Title: Interventions for improving coordination of reach to grasp following stroke: Systematic Review

Centres conducting review:
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Commencement date: 01/10/2009
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Background
Scope of the problem
Damaged brain tissue from stroke is caused when the supply of oxygen and nutrients is interrupted, usually because a blood vessel bursts or is blocked by a clot. It is estimated that over 100,000 people in England and Wales suffer a first stroke every year. The psychological and economic burden related to unemployment, functional dependency and impoverished participation following stroke is therefore considerable. Upper limb motor deficit is the most common symptom following acute stroke with approximately 77% of patients demonstrating symptoms. Traditionally the prognosis for functional recovery of the upper limb has been unpromising. A recent study reported complete functional recovery in just 12% of hemiplegic patients without severe cognitive impairment after primary stroke at 6 months. A further 26% of patients had some recovery of dexterity. Whilst this overall picture does not take into account the initial level of impairment, the amount and type of therapy or the amount of unsupervised patient practice, it highlights the variable and poor level of recovery seen in stroke survivors. One reason for poor recovery could be the limited effectiveness of current therapies, in which case a review of contemporary practice and its effectiveness is needed. Two major goals of rehabilitation are to retrain selective movements of the arm and the smooth coordination of reach to grasp. There is incomplete information for both of these aspects, particularly about the treatments for coordination deficits and their effectiveness.

Reach to grasp coordination
Independence in activities of daily living and participation in leisure or recreational pursuits is largely contingent upon effective motor control for reach to grasp. Spatial and temporal coordination between multiple joints of the hand, elbow and shoulder are evident during skilled reach to grasp. Accurate and seamless movement relies upon the integration of visual and proprioceptive information to plan motor coordinates, make on-line error adjustments and to respond to changes in the environment. Normal cost efficient, segmental movements show characteristic patterns which meet the complex and varied spatiotemporal demands of different tasks. Studies suggest for example that although the arm and hand are controlled separately, they are coordinated according to key temporal and spatial events. The magnitude of grasp aperture is adjusted to the size of the object intended for manipulation, the speed of the movement and the movement end goal.
It was conceived \cite{15} that motor representations for learned reach to grasp movements are stored by the central nervous system and consist of a series of neural commands, which activate muscles to produce a particular sequence of coordinated activity. The stored representation is updated with sensory feedback regarding the movement outcome which enables ongoing skill development. Learning results in persistent changes in the strength of the neural connections (long-term potentiation) which occur in the motor and sensory cortex, the cerebellum and the visual cortex \cite{16,17} as a result of synaptic growth (synaptogenesis).

**Effect of stroke in reach-to-grasp**
Following stroke people demonstrate deficits both in accuracy and efficiency \cite{18} during reach to grasp. Upper extremity function can be directly affected by motor and sensory impairments as well as adaptive changes in response to stroke. Motor impairments resulting from the lesion itself include muscle weakness, disordered coordination and spasticity. Sensory impairments impact upon reach to grasp both in terms of tactile or proprioceptive sensory loss as well as perceptual-cognitive problems such as visuospatial impairments and attentional problems. Secondary physiological adaptations such as muscle atrophy, altered soft tissue length and joint contracture also cause mechanical and functional changes. Common problems with anticipatory hand shaping, premature hand closure, inadequate aperture, dysmetria, segmented and slowed movements all contribute to clumsy function or disuse after stroke. In comparison to healthy controls coordination of key spatiotemporal events, such as the correlation between the time of maximum aperture and peak deceleration, are not as tightly coupled in patients with moderate recovery after stroke \cite{19}.

