Is Cerebral Palsy Research Focusing on the Right Outcome Measures and Using the Right Methodology?

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Abstract

Background: Cerebral palsy (CP) is the most prevalent lifelong disability in the UK and affects around 1 in 400 live births. Treatment of this disorder has not focused on the needs of the patients. This is largely due to problems with outcome measures and methodology used by numerous disciplines. Methodological issues in rehabilitation techniques largely stem from a lack of a proper control group.

Aims/Objectives: To highlight the inconsistencies in outcome measures and issues concerning methodologies used in the research of CP treatment and rehabilitation. A comprehensive review was undertaken to identify ways in which treatment of CP can be improved and enhanced.

Conclusions: Outcome measures differ between pharmacological and rehabilitation research. Overall, the outcome measures tend to be near-transfer effects rather than far-transfer effects. The methodological techniques in rehabilitation approaches are inadequate and need to use randomised control trials and crossover designs. The role of metacognition has been ignored to date. Virtual reality may provide the potential to employ motor/mental imagery training in a more suitable and economical way. Future research needs to investigate pharmacological treatment for dyskinesia and ataxia, but must also increase consultation with patients with CP and their families/carers. Null findings need publishing to enhance future research.

1. Introduction

1.1. Definition of Disability

According to the World Health Organization (WHO; 2001), disability is defined as: ‘Disabilities is an umbrella term, covering impairments, activity limitations, and participation restrictions. An impairment is a problem in body function or structure; an activity limitation is a difficulty encountered by an individual in executing a task or action; while a participation restriction is a problem experienced by an individual in involvement in life situations. Disability is thus not just a health problem. It is a complex phenomenon, reflecting the interaction between features of a person’s body and features of the society in which he or she lives.’ However, there are many different types of disability and this paper focuses on cerebral palsy (CP) and whether the researchers investigating treatments into CP are using the correct outcome measures and methodology in their research.

It is difficult enough to define a person as disabled, because when one reads the WHO definition there is no clear dividing line for what constitutes a disability. There are many other definitions of a disability and they tend to refer to an inability to participate in “normal life activities”. It is questionable how to define “normal life activities” and whether these differ between countries or even within communities. In the UK, the government is struggling to identify the definition of disability with regards to benefits and eligibility to rehabilitation or health care. With regards to CP this is not clear cut as individuals with CP can have a very wide spectrum of disabilities.

1.2. Cerebral Palsy (CP)

CP is caused by hypoxia at birth or foetal development (e.g., Yarnell & O'Reilly, 2013; Beukelman & Mirenda, 1999). Hypoxia at pre-, peri- or neonatal occurrence causes brain damage to the cerebellum, basal ganglia (BG) and the thalamus (e.g. Almond & Chakrabarty, 2017), which have knock on effects in neuronal development in other areas of the brain and spinal cord. CP is an umbrella term which covers a number of motor coordination problems in individuals and is non-progressive. However, there are other causes of CP that include brain malformations during development that account for between 10-15% of cases. There are four facets of CP, which are not mutually exclusive to one person (i.e. an individual can suffer from all four depending on their damage to the brain). The four facets are; dyskinetic/athetoid, spastic, ataxic and/or hypotonic CP (see Almond & Chakrabarty, 2017 for full definitions).

CP has also been separated on the effected areas of the body that the disorder affects. These can be separated into three sub-groups; quadriplegic, hemiplegic (or hemiparesis) or diplegic. Patients with quadriplegic CP (also known as tetraplegic) have motor coordination and/or muscle tone dysfunction with or without spasticity in all four limbs as well as their trunk and typically the neck/face. Hemiplegic CP individuals have a motor coordination deficit and/or spasticity as well as the possibility of dyskinesia in one side of their body (either the right or left arm and/or leg are affected). Diplegic cerebral palsy refers to when the upper or typically the lower limbs are affected by spasticity, dyskinesia and/or ataxia (e.g., Molina et al., 2015).

