complex systems when new patterns are explored and is believed to be a necessary property of behavior that enables better patterns to be discovered (Haken, Kelso, & Bunz, 1985; Zanone & Kelso, 1992). They also mark shifts from one stable state to another. From this dynamic systems point of view, the variability, reflecting neuromuscular plasticity is a necessary feature for learning; through exploration of workable options we find patterns that "fit" the task and then strengthen the neural connections via practice.

Plasticity: Signs of the Learning Process Starting in Utero?

The studies cited above stress that infant gait development is not trivial or prescribed. Infants need time and lots of repetitions of action in their environment to discover and learn efficiencies- producing stable yet adaptive movements. Recently researchers have reported data arguing that the learning process is already going on in utero for hand-to-face and mouth movements, showing that fetuses learn to control their arms and anticipate contact by opening their mouths with repeated contacts (Reissland, Francis, Aydin, Mason, & Schaal, 2014; Zoia et al., 2013). Fetuses initially contact many parts of their face but, with repetitions, reduce the dispersion of contact points and make more focused contact with oro-facial areas. Anticipatory opening of the mouth also begins to appear as the hand approaches. The researchers argue this changing pattern is potentially due to neural development of the somatosensory cortex with practice. Taken together, as technology allows more refined observations of human fetuses data suggest that motor patterns and control progressively evolve. We propose that neurophysiological growth, the environment and experience are inextricably intertwined in this process.

While the evidence for learning processes starting in utero and continuing at and well-after birth is becoming well established for goal oriented activity like reaching, it seems harder for the scientific community to accept a similar possibility for gait-like movement. Nevertheless, studies on animals are making progress in showing the link between evolving stepping patterns in utero and behavior expressed at birth. In fact, studies in rats show that during the fetal period, changes in leg flexions and extensions are shaped by the joint influence of neural resources, biomechanical constraints, proprioceptive feedback, and constraints imposed by the intrauterine environment and shape the coordination seen in the post-natal period (for details, see Brumley and Robinson, 2010). If we conceive of the possibility that human infants can, as well as rat pups, discover and change leg coordinations in utero, like they do with hand-to-mouth movements, perhaps it is the case that neurons underlying alternating leg flexions and extensions (step-like patterns) begin to be strengthened prior to birth, in ontogenetic fashion. That is, the core neural network linking leg muscles to stepping actions observed in newborns is part of an ongoing developmental and emergent process. When neonates are supported upright with their typical flexor-dominant joint posture, some forms of stimuli, such as dynamic tactile and pressure on the feet and stretch of joint receptors may elicit the leg flexions and extensions practiced in utero. Perhaps, too, researchers can intervene at this opportune moment in infants' developmental history to create new early therapies. In the past, clinical approaches to helping infants with neuromotor disabilities advised waiting until the child initiated attempts to walk before intervening to help the baby practice. More recent studies show that waiting ignores not only basic science and contemporary developmental theory but also reflects missed opportunities to optimize outcomes.

CLINICAL IMPLICATIONS

Mapping Theory to Application

Contemporary developmental theory suggests that healthy infants demonstrate self-organization and discovery of new patterns, whether the goal is to roll over, reach for interesting objects, or crawl and walk (Adolph, 2008; Thelen et al., 1993). But when studying the infancy period scholars tend to focus on common patterns, universal ones that all babies acquire. So, it is easy to fall into the trap of assuming they were preprogrammed into the genetic code. When infants have diagnosed disabilities with subsystems that diverge from typical, discovery and the need for many repetitions and practice to achieve their motor goals becomes more obvious.

One beautiful example of self-organization and discovery is the patterns infants use to accomplish the motor milestone of shifting posture from prone to seated. The common approach discovered by infants with typical development (TD) is to push their trunk upward by extending both arms, then shift their weight to one side while flexing their hips and knees to bring both legs forward together along the other side until they are in front. When infants with Down syndrome (DS) recognize the goal of moving from face down to sitting up and explore their options, they discover a completely different solution. They begin like their peers with TD, by using their arms to push their trunk upward, but the similarities end there. At that point babies with DS slide one leg forward on each side of their bodies in what looks like they are doing a "split," continuing until the legs end up in front (Fig. 2). They are not genetically coded to do this; it occurs because some of their subsystems differ substantively from those of TD babies. Perhaps the most important difference for this behavior is their hip joint laxity. Thus, babies with DS discover their own path of least resistance to achieving their goals, given their available resources. Both populations find coordination patterns that get the job done!