**Treatment can promote recovery**
Neural recovery after stroke refers to the restoration of function in the neural tissue that was lost after the event \cite{20}. It can be measured using imaging techniques, usually as the activation of areas surrounding the lesion (penumbra) and in the functionally connected areas (diaschisis) inactivated by the brain injury. Functional magnetic resonance imaging (fMRI) provides an indirect measure of neural activity according to the haemodynamic response of active and inactive neurons. Functional gains seen in clinical scales may represent true motor recovery (reacquisition of previously learned motor patterns) or alternative compensations in the absence of neural recovery. Additional measures of impairments such as strength, coordination and sensation help to distinguish between recovery and compensation \cite{21}.
It would appear that targeted upper extremity therapy post-stroke can promote neural recovery. A link between behavioural experience and structural plasticity after brain injury was first suggested in animal research 22-24 which found training induced synapopogenesis in the lesioned hemisphere. The last decade has seen the development of a number of controlled research studies which indicate that targeted treatments can promote neural recovery in chronic stroke in humans. Scientific knowledge regarding the mechanisms for motor control and long term potentiation following stroke has developed together with an associated increase in the quantity and quality of rehabilitation research. It is now widely accepted that experience and training after stroke induce physiological and structural changes in the brain as they do in healthy individuals 25. Functional recovery over time has also been linked with increased task-related activation of the motor system in fMRI after stroke 26. More recently it was suggested that post stroke recovery involved alternative inputs to the corticospinal system via spared parallel networks and residual distributed systems 27.

More specifically there is compelling fMRI evidence 28 for adaptive neural plasticity associated with functional gains after targeted upper extremity therapy. The meta-analysis included 5 well controlled studies which showed significant neural activity increases in the areas of the sensorimotor cortex for the paretic arm which were associated with treatment directed at upper extremity function. Further studies 29-31 also show therapy-related improvements in upper extremity movement linked to increased fMRI activity. The larger of these studies found increased activation contralateral (on the opposite side) to the affected arm and bilaterally (on both sides) in the cerebellum 29. This recent evidence includes several types of movement-dependent training and a variety of treatment durations but together the significance of these results supports the overall argument for therapy induced neural changes post-stroke.

**Rehabilitation**

Despite prolonged rehabilitation, one earlier study 6 found that more than half of patients with upper extremity weakness following stroke remained severely impaired. In the past, traditional approaches to stroke rehabilitation failed to promote strengthening exercises and intensive, repetitive task based practice, fundamental aspects of treatment which have now been recognised 32;33. A growing body of evidence 34-38 highlights the potential for rehabilitation to improve upper extremity function, even in the chronic phase where patients were previously thought to plateau 39. Improved coordination of reach to grasp may depend upon task specific practice which involves the use of grasp and transport together with specific emphasis on
planning and executing the 2 components together \(^{19}\). Whereas, conventional therapy has perhaps failed to appreciate the importance of spatiotemporal links between the hand and arm, focusing instead upon more general aspects of upper limb function.

**Why is this study important?**

An initial scoping review revealed a small number of published reviews for treatment interventions of the upper limb following stroke \(^{40-43}\). The most recent of these \(^{40}\) identified potentially effective treatment interventions for the overall management of the paretic upper limb. The present study aims to build upon previous reviews and to provide more detailed analysis by focusing specifically upon treatments targeted at coordination of reach to grasp. To our knowledge there are no published articles which provide a detailed review of interventions which are specifically aimed at improving coordination of the reach to grasp following stroke. A general evaluation of the literature reveals a series of pilot studies and Randomized Controlled Trials (RCTs) evaluating specific physical interventions aimed at improving coordination. These include constraint induced movement therapy \(^{44}\), bimanual upper extremity exercise \(^{45}\), task orientated functional training \(^{46}\), functional electrical stimulation \(^{47}\), robotic devices and virtual reality based rehabilitation \(^{48}\). These studies have examined heterogenous stroke populations (in terms of site and size of lesion, functional impairment and time since onset); mixed intensities and durations of training; and have utilized a range of outcome measures. It is therefore difficult for clinicians to draw conclusions regarding best practice for specific types of patients. A systematic review with considered synthesis of results would therefore provide a valuable tool for therapists. It is therefore imperative to provide a systematic review of the research which will help to steer guidelines for retraining coordination of the upper limb following stroke.

