The effect of constraint-induced movement therapy assessed by accelerometry: the impact on daytime activity and sleep in children with cerebral palsy

O efeito da terapia por contensão induzida avaliada por meio de acelerômetros: o impacto na atividade diurna e no sono em crianças com paralisia cerebral

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Abstract

Introduction: Spastic hemiparetic cerebral palsy (CP) is the most prevalent type of CP. Children with spastic hemiparesis experience difficulties when using their affected upper extremities, and one effective treatment is the Constraint-Induced Movement Therapy (CIMT). The study of rest-activity patterns provides information on children's daily activities with spastic hemiparetic CP during the day and sleep. **Objective:** To investigate the effect of CIMT on the rest-activity patterns in children with spastic hemiparetic CP vs in a healthy group. **Methods:** Nonrandomized controlled trial was conducted at the Neuropediatric Center of the Hospital de Clínicas Complex, in Curitiba, Brazil. Children with spastic hemiparetic CP between 5 and 16 years old participated in the study group and receive the CIMT. The healthy group was composed of children between 5 and 15 years old. Both groups used accelerometer to record rest-activity patterns, that may be studied through nonparametric variables of accelerometer: M10 (an individual's most active 10h); L5 (an individual's least active 5h); and RA (relative amplitude of the circadian rest-activity patterns). **Results:** Forty-five children were recruited, and 38 were included in the analyses (19 allocated to each group). In the study group, there was a significant increase in M10 and L5 ($p < 0.001$) after CIMT. The values of M10 and L5 were significantly higher ($p < 0.001$) in the healthy group compared to the study group after CIMT. **Conclusion:** Our results showed that children with spastic hemiparetic CP became more active and participant in their daily life during the day as well as more efficient sleeping.

Keywords: Accelerometer. Cerebral palsy. Children. Constraint Induced Movement Therapy. Rest activity patterns.

Resumo

Introdução: *A paralisia cerebral (PC) hemiparética espástica é o tipo de PC mais prevalente. Crianças com hemiparesia espástica apresentam dificuldades ao usar as extremidades superiores afetadas e um tratamento eficaz é a Terapia por Contensão Induzida (TCI). O estudo dos padrões de atividade-repouso fornece informações sobre as atividades diárias de crianças com PC hemiparética espástica durante o dia e o sono.* ***Objetivo:*** *Investigar o efeito da TCI nos padrões de repouso-atividade em crianças com PC hemiparética espástica versus um grupo saudável.* ***Métodos:*** *Realizou-se um ensaio controlado não randomizado no Centro de Neuropediatria do Complexo do Hospital de Clínicas, Curitiba, Brasil. Crianças com PC hemiparética espástica entre 5 e 16 anos participaram do grupo de estudo e receberam a TCI. O grupo saudável foi composto por crianças entre 5 e 15 anos. Ambos os grupos utilizaram um acelerômetro para registrar padrões de atividade-repouso, os quais podem ser estudados através de variáveis não paramétricas do acelerômetro: M10 (10h mais ativas de um indivíduo); L5 (5h menos ativas de um indivíduo); e AR (amplitude relativa dos padrões de atividade-repouso).* ***Resultados:*** *Foram recrutadas 45 crianças e 38 foram incluídas nas análises (19 alocadas em cada grupo). No grupo de estudo, houve aumento significativo de M10 e L5 (p < 0,001) após TCI. Os valores de M10 e L5 foram significativamente maiores (p < 0,001) no grupo saudável em comparação ao grupo de estudo após TCI.* ***Conclusão:*** *Os resultados do presente estudo mostraram que crianças com PC hemiparética espástica tornaram-se mais ativas e participantes de sua vida diária durante o dia, bem como dormiram mais eficientemente.*

Palavras-chave: *Acelerômetro. Paralisia cerebral. Crianças. Terapia por Contensão Induzida. Padrões de atividade-repouso.*