If we accept that the behaviors of infants with neuromotor disabilities like DS are open to being influenced by many intrinsic and extrinsic factors and that the ability to walk is a skill that must be discovered and practiced for it to be acquired, we have opportunities to facilitate development, using specific contexts like the pediatric treadmill.

Are Treadmill Stepping Responses Similar in Infants With Neuromuscular Disabilities?

Behavioral plasticity must be supported by plasticity in central and peripheral nervous systems. Is there evidence for this sort of behavioral plasticity in infants

FIGURE 2 Infant with Down syndrome shifting posture from prone to seated by doing the "splits."

born with compromised nervous systems and can they demonstrate adaptation and functionally relevant responses in the context of being supported on a pediatric treadmill?

Two of the most common neuromuscular disabilities that are diagnosed at or before birth are DS and the myelomeningocele (MMC) type of spina bifida. In each of these conditions infants present with an array of subsystems that vary distinctly from those of the typical healthy infant. For example, infants with DS have smaller brain mass with fewer neurons, particularly in the cerebellum, they have lower levels of 5 hydroxytryptophan (a hormone) and high ligamentous laxity. MMC is a neural tube defect involving an incomplete spinal lesion (usually at the lumbar or sacral level) that is reflected in diminished sensory and motor nerve conduction at levels below the lesion. When intrinsic subsystems vary, plasticity may enable the neural and muscle systems to create some limb movements but they may not look like that of a healthy infant, show the same developmental trajectory or timing. These are, of course, empirical questions.

Figure 3 combines data across several studies to illustrate that, when infants with DS and babies with MMC were supported upright on a motorized treadmill they did, like their peers with TD, respond by producing step patterns. In each population a nonlinear shift from minimal stepping to a rise in rate of alternating steps emerged over developmental time, with that shift occurring significantly later in both disability groups yet long before they self-initiated stepping (Lee & Ulrich, in progress; Teulier et al., 2009; Thelen & Ulrich, 1991; Ulrich, Ulrich, Collier, & Cole, 1995). Factors that caused infants' systems to shift into improved alternation varied by population. For infants with TD, the shift emerged as they achieved greater leg extensor dominance and abductor strength, which kept legs from rotating inward and crossing each other (Thelen & Ulrich, 1991). Infants with DS shifted as they gained greater pelvic and leg strength but also reduced body fat relative to muscle (Ulrich et al., 1995).

Interlimb coordination varied during the early stepping responses of babies in all three populations. Perhaps early stepping is so varied because the degrees of freedom are high, that is, many different leg actions are possible when one is supported upright and babies are empowered simply to explore. Perhaps the increase in step responses overall reflects the integrity of the underlying neural transmissions; both motor and sen-