The severity of the brain damage can cause a number of other neurological and developmental problems, such as; epilepsy, learning difficulties, sensory impairment and perception problems during life (Rosenbaum et al., 2007). However, the purpose of this paper is to identify whether current rehabilitation techniques are using the correct methodology and outcome measures when treating CP.

According to the National Health Service in the UK, 1 in 400 (however, this is significantly higher in developing countries) people are affected by some form of CP, which equates to roughly 150,000 people. This is critical in two ways: first, rehabilitation must improve the everyday lives of individuals with CP and not just on the trained tasks of rehabilitation techniques. Second, individuals with CP (with or without learning difficulties or associated disabilities) can lead more fulfilling lives and take part in employment opportunities, which is one of the main aims of the UK and western governments; this will also reduce the burden on care services and the NHS.

1.3. Aims of this Paper

Pharmaceutical research into CP has a vigorous testing regime, whereby participants are tested at baseline for numerous outcome measures including the Gross Motor Functioning Classification System (GMFCS; Palisano et al., 1997), The Gross Motor Function Measure (GMFM; Russell et al., 1989), as well as many other measurements of everyday functioning such as Goal Attainment Scoring (GAS; Kiresuk, Smith & Cardillo, 1994) etc. Furthermore, pharmaceutical testing normally involves a crossover design or a between-subjects design; therefore, one can eliminate possible placebo or natural development effects. Physiotherapy, conductive education (CE), Bobath/neurodevelopmental training (NDT) and motor/mental imagery (MI) do not employ these techniques to either assess the outcomes of their techniques against valid and reliable measures of disability or to rule out the fact that participants may be developing naturally.

The main goal of rehabilitation is not only to focus on the trained task (e.g. strength in physiotherapy), but is also to enhance the quality of life for patients and their carers with CP. MI may be the only rehabilitation approach that is attempting to extend the therapeutic technique to encompass everyday life; however, this is still in its infancy and further research is needed to recruit specialists outside of the MI field. In all rehabilitation therapies, there are clear near-transfer effects; however, there need to be far-transfer effects in order that the treatment benefits everyday life and enables individuals with CP to undertake work and social activities on an equal footing to able-bodied persons.

2. Methodological Issues with Rehabilitation Techniques

With regards to physiotherapy, CE, Bobath/NDT and Vojta therapy, the majority of published articles do not use a no-contact control group (see Almond & Chakrabarty, 2017 for a comprehensive review). The main argument for this is that it would be unethical to deny patients with CP treatment. Conversely, pharmaceutical trials repeatedly use a placebo control group or crossover trials when testing a new medication for CP and other conditions. For example, baclofen is the most commonly prescribed medication to counteract spasms in CP and there are numerous studies that have used a double-blind approach when testing the efficacy of intrathecal baclofen (e.g. Morton, Gray & Vloeberghs, 2011; Gilmartin et al., 2000; Milla & Jackson, 1977).

2.1. Physiotherapy Methodological Issues

There has also been research that has investigated the effect of intensive physiotherapy or Bobath/NDT where participants have not received either treatment for a period of weeks or months (e.g. Brunner, Rutz, Juenemann & Brunner, 2014; Christiansen & Lange, 2008; Trahan & Malouin, 2002). Therefore, there is no reason why one cannot investigate other rehabilitation techniques using a crossover design over a three month period, for example. Fine motor control develops in the first five to seven years of life (e.g. Friel, Williams, Serradj, Chakrabarty & Martin, 2014; Friel, Chakrabarty, Kuo & Martin, 2012); therefore, a break from physiotherapy or any other rehabilitation technique should not make a massive impact on central nervous system (CNS) development, but it would allow an investigation into whether physiotherapy was having a direct effect on multiple outcome measures.

