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ORIGINAL ARTICLE

Evidence of training influence on infant manual behavior: a systematic review

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Open acess

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Resumo

Introdução: Pesquisadores tem amplamente investigado como o treino pode melhorar comportamentos manuais em lactentes. No entanto, nenhuma revisão sistemática foi encontrada sobre este tópico.

Objetivo: Analisar a qualidade da evidência científica considerando a qualidade metodológica e o nível de evidência por tipo de estudo em pesquisas sobre treino de comportamentos manuais direcionados a objetos em lactentes nos primeiros 18 meses de vida.

Método: Foram utilizadas as bases de dados da Biblioteca Nacional de Medicina (PubMed / MEDLINE), Literatura Latino-Americana e do Caribe (LILACS), Biblioteca Virtual em Saúde (BIREME / BVS), Science Direct, SciELO e Physiotherapy Evidence Database (PEDro). Apenas ensaios clínicos que avaliaram os benefícios do treino manual orientado a objetos em lactentes e que foram publicados até fevereiro de 2018, em inglês, foram incluídos. O Modelo de Colaboração Cochrane foi adaptado para extrair dados bibliográficos dos artigos e sua qualidade metodológica foi avaliada pela escala PEDro e pelo Nível de Evidência Científica por Tipo de Estudo de Oxford.

Resultados: Vinte e um ensaios clínicos foram incluídos. Os estudos investigaram lactentes nascidos a termo, prematuros e lactentes de risco para distúrbios do espectro autista. Os treinos foram administrados aos lactentes por meio das abordagens do paradigma de "luvas aderentes", prática específica da tarefa ou reforço de contingência. A maioria dos estudos apresentou qualidade metodológica razoável ou fraca. Apenas os estudos que utilizaram a prática ativa específica da tarefa apresentaram qualidade metodológica alta.

Conclusão: Há evidência de alta qualidade de que o treino específico da tarefa aprimora comportamentos manuais orientados a objetos em lactentes com desenvolvimento típico e lactentes prematuros nos primeiros 2-4 meses de vida. Estudos abordando lactentes com diagnósticos estabelecidos de disfunção do desenvolvimento não foram encontrados.

Palavras-chave: desenvolvimento infantil, lactente, intervenção precoce, destreza motora.

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Síntese dos autores

Por que este estudo foi feito?
Esta é a primeira revisão sistemática que aborda a qualidade metodológica dos ensaios clínicos que investigaram os efeitos de diferentes tipos de treino de comportamentos manuais em lactentes, servindo como um guia para a tomada de decisão sobre estratégias de estimulação ou intervenção sensório-motora focadas em comportamentos manuais nos primeiros meses de vida.

O que os pesquisadores fizeram e encontraram?
Foram detalhadas as principais características metodológicas e os achados de ensaios clínicos que examinaram os efeitos de diferentes tipos de treino de comportamentos manuais em lactentes típicos e de risco de até 18 meses de idade. A qualidade da evidência desses estudos foi classificada e discutida, sendo finalmente fornecidas recomendações para a prática clínica. Estudos que aplicaram treino ativo e específico da habilidade de alcançar apresentaram alta qualidade de evidência, enquanto treinos que utilizaram abordagens com luvas aderentes ou reforço contingente apresentaram qualidade moderada ou fraca.

O que essas descobertas significam?
Uma vez que os desfechos de treinos específicos do alcance apresentam alta validade interna e excelente nível de evidência, essa abordagem é a mais recomendada para a prática clínica quando o intuito for estimular e aprimorar o alcançar em lactentes típicos e prematuros no período de aquisição dessa habilidade.

INTRODUÇÃO

Infants are able to interact with objects since the first days of life[1]. Gradually, by means of spontaneous practice over days and months, infants become skilled in reaching, grasping and exploring objects. These early object-directed manual behaviors are essential motor milestones as they allow infants to gather new information about the environment and learn further motor strategies from that[2-4].

Due to developmental importance of these manual behaviors, researchers have widely investigated how interventions by means of induced practice (training) could improve them in infants. Several training approaches have been addressed in literature, including the "sticky mittens" paradigm, task-specific training, or contingent reinforcement. In the "sticky mittens" paradigm, 3-month-old infants were seated on a parent's lap in front of a table, on which Velcro covered toys are placed. As infants wore Velcro covered mittens and were encouraged to reach for the toys, the toys adhered to the mittens as if the infants had grasped them[5-7]. During task-specific trainings, pre-reaching infants were induced to repeat toy-oriented arm movements organized in steps of activities. Activities included haptic contact with the toy and assisted and active toy-oriented hand movements[8-10]. In the contingent reinforcement approach, 3-month-old infants were exposed to moving/sounding toys or a mobile which could be activated contingently upon infants' upper limb actions[11].

These movement experiences have been used as induced trainings to advance or enhance the amount and duration of object-directed manual behaviors in typically developing infants and at-risk infants over 1-2 brief-term sessions or daily sessions. In general, authors have suggested these trainings provide infants with opportunities to improve upper limb control[8,9,11], select more efficient movement patterns[6,8,9,11], become motivated and engaged[10,12], and learn to couple object perception and movement action[6,10]. These trainings, therefore, can be considered interesting tools to potentiate early manual development in typical infants and to prevent or minimize manual impairment in infants at risk for developmental disorders during early intervention practice.

Despite the relevance of this topic, only one article has characterized and discussed studies related to training for upper extremity behaviors in infancy[13]. No systematic review has been found on this topic. Therefore, this article systematically reviewed studies that used training of object-directed manual behaviors to advance their acquisition or improve their development in infants over the first year and half of life. Its purpose was to identify the studies methodological characteristics and analyze their quality of evidence considering methodological quality and level of evidence by type of study.