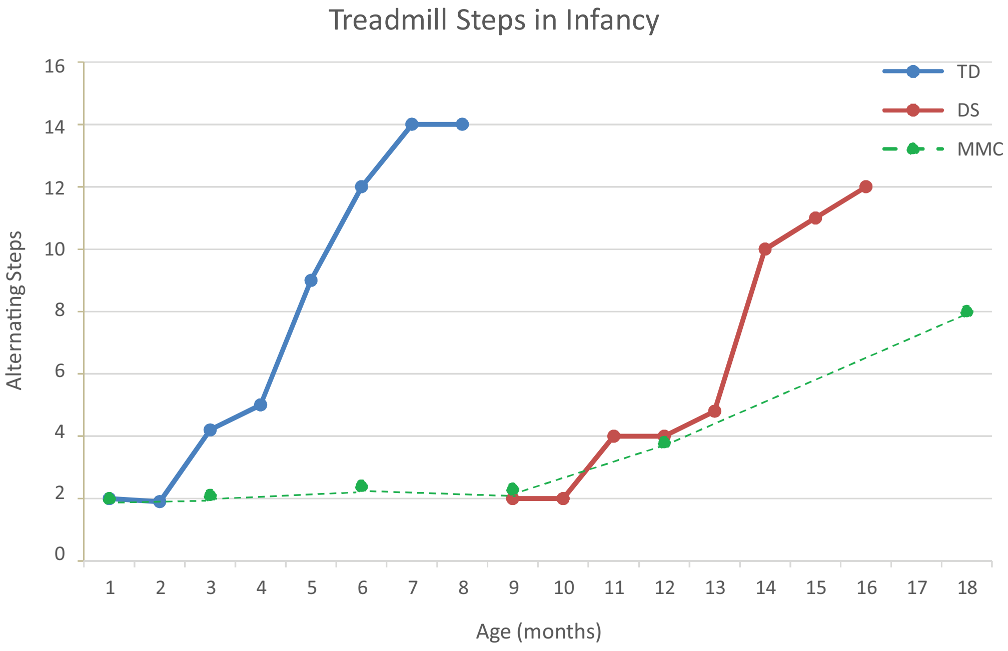

FIGURE 3 Composite figure representing the shape of the developmental trajectory of treadmill alternanting steps produced by infants with typical development (TD), Down syndrome (DS) and myelomeningocele (MMC). Example experimental papers on which these data trajectories are based include Thelen & Ulrich, 1991 for infants with TD ; Ulrich et al. (1995) for infants with DS; Teulier et al. (2009) and Lee & Ulrich, in progress for infants with MMC. All represent longitudinal data for infants but for MMC the data points are connected with a dashed line because collections occurred two to three months apart.

sory systems are becoming better myelinated and stable as babies move and grow. While we know stepping emerges and resolves to alternating more slowly for infants with DS and MMC in comparison to those with TD we have very little direct evidence specifying their neural development in relation to motor control. When infants stepped at all ages, those with TD produced a higher proportion of alternating steps than their peers in the other groups, for whom alternation did not become the modal response until about 10 months (DS) (Ulrich et al., 1995) or beyond a year (MMC) (Lee & Ulrich, in progress; Teulier et al., 2009).

Perhaps what is most striking is the muscle activity that underlies these steps. In highly skilled children and adult walkers the pattern of muscle activity in the legs is rhythmic and dominated by a temporal sequence of activations by core gait muscles, the quadriceps, hamstrings, gastrocnemius-soleus, and tibialis anterior. That would make sense for a behavior driven by populations of neurons that have built up stable connections over many repetitions. But, consider that each leg and foot has about 44 muscles available to act on relevant joints. Consider further that to be a step, legs must simply demonstrate a stance phase followed by a swing phase. That is, in stance any combination of muscles that creates a net extensor torque can work and combinations that create net flexor torques can facilitate (along with gravity and motion-dependent torques) a swing. When infants step on a treadmill we see exactly that, many variations in the combinations of muscles activated at varied times within the stride cycle, in babies with TD (Sansom et al., 2013) and MMC (Teulier, Sansom, Muraszko, & Ulrich, 2012). While differences among these groups occur, most notably lower frequencies of muscle activations in infants with MMC than TD, the consistency is variability! Infants have many options for creating these net torques and only with much practice will they discover those that are functional for independent upright locomotion and, subsequently, those that are optimal (Chang et al., 2006; Chang, Kubo, & Ulrich, 2009).

Is There Evidence for Its Utility?

The fact that babies with DS and MMC can respond to the partial bodyweight supported treadmill context by producing steps and that their nervous systems demonstrate the capacity for change- plasticity rather than stereotypic or fixed neuromuscular patterns- suggests that supported treadmill stepping practice may be useful as an early therapeutic intervention. It provides a context as similar to upright locomotion as possible, engages many sensory systems in coupling with the motor system, and may enhance muscle and bone strength as well as neural control. It provides a context as similar to upright locomotion as possible, engages many sensory systems in coupling with the motor system, may enhance muscle and bone strength as well as neural control. But theory and basic science do not provide recipes and, thus, studies must be conducted with specific choices about many design details to determine how and why these ideas might be used effectively to facilitate development.

