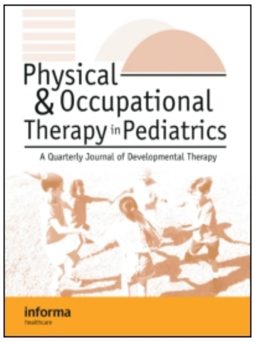

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Using Contingent Reinforcement to Augment Muscle Activation After Perinatal Brachial Plexus Injury: A Pilot Study

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ABSTRACT
Aim: Examine the feasibility of increasing muscle activation with electromyographically (EMG)-triggered musical-video as reinforcement for children with perinatal brachial plexus injury (PBPI). *Methods*: Six children with PBPI (9.3 $\pm$ 6.3 months; 5 female, 1 male) and 13 typically developing (TD) controls (7.8 $\pm$ 3.5 months; 4 female, 9 males) participated. The left arm was affected in 5/6 children with PBPI. We recorded the integral (Vs) of biceps activation with surface EMG during two conditions per arm in one session: (1) 100 second (s) baseline without reinforcement and (2) 300 s reinforcement (musical-video triggered to play with biceps activation above threshold [V]). We examined the relation between the mean integral with reinforcement and hand preference. *Results*: Mean biceps activation significantly increased from baseline in the affected arm of the group with PBPI by the 2nd ($p < .008$) and 3rd ($p < .0004$) 100 s intervals of reinforcement. Six of 6 children with PBPI and 12/13 TD controls increased activation in at least one arm. A lower integral was linked with hand preference for the unaffected right side in the PBPI group. *Conclusion*: This study supports contingent reinforcement as a feasible method to increase muscle activation. Future work will examine training dose and intensity to increase arm function.

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Brachial plexus injury; contingent reinforcement; electromyography; infants; muscle activation

Perinatal brachial plexus (C5-T1) traction injuries cause muscle and sensory denervation in the affected arm at an incidence of 1.3–5.1 per 1,000 live births in the United States and other countries (Chauhan et al., 2014; Foad et al., 2008). Two-thirds of infants with perinatal brachial plexus injury (PBPI) recover arm strength and sensation by 1–2 years of age following reinnervation, yet, up to one-third experience delayed or no recovery (Hale et al., 2010; Mollberg et al., 2005). Persistent delay in recovery can lead to muscle imbalances that contribute to muscle shortening, joint contracture, and posterior glenohumeral joint subluxation limiting prehensile function (Mollberg et al., 2005). Factors that influence recovery and outcome include the severity and location of the plexus lesion as well as surgical and rehabilitation strategies (Hale et al., 2010).

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The timing of return in biceps brachii muscle function is a common predictor of recovery (Gilbert and Tassin, 1984). If full active elbow flexion against gravity is not achieved between 3–8 months of age, microsurgical intervention such as nerve transfers or grafting are indicated to improve motor and sensory function (Bain et al., 2009; Little et al., 2014). Infants who are not surgical candidates, yet display delayed recovery, often receive rehabilitation to minimize secondary impairments and activity limitations associated with weakness, joint or muscle contractures, and prehensile dysfunction. Therapeutic intervention for young infants after PBPI often includes passive range-of-motion (PROM) and positioning (Duff et al., 2004 unpublished). However, methods used to increase muscle activation and function are not well documented.

Due to weakness in the affected muscles, infants and toddlers with PBPI often use compensatory patterns during affected arm motion, relying on activation of muscles which are fully innervated (Duff et al., 2007). Insufficient activation in the affected muscles can contribute to muscle imbalances, secondary impairments, and developmental disuse of the affected arm (Duff et al., 2007). Thus, the unaffected arm is often preferred for prehensile tasks since it is fully functional and more efficient. To progressively increase strength and function in the affected arm it is not sufficent that children with PBPI merely practice moving it, as the movement often involves compensatory strategies. Instead, these children should frequently activate the affected muscle(s), to foster neuromotor recovery and an increase in muscle strength and arm function. Since reach to grasp behaviors typically begin between 3–5 months of age (Thelen et al., 1993) it is important to foster strength and function early.