MÉTODOS

Definition of the research questions

The following questions guided this review:
1) Which methodological aspects the studies have been using to examine the influence of trainings of object-directed manual behaviors in infants?
2) What have these studies found?
3) What is the quality of evidence on the effects of those trainings?

Inclusion criteria

Clinical trials that assessed the efficacy of manual object-directed training were included. The World Health Organization[14] defines clinical trial as a research study that assess the effects of health-related interventions using human participants. For this review, non-randomized, randomized or quasi-randomized clinical trials with at least one control group were included. At least one object-directed manual behavior (reaching, grasping, or object exploration) should be an outcome variable. The target population was infants from 0 to 18 months of age with typical development, at risk or with established diagnosis of developmental disorders. The studies should have been published up to February 2018, in English. All of the criteria needed to be met for inclusion in this review.

Exclusion criteria

Studies were excluded if/in case of: 1) at least one manual behavior was not an outcome variable; 2) no manual behaviors were trained; 3) animal studies; 4) project reports, review articles or case studies.

Search strategy

The articles were selected from the following electronic databases: National Library of Medicine (PubMed/MEDLINE), Latin American and Caribbean Health Sciences (LILACS), Virtual Health Library (BIREME/BVS), Science Direct, SciELO, and Physiotherapy Evidence Database (PEDro). The search employed keywords and Pubmed medical subject headings (MeSHs) terms, combined by the Boolean operators AND and OR: reaching, grasping, exploration, training, intervention, practice, learning, motor skills, infant, movement, hands, movement training. In addition, the reference list of the selected studies were used to retrieve potential articles. Each reviewer conducted the search several times to avoid losing articles and the final search was on March 2018.

Selection and data extraction

Two independent reviewers worked on the searches and initial selection of the articles. The reviewers selected articles based on their titles, excluding duplicate articles and those that clearly were not related to the review subject. After reading the abstracts and the entire articles independently, the reviewers discussed together, reached a consensus and determined a final selection.

A third reviewer was consulted when necessary. The Cochrane Collaboration Model[15] was adapted to extract bibliographical data from the included articles. Data consisted of methodological characteristics of the studies and the results of training.

Assessment of the quality of evidence

The methodological quality of the studies was assessed using the PEDro scale[16-18]. The scale consists of a checklist of scored dichotomous (yes or no) questions/ criteria that predict bias. It guides users to trials that are more likely to be valid (internal validity) and to contain sufficient information to base clinical practice. The following criterion comprise the scale: 1) Subjects were randomly allocated to groups (quasi-randomized allocation does not satisfy this criterion), 2) Allocation was concealed; 3) Groups were similar at baseline regarding the most important prognostic indicators; 4) There was blinding of all subjects; 5) There was blinding of all persons who administered the intervention; 6) There was blinding of all assessor who measured at least one key outcome; 7) Measures of at least one key outcome were obtained from more than 85% of the subjects initially allocated to groups; 8) All subjects for whom outcome measures were available received the treatment or control condition as allocated or, where this was not the case, data for at least one key outcome was analyzed by "intention to treat", 9) The results of between-group statistical comparisons are reported for at least one key outcome; 10) The study provides both point measures and measures of variability for at least one key outcome. Each criterion is awarded with 1 (yes) or 0 (no). Thus, the PEDro score is out of 10. Points are only awarded when a criterion is clearly satisfied. The methodological quality of each study was classified as "high" (6-10 points), "fair" (4-5 points), or "poor" (below 4 points). Three examiners (authors) applied the scale together and reached 100% agreement regarding the studies scoring in each criterion.

In addition, the studies were analyzed using the Oxford Centre for Evidence-Based Medicine's (CEBM) Levels of Evidence[19]. The tool was designed so that it can be used as short-cut for clinicians, researchers and patients with limited time. It consists of a hierarchy of the likely best evidence that considers mainly the type of the study methodological design (eg.: cohort study, systematic review, randomized trial, etc.). The studies can be classified within a hierarchy of levels of evidence (1a, 1b, 1c, 2a, 2b, 2c, 3a, 3b, 4, 5) and grades of recommendation (A, B, C, D). Level 1 studies, the best level of evidence, present grade of recommendation A; level 2 or 3 studies present grade of recommendation B; level 4 studies present grade of recommendation C; and level 5 studies present grade of recommendation D. Therefore, studies with evidence level 1 and grade of recommendation A present the best evidence. For this review, only the two possible levels of evidence for clinical trials (1b and 2b) were considered as only clinical trials were included. Individual randomized controlled trials with narrow Confidence Interval were classified as level 1b; low quality clinical trials (e.g., <80% follow-up, non-randomized) were classified as level 2b. In these cases, the grades of recommendation could be A (consistent level 1 studies) or B (consistent level 2 studies). Three examiners (authors) reached 100% agreement regarding the classifications.

RESULTADOS

The electronic search found 367 potential articles, all published in English. Initially, 82 articles were selected based on their titles and 25 studies were added from their references lists, thus totaling 107 articles. The abstracts were read and 85 articles were excluded for the following reasons: manual behaviors were not outcome variables

Table 1: Data extracted from the included articles. Sample, infants' characteristics, study design and country.

Authors	Sample size	Biological characteristics	Age	Study design	Country
Needham et al., 2017[27]	74	TD, full-term (>37 weeks)	3-4 months	RCT	USA
Wiesen et al., 2016[24]	32	TD, full-term (>37 weeks)	2-3 months (before reaching onset)	RCT	USA
Williams & Corbetta, 2016[11]	35	TD, full-term (>37 weeks)	2,9 months (before reaching onset)	RCT	USA
Williams et al., 2015[7]	37	TD, full-term (>37 weeks)	2 months and 21 days (before reaching onset)	QRCT	USA
Guimarães & Tudella, 2015[22]	16	AR, preterm (<33 weeks), low birth weight	12 weeks corrected age (few days after reaching onset)	RCT	Brazil
Cunha et., 2015[8]	30	TD, full-term (>37 weeks)	12-16 weeks (few days after reaching onset)	RCT	Brazil / USA

Continuation - Table 1: Data extracted from the included articles. Sample, infants' characteristics, study design and country.