**Objectives**

The purpose of this systematic review will be two-fold. Firstly, we aim to provide a comprehensive account of the existing interventions targeted at coordination of arm and hand segments for reach to grasp following stroke. Secondly, we aim to determine the effectiveness of current treatments for improving coordination of reach to grasp after stroke.

**Criteria for considering studies for this review**
**Types of studies**
For the purpose of answering the first question, the review will be inclusive with regard to study design, in order to source all the existing and potential interventions for upper limb coordination. We will include experimental studies including randomised, quasi-randomised and non-randomised controlled trials, cross over trials, and observational studies including case-control studies and cohort studies that investigate the degree or extent of a physiological condition. Studies must include an intervention or experimental manipulation targeted to improve coordination of the hand and arm following stroke. Studies concerned with the coordination of the shoulder and elbow will be excluded if the hand is not involved in some aspect of the task, such as holding an object. Only studies written in the English language will be included.

**Types of participants**
Participants will be adults (18 years and older) with a clinical diagnosis of stroke, defined by the World Health Organization as ‘a syndrome of rapidly developing symptoms and signs of focal, and at times, global, loss of cerebral function lasting more than 24 hours or leading to death, with no apparent cause other than that of vascular origin’. Inclusion will be regardless of lesion site, time since onset, co-morbidities, previous strokes, where intervention is carried out, initial motor impairment, or ability to follow instructions. We will include studies that also recruited participants with other neurological disorders if the data on stroke subjects can be extracted from the data of non-stroke subjects (i.e. data from different groups should not be pooled). Subjects must have a movement deficit in the upper limb. We will include subjects with other additional movement deficits (e.g. of the lower limb or aphasia). We will collect and document data on these participants, and use it to describe subgroups, such as time since lesion, lesion site and severity of stroke.

**Types of intervention**
Studies, in any setting, must include an intervention or manipulation aimed at improving coordination of the upper limb during reach and grasp. For the purposes of this review, we have defined coordination as ‘the ability to manage interaction between movements of different body segments for the production of purposeful movement’. Studies must have a specific design objective related to coordination of the upper limb. We will include studies that use a single intervention, and also studies that deliver a treatment for coordination as part of a more complex package. The intervention could occur in reach and grasp, or could be delivered as a treatment separate from reach and grasp, if the aim is to improve coordination of hand and arm segments
for reach and grasp. The intervention should therefore involve the hand either grasping an object or opening and closing. Treatments must be prescribed, supervised or delivered by an allied health care professional, or delivered as part of a manipulation in an experimental study which investigates the degree or extent of a physiological condition. Studies of bilateral arm training will only be included if they include measures of intra-limb coordination on the affected side. Any duration or intensity of programme will be included and subgroups will be described.

**Types of outcome measures**

I. In order to provide a comprehensive account of the range of interventions, the review will include studies with an intervention aimed at improving upper limb coordination, regardless of whether they incorporate an outcome measure.

II. To determine effectiveness of interventions, studies with any measurement of upper limb coordination will be included. These are likely to include:

i. Coordination measures that exist within impairment measurement scales such as the Fugl-Meyer Motor Assessment Scale.

ii. Specific measures of coordination such as movement velocity, acceleration, deceleration and movement duration, maximum hand aperture and reaction time.

iii. The types of measurements used will be documented and described.

**Search methods for identification of studies**

Prior to commencing the review, contact will be made with the Joanna Briggs Institute and the Cochrane Collaboration to identify previous or current activity related to the review topic.

Electronic searches will seek to identify published research from the following databases:-

- Cochrane Central Register of Controlled Trials (CENTRAL) (The Cochrane Library, latest issue)
- MEDLINE (1950 to present)
- EMBASE (1980 to present)
- CINAHL (1982 to present)
- AMED (1985 to present)
- ProQuest Dissertations and Theses (International)
- ISI Proceedings (Conference)

The grey literature search will include:

- Mednar
- Dissertation International
- Conference Proceedings
We will also search the following therapy databases:

- REHABDATA (http://www.naric.com/research/rehab/default.cfm)

We will use the following search strategy, using a combination of controlled vocabulary (MeSH) and free text terms, for MEDLINE and will modify it to suit other databases.