We propose that activation of the biceps muscle, frequently affected after PBPI and an indicator of C5-C6 innervation, could be augmented with age-appropriate biofeedback as a form of contingent reinforcement. Contingent reinforcement involves the use of motivating stimuli, provided when a person exhibits a specific behavior or motion. A contingency paradigm linking an overhead mobile to movement has been used to study memory and learning in infants developing typically (Rovee-Collier & Barr, 2010), as well as those with congenital heart disease (Chen et al., 2015), Down syndrome (Ohr and Fagen, 1991), spina bifida (Taylor et al., 2013), and infants born preterm (Gekoski et al., 1984; Haley et al., 2006, 2008; Heathcock et al., 2004, 2005). For example, when arm or leg movements are reinforced with sound and motion of an overhead mobile, 3–6 months old infants increase the frequency of movement in the reinforced limb (Rovee-Collier and Gekoski, 1979). The mobile contingency paradigm was recently investigated as a method to promote selective hip-knee coordination in infants developing typically (TD) (Chen et al., 2002; Sargent et al., 2014) and infants born very preterm at risk for motor incoordination (Sargent et al., in review). It is not known if muscle activation could be increased with contingent reinforcement. Thus, the purpose of this study was to examine if infants and toddlers with PBPI and those who are TD could increase bicep activation using a contingency paradigm, involving triggered musical-video reinforcement in one session.

Method

Participants

Nineteen children less than 2 years of age completed this feasibility study; 6 had PBPI (9.3 $\pm$ 6.3 months; 5 female, 1 male) and 13 were typically developing (TD) (7.8 $\pm$ 3.5 months; 4 female, 9 males)(Table 1). Two children did not complete the study due to scheduling difficulty. All participants met the following inclusion criteria: (1) $<$ 2 years of age; (2) scored $\geq$ the 25th percentile on the motor portion of the Bayley Scales of Infant and Toddler

Table 1. Participant demographics.

Participant	Initial lesion	Age (mos)	Affected arm	AMS total (105)	AMS elbow flexion (7)	BSITD III motor percentile	Gender	Race-ethnicity
BP02	C5-T1	4.5	Left	44	1	88th	Female	White H
BP03	C5-T1	8.75	Left	43	2	84th	Female	White H
BP04	C5-C6	4.5	Left	44	3	88th	Male	White NH
BP05	C5-C7	11.25	Left	99	6	88th	Female	Black NH
BP06	C5-T1	5.5	Left	83	3	75th	Female	Black NH
BP07	C5-C7	12.25	Right	65	4	92nd	Female	Black NH
TD01	NA	7.5	NA	105	7	98th	Male	White NH
TD02	NA	10.0	NA	105	7	84th	Female	White NH
TD03	NA	4.75	NA	102	7	92nd	Female	Black NH
TD04	NA	22.0	NA	105	7	96th	Male	White NH
TD06	NA	5.75	NA	105	7	96th	Male	While NH
TD07	NA	13.0	NA	105	7	27th	Female	White H
TD08	NA	5.75	NA	102	7	99th	Male	White NH
TD09	NA	4.75	NA	102	7	99th	Female	White NH
TD10	NA	3.0	NA	99	7	95th	Male	White H
TD11	NA	9.75	NA	105	7	95th	Male	White NH
TD12	NA	4.75	NA	102	7	92nd	Male	White NH
TD13	NA	8.0	NA	105	7	68th	Male	White NH
TD14	NA	22.0	NA	105	7	58th	Male	White NH

Note. PBPI = perinatal brachial plexus injury, TD = typically developing, C = cervical, T = thoracic, mos = months, AMS = active movement scale (affected and right arm), BSID III = Bayley scales of infant and toddler development, Third Ed, H = hispanic, NH = nonhispanic.