Authors	Sample size	Biological characteristics	Age	Study design	Country
Guimarães et al., 2015[20]	16	AR, preterm (<33 weeks), low birth weight TD, full-term (>37 weeks)	3 months (few days after reaching onset)	NRCT	Brazil
Libertus et al, 2016[25]	40	TD, full-term (>37 weeks)	3 months, 15 months	NRCT	USA
Needham et al., 2014[12]	57	TD, full-term (>37 weeks)	3 months	NRCT	USA
Libertus & Landa, 2014[5]	89	AR, family history of ASD (full-terms and one 35-week-gestation preterm)	3 months (few days after reaching onset)	NRCT	USA
Gerson & Woodward, 2014[21]	90	TD, full-term (>37 weeks)	3.5 months	NRCT	USA
Libertus & Needham, 2014[36]	72	TD, full-term (>37 weeks)	3 months (before reaching onset)	NRCT	USA
Soares et al., 2013[10]	36	AR, late preterm (34-36 weeks)	14-17 weeks (few days after reaching onset)	RCT	Brazil / Netherlands
Cunha et al, 2013[37]	24	TD, full-term (>37 weeks)	12-15 weeks (few days after reaching onset)	QRCT	Brazil
Cunha et al., 2013[34]	33	TD, full-term (>37 weeks)	12-14 weeks (few days after reaching onset)	QRCT	Brazil / USA
Libertus & Needham, 2010[33]	58	TD, full-term (>37 weeks)	2-3 months and 5 months (before reaching onset)	NRCT	USA
Lobo & Galloway, 2008[26]	42	TD, full-term (>37 weeks)	8-11 weeks (before reaching onset)	RCT	USA
Heathcock et al., 2008[9]	39	AR, preterm (<33 weeks), low birth weight TD, full-term (>37 weeks)	8.5 weeks (before reaching onset)	RCT	USA
Sommervillle et al., 2005[35]	30	TD, full-term (>37 weeks)	3-4 months (few days after reaching onset)	RCT	USA
Lobo et al., 2004[28]	30	TD, full-term (>37 weeks)	2-3 months (before reaching onset)	RCT	USA
Needham et al., 2002[6]	32	TD, full-term (>37 weeks)	3 months - 3 months and 19 days (before reaching onset)	NRCT	USA

TD, Typically developing infants; AR, at-risk infants; ASD, autism spectrum disorder; RCT, randomized controlled trial; NRCT, non-randomized controlled trial; QRCT, quasi-randomized controlled trial; USA, United States of America.

(n=20), manual behaviors were not trained (n=29), infants' age over 18 months (n=4), animal studies (n=3), project reports, review articles or case studies (n=14); two or more of these criteria (n=15). Hence, 22 articles were read in full. Of these, 1 was excluded because the outcome measure was the infant's brain response during the training. After the final selection, 21 articles were included. The most recent study was published in

February 2017. Seventeen studies were carried out in the United States and 6 in Brazil (Table 1).

Ten of the included studies could be characterized as randomized controlled trials. Sixteen studies investigated only typically developing full-term infants. Their sample sizes ranged from 16[20] to 90[21]. Other 5 studies included infants at risk for developmental disorders: three studies with preterm infants with less than 34 weeks of gestation and low birth weight, with sample size from 16 to 39[9,20,22]; one study with 32 late preterm infants (34 a 36 6/7 weeks of gestation) with adequate birth weight[10]; and one study with 17 infants with familiar history (high risk) for autism spectrum disorders (ASD) mostly born full-term[5]. This latter study included 72 additional infants from previous research. Infants' age ranged from around 2 to 15 months (Table 1).

Table 2 shows data on studied manual behaviors and main methodological procedures. The studies addressed 3 types of early object-directed manual behaviors: reaching, grasping (holding), and object manual exploration. Although some studies did not label their dependent measures as "reaching", we considered them as reaches

Table 2: Studied manual behaviors and procedures of the included articles.

Authors/Year	Training administration	Object-directed manual behaviors	Body position for training	Toys	Assessments	Training duration
Needham et al., 2017[27]	Researcher	Manual exploration	Seated	Plastic blocks and other infant toys.	Pre-training Post- training	Single session of 10 minutes
Wiesen et al., 2016[24]	Caregiver	Reaching Grasping Manual exploration	Seated	Lightweight toys	Pre-training Post-training Post-training 2	Daily sessions of 10 minutes over 2 weeks
Williams & Corbetta, 2016[11]	Researcher	Reaching	Seated reclined at 10º	Colorful blocks and plastic animal squirt toys	Pre-training Post-training	105 minutes in 16 consecutive days
Williams et al., 2015[7]	Researcher	Reaching	Seated reclined at 10º	Rubber duck, plastic blocks	Pre-training Post-training	80 minutes in 16 consecutive days
Guimarães & Tudella, 2015[22]	Researcher	Reaching	Seated reclined at 45º	Malleable rubber mouse	Pre-training Post-training	Single session of 5 minutes
Cunha et al., 2015[8]	Researcher	Reaching	Seated reclined at 45º	Malleable rubber mouse	Pre-training Post-training Post-training 2	3 sessions of 4 minutes in 2 days
Guimarães et al., 2015[20]	Researcher	Reaching	Seated reclined at 45º	Malleable rubber mouse	Pre-training Post-training	Single session of 4 minutes
Libertus et al., 2016[25]	Researcher	Grasping Manual exploration	Seated	Plastic blocks and other infant toys	Pre-training Post-training Follow up	Daily sessions of 10 minutes over 2 weeks
Needham et al., 2014[12]	Researcher	Reaching Manual exploration	Seated	Plastic blocks and other infant toys	Pre-training Post-training	Single session of 9 minutes
Libertus & Landa, 2014[5]	Caregiver	Grasping	Seated	Plastic blocks, rattle, other infant toys.	Pre-training During training period Post-training	Daily sessions of 10 minutes over 2 weeks

Continuation - Table 2: Studied manual behaviors and procedures of the included articles.