During an extensive search, only a few studies were found that attempted to use controlled trials to investigate the effect of physiotherapy on CP. These studies have tended to investigate different intensive levels of standard physiotherapy, whether intermittent or continuous physiotherapy is more effective, or comparing physiotherapy to different rehabilitation approaches. Trahan and Malouin (2002) investigated whether intermittent intensive blocks of physiotherapy followed by a rest period were more effective than continuous physiotherapy. In this study, a crossover design was used and during the intensive block physiotherapy period children had eight weeks without any physiotherapy, which would be an ideal opportunity to statistically investigate whether a period without physiotherapy has any effect on multiple outcome measures. However, unfortunately Trahan and Malouin (2002) only recruited 5 children, which would not allow for appropriate statistical outcome measures (see below for discussion of outcome measures). Mann et al. (2016) have argued that smaller data may provide greater insight into unique sample populations; that then can feed into a larger database or meta-analysis.

Christiansen and Lange (2008) conducted a similar study to Trahan and Malouin (2002), however, with a larger sample population (n=25). In this study, the larger sample population would allow for more in depth statistical analysis, however, the period of time when participants were not undertaking physiotherapy was reduced to six weeks. Furthermore, one major problem with this research was that the type of CP was not reported; hence, it is difficult to ascertain whether intensive intermittent or continuous physiotherapy with different subcategories of children with CP was effective. This is also the case with Brunner et al. (2014), however, the break period was only four weeks. Also, participants received different types of rehabilitation techniques (e.g. standard physiotherapy, CE, Bobath/NDT or Vojta therapy) and this may have been tailored on the participant’s individual needs or rehabilitation regime.

Regarding the above three investigations, there are a number of methodological problems that need to be addressed when conducting controlled crossover trials. First, the severity of CP (based on the GMFCS) differed in the three studies. The age of the participants differed in all three studies, which is critical as CNS and neurological development are time specific. Third, it is important to report the type of CP as it needs to be reported and investigated in post-hoc analysis. Fourth, the durations and the amount/type of rehabilitation must be matched and the resting periods should also be matched to allow for further analysis regarding outcome measures (see below). Finally, there must be a minimum number of participants taking part to allow for an appropriate statistical analysis.

2.2. Alternative Therapy Methodological Issues

Alternative rehabilitation techniques, specifically CE, Bobath/NDT and Vojta therapy are explained in depth in Almond and Chakrabarty (2017). Almond and Chakrabarty (2017) conducted a rigorous systematic review of the alternative therapies and found that controlled trials only compared these alternative therapies to standard physiotherapy or the education of parents in occupational therapy (e.g. Dalvand, Dehghan, Feizy, Amirsalai & Bagheri, 2009); that is, there was no randomised control trial involving a no-contact control group. This raises major issues regarding the validity of these studies.

For example, Dalvand et al. (2009) undertook a randomised control trial that involved children with a mixture of CP; however, the GMFCS was not reported and it was unclear as to whether participants had one or multiple subtypes of CP. The results were mixed due to the measurements taken as outcome measures depending on the settings/situations. This has a methodological implication as results of interventions can differ significantly depending on where and who compiled the outcome measures.

A reoccurring theme was present, in that the baseline measures were sparse and did not include key factors of the participants. If one takes Dalvand et al. (2009) as an example, there were only 15 participants in each experimental group and no control group. Statistics require a minimum of 30 participants in each group to allow for the normal distribution and therefore, parametric statistical analysis. When considering the CP population, there is a large degree of heterogeneity and therefore, a larger sample population is required, especially when using a between-subjects technique.

Finally, CP is a lifelong condition and treatments, such as physiotherapy continue into adulthood and even old age. Even though there is a great deal of evidence that rehabilitation is more effective in children when the CNS is at its most plastic, when individuals with CP age then the everyday activities and social activities change. This means that a person’s requirements may change, for example, they may wish to live independently or they may be taking up an academic or work opportunity that requires a different set of physical skills. In a recent review, a lack of research regarding adults with CP and rehabilitation techniques was found, however, there is a great deal of information about rehabilitating stroke survivors (e.g. Crajé, van der Graaf, Lem, Geurts & Steenbergen, 2010) that may be transferrable to adults with CP.