Development, 3rd edition (BSITD-III; Bayley, 2005); and (3) scored ≥ 1 out of 7 for elbow flexion (an isometric contraction) on the Active Movement Scale (AMS; Clarke & Curtis, 1995). A university-affiliated institutional review board approved this study and parents gave written informed consent.

Procedure

The study took place over two, 1-hour laboratory sessions. The BSITD-III, the AMS and the Almli test of handedness (Almli, 2006 unpublished) were completed in session 1. The training program occurred during session 2 (same day or one day later).

During training, participants sat in a corner seat with a tray and 1–2 graspable toys (Fig. S1, supplement). The toys induced biceps muscle activation during grasping. Each session was taped with two digital video cameras (Canon HG10 and HF R400). One camera was superior to the monitor and anterior to the infant to observe the child's visual attention on the video. The second camera was behind the infant to capture a posterior-lateral facial view, and the video image on the monitor.

Each volar upper arm was prepared with alcohol, followed by water. Disposable (nonallergic) adhesive tape and Coban wrap® were used to secure a bipolar active electrode to the skin over the mid-belly of each biceps and a ground electrode over one scapula. The two parallel bars on each electrode were 1-cm apart and each contact point was 1-mm wide × 1-cm long. Biceps muscle activity was recorded in volts (V) with surface electromyography (SEMG; 1,000 Hz; DelsysBagnoli System, Boston, MA) and captured using a laptop computer equipped with a custom MATLAB® program.

SEMG Data Reduction

Biceps activity was collected in both arms for 100 seconds at *baseline* (no reinforcement) and during a 300 second (5 minute/arm) musical-video reinforcement condition. Given the age of the participants, we could not use the percent of maximum muscle contraction. Instead we quantified muscle activity by capturing the integral of suprathreshold biceps SEMG activity. This integral (Saavedra et al., 2012), expressed in units of volts*seconds (Vs), was the primary outcome measure of muscle activity.

Online SEMG Smoothing

The data were smoothed, integrated, and postprocessed using a custom MATLAB® program. To smooth the SEMG signal in real-time without delays associated with common SEMG postprocessing filters, we used a custom algorithm that created an on-line linear envelope of the signal. A running variable, encoding smoothed SEMG, increased if the current instantaneous SEMG signal exceeded the smoothed SEMG (increase was 10% of the difference between current instantaneous and smoothed signal). The smoothed SEMG decreased if the current instantaneous SEMG signal was lower than the smoothed SEMG (decrease was 10% of the difference between current instantaneous and smoothed signal). Thresholds for triggering musical-video reinforcement were set based on the average smoothed SEMG signal from each arm, during a period of EMG activity, determined from the 100 second baseline for each participant.

Training Protocol

The integral of muscle activity above threshold (Vs) was quantified for each arm during the 100 second baseline condition and during the 300 second reinforcement condition (divided into three 100 second segments for analysis) for each arm. During *reinforcement*, whenever a participant contracted the biceps of one arm greater than the preset SEMG threshold value (V) for that arm, for 0.5 second, an age appropriate musical video (e.g., Cookie Monster singing) was projected on a monitor and music played from a speaker. We counterbalanced the first arm used for training across participants as the affected or unaffected arm for the PBPI group and the right or left arm for TD controls.

Visual Attention

We calculated the mean percent time of visual attention on the musical video when it was triggered to play during reinforcement for all participants. Recorded participant videotapes were coded for visual attention and looking time (s) by an evaluator who was blind to group. The scale for attention was described as: 0 = not looking at the monitor while the video played; and 1 = looking at the monitor while the video played. Looking time was calculated as the percent of time the child attended to the monitor while the video played. This coding strategy has been used with infants in previous work (Sargent et al., 2014; Tiernan & Angulo-Barroso, 2008).