Authors/Year	Training administration	Object-directed manual behaviors	Body position for training	Toys	Assessments	Training duration
Gerson & Woodward, 2014[21]	Caregiver	Manual exploration	Seated	Balls, ted bears, blocks.	Pre-training Post-training	Single session of 3 minutes
Libertus & Needham, 2014[36]	Caregiver	Reaching Grasping	Seated	Plastic blocks, rattle, other infant toys.	Pre-training During training period Post-training	Daily sessions of 10 minutes over 2 weeks
Soares et al., 2013[10]	Researcher	Reaching Grasping	Seated reclined at 45º	Malleable rubber mouse.	Pre-training Post-training Retention	Single session of 4 minutes
Cunha et al., 2013[37]	Researcher	Reaching Grasping	Seated reclined at 45º Supine	Malleable rubber mouse.	Pre-training Post-training	Single session of 4 minutes
Cunha et al., 2013[34]	Researcher	Reaching	Seated reclined at 45º Supine	Malleable rubber mouse.	Pre-training Post-training	Single session of 4 minutes
Libertus & Needham, 2010[33]	Caregiver	Reaching Grasping Manual exploration	Seated	Plastic blocks, rattle.	Pre-training During training period Post-training	Daily sessions of 10 minutes over 2 weeks
Lobo & Galloway, 2008[26]	Caregiver	Reaching Manual (haptic) exploration	Supine Seated	Toys with varied characteristics (shape, size, texture, rigidity), toy activated by switch.	Pre-training During training period Post-training Follow up	Daily sessions of 15 minutes over 3 weeks
Heathcock et al., 2008[9]	Caregiver	Reaching	Supine Seated	Infant toys	Pre-training During training period Post-training	Daily sessions of 15-20 minutes over 8 weeks
Sommervillle et al., 2005[35]	Researcher	Reaching Manual exploration	Seated	Balls, ted bears.	Pre-training Post-training	Single session of 6 minutes (380 s)
Lobo et al., 2004[37]	Caregiver	Reaching	Supine Seated	Infant toys	Pre-training Post-training	Daily sessions of 20 minutes over 2 weeks
Needham et al., 2002[6]	Caregiver	Reaching Grasping Manual exploration	Reclined Seated	Wooden blocks, plastic rings, plastic cubes, rubber theeters, wooden theeters.	Pre-training Post-training	Daily sessions of 10 minutes over 2 weeks.

(or pre-reaches) because they were characterized as the movement of one or both hands towards a toy in an attempt to obtain it[23]. Reaching was assessed in 17 studies as a dependent measure. Infants were mostly assessed and trained seated. The studies predominantly used similar toys for assessments and training. However, most of the studies did not provide complete information on the physical characteristics (color, texture, size, rigidity and type of material) of the toys used as stimulus (Table 2).

All 21 studies presented at least one assessment after training (post-training). However, only 5 studies[8,10,24-26] presented at least one retention measure (after the post-training) or weekly follow-up assessments during or after the training weeks. Most of the studies analyzed the infants' behaviors using video recording (Table 3).

In 12 studies, training was administered by the researcher; in 9 studies training was administered by parents/caregivers. As to training duration, the protocols were constituted of daily practice of 10-20 minutes over 2-8 weeks; single 3-10 minutes session of practice; or 3 sessions of 4-minute practice divided in two consecutive days. The protocols varied from daily practice throughout weeks to a single session. Velcro covered mittens (sticky mittens paradigm) were used to train infants in most of the studies (n = 11). The other studies trained infants by means of task-specific training in itself without mittens (n = 8) or contingent reinforcement (n = 2) (Table 3).

Table 3 shows the outcomes of the studies. In summary, increased reaching, grasping and exploratory activity were found after daily training over 2 weeks

Table 3: Main training approaches and outcomes related to the studied manual behaviors.

Study		Main training approach	Outcomes
Needham et al., 2017[27]	Experiment 1: G1: sticky mittens; G2: non-sticky mittens; Experiment 2: G1: sticky mittens associated to toy with auditory feedback; G2: sticky mittens associated to toy with low auditory feedback.	Reaching for Velcro-covered toys offered on a table while wearing Velcro-covered mittens (sticky mittens paradigm)	Experiment 1: G1 sustained object touching and G2 decreased object touching from pre- to post-training. Experiment 2: G1 presented more robust increase in exploratory activity from pre- to post-training compared to G2.
Wiesen et al., 2016[24]	G1: sticky mittens; G2: non-sticky mittens.	Sticky mittens paradigm	G1 presented greater duration of manual exploration than G2 at post-training 2. Both groups increased the amount of reaches from pre- to post-training 2.
Williams & Corbetta, 2016[11]	G1: contingent group, a toy target moved and sounded upon contact only; G2: continuous group, the toy moved and sounded continuously, independent of hand-toy contact. G3: control group (no training).	Contingent reinforcement using a moving and sounding toy.	Both intervention groups showed gains in reaching. Only G1 presented more hand-toy contacts than the control group.
Williams et al., 2015[7]	G1: sticky mittens; G2: non-sticky mittens; G3: control (without mittens)	Sticky mittens paradigm	G2 made significantly more intentional contacts with the toy than G3, but G1 did not. G1 showed a significant increase in the speed of movement of the hand.
Guimarães & Tudella, 2015[22]	G1: reaching training; G2: control (no training).	Task-specific training of reaching	G1 increased the amount of reaches from pre- to post-training. G1 presented slower reaches, with greater adjustment and lower number of movement units than G2.