In two studies involving 66 infants with DS researchers have identified an early intervention treadmill practice design that has proven successful in enabling these infants to learn to walk significantly earlier than infants with DS receiving traditional physical therapy alone (Ulrich, Lloyd, Tiernan, Looper, & Angulo-Barroso, 2008; Ulrich, Ulrich, Angulo-Kinzler, & Yun, 2001). Babies with DS, on average, learn to walk at about 2 years of age, or one year later than infants with TD. In both studies, families of infants between the ages of 8 and 10 months were given small treadmills and asked to support their babies upright on them, in their homes, for 8 to 10 minutes a day, 5 days a week. Gradually, babies' stepping became more consistent and a small ramp was added to the end of the treadmill so parents could "walk" their baby through space rather than have them step only in place. Experimental group babies achieved related motor milestones earlier as well, such as the skill of pulling to standing and cruising (Ulrich et al., 2001). In the second study (Ulrich et al., 2008), as individual babies' step frequency improved to reach predetermined performance markers, the researchers increased the movement challenge by modifying the context via small weights added to the legs and increasing the belt speed. These additional challenges helped babies improve faster and reach walk onset earlier. Moreover, follow-up examination showed that infants who received early treadmill intervention retained benefits up to a year beyond the end of their involvement. A principal component analysis showed better gait parameters for the group who received intervention (Angulo-Barroso, Wu, & Ulrich, 2008). Thus, sustained, relevant, challenging practice of stepping can have long-lasting functional effects on neuromotor pathways.

Some of the quandaries faced by early intervention researchers are to determine effective timing (age of onset or developmental level), intensity (dose-response levels), and appropriate motivational characteristics of the therapy. In the motor realm this expands to include determining which subsystems need to be affected and which must be supported. In a recent pilot study Lee and Ulrich (in progress) began the process of sorting through these challenges in an effort to find new and successful early intervention strategies for helping babies with MMC build their subsystems and develop leg control for stepping. These infants show reduced levels of leg activity in infancy and learn to walk at about 3 years of age (Rademacher, Black, & Ulrich, 2008; Williams, Broughton, & Menalaus, 1999). In an effort to take full advantage of early neural plasticity they chose to enroll infants as early as possible, with onset age, on average, of 2 months (corrected age). As had been done for infants with DS in previous studies, pediatric treadmills were provided to parents who helped their babies practice using their legs and stepping, 5 days a week for 10 min a day, for one year. Intensity varied in minutes per day, with parents starting slow and ramping up durations as babies seemed capable. To keep parents and babies motivated, early practice was varied, combining time spent in each of three options for encouraging babies to move their legs: attempts to elicit newborn stepping (treadmill belt was stationary), bouncing the baby on their laps (attempting to elicit leg extensor action after contact), and partial bodyweight supported treadmill stepping. At multiple time points across the year (including pre and post testing) muscle activity, bone mineral content, motor milestones and stepping responses were assessed.

The classic desired behavioral outcome of faster rate of stepping development on and off the treadmill was not clearly supported. At pre-test and after 6 months of practice, infants in the pilot study did no better than infants who did not receive this practice. By post-test, four of the infants were stepping well above the mean for the comparison group, but four were performing below the mean (two failed to complete the intervention). However, by comparing the Bayley Scales of Infant Development motor items between these same two groups, it was clear that other aspects of their neuromotor control were improving more rapidly than in the comparison group. Mean age of onset for motor items related to locomotion favored the practice group and showed high effect sizes or statistically significant differences for five of eight items (Fig. 4). Further, as part of another study the bone mineral content (BMC) of infants in this pilot study was compared to infants with MMC who did not receive treadmill practice and infants with TD over the first 18 months (Lee, Muraszko, & Ulrich, submitted). All neonates showed similar low levels of leg BMC. With age, infants with TD and those with MMC who practiced stepping showed steady rates of increase; infants with MMC who did not receive stepping practice showed little change and significantly lower BMC compared to their peers who received this intervention (Fig. 5). Thus, some underlying subsystems seemed to benefit from the intervention but the design itself needs to be modified, depending on the outcomes desired.