Hand Preference

We documented current hand preference for each participant with the Almli test of handedness (Almli, 2006 unpublished). The Almli was administered while the child sat in the corner seat with a waist-high table placed anteriorly. Four spools (red, blue, yellow, and green), were placed on the table one at a time, at 50%–75% of arm reach in midline for two repetitions each. Eight trials were videotaped for each child. The frequency of right, left and bimanual grasps were tallied to calculate a laterality index (see Appendix for formula); an estimate of hand preference (Almli, unpublished). We categorized the results for hand preference based on the calculated scores. A score <-1 represented a left hand preference and a score $>+1$ a right hand preference. Scores ranging from -1 to 1 denoted a mixed hand preference.

Statistical Analysis

We used mixed effects linear regression to model the integral of muscle activation as a function of sequence and arm. Sequence included a baseline condition of 100 seconds and 3 reinforcement intervals of 100 seconds each. A direct product structure was assumed for the residual covariance matrix to model the correlation between arms at each time and among repeated measures over time. Models were fit separately for children with PBPI and TD controls. For those in the PBPI group, arm referred to the affected vs. unaffected limb. For the TD group, arm referred to the right vs. left limb. Within each model, the average change from baseline to each interval during reinforcement was estimated for each arm. Model residuals were examined graphically to evaluate the suitability of the normality assumption. Using a Bonferonni adjustment for each group for 6 comparisons, we would require $p < .0083$ for significance.

We used mixed effects linear regression to compare the mean integral of biceps activation during baseline and the reinforcement period. This was used at each interval, between the two groups and separately between arms for the PBPI group (affected vs. unaffected) and the TD group (right vs. left). With a Bonferroni adjustment, $p < .0125$ was needed for significance of between-group comparisons at each interval. We used a Spearman correlation (rho) to examine the association between the laterality index for grasp and the mean integral of biceps activation during the reinforcement period in both groups.

Results

Figure S2 (supplement) depicts a representative raw SEMG time series from the right arm of TD03 recorded at baseline (100 seconds) and reinforcement (300 seconds divided into 3 intervals of 100 seconds each). The graph and magnified inset display muscle activation at zero volts, the preset threshold (V), and the integral of activation (Vs) at baseline and reinforcement.

Biceps Activation

At baseline, there was not a significant group difference in the mean integral of biceps activation above threshold (Vs, $p = 0.0298$). Yet, as seen in Figure 1, at each interval of reinforcement the mean integral above threshold was significantly greater in the PBPI group compared to the TD group ($p < .0053$, $p < .0049$, $p < .0066$, respectively). There was no significant difference between arms in the integral at baseline nor in the 3 reinforcement intervals for either group ($p > .0125$).

During reinforcement, the mean integral of activation for the PBPI group significantly increased in the affected arm from baseline by the second ($p < .0080$), and third ($p < .0004$) 100 second intervals (see Figure 1). The integrals above threshold increased from baseline to at least one 100 second reinforcement interval in one arm, for 6 of 6 children with PBPI and 12 of 13 controls (Figure 2). Thus, 87% of participant arms increased biceps activation, from baseline when compared to the 3 reinforcement intervals.

Visual Attention

When the musical-video played during reinforcement, the mean visual attention on the monitor across all participants was 81.7% $\pm$ 18.8%. Upon review of the recorded video, participants