Continuation - Table 3: Main training approaches and outcomes related to the studied manual behaviors.

Study		Main training approach	Outcomes
Cunha et al., 2015[8]	G1: reaching training; G2: control (social training);	Task-specific training of reaching	G1 presented higher frequency of object contacts, shorter and smoother reaching, and better hand positioning than G2.
Guimarães et al., 2015[20]	G1: reaching training (preterm)G2: control (social training – term)	Task-specific training of reaching	G1 presented greater amount of reaches with oblique and semi-open hand compared to G2.
Libertus et al., 2016[25]	G1: active training (sticky mittens) G2: passive training; G3: no training	Sticky mittens paradigm	G1 presented more grasping activity than G2. G1 presented more object exploration than G2 and G3 12 months later.
Needham et al., 2014[12]	G1: active training; G2: observational experience;	Contingent reinforcement using a mobile attached to infants' wrist.	G1 moved the mobile more times than G2 during the experience. G1 increased the amount and duration of reaches from pre- to post-training.
Libertus & Landa, 2014[5]	G1 active training (sticky mittens) - HR; G2: active training (sticky mittens) - LR; G3: passive training - LR; G4: encouragement experience - LR; G5: movement training - LR.	Sticky mittens paradigm	G1 and G2 groups presented increase in grasping duration from pre- to post-training. G1 presented longer grasping duration than G3, G4 and G5. There were no differences between G1 and G2.
Gerson & Woodward, 2014[21]	G1: active training (sticky mittens) G2: observational experience; G3: generalization experience.	Sticky mittens paradigm	G1 presented a positive relation between their level of engagement in object-directed actions during training.
Libertus & Needham, 2014[36]	G1: encouragement experience; G2: movement experience; G3: active training; G4: passive training.	Sticky mittens paradigm	Between-assessments and inter-group analyses showed that only G1 presented increased reaching and grasping behaviors. G2, G3 and G4 did not change.
Soares et al., 2013[10]	G1: blocked sequence practice; G2: serial sequence practice; G3: control (social training).	Task-specific training of reaching (sequences of activities)	Only G2 showed increased number of total reaches and bimanual reaches after practice; this increase was not maintained in the retention test performed one day later.

Continuation - Table 3: Main training approaches and outcomes related to the studied manual behaviors.

Study		Main training approach	Outcomes
Cunha et al., 2013[30]	G1: trained in reclined position;G2: trained in supine position;G3: control (no training).	Task-specific training of reaching (body positions).	G1 and G2 presented increased number of reachs, unimanual reachs and reaches with the semi-open and oblique hand from pre- to post-training. Improvements occurred only in supine for G2, and in supine and reclined positions for G1.
Cunha et al., 2013[6]	G1: trained in reclined position;G2: trained in supine;G3: control (no training).	Task-specific training of reaching (body positions).	G1 presented shorter and faster reaches compared to G2 and G3. G1 and G2 decreased reaching duration from pre- to post-training. Only g1 increased the number of movement units from pre-to post-training.
Libertus & Needham, 2010[28]	G1: active training (sticky mittens);G2: passive training;	Sticky mittens paradigm	G1 showed increased reaching and grasping behaviors compared to G2.
Lobo & Galloway, 2008[21]	G1: control (social experience);G2: postural experience;G3: object-oriented experience.	Task-specific training of reaching (and body positions).	G1 and G2 advanced reaching, haptic exploration of objects, and developing means – end behavior compared to G3. G2 out performed G1.
Heathcock et al., 2008[9]	G1: movement training (preterm);G2: social training (preterm);G3: social training (full-term).	Task-specific training of reaching	G1 performed more reaches than G2 after 4 weeks and more reaches than G3 after 8 weeks of training. G1 and G3 presented similar duration of hand-toy contacts and more contacts with open hand and ventral hand surface than G2 after 8 weeks.
Sommervillle et al., 2005[35]	G1: reach first (sticky mittens);G2: watch first (sticky mittens).	Sticky mittens paradigm	G1 presented greater number of hand-toy contacts than G2.
Lobo et al., 2004[28]	G1: general experience;G2: task related experience;G3: control (no experience).	Task-specific training of reaching (and general experience)	G1 and G2 increased the number of hand-toy contacts when compared to G3. G2 displayed higher amounts of reaching relative to G1.
Needham et al., 2002[6]	G1: sticky mittens;G2: control (no experience).	Sticky mittens paradigm	G1 presented greater object exploration percentages than G2.

HR, high-risk infants; LR, low-risk infants.

and single-session training of 3-10 minutes using the sticky mittens paradigm. Task-specific training resulted in improved reaching performance after daily sessions over 2-8 weeks and single session training of 4-5 minutes. Contingent reinforcement leaded to improvements in reaching after daily training over 2 weeks and single session training of 9 minutes.

Table 4 presents the methodological quality of the studies classified using the PEDro scale and the Oxford (CEBM) Levels of Evidence. Three studies[10,22,26] presented high methodological quality and level of evidence 1b (grade of recommendation A) (Table 4).

Table 4: Quality of evidence of the articles.