1. ((cerebrovascular disorders/ or exp basal ganglia cerebrovascular disease/ or exp brain ischemia/ or exp carotid artery diseases/ or cerebrovascular accident/ or exp brain infarction/ or exp cerebrovascular trauma/ or exp hypoxia-ischemia, brain/ or exp intracranial arterial diseases/ or intracranial arteriovenous malformations/ or exp 'Intracranial Embolism'/ and Thrombosis'/) or exp intracranial hemorrhages/ or vasospasm, intracranial/ or vertebral artery dissection)/ (46227)
2. (stroke or poststroke or post-stroke or cerebrovasc$ or brain vasc$ or cerebral vasc$ or cva$ or apoplex$ or SAH).tw. (125782)
3. ((brain$ or cerebr$ or cerebell$ or intracran$ or intracerebral) adj5 (isch?emi$ or infarct$ or thrombo$ or emboli$ or occlus$)).tw. (56505)
4. ((brain$ or cerebr$ or cerebell$ or intracerebral or intracranial or subarachnoid) adj5 (haemorrhage$ or hemorrhage$ or haematoma$ or hematoma$ or bleed$)).tw. (32535)
5. hemiplegia/ or exp paresis/ (13294)
6. (hemipleg$ or hemipar$ or paresis or paretic).tw. (20165)
7. 1 or 2 or 3 or 4 or 5 or 6 (222029)
8. rehabilitation/ or ‘activities of daily living’/ or exercise therapy/ or occupational therapy/ (40729)
9. physiotherapy/ or physical therapy/ or facilitation/ or treatment/ or intervention$ (7051)
10. ((motor or movement$ or task$ or skill$ or performance) adj5 (repetit$ or repeat$ or train$ or re?train$ or learn$ or re?learn$ or practic$ or practis$ or rehears$ or rehers$)).tw. (41285)
11. ((recovery or regain) adj3 function$).tw. (17367)
12. 8 or 9 or 10 or 11 (105168)
13. (upper adj3 (limb or extremity)).tw. (16668)
14. (arm or shoulder or elbow or forearm or wrist or finger$).tw. (188903)
15. 13 or 14 (199927)
16. (reach$ or transport or grasp or grip or prehen$ or dexterity or grip).tw. (424347)
17. (aperture adj1 (hand or grip or finger$)).tw. (154)
18. (coord$ or synchron$ or manipul$ or timing or skill).tw. (272153)
19. 16 or 17 or 18 (682974)
20. 7 and 12 and 15 and 19 (241)

N.B. Numbers in brackets represent the number of papers provisionally found using this search strategy.
Assessment criteria

Identification of relevant trials
Two review authors will independently read the titles of the identified references and eliminate any obviously irrelevant studies. We will then obtain the abstracts for the remaining studies and, based on the inclusion criteria (types of studies, types of participants, type of interventions), two review authors will independently rank these as ‘possibly relevant’, or definitely irrelevant’. If both review authors identify a trial as ‘definitely irrelevant’ we will exclude this trial at this point. We will retrieve the full text of trials categorised as ‘possibly relevant’, review them, and classify them independently as ‘include’, ‘exclude’ or ‘unsure’. We will exclude trials classified as ‘exclude’ by both review authors. If there is disagreement between review authors, or a decision cannot be reached, we will seek consensus through discussion, including a third review author if necessary.