2.3. Summary of Methodological Issues in CP Research

Overall, the methodologies of researching physiotherapy or alternative therapies have not used a control group (e.g. Ödman & Öberg, 2005) or have not taken the correct measurements of CP at baseline. This means that it is impossible to determine whether the therapeutic technique is not due to a placebo effect or simply due to the fact that the participants are receiving more social interaction that can benefit their development. Due to the large degree of heterogeneity in CP patients it is questionable whether a between-subjects design should be used; people with CP show contrasting responses to different therapies and therefore, a within-subjects crossover design is required. Furthermore, there is a lack of research investigating rehabilitation in older adults with CP. This is especially important as CP is a lifelong condition and there need to be controlled trials to investigate the impact of various rehabilitation techniques for adults with CP. Finally, there is an inconsistency with the reporting of the severity or type of CP that participants have when undertaking randomised control trials.

3. Outcome Measures

3.1. Theory Driven Research vs. Problem Based Learning Hypotheses

In science, one has either theory driven research or problem based learning (PBL) hypotheses. Unfortunately, physiotherapy, CE, Bobath/NDT and Vojta therapy have used the theory driven technique to increase acceptance for publication. This is not isolated to CP research as journals tend not to publish null findings. However, in the area of CP there is a lack of researchers who can identify a problem and devise a technique to enable individuals with CP to undertake more fulfilling lives. Within the realms of CP research it is almost impossible to find published research where the rehabilitation techniques have not been successful (i.e. reporting null findings). The main reason for this is that outcome measures are specifically selected to measure the effectiveness of the treatment. One example can be Kerem, Livanelioglu and Topcu (2001); whereby the researchers investigated whether Bobath/NDT was more effective with or without splints. In this research, there was no control group who did not undertake Bobath/NDT; hence, the hypothesis was that Bobath/NDT was beneficial to individuals with CP. The major error in this research was to assume that Bobath/NDT was effective for children with spastic diplegic CP. However, there are no randomised controlled trials that confirm that Bobath/NDT is beneficial using the outcome measures of Kerem et al. (2001).

3.2. Targeting the Correct Outcome Measures

There are major problems with outcome measures regarding pharmaceutical treatment, physiotherapy, CE, Bobath/NDT, Vojta therapy and to some extent MI research. During a recent focus group (Lewis, Almond, Chakrabarty & Mon-Williams, *unpublished*) patients with CP and their carers/families expressed displeasure with the lack of communication between the patient group, healthcare professionals and researchers. The main outcome of this focus group was that the everyday needs or activities of individuals with CP were not being targeted or taken into account by researchers or healthcare professionals. This means that there is a large unmet medical need that the researchers are failing to address, in particular, the everyday issues facing people with CP.

Multiple outcome measures have been developed over decades to assess the suitability of both pharmacological interventions and therapeutic approaches. These include the Modified Ashworth Scale (MAS; Ashworth, 1964), the GMFM-66 and GMFM-88 (Russell et al., 1989), Paediatric Evaluation of Disability Inventory (PEDI; Wilson, Kolobe, Arnold & McEwen, 2015), Assessment of Everyday Living (ADL; Katz, Downs, Cash & Grotz, 1970), assistive hand assessment (AHA; Krumlinde-Sundholm & Eliasson 2003), ABILHAND-kids (Arnould, Penta, Renders & Thonnard, 2004), GAS (Kiresuk et al., 1994), Caregiver's Health Questionnaire (CHQ; Deeken, Taylor, Mangan, Yabroff & Ingham, 2003), Penn Spasm Frequency Scale (SFS; Priebe, Sherwood, Thornby, Kharas & Markowski, 1996), Parental Stress Index (PSI; Reitman, Currier & Stickle, 2002) and the Questionnaire on Resources and Stress (QRS-F; Honey, Hastings, & McConachie, 2005).