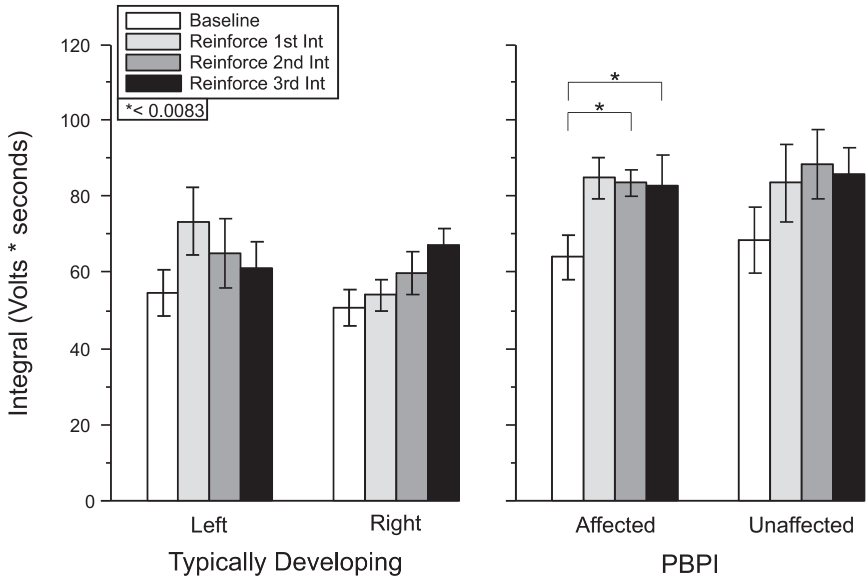

Figure 1. Mean integrals of biceps activation at baseline and during reinforcement (reinforce) for typically developing (TD) children (left) and children who sustained perinatal brachial plexus injury (PBPI, right). Mean biceps activation (integral) significantly increased from baseline (100s) by the 2nd ($p < .0080$), and 3rd ($p < .0004$) intervals (Int) for the PBPI group. The unaffected arm of the PBPI group and both arms of the TD group did not reach significance ($p > .0083$).

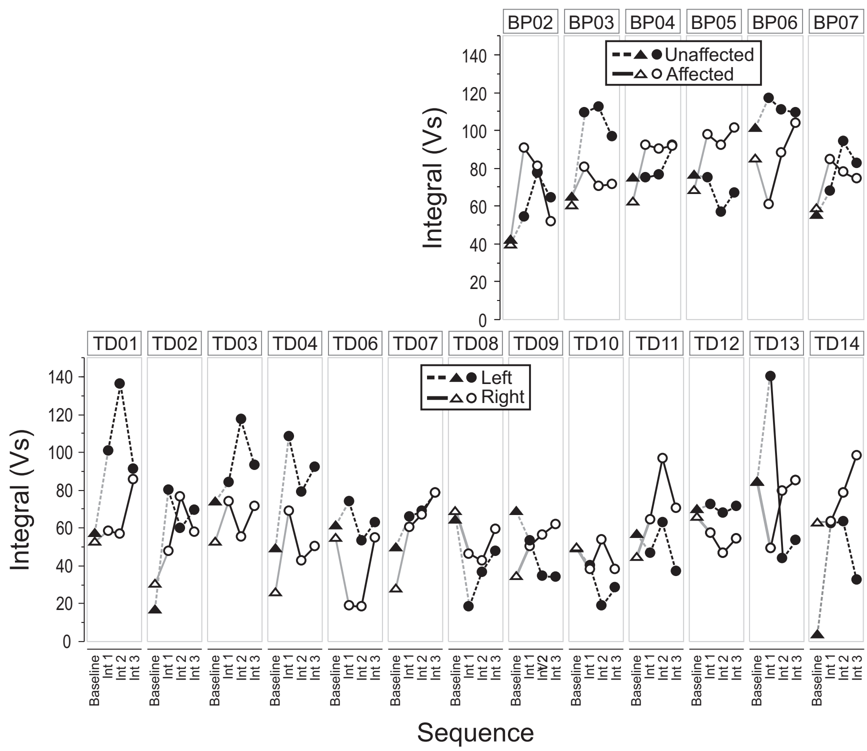

Figure 2. Integral (Volts*seconds [Vs]) of biceps activation at baseline (100s) and three, 100s training intervals (Int) for all participants (top graph – children with the perinatal brachial plexus injury [PBPI]; bottom graph – typically developing [TD] children).