Introduction

Cerebral palsy (CP) is the most common cause of childhood disability. It has a prevalence of 0.33 per 1,000 live births. Spastic hemiparetic CP is the most prevalent type of CP.[1] It is considered to be a condition that affects muscle control and function on one side of the body.[2] Children with spastic hemiparesis experience difficulties using their affected upper extremities in their daily lives. Constraint-Induced Movement Therapy (CIMT)[3,4] is an intensive and most effective treatment to improve bimanual function and performance. The study of rest-activity patterns provides information on the daily activities of children with spastic hemiparetic CP during the day and sleep.[5,6] Several systematic reviews strongly support the conclusion that CIMT is one of the few therapies that produce clinically significant benefits for children with hemiparesis.[4,6] In addition to the consolidated satisfactory clinical results, Coker-Bolt et al.[5] published a study that quantitatively measured the increased use and, thus, the improvement of the most affected upper extremity after CIMT. Although some studies evaluated the performance of the most affected upper extremity during daytime activity (wakefulness), none simultaneously analyzed its activity during the period of rest (sleep), i.e. circadian rest-activity patterns. The circadian rest-activity pattern is one of the 24-hour circadian cycles observed in healthy individuals, produced by a complex interaction of endogenous (e.g. physiological functions) and exogenous (e.g. environmental influences - ambient light, physical activity, and meal times) factors.[7,8] Desynchronization of rest-activity patterns in children has been associated with sleep disorders, obesity, diabetes, and attention-deficit hyperactivity disorder. In addition, sleep onset and duration changes, wakefulness (daytime sleepiness), changes in mood, learning, and memory deficits are commonly observed.[7,8]

Although published studies on rest-activity patterns may provide detailed physiological data in healthy children, studies in these settings may not reflect the variations in sleep-wake behaviors in children with spastic hemiparetic CP. A non-invasive way to collect data on rest-activity patterns is through accelerometer. Accelerometer has been widely recognized in pediatrics since capturing activity at various times over several days, which can be a useful feature in the studied population. Children often behave differently in a clinical setting compared to their everyday lives.[7,9]

Consolidated scientific evidence indicates that CIMT is an effective treatment to reverse learned non-use, to improve the quantity and quality of use of the less affected upper extremity.[3] CIMT is considered an intensive treatment, but there is a lack of literature about its effects on circadian rest-activity patterns. In other words, what is the impact of CIMT on these children's wakefulness period (e.g. they become more active, participative in their activities) and what is the consequence of this effect on the night period (for example, on sleep, if there is any impairment in sleep of these children).[8] It is suggested that alterations in the period of wakefulness and a period of non-restorative rest, with many nocturnal awakenings, may negatively interfere with several aspects of children's lives in general, with difficulties in learning, attention, memory, mood and metabolic disorders, which may be exacerbated in a population with CP.[10-12] Although literature has expanded on the consequences of rhythm fragmentation and poor sleep on human health, few studies have demonstrated the rest-activity patterns among children up to 16 years with CP. Therefore this study aimed to investigate the effect of CIMT on rest-activity patterns of children with spastic hemiparetic CP.

Methods

This study was a nonrandomized controlled trial (NRCT) in which children with spastic hemiparetic CP receive the CIMT (study group) versus a comparison group consisting of healthy children (healthy group). The study was conducted at the Neuropediatric Center of the Hospital de Clínicas Complex at the Federal University of Paraná (HC-UFPR), Curitiba, Brazil. In the study group, 45 days' worth of accelerometer data were collected before, during, and after the CIMT protocol. In the healthy group, accelerometer data were collected over 15 days.

This trial was approved by the Ethics Committee on Human Research of the HC-UFPR (CAAE: 61969016.6.0000.0096). The consent or agreement of each participant, depending on their legal age, was obtained at the initial clinical visit. All participants agreed to be part of this study, and their parents consented. No changes to the study design were made after the beginning of the study.

Participants

Participants of the study group: female and male children and adolescents (5-16 years) with a confirmed diagnosis of spastic hemiparetic CP. The pediatric neurology diagnosed spastic hemiparetic CP in the study group participants was based on their complete clinical history, standardized physical examination, and neuroimaging exams.[13] The exclusion criteria were botulinum toxin application in the previous three months, surgical procedure in the previous six months, and invalid accelerometer data.

Participants of the healthy group: female and male children and adolescents (5 - 16 years). The exclusion criteria for this group were participants with structural brain disease, neurological impairment or autistic spectrum disorder. Invalid accelerometer data were excluded.