Study	PEDro												Oxford	
	A	B	C	D	E	F	G	H	I	J	Total Score /10	Quality Classification	Grades of recommendation	Level of Evidence
Needham et al., 2017[27]	1	0	1	0	0	0	0	0	1	1	4	Fair	A	1b
Wiesen et al., 2016[24]	1	0	1	0	0	0	0	0	1	1	4	Fair	A	1b
Williams & Corbetta, 2016[11]	1	0	1	0	0	0	0	0	1	1	4	Fair	A	1b
Williams et al., 2015[7]	0	0	1	0	0	0	1	0	1	1	4	Fair	B	2b
Guimarães & Tudella, 2015[22]	1	1	1	0	0	0	1	0	1	1	6	High	A	1b
Cunha et al., 2015[8]	1	0	1	0	0	1	0	0	1	1	5	Fair	A	1b
Guimarães et al., 2015[20]	0	0	0	0	0	1	0	0	1	1	3	Poor	B	2b
Libertus et al., 2016[25]	0	0	1	0	0	0	0	1	1	1	4	Fair	B	2b
Needham et al., 2014[12]	0	0	1	0	0	1	0	0	1	1	4	Fair	B	2b
Libertus & Landa, 2014[5]	0	0	1	0	0	0	0	0	1	1	3	Poor	B	2b
Gerson & Woodward, 2014[21]	0	0	1	0	0	1	0	0	1	1	4	Fair	B	2b
Libertus & Needham, 2014[36]	0	0	1	0	0	0	0	0	1	1	3	Poor	B	2b
Soares et al., 2013[10]	1	1	1	0	0	1	1	0	1	1	7	High	A	1b
Cunha et al., 2013[37]	0	0	1	0	0	1	0	0	1	1	4	Fair	B	2b
Cunha et al., 2013[34]	0	0	1	0	0	1	0	0	1	1	4	Fair	B	2b
Libertus & Needham, 2010[33]	0	0	1	0	0	0	0	0	1	1	3	Poor	B	2b
Lobo & Galloway, 2008[26]	1	0	1	0	0	1	1	0	1	1	6	High	A	1b
Heathcock et al., 2008[9]	1	0	1	0	0	1	0	0	1	1	5	Fair	A	1b
Sommervillle et al., 2005[35]	1	0	0	0	0	1	0	0	1	1	4	Fair	A	1b
Lobo et al., 2004[28]	1	0	1	0	0	1	0	0	1	1	5	Fair	A	1b
Needham et al., 2002[6]	0	0	0	0	0	0	0	0	1	1	2	Poor	B	2b

PEDro scale: A, random allocation; B; concealed allocation, C, baseline comparability; D, blind subjects; E, blind therapists; F, blind assessors; G, adequate follow-up; H, intention-to-treat analysis; I, between-group comparisons; J, point estimates and variability; 1, Yes; 0, No. Points were only awarded when a criterion was clearly reported on the article. *Study in which points were awarded by PEDro database. Oxford CEBM Levels of Evidence: 1b (grade of recommendation A): individual randomized controlled trial; 2b (grade of recommendation B): low quality randomized controlled trials. [a]Quasi-randomization methods such as allocation by alternation are not considered strictly random.

DISCUSSÃO

This systematic review examined articles that investigated the effects of training on object-directed manual behaviors in typically developing infants and at-risk infants in the first 18 months of life. All studies reported enhancement of object-directed manual behaviors as a result of active experience exploring Velcro covered objects with Velcro covered mittens, task-specific experience in itself, or contingent reinforcement. All studies with high methodological quality and best level of evidence used task-specific training.

Which methodological aspects the studies have been using to examine the influence of trainings of object-directed manual behaviors in infants?

Few studies included infants at risk for developmental disorders[5,9,10,20,22]. They addressed infants born preterm or at risk for ASD. Studies with established disorders which potentially hamper early manual function, such as Down syndrome or cerebral palsy, are lacking. This is not surprising as learning mechanisms need to first be tested in typically developing infants before atypical samples. However, we highlight the essential importance of promoting further research on early interventions for manual behaviors in those population with established disorders.

Among the studied manual behaviors, reaching was the most assessed and trained one. Most of the studies started the training before or within a few days after reaching onset, thus minimizing the influence of spontaneous practice as a confounding factor that could bias the outcomes. On the other hand, some studies did not report on the infants' skill level[21-23,27], which makes it more difficult to conclude on how much the training improved reaching regardless of the influence of spontaneous practice. Future studies must be attentive to this issue.

Another important issue is that most of the studies did not report the size of the toys used as stimulus. In addition, two studies did not provide specific information or at least illustration on the main physical characteristics (color, texture, rigidity, type of material) of the toys[24,28]. Such characteristics should be always clear as they may influence the outcomes of the studies. For example, malleable toys can produce more reaches than rigid ones, whilst big rigid toys can produce more bimanual than unimanual reaches[29]. Considering studies that have found influence of the physical properties of objects on manual skills in infants[29,30], reporting a maximum of physical characteristics of the used toys in the studies are of essential relevance to allow methodological replications in other research and clinical practice.

As to assessments, only few studies included at least one retention test or follow-up assessments after the first post-training assessment[8,10,24,26]. This hampers the conclusions that could be drawn on the duration of observed effects of training, since it is not possible to evidence whether initial changes in motor behavior were only immediate or more long lasting.

Training was predominantly administered by parents. Parents were trained, monitored and could consult with the researchers about questions regarding the execution of the training protocol. When the training is administered by the researcher, the chance of experimental error is minimized; however, the infant may not respond naturally to the intervention administered by an unfamiliar person. Training administration by parents may be more natural for infants and more convenient for researchers; however, in this case there is more risk of error during the procedure as parents could offer excessive stimuli to the infant, for example. Despite this point of view, it is valuable that studies investigate trainings that can be easily administered by parents and caregivers so that they can apply the intervention at home without difficulties. This is especially important because some at-risk infants do not qualify for professional assistance in early intervention programs due to their clinical similarities to health infants at birth[31,32].