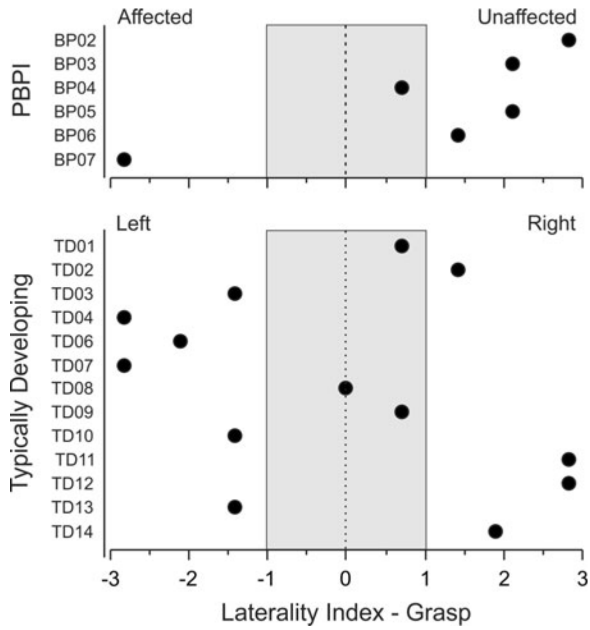

Figure 3. Laterality Index for grasp based on the Almli Test of Handedness. Top graph–children with perinatal brachial plexus injury (PBPI); and bottom graph–typically developing (TD) children. The shaded area, −1 to +1, represents a mixed hand preference.

predominately turned toward the monitor when the music turned on. The music apparently attracted the attention of participants toward the video.

Hand Preference

Data from the Almli test of handedness are shown in Figure 3. For children with PBPI; one had a left hand preference (unaffected arm, <-1), four had a right hand preference (unaffected arm, $>+1$) and one had a mixed hand preference (-1 to 1). Six TD children displayed a left hand preference (<-1), 4 had a right preference ($>+1$) and 3 had a mixed hand preference (-1 to 1). To determine the Spearman correlation, a laterality index of -2.83 was assigned the lowest rank (1) and an index of $+2.83$ the highest rank (6). There was a moderate negative correlation between ranks for the laterality index and the integral during reinforcement for the participants with PBPI ($r = -0.42$, $p = 0.18$) whereas the TD participants had a low positive correlation ($r = 0.15$, $p = 0.48$) (Fig. S3, supplement). Thus, for the PBPI group, a lower integral was associated with a right hand preference or the unaffected arm, whereas, for the TD group a higher integral was linked with a right hand preference.

Discussion

This study investigated the feasibility of using SEMG-triggered musical-video reinforcement to increase biceps muscle activation in participants who sustained PBPI as well as controls who were TD. The primary impairment after PBPI is muscle weakness, and this group often compensates by recruiting unaffected muscles to move the affected arm during prehensile tasks (Duff et al., 2007). There are few evidence-based rehabilitation strategies designed to increase muscle activation and strength in infants and toddlers (Berggren & Baker, 2015; Pantall et al., 2012). Among reported strategies, are the use of reciprocal electrical stimulation to opposing muscle groups which was recently supported as a beneficial treatment method in a case report of a toddler with PBPI (Berggren & Baker, 2015). However, for this study, we drew on the concept of contingent reinforcement to increase arm movement as used in the mobile paradigm (Chen et al., 2002; Needham et al., 2014; Rovee & Rovee, 1969; Sargent et al., 2014). We modified the paradigm to be uniquely targeted to the primary impairment of weakness through triggered activation of the biceps, an indicator of C5-C6 innervation. The results support this paradigm as feasible for the group with PBPI.

Treatment strategies that encourage an increase in muscle activation as reinnervation occurs may foster arm use and limit compensation. Optimal use of the biceps in functional tasks such as hand-to-mouth behavior may hasten recovery in this group. Previous work with infants with TD using the reinforcement of an overhead mobile has shown that reach-to-grasp behaviors improved most when movement triggered the mobile to play versus when the mobile played continuously (Needham et al., 2014). Thus, to support the efficacy of triggered reinforcement with a musical-video as a modality, a comparison between increasing muscle activation with triggered vs. continuous reinforcement should be completed in children with PBPI.