Intervention

CIMT was provided in the physiotherapy clinic and applied by a physiotherapist at the Neuropediatric Center of the HC-UFPR. All study participants received physical therapy treatment. The less affected upper extremity was constraint through a synthetic cast covering the arm and fingers used 24 hours a day, during the first 13 days of treatment. After the removal of the cast, the last days of therapy focused on bimanual treatment to promote the integration of the new skills acquired at the beginning of treatment.[14] A rigorous and systematic daily follow-up schedule was developed to support the tasks according to the development of gross and fine motor function activity and to check daily progress.[5] The main components of CIMT involve the use of a constraint (in this case, a cast), shaping, and the repetitive practice of tasks for several hours a day, many days a week, and for several weeks. Shaping and repetitive task practice are grounded in learning theory, which was initially developed in CIMT for adults, and whose effectiveness is consolidated.[15] During the CIMT application period, the physiotherapist responsible for the study designated motor activities to be carried out at home (under the supervision of parents), during the period in which the participants were not in the treatment environment. Some examples of designated motor activities included: transferring grains (corn, beans) from one plate to another; place objects/toys of different sizes on a box (the box was far from the participant); with the help of a towel, cleaning a surface; throw small balls into a box/basket; with the help of clothes pegs, nail objects (for example, hanging clothes) and playing ball with both hands (during the period without the cast).

The main emphasis of treatment is promoting the use and abilities of the most affected upper extremity to be functional in the child's general repertoire. Furthermore, intensive practice searches to increase automaticity and, consequently, ease the execution of new motor functions in various everyday situations.[15] This study considered three daily hours of therapy, 5 days a week, for two weeks (Figure 1).

Figure 1 - Constraint-Induced Movement Therapy with accelerometer during various activities.

Functional assessment

In this study, accelerometer data were considered as a primary result, with the aim of verifying the effect of CIMT on rest-activity patterns in the most affected upper extremity of children with spastic hemiparesis. This article presents data on functional outcome measures: Pediatric Upper Extremity Motor Activity Log (PMAL)[16] and Teenager Upper Extremity Motor Activity Log (TMAL).[17] These instruments were used in early studies with CIMT and can be applied across a wide range of ages and ability levels.[15]

PMAL and TMAL are standardized instruments in which parents assess their child's abilities using a six-point Likert scale and the subscales quality of movement (0 = no use and 5 = normal) and amount of use (0 = never and 5 = very often) for each of the arm and hand activities (e.g. holding a cup or bottle, putting the arm through sleeves, throwing a ball). TMAL is an adaptation of PMAL for adolescents; the first's age range covers 9 to 16 years, while PMAL covers 2 to 8 years.[16,17] In this study, we used the PMAL and TMAL versions, developed by the original authors of the tool due to its widespread use in other studies.[5,14,15] Gross Motor Function Classification System (GMFCS) was used for the classification of the ability to perform functional tasks into five levels of gross motor function: from Level I (most able) to Level V (most limited).[18]

Outcome measures

Participants in this study were required to wear a wrist accelerometer (ActTrsut -Condor Instruments, São Paulo, Brazil) on 24 hours a day (except for swimming). In the study group, accelerometers were used in both upper extremities during the pre-treatment period. During treatment, the accelerometers were used in the most affected upper extremity; after treatment, the devices were used in both upper extremities. The accelerometers were used in the non-dominant upper extremity in the healthy group. A paper diary was provided for participants to report all the times their accelerometer was removed. At the end of the period, participants returned their accelerometers in person; data were downloaded using ActStudio software (Condor Instruments, São Paulo, Brazil). We considered a valid day to be >10 hours of gathered activity. The days needed to be consecutive, and weekends were included. Participants in the study group had to provide 45 days of recordings to be included in our analysis, and the healthy group 15 days. All files were visually examined at the data collection site before being processed by the ActAnálise software.[19] The accelerometers were initialized in zero crossing mode, collecting data at 1-min epochs.