There is a major issue regarding questionnaires such as the ADL (Katz et al., 1970) and other questionnaires such as the PSI (Reitman et al., 2002) and the QRS-F (Honey et al., 2005) as these mainly focus on children with CP and not adults with the condition. Furthermore, the condition of the person with CP can distort the outcome of these questionnaires and; therefore, there needs to be a new questionnaire developed which takes into account the age, GMFCS and the type of daily activities that the individual with CP and their carers' undertake. For example, an individual with a GMFCS score of I-II may have different ideas of daily living, such as being able to attend work and take part in social activities. Alternatively, an individual with a GMFCS score of IV-V may be in long-term care and have totally different aspirations for everyday life. This has not been taken into account for older adults with CP.

3.3. Choosing the Right Outcome Measures

A critical issue regarding rehabilitation research, especially physiotherapy, CE, Bobath/NDT and to a lesser extent MI, is that researchers cherry pick outcome measures that will support their research objectives. This is also the case with pharmaceutical controlled trials; however, to a lesser extent. A full review of pharmacological, physiotherapy and alternative treatments can be found in Almond and Chakrabarty (2017). The outcome measures largely neglect the everyday functioning of individuals with CP.

One recent example is Brunner et al. (2014) where the only outcome measure was the GMFM-66. Unfortunately, the GMFM does not take into consideration the social or academic functioning of the child and it does not take into account the experience of the parent/carer of the child with CP. This is symptomatic of the majority of research into physiotherapy, CE, Bobath/NDT, pharmaceutical research and to some degree MI (Lust, Wilson & Steenbergen, 2016; Shire et al., 2016; Labaf, Shamsoddini, Hollisaz, Sobhani & Shakibaee, 2015; Brunner et al., 2014; Nasiri & Kargar, 2014; Christiansen & Lange, 2008; Tsorlakis, Evaggelinou, Grouios & Tsorbatzoudis, 2004; Knox & Evans, 2002; Trahan & Malouin, 2002; Arvio & Merikanto, 2001; Brunstrom, Bastian, Wong & Mink, 2000; Gilmartin et al., 2000; Ford, Bleck, Aptekar, Collins & Stevick, 1976). The case is that the majority of research has only focused on select outcome measures and, on the whole, neglected to include outcome measures that focus on socialisation, academic/work activities and the pressure on parents/carers.

Once again, older adults with CP have not been assessed properly with regards to outcome measures. The GMFM is only suitable for individuals up to the age of 16-18 and therefore, there needs to be an appropriate measure of motor functioning in adults with CP. There is also a lack of outcome measures that assess adults, who have CP, and undertake potential rehabilitation therapies (including pharmacological treatments) regarding social activities, work related activities and the pressure on health care professionals and/or parents/carers. The current outcome measures that focus on physical abilities are, arguably, not suitable for adults with different severities or classifications of CP. Urgent research is needed to develop a model based on the GMFM for adults with CP that can be used to assess rehabilitation approaches for individuals aged over 18 years old. Much of the research from stroke survivors undertaking rehabilitation could be implemented in the rehabilitation of adults with CP.

3.4. Summary of Outcome Measures

In summary, there is a dearth of outcome measures that focus on social/academic or work activities, as well as the pressure on health care professionals or carers/parents of children and adults with CP. Several published intervention studies have missed the opportunity to employ multiple outcome measures that focus on far-transfer effects and not just on the efficacy of the intervention. This is supportive of Meghi et al. (2012), who argued for a checklist so that physiotherapists and patients or carers/families could improve communication regarding outcome measures of rehabilitation. Pharmacological research has largely focused on spastic symptoms and not on the needs of individuals with CP, such as, dyskinesia or ataxia. Finally, there is insufficient research to investigate outcome measures in older adults with CP. This is critical as the burden on carers, social services and the NHS is astronomical when caring for people with disabilities such as CP.