Documentation of methodological quality
Two review authors will independently assess the methodological quality of the studies using standardised critical appraisal assessment forms (Appendix I) from the JBI-MAStARI (Joanna Briggs Institute-meta-analysis of statistics assessment and review instrument). For case control and cohort studies the JBI Critical Appraisal Checklist for Comparable Cohort/ Case Control will be used. The JBI Critical Appraisal Checklist for Experimental Studies will be used to assess experimental studies. For rigour and detail, additional questions about quality from the checklist for assessment of the methodological quality described by Downs and Black as follows 49:

1) Is the hypothesis/aim/objective of the study clearly described?
2) Is there a sound theoretical basis on which the hypothesis is based?
3) Are the characteristics of the people included in the study clearly described?
4) Is the experimental design reliable & valid?
   a. Randomization or counterbalance of intervention or experimental manipulation
   b. Baseline comparisons between groups or conditions
   c. Control condition/group comparisons or Pre-post comparisons
   d. Blinding (where applicable)
5) Were outcomes measured in a reliable way?
6) Were outcomes measures valid?
7) Were the main findings of the study clearly described?
Each question will be answered as either ‘yes’, ‘no’, or ‘unclear’. Where insufficient information is provided, we will contact the authors for further information.

**Data extraction**

Two review authors will independently extract data from the studies using a standard data extraction form the JBI-MAStARI (Appendix II) If possible we will also document:

1) participant details (including age, gender, type of stroke, time since stroke, initial upper limb impairment, co-morbid conditions, pre-morbid disability)
2) sample size for each outcome for the intervention group and for any comparison groups.
3) the inclusion and exclusion criteria for recruitment of patients, and sampling frame for participant selection
4) a description of the coordination/reach to grasp intervention (including whether delivered as part of a package of treatment or as a specific intervention.)
5) the duration/intensity/frequency of intervention
6) setting in which the intervention was delivered
7) the comparison intervention, if there was one or pre and post comparisons in non-control condition studies
8) person delivering the intervention and their qualifications and experience
9) the outcomes measurement used to describe coordination
10) the outcomes measurement used to describe reach to grasp function
11) for each outcome, the mean and standard deviation for the intervention group and comparison groups.

Data extracted will be entered into a database. Data will be organised in tables (Appendix III) according to the type of intervention/ manipulation using the following categories:

- Bobath or Neuro-developmental approach
- Exercise therapy including isolated repetitive movements or isometric contractions, assisted and resisted strength training.
- Bilateral training
- Task specific practice / functional training
- Constraint induced therapy
- Biofeedback or electrical stimulation
- Robot therapy or computerised training
- Other including brief or prolonged passive soft tissue stretching

If a study includes an experimental manipulation or condition as opposed to a direct intervention it will still be categorised under the appropriate heading above. For example, repeated trials of
reach to grasp will be categorised under task specific practice, pedalling with the arms to improve upper limb coordination will be categorised under bilateral training.

Data synthesis
Details of the included studies will be recorded in a table, with details of the above items in the data extraction list. Coordination interventions will be described in detail. Theoretical bases for the interventions, provided in the included studies, will be extracted and recorded. Studies without a sound theoretical basis will be identified. A sound theoretical basis may include either experimental evidence from studies with stroke subjects, extrapolation of research findings from studies on the healthy population, or excellent theoretical reasoning. The stated aims of each of the intervention types will be documented.

The psychometric properties of each measurement of coordination used will be tabulated, indicating whether the measure has been investigated for each property and the result of these investigations recorded (e.g. Kappa statistic for reliability).

Descriptive statistics will be used to summarise the findings. Frequencies of items of interest will be recorded, such as number of studies with coordination interventions for upper limb or reach to grasp, number of studies that found a difference in outcome between the coordination intervention and another group (no treatment, placebo, or alternative intervention). Means and standard deviations will be reported where appropriate, e.g. mean age of subjects, mean time since stroke and mean duration of treatment.

Comparative statistical analyses will only be performed if a sufficient number of studies within each intervention type category employ the same measures and will only be performed within a category of intervention type. Studies to be included in meta-analysis will be analysed using JBI-MAStARI software. The approach used to summarise the main effects will be determined by the type of data. Either weighted mean difference or standardised mean differences will be used for continuous data as appropriate. Confidence intervals (95%) will be calculated for all data. If statistical pooling of results is not appropriate the findings will be summarized in a narrative form.
Acknowledgements
This review is part of an Allied Health Research bursary funded by the Stroke Association awarded to Dr. van Vliet, Prof. Wing and Miss Pelton.