Nonparametric variables

Rest-activity patterns do not perfectly follow a sinusoidal waveform, so it is important to consider alternatives such as nonparametric approaches to investigate 24-hour rest-activity patterns.[7,20] In this study, we calculated the following nonparametric variables:

1) Least active five-hour period or nocturnal activity (L5): is the average activity count during the least five-hour period used for measuring rest phase. A low value of L5 indicates more consolidated sleep and less

fragmented rhythm. The lower the L5 values, the more restorative sleep, with few nocturnal awakenings.[20]

2) Most active ten-hour period or diurnal activity (M10): is the average activity count of the most active 10-hour period. A low value of M10 may be associated with motor difficulty, exercise reduction or circadian timing system degeneration. High M10 values indicate a period of more active wakefulness.[20]

3) Relative amplitude (RA): activity's RA is calculated as follows: (M10-L5)/(M10+L5). Higher RA values indicate more robust 24-hour rest-activity patterns representing higher activity during wakefulness and less activity during sleep. In other words, a more restful sleep, therefore healthier sleep.[20]

Data analysis

Participants were recruited through convenience sampling. Based on a pilot study, the standard deviations of the rest-activity patterns were estimated. Sample sizes were calculated for estimating the movements' mean with a precision of 3% and a confidence level of 95%. We aimed to evaluate 19 children from the study group and 19 from the healthy group.

Analyses were performed using IBM SPSS v.20.0. (Armonk, NK; IBM Group). The Jarque-Bera test was used to determine data distribution normality. Both groups were compared by age and sex (Student's t-test). We describe the mean activity and rest scores for each study stage: before, during, and after treatment with CIMT. For the accelerometer data, Student's t-test was used to compare the changes in the rest-activity patterns before, during, and after treatment with CIMT. To compare linked sample data, we used Friedman's non-parametric test, and to compare the quantitative variables of the rest-activity patterns between the study group and the healthy group, we used the non-parametric Mann-Whitney test; $p < 0.005$ was considered statistically significant.

Results

In the study group, 25 children met the inclusion criteria. Three children were excluded due to incomplete recorded data by the accelerometers and three dropped out of the study. In the healthy group, 20 children met the inclusion criteria. One was excluded due to the lack of collected data by the accelerometer. Thus, 38 children participated in the study, 19 from the study group and 19 from the healthy group (Figure 2). The recruitment period was from January 2017 to October 2019, and the study was closed once the sample size was reached. There were no adverse events. Participants in the study and healthy groups did not differ significantly in age ($p = 0.578$) and sex ($p = 0.103$). Table 1 presents the demographic information for both groups.

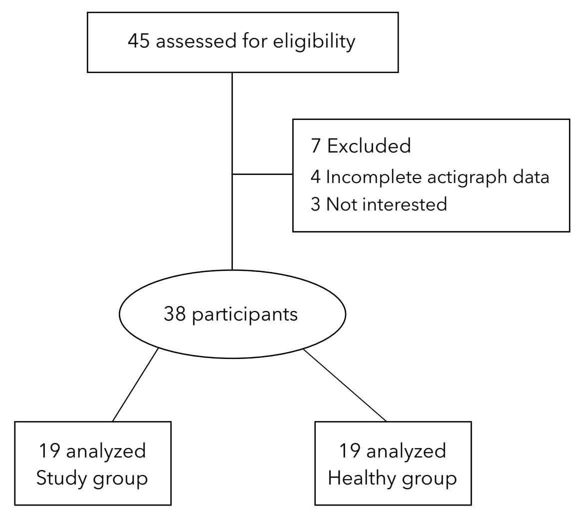

Figure 2 - Flowchart of sample selection.

Table 1 - Characteristics of children with spastic hemiparetic cerebral palsy (study group - SG, n = 19) and healthy group (HG, n = 19)

Characteristics	SG n (%)	HG n (%)
Sex		
Male	11 (57.90)	6 (31.57)
Female	8 (42.10)	13 (68.43)
Age (years)		
Range	5 - 16	5 - 15
Mean (SD)	9.31 (3.07)	9.84 (2.69)
Right hand dominance	8 (42.10)	19 (100)
GMFCS level		
I	14 (73.68)	NA
II	5 (26.32)	NA
Maternal educational level		
High school diploma	14 (73.68)	19 (100)

Note: GMFCS = Gross Motor Function Classification System; SD = standard deviation; NA = not applicable.