Implications of Manipulating Sensory Input for Clinical Benefit

Motor behavior researchers refer to control of human movements as sensorimotor control but have focused little research on the unique contributions of the developing sensory subsystems in relation to the motor actions of babies. As we pointed out above, the number of steps produced by healthy neonates when supported on a pediatric treadmill tends to be very low, as was true also for young infants with DS and MMC. Yet, the importance of starting interventions as early as possible for babies born with neuromotor disabilities is supported by our knowledge of how the nervous system is developing in these early months. We know that this is a time of exuberant overproduction of synapses and that pruning of neurons has already begun. While synapses are being produced they are also being strengthened by use, or the demands placed on them to support function. Plasticity is high but so is competition for this strengthening neural organization that underlies sensorimotor development and control. Thus, interventions need to target this adaptive plasticity (Johnston, 2009) and the sensory systems may offer new pathways to this goal.

For healthy neonates and ones with medically fragile systems, the pediatric treadmill may be a greater challenge than they can respond to voluntarily but Barbu-Roth and colleagues have been studying the visual system as another pathway to encourage young infants to step (Barbu-Roth et al., 2009; Barbu-Roth et al., 2014). Her team showed that 3-day-old healthy infants who produced some steps when simply supported upright in the air (air-stepping) increased their step frequency when exposed to a pattern of visual flow below their feet that mimicked forward displacement. This line of work is particularly exciting because of its potential for early impact. The power of visual input to elicit goal-oriented motor output was demonstrated by van der Meer and colleagues, though for arm, rather than leg movements (van der Meer, 1997; van der Meer van der Weel, & Lee, 1995, 1996). In three different paradigms they demonstrated that supine newborns who are able to see one of their arms will, during unrestrained movement maintain that arm in view and, when researchers gently displaced it from view would move it back into view. Together these studies are exciting because they argue not only for voluntarily initiated goal-directed actions very early post birth but also that the visual system, generally