What have these studies found?

All training protocols were based on the repetition of a set of hand movements towards toys offered on a table or at the infants' trunk midline. The protocols varied from daily practice throughout weeks (long-term)[5-7,9,11,24, 26,28,33] to single session practice (short-term)[8,10, 22-25,27,34,35].

Velcro covered mittens (sticky mittens paradigm) were used during training in most of the studies[5,7,10,21,24,25,36,37]. Infants wore Velcro covered mittens and were offered Velcro covered toys on a table. As infants moved their arm while wearing the mittens, the toy could easily adhere to the mittens, thus providing opportunities for infants to "grasp" the toys before acquiring this skill. In these studies, training was based on the active or passive (observation) repetition of toy-mitten sticking. Ten minutes of daily active training over 2 weeks benefited the number of reaches and grasps and favored the interest to explore objects and start contacting them in pre-reaching typically developing infants[6,24,33,36]. Two to 10 minutes of the training in a single session[21,27,35] or 3 sessions[25] improved the infants' engagement contacting toys manually during the active training with the mittens. The studies also suggested that the observed effects in typically developing infants can last 2 to 12 months after training ceases[11,24]. One sole study used the sticky mittens paradigm in at-risk infants. Daily 10 minutes of the active training over 2 weeks benefited grasping activity in infants at familial history (high risk) for ASD[5]. One study found no clear advantage of daily 10-minute training with open-fingers sticky mittens over 2 weeks in pre-reaching typically developing infants and concluded that providing opportunities for infants to repeat active hand-toy interaction is possibly enough to enhance reaching regardless of the toy-mitten sticking provision[7].

In most of the other studies, training was based on the repetition of active hand-toy interaction in itself (task-specific experience), mostly in the supine position. In general, these trainings were organized in sequential steps of activities essentially constituted by presentation of the toy and the infant's hand at his/her visual field for a few seconds, assistance of the infant's hand movement to his/her midline to touch the toy, and offering the infant opportunities to reach actively for the toy over some minutes. Two weeks of this daily training for 20 minutes

followed by active manual and oral exploration of toys with varied texture, sizes and rigidity advanced the emergence of reaching and increased the number of hand-toy contacts in 2 month-old typically developing infant[35]. In addition, 3 weeks of 10-15 passive toy-oriented reaches followed by 5 minutes of active toy-oriented reaching enhanced reaching with more functional behaviors (with open hand and hand closer to the toy) in 2 month-old typically developing infants[26]. In pre-reaching preterm infants born with less than 33 weeks of gestation and low birth weight (<2500g), daily training during 15-20 minute over 4 weeks leaded to more reaches than untrained controls after 4 weeks[9].

Infants also received task-specific training in steps of activities during a single session. The activities were constituted by assisted and active hand-toy contact at the infant's midline, tactile stimulation of the infant's upper limb with the toy, followed by offering the infant opportunities to perform toy-oriented reaching actively for some minutes, in the reclined seated position. In typically developing infants, 4-5 minutes of the training in a single session resulted in more functional behaviors to reach[8,34,37]. These effects were likely to be specific to body position when infants were trained in the reclined position; on the other hand, when infants were trained in supine, the effects were found in both supine and reclined positions[34]. In newly reaching preterm infants born from 30 to 36 6/7 weeks of gestation, a similar training applied in a serial sequence of activates resulted in immediate increase in the number of reaches, mainly bimanual reaches[10], and in the amount of motor strategies to gain success in reaching and pre-grasping attempts[10,20,22]. The effects of these brief-term trainings, however, seem to be only temporary as they were not maintained in the following day after the session, at least in the preterm infants[10]. Hence, whilst task-specific adaptations in manual behavior start and can be observed in the initial minutes of motor experience[10], long-term training is required for long lasting adaptations[10].

The other approach used to train infants' manual behavior was contingent reinforcement, in which infants were induced to notice the consequences their upper limbs' actions have on nearby objects by means of a mobile[12] or moving/sounding toys[11]. Active training moving a mobile with the arm during a single session of 9 minutes benefited the number of hand-toy contacts in pre-reaching typically developing infants[12]. Three-month-old infants' hand-toy contacts were also benefited from a daily 10-minute training actively boosting a sounding and moving toy with the hand over 2 weeks[11].

Overall, the studies have suggested offering opportunities for infants to self-produce toy-oriented movements potentiates their ability to learn from the sensory properties of the objects and the biomechanical strategies than can be adopted by their upper limbs for manual action. As a result, infants seem to become more engaged and improve perception on objects and motor control to move the hands toward the toys to attempt to touch and explore them.

What is the quality of evidence on the effects of those trainings?

Considering the PEDro scale, the majority of the studies presented fair methodological quality[7,8,11,12,21,24,25, 27, 34,37]. They especially failed on reporting or performing two or three key criteria required for avoiding biased outcomes: randomization, allocation concealment, and blinding of outcome assessors. Proper randomization in clinical trials ensures that subjects in groups are systematically equal, which avoids biased results due to the influence of imbalance of covariates[38]. In addition, allocation concealment and blinding of outcome assessors ensure that researchers and participants do not know to which group subjects were assigned and therefore avoid selection and measurement biases that tend to overestimate treatment effects[38,39]. As a general consequence, treatment groups may have been systematically different in those studies and their results may be biased. On the other hand, among those studies with fair methodological quality, seven studies[8,9,11,24,27,28,35] presented level of evidence 1b, grade of recommendation A, which represents the clinical trials with best quality according to the Oxford CEBM Levels of Evidence. These differences between the tools classifications occur because the PEDro scale evaluates the reporting and performance of several methodological criteria that allow appraising the study internal validity, as mentioned earlier, whilst the Oxford CEBM Levels of Evidence was designed for rapid appraisals and considers the study design type as the main criteria to classify the likely best evidence. Therefore, considering both classifications is important to a more definitive judgment of the quality of evidence in clinical decision-making.