Rest-activity patterns

During pre-treatment, study group participants presented a higher M10 activity mean in the less affected upper extremity compared to the most affected upper extremity (p < 0.001). Participants also demonstrated a significant increase in the M10 of the most affected upper extremity during each day of treatment compared to pre-treatment data (median: 236.6, p = 0.005), as illustrated in Figure 3. During post-treatment, there was higher M10 activity mean in the less affected upper extremity compared to the other upper extremity (p < 0.001). Regarding the mean L5 level, during pre-treatment, the highest activity was found in the less affected upper extremity (p < 0.001).

There was no difference when comparing the L5 variable daily during treatment to pre-treatment (median: 3.3, p = 0.900) (Figure 3).

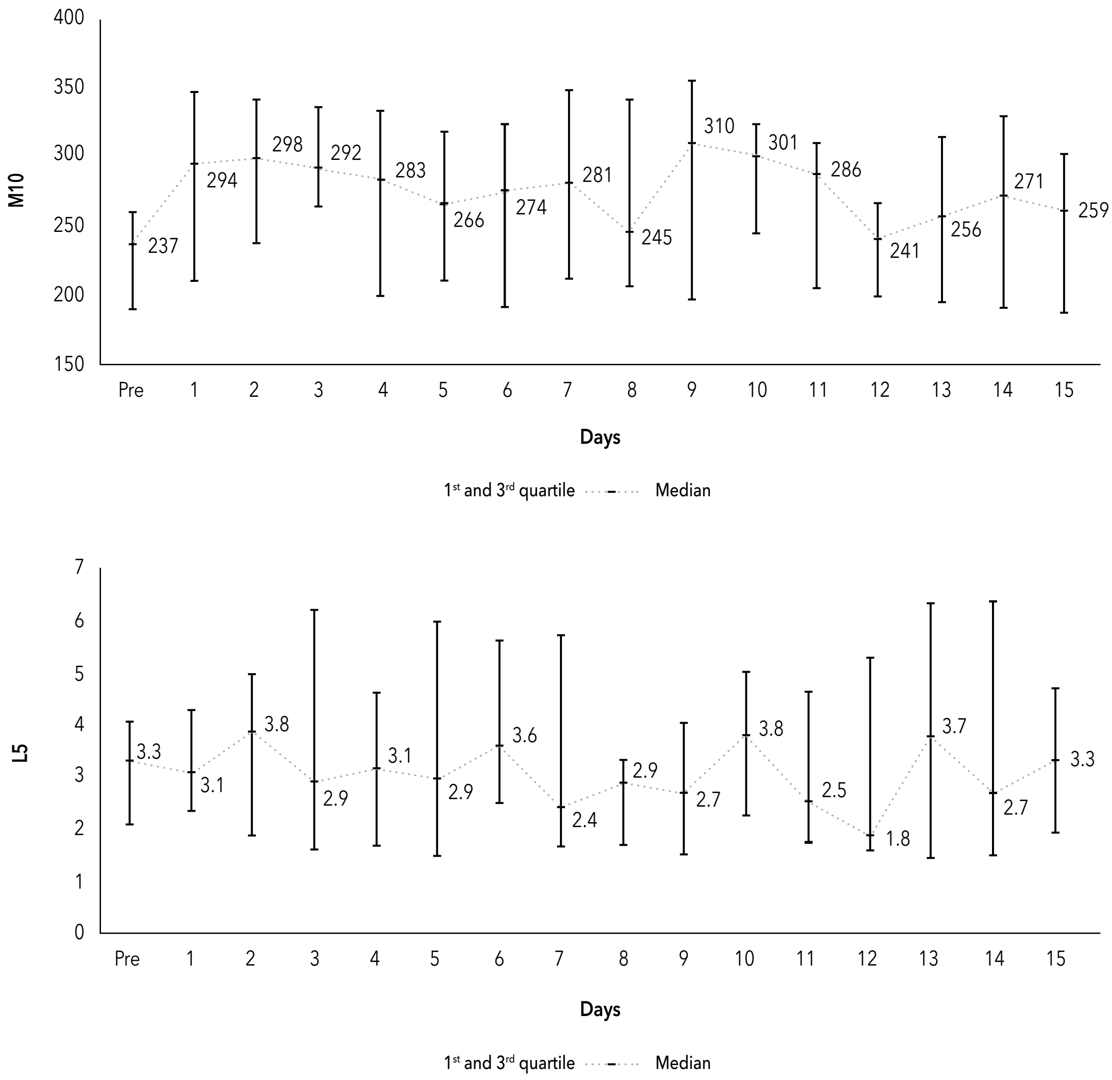

Figure 3 - The most-active 10-h period (M10) duration of the most affected upper extremity increased during CIMT compared to the baseline (pre-CIMT), and the less-active 5-h period (L5) duration of the most affected upper extremity stabilized during the CIMT compared to the baseline (pre-CIMT) in the study group.

Note: CIMT = Constraint-Induced Movement Therapy (day 1 -15).

At the end of the treatment, the results pointed out that the mean L5 activity level was significantly higher in the less affected upper extremity ($p < 0.001$, Student's t-test) (Table 2). There was no difference between RA and the periods before, during, and after treatment with CIMT regarding the most affected upper extremity (median = 0.97, $p = 0.254$, non-parametric Friedman's test).

In the healthy group, the mean M10 activity of the non-dominant upper extremity was 355.8 (±72.2), ranging from 267.8 to 499.3. The median L5 activity was 5.8 (±2.5), ranging from 3.7 to 13.9. The healthy group showed higher M10 and L5 activity than the study group during pre-treatment ($p < 0.001$, for both