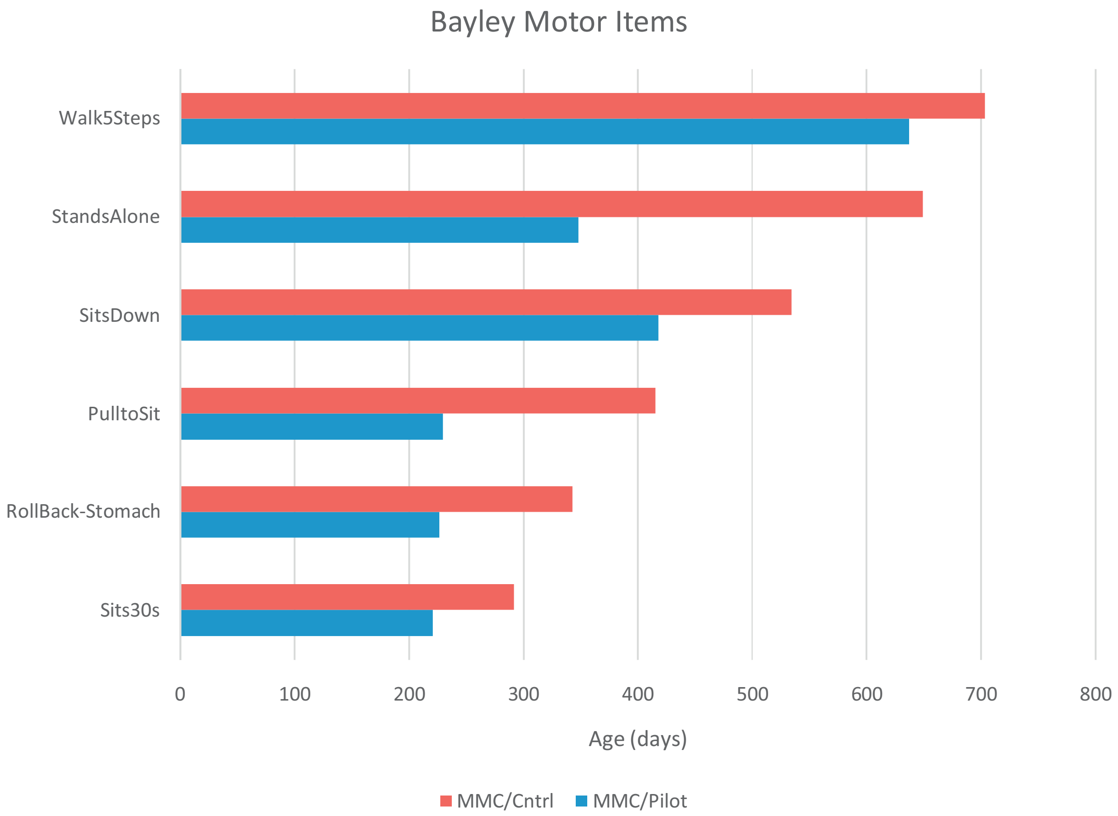

FIGURE 4 Mean values for gross motor items for infants with myelomeningocele (MMC) who participated in the pilot study of the effects of in-home treadmill stepping practice and infants with MMC in a comparison group who did not receive treadmill practice.

considered to be the most poorly developed of the sensory systems at this point, still function sufficiently well to link to and drive motor control.

The use of visual flow to increase baseline treadmill stepping responses of infants has been addressed in a few studies. For infants with TD, across ages 2 to 10-months, a black and white checkerboard covered treadmill belt increased step frequency- specifically during periods in which infants appeared to attend to the belt (Moerchen & Saeed, 2012). For infants with MMC, however, the effect was not significant for younger infants; only in the 7 to 10-month-olds did this visual flow pattern enhance step frequency (Pantall et al., 2011). Alternative sources of sensory input at different ages and in different task conditions may be more salient than visual input alone. For example, babies with MMC at ages 3–5 months who did not respond well to visual input when supported on a treadmill increased step frequency when friction on the foot sole was created via a tacky belt surface (Pantall et al., 2011). Infants with DS (mean age 13 months) increased their treadmill step frequency both when wearing Velcro socks (with a Velcro treadmill belt) and when barefoot but with a nubbly belt surface (Ulrich et al., 1998). Angulo-Kinzler and colleagues (Angulo-Kinzler, Ulrich, & Thelen, 2002) found that healthy 3-month-old infants ages learned to control a mobile suspended over their cribs much better when their supine kicking was rewarded not just with the movement of the mobile (visual feedback) but also with concurrent auditory feedback from wind chimes attached to the mobile. The take-home message from these studies is that sensory systems have been largely ignored in research on the development of motor control in humans but finding contexts that stimulate them is the key to creating efficient early therapies for gait development. Nevertheless, as each population has its own organismic constraints, each context needs to be tested first, before being implemented in specific early therapies.

CONCLUSION

Today we have a better understanding of stepping and walking development over the first year post birth and the concurrent plasticity of subsystems contributing to

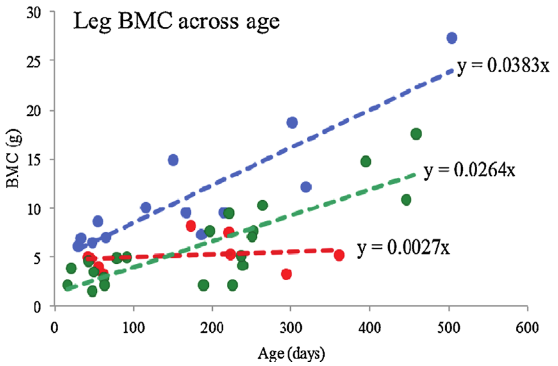

FIGURE 5 Scatterplot of individual data points and subgroup regression lines showing changes in bone mineral content (BMC) in the legs of infants across ages 1–18 months. Blue line represents infants with typical development; green line shows infants with myelomeningocele who received treadmill stepping practice; red line reflects infants with myelomeningocele who did not receive treadmill stepping practice.

these behavioral outcomes. The work we summarized here suggests that when applying basic science and theory to clinical intervention efforts, perhaps nature and nurture must be considered separately along with the imperative understanding that functionally they cannot be separated. That is, we need to recognize the inherent neurophysiological resources available (or not) to the child while identifying potentially nurturing contexts that can be designed to interact with nature to facilitate improvements in the cascading outcomes. Developmental neuromotor control science suggests that the earlier interventions can be accessed the better able one is to optimize outcomes. But, this does not provide a recipe and thoughtful designs must still be tested empirically before they are adopted in practice. The need remains for much more basic science focused on identifying functionally relevant contexts to which infants are capable of responding and to which they are sufficiently motivated to do so, repeatedly.

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