In this sense, we highlight the three randomized controlled trials that used task-specific active training and presented not only high methodological quality (PEDro scale) but also the best level of evidence (Oxford CEBM Levels of Evidence)[10,22,26]. Their results are likely to be valid for clinical practice. In these studies, which presented background from Physical Therapy, training was administered to preterm infants in a single 4-5 minute session[10,22] or to typically developing infants in a daily 10-minute basis over 2 weeks[26]. This latter protocol could be recommended by clinicians when the intention is to use stimulating play in daily life to improve reaching and object exploration in typically developing infants as health promotion strategy. When the intention is to benefit reaching behavior in preterm infants, clinicians could use the brief-term training protocol as part of a session of early intervention practice.

The studies with fair or poor methodological quality[5-9,11,20,24,27,25-33,35] and/or level of evidence "2b", degree of recommendation "B",[5-7,20-33], addressed the three approaches discussed earlier - sticky mittens paradigm, task-specific training, and contingent reinforcement -, but most of them used the sticky mittens paradigm. It calls attention that none of the studies using the sticky mittens paradigm scored highly in the methodological quality. Considering their

background from Psychology, it is possible that these studies were not directly intended to guide intervention for clinical practice and therefore researchers may not have engaged in a full clinical trial standard. They were predominantly non randomized controlled trials. Despite of this, it is valid to observe the high degree of agreement between these studies outcomes, with almost all showing some benefit of the training for manual behaviors. This may suggest some consistence in the effectiveness of their manipulation.

Overall, this systematic review shows there is strong evidence for the effectiveness of training for object-direct manual behaviors, specially reaching. It is important to caution readers that the PEDro scale and the Oxford CEBM Levels of Evidence should not be used as a measure of the validity of the study conclusions as they do not judge, for instance, whether the study results are clinically important. However, this review suggests that future studies report more detailed and clear information of their methods and try to follow methodological standard criterion known for reducing bias.

Recommendations for clinical practice and future research

The outcomes of the studies with high methodological quality are likely to present high internal validity and excellent level of evidence to guide clinical practice. Therefore, considering their main methodological settings (infant, therapist and toy position; type of activities), intervention to stimulate and improve early manual behaviors should be constituted by these basic points:

(1) infants placed supine, reclined on the therapist's thighs (both face-to-face), or seated in a baby seat slightly reclined; (2) toy offered in the infant's midline at an arm-length distance; (3) repetition of assisted and active hand and arm movements towards the toy; (4) tactile stimulation of infants' upper limbs; (5) active upper limb movements towards the toy.

The expected effects may be: a) more functional hand shape and position to act upon small toys, and b) increased number and time of hand-toy exploration. Such effects can be temporary (intra-session) or more lasting and seem to result from improvement of motor control, selection of more efficient movement patterns, intrinsic motivation and better perceptual and motor coupling.

We stress the lack of studies addressing infants with established diagnoses of developmental dysfunction, such as Down syndrome and cerebral palsy. Considering these conditions affect early manual behavior and have impaired a growing population of children worldwide[40,41] addressing them in future research on this topic will be of valuable importance for clinical practice. In addition, as the majority of the studies did not use or report basic methodological criteria known to reduce biased results (eg.: randomization, allocation concealment), we recommend researchers engage in high quality standards for clinical trials in future studies. To allow proper replication, it is also important to provide detailed information on the objects used as stimuli during training. Moreover, as few studies performed follow-up tests, future studies could include at least one additional assessment after post-training.

CONCLUSÃO

There is high quality evidence for the benefits of task-specific training for improving manual behaviors in typically developing infants and preterm infants in the first 2-4 months of life. Additional randomized controlled trials that use high methodological standards to minimize bias may help to endorse or refute the studies findings.

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Abstract

Introduction: Researchers have widely investigated how interventions by means of training can improve manual behaviors in infants. However, no systematic review has been found on this topic.

Objective: To analyze the quality of scientific evidence considering the methodological quality and level of evidence by type of study in research on training of object-directed manual behaviors in infants in the first 18 months of life.

Methods: National Library of Medicine (PubMed/MEDLINE), Latin American and Caribbean Health Sciences (LILACS), Virtual Health Library (BIREME/BVS), Science Direct, SciELO, and Physiotherapy Evidence Database (PEDro) databases were used. Only clinical trials that assessed the benefits of manual object-directed training in infants and were published up to February 2018, in English, were included. The Cochrane Collaboration Model was adapted to extract bibliographical data from the articles and their methodological quality was assessed using the PEDro scale and the Oxford Centre for Evidence-Based Medicine's Levels of Evidence.

Results: Twenty one clinical trials were included. Studies investigated typically developing full-term infants, preterm infants, and infants at risk for autism spectrum disorders. Trainings were administered to infants by means of "sticky mittens" paradigm, task-specific practice, or contingency reinforcement. Most of the studies presented fair or poor methodological quality. Only studies that used task-specific active practice presented high methodological quality.

Conclusions: The results indicate there is high quality evidence that task-specific training improves object-directed manual behaviors in typically developing infants and preterm infants in the first 2-4 months of life. Studies addressing infants with established diagnoses of developmental dysfunction are lacking.

Keywords: child development, infant, early intervention, motor skills.