Muscle Activation

Both groups displayed a mean increase in the integral of muscle activation from baseline during the reinforcement period. However, only the increase for the group with PBPI was statistically significant by the 2nd and 3rd intervals in the affected arm based on the multiple comparisons. Thus, with reinforcement, the PBPI group showed that they could increase biceps muscle activation within one session of training. Although muscle activation was associated with the reinforcement, it is possible that the infants learned that a specific arm motion was linked to the musical video instead.

The results showed that children with PBPI significantly increased mean biceps activation above threshold from baseline during reinforcement to a greater degree than the control group. Studies using animal models suggest that changes in muscle activation patterns and the development of contractures may be due to impaired muscle growth and force changes secondary to full or partial denervation (Cheng et al., 2015; Nikolaou et al., 2015). Cornwall and colleagues found muscle spindle degeneration and loss of spindle ErbB (tyrosine kinase receptors) signaling activity after postganglionic brachial plexus nerve injury in an animal model. Thus, there may be significant changes in muscle spindle integrity in children who experience partial plexus denervation. A loss in the number of muscle spindles in the affected muscles may dampen the available sensory feedback. This change in sensory feedback, could lead to greater effort and higher muscle activation by children with PBPI (Navarro et al., 2007). Alternatively, as axon regeneration progresses resting muscle activation may naturally increase resulting in a higher level of activation during isometric or isotonic tasks (Udina et al., 2011). Sheffler et al. (2012) found that surface EMG activity in the long head of the biceps in the affected arm of children with PBPI was higher than the unaffected arm during hand to head and high reach tasks. The authors (Sheffler et al., 2012) postulated that this finding may contribute to elbow flexion contractures. The rationale for why muscle activation was higher in both arms for the PBPI group during reinforcement requires further examination.

Hand Preference

It was not surprising that the hand linked with the unaffected arm in the group with PBPI was preferred for grasping and that controls show a wide distribution for hand preference.

Interestingly, for the group with PBPI, a negative correlation between the laterality index and the integral of muscle activation during reinforcement suggests that the arm with the strongest hand preference had the lowest integral. Conversely, the positive correlation between the laterality index for the control group and the higher integral of activation during reinforcement suggests that the integral was slightly higher when the right hand was preferred for grasping. The implications of hand or arm preference on the amount of muscle activation during task performance require further investigation.

Limitations

We found our paradigm to be feasible for the group with PBPI, yet there were limitations. First, the sample size was small and the age range of participants broad. Yet, the findings were evident across all children with PBPI regardless of age, strengthening the feasibility of this paradigm for this group. Second, there may have been crosstalk between muscle groups, in particular between the biceps and the brachialis. However, given that the brachialis muscle is also innervated primarily by cervical 5–6 spinal nerves, activation of either muscle provides evidence of recovery. Third, we did not assess learning via retention so we do not know if one training session led to a permanent change in biceps muscle activation. To sufficiently boost muscle activation and support neuromotor recovery a substantially longer period of training may be required. Finally, although we documented a mean of 81% visual attention on the musical-video when it played, some children did not attend to it as long as others as noted by the 18% standard deviation. For some infants and toddlers a movable toy or music may be a stronger form of reinforcement. Further research should examine longer training periods, alternate forms of reinforcement, and retention in a larger sample size.

Conclusion

In this feasibility study, mean biceps activation in the affected arm of participants with PBPI significantly increased with contingent reinforcement. Further study will help determine the best dose for training and whether an increase in muscle activation supports neural recovery, minimizes secondary impairments, and optimizes function. It is also important to determine if an increase in muscle activation is retained and transferred to other tasks. A tighter age range using alternative modes of reinforcement may further support the efficacy of this paradigm for children with PBPI who present with muscle weakness.

Declaration of Interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of this article.

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Appendix

Calculation of the laterality index for grasp is as follows: LI = number of right hand grasps – (number of left hand grasps + number of bilateral grasps)/square root of the number of trials.