Student's t and non-parametric Mann-Whitney tests). During post-treatment, M10 and L5 were significantly higher in the healthy group compared to the study group ($p < 0.001$, for both Student's t and non-parametric Mann-Whitney test). No differences were found between RA in the healthy group (median = 0.96) and study group pre- (median = 0.97) and post-treatment (median = 0.97) ($p = 0.170$ and $p = 0.157$, non-parametric Mann-Whitney test, respectively).

Relating to PMAL and TMAL, an increase in the frequency of use (< 0.001) and in the quality of use of the most affected upper extremity ($p < 0.001$) was observed after CIMT.

Table 2 - Description of rest-activity pattern study group

CIMT	L5			M10		
	Most affected upper extremity (mean)	Less affected upper extremity (mean)	p*	Most affected upper extremity (mean)	Less affected upper extremity (mean)	p*
Pre-treatment	3.5 (±2.1) **0.9 - 9.4	7 (±3.1) **3.1 -11.9	< 0.001	221.9 (±59.5) **104.2 - 318.5	344.4 (±77.3) **173.4 - 444.2	< 0.001
Treatment	4.4 (±3.3) **1.6 - 16.1	NA	NA	283.1 (±58.9) **168.4 - 365.7	NA	NA
Post-treatment	3.9 (1.9) **1.3 - 8.3	8.6 (±5.2) **1.6 - 22.8	< 0.001	255.7 (±55.5) **154.9 - 332.6	342.2 (±87.7) **157.1 - 473.8	< 0.001

Note: CIMT = Constraint Induced Movement Therapy; L5 = less active 5 hours; M10 = most active 10 hours; NA = not applicable. *Student's t-test. **Minimum-maximum.

Discussion

TThis is, to our knowledge, the first study to investigate the effect of CIMT on the rest-activity patterns of children with spastic hemiparetic CP. We found that CIMT improved the spontaneous activity of the most affected upper extremity and that there was no impairment to the resting period. In addition, the less affected upper extremity had higher activity peaks in both daytime and nighttime. We also observed differences in the rest-activity patterns between the study and the healthy group; the study group had the least stable circadian rest-activity patterns.