Potential conflict of interest
The authors are not aware of any conflicts of interest.
Reference List


## Appendix I: Critical Appraisal Checklists

### JBI Critical Appraisal Checklist for Experimental Studies

Reviewer ___________________  Date __________
Author _____________________  Year __________  Record Number ______

1. Was the assignment to treatment groups truly random?  
   - Yes  
   - No  
   - Unclear

2. Were participants blinded to treatment allocation?  
   - Yes  
   - No  
   - Unclear

3. Was allocation to treatment groups concealed from the allocator?  
   - Yes  
   - No  
   - Unclear

4. Were the outcomes of people who withdrew described and included in the analysis?  
   - Yes  
   - No  
   - Unclear

5. Were those assessing outcomes blind to the treatment allocation?  
   - Yes  
   - No  
   - Unclear

6. Were the control and treatment groups comparable at entry?  
   - Yes  
   - No  
   - Unclear

7. Were groups treated identically other than for the named interventions?  
   - Yes  
   - No  
   - Unclear

8. Were outcomes measured in the same way for all groups?  
   - Yes  
   - No  
   - Unclear

9. Were outcomes measured in a reliable way?  
   - Yes  
   - No  
   - Unclear

10. Was appropriate statistical analysis used?  
    - Yes  
    - No  
    - Unclear

**Overall appraisal:**  
- Include  
- Exclude  
- Seek further info.

**Comments (Including reasons for exclusion)**
**JBI Critical Appraisal Checklist for Comparable Cohort/ Case Control**

Reviewer ___________________  Date ____________  
Author _____________________  Year ____________  Record Number ______

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<th>Yes</th>
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<td>1. Is sample representative of patients in the population as a whole?</td>
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<td>2. Are the patients at a similar point in the course of their condition/illness?</td>
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<td>3. Has bias been minimised in relation to selection of cases and of controls?</td>
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<td>4. Are confounding factors identified and strategies to deal with them stated?</td>
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<td>5. Are outcomes assessed using objective criteria?</td>
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<td>6. Was follow up carried out over a sufficient time period?</td>
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<td>7. Were the outcomes of people who withdrew described and included in the analysis?</td>
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<td>8. Were outcomes measured in a reliable way?</td>
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<td>9. Was appropriate statistical analysis used?</td>
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Overall appraisal: Include □  Exclude □  Seek further info □

Comments (Including reason for exclusion)
# Appendix II: Data Extraction Form (Quantitative Data)

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Number of Participants

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Interventions

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### Outcome Measures

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### Results

#### Dichotomous Data

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<td>Number/total number</td>
<td>Number/total number</td>
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#### Continuous Data

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<td>Mean &amp; SD (number)</td>
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### Authors Conclusion

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### Reviewers Conclusion

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Appendix III: Database Tables

**i. Participant Information**

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<th>Final n</th>
<th>Inclusion criteria</th>
<th>Exclusion criteria</th>
<th>Male/female</th>
<th>Age (yrs) - Mean, Range, (SD)</th>
<th>Time since stroke (mths) - Mean, Range, (SD)</th>
<th>Baseline measures of impairment - mean (SD)</th>
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**ii. Intervention Information**

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<tr>
<th>Study</th>
<th>Comparison Groups</th>
<th>Aim</th>
<th>Type</th>
<th>Delivery</th>
<th>Duration, intensity, frequency</th>
<th>Setting</th>
<th>Person delivering the intervention</th>
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<td>Intervention A&amp;B or ABA design</td>
<td>e.g. Function during reach to grasp or coordination of reach to grasp</td>
<td>e.g. task specific practice or strength training</td>
<td>e.g. complex intervention or experimental manipulation.</td>
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<td>e.g. research lab, home or hospital</td>
<td>e.g. researcher or PT</td>
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**iii. Outcome Measures**

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