Despite the proven efficacy of CIMT recently, there is still a need to quantify the improvement of the most affected upper extremity.[7,8] The children in this study presented a significant increase in M10. This finding is based on one of the mechanisms by which CIMT achieves its therapeutic effect, which is the overcoming of learned non-use and plastic changes in the structure and function of the brain.[21] Furthermore, our results point to significant improvements in the quality of movement of the most affected upper extremity after CIMT. It is suggested that due to repetitive practice associated with sensory-motor stimuli, brain excitability increased related to the stimulated area, thus promoting an improvement in motor performance.[22] Coker-Bolt et al.[5] found that children with spastic hemiparesis undergoing intensive training protocols such as CIMT may increase the quantity and quality of spontaneous activity in the most affected upper extremity and retain these gains as long as they are subjected to high-intensity protocols (> 30 hours) so that the repetitive practice of tasks occurs in a sufficient manner, which allows the automation of spontaneous movements and indicates that motor learning has occurred, which needs to be transported to real life. Goodwin et al.[23] reported that other strategies or home exercise programs can optimize the use of the most affected upper extremity after CIMT, making this extremity more functional in activities of daily living. Additionally, according to Coker-Bolt et al.,[24] accelerometers are an effective and safe tool for quantitatively measuring the spontaneous activity of the most affected upper extremity in everyday situations.

Regarding nocturnal activity, we observed an increase in L5 after CIMT. This result indicates that CIMT promoted the forming of a new network of neuronal circuits, which increased the movement of the most affected upper extremity during sleep. This result suggests a positive effect during the day, when the upper extremity may become more active.[21,25]

The present study shows that the most affect upper extremity had lower values for M10 and L5 compared to the less affected upper extremity. The lower motor activity of the most affected upper extremity is related to the location of the brain lesion, size, and amount of lesions.[26,27] Hoyt et al.[28] found significant M10 asymmetry between the upper extremities of children with spastic hemiparetic CP attributed to identified brain injury, such as perinatal stroke. Furthermore, for the authors, accelerometer proved to be a reliable resource for the early detection of this asymmetry between the upper extremities, hence allowing targeted interventions.

There were no RA adverse effects after CIMT, suggesting that the intensive treatment kept the sleep-wake period stable and without fragmentation. In other words, sleep was efficient, and the children were more active during the day, which reflected positively on their health.[20,29]

When we analyzed the rest-activity patterns of the study group compared to the healthy group during the three research phases, we noticed that the healthy children presented higher values of M10 and L5. This tells us that healthy children are more active during the day and that their upper extremity moves more during sleep. Furthermore, the results point out that children with spastic hemiparesis present a decrease in their motor activity both during the day and night. This occurs due to cortical lesions that plan and initiate motor activities.[30,31] It is essential that, during the daytime, these children present efficient and functional motor activity so they become more participative at school, in leisurely activities, and in the community. Moreover, efficient sleep helps form different neural networks and consolidate and retain motor learning, which is perceived in the movement of the upper extremity affected during sleep.[32]

The present study was a nonrandomized controlled trial, in which sample selection was by convenience; therefore, selection bias is possible. We find this unlikely, as we recruited participants eligible for treatment from the sample selection. Other limitations include that parents or family members carried out accelerometer care. Although we are confident of the results, the accelerometers may have been misused. To estimate the potential magnitude of expectancy bias, we did not assess the rest-activity patterns in younger children (below 5 years). Future studies with larger and younger samples should be carried out so that the rest-activity patterns and the treatment findings can be more widely verified.

Conclusion

This study begins to fill a gap on literature as there are already publications on the use of accelerometers and CIMT in children with spastic hemiparetic CP, however, they have not been applied to investigate the effects of this intervention on the rest-activity patterns, i.e. during the period of activity and sleep. Our findings indicate that CIMT effectively promotes increased motor activity of the most affected upper extremity both during the day and during sleep. They also point out that our metrics with accelerometer may be useful tools to quantify the improvement in daytime activity in children and adolescents undergoing CIMT. The data provide preliminary evidence of a benefit in the rest-activity patterns after CIMT, resulting in the children and adolescents being more active and participatory during the day and presenting stable sleep. Overall, our study presents a starting point for investigations based on the rest-activity patterns in the CP population, as well as generating new hypotheses to investigate the implications for health in the variation of the rest-activity patterns throughout life.

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Authors' contributions

MFA, MBZ and ACC were responsible for the study design. MFA and AO, for data collection; and MFA and MBZ, for data analysis. MFA wrote the manuscript, while ACC and MBZ, review it and supervised the study. All authors approved the final version.

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