4. Future Research and Far-Transfer Effects

4.1. Far- vs. Near-Transfer Effects

As discussed above, any type of rehabilitation (for CP patients) must have far-transfer effects. That is, an intervention may benefit the ROM or reduce spasticity in individuals with CP; however, this is practically useless unless it allows people to lead a more “normal” life. This could be undertaking computer games on an equal footing (with non-disabled children) for children with CP or it could be increasing the independence of children or adults with CP in their everyday lives. MI training has a great potential of doing this, however, it is still in its infancy and further research is needed to investigate which individuals with CP may benefit from MI training and how this can be implemented in a cost effective way.

4.2. Overt vs. Covert MI Training

For example, there is a difference on the effectiveness of covert versus overt MI training based on the age of the participants and their type of CP the participant has got. Covert MI training asks participants to make judgments on whether it is a right or left hand and which angle it is rotating at. Researchers then ask them to perform a manual dexterity task. This is normally done with people with hemiplegic CP and researchers investigate whether the mental imagery benefits some kind of motor performance in their impaired hand. Overt MI training is when participants are literally asked to imagine doing a task before completing it; this could be moving a joystick to a target on a screen or thinking about walking a certain distance for people with diplegic CP.

One major breakthrough was made by Steenbergen, Meulenbroek and Rosenbaum (2004) who found that overt MI training was not effective in individuals with left hemiplegic CP (i.e. right brain damage); however, it was effective in adolescences with right hemiplegic CP (i.e. left brain damage). Further research also showed that overt MI training was beneficial for individuals with quadriplegic CP. This indicated that the right side of the brain is critical for motor planning and was supported by Chinier et al. (2014). Therefore, MI training needs to use either covert or overt techniques when rehabilitating CP patients with different types of brain damage and severity of the disorder.

Steenbergen, Crajé, Nilsen and Gordon (2009) also suggested a direct link between executive functioning and overt MI training. Subsequent research has indicated that individuals with a high degree of executive functioning show a greater benefit of overt MI training (e.g. Shire et al., 2016; Spruijt, van der Kamp & Steenbergen, 2015; Spruijt, Jongsma, van der Kamp & Steenbergen, 2015; Braun, Beurskens, Brom, Schack & Wade, 2006). However, as mentioned earlier, the outcome measures were limited and did not include everyday functioning (see Sharma, Pomeroy & Baron, 2006).

4.3. Executive Functioning and Meta-cognition in MI Rehabilitation

Executive functioning is closely related to metacognition (Souchay & Isingrini, 2004) and therefore, it is possible that metacognition may have a significant impact on MI training; specifically overt MI techniques. It is no coincidence that executive functioning and metacognition develop at the age of five to seven years old and that overt MI training seems to be more beneficial in children with CP who are aged over 7 and have a high level of executive functioning (e.g. Steenbergen et al. 2009). The theory of metacognition (e.g. Nelson & Narens, 1990) has been largely overlooked in the field of rehabilitation of CP patients; however, this is discussed in depth in Almond and Chakrabarty (2017).

In brief, the metacognition system may provide additional insights into why some individuals with different categories of CP or higher cognitive functioning may benefit from overt MI training. One suggestion is that the monitoring pathway is intact in individuals who have quadriplegic and right hemiplegic CP, but not necessarily in persons with left hemiplegic CP. If this is the case, then metacognitive training may benefit individuals with higher executive functioning who suffer from right hemiplegic CP, quadriplegic and mild diplegic CP in combination with overt MI training. This requires further research and requires involving cognitive psychologists who are experts in metacognition. If a combination of MI and metacognitive training can enhance the multiple outcome measures by strengthening the control pathway of metacognition then this may be a fruitful avenue to explore.

4.4. Virtual Reality (VR)

Furthermore, the role of VR in combination with MI (and potentially metacognition) training has a great potential for a number of reasons. Wilson, Green, Caeyenberghs, Steenbergen and Duckworth (2016) conducted a recent review of the use of VR with children who were diagnosed with CP or Developmental Coordination Disorders (DCD). The results suggest that; first, VR can benefit coordination in individuals with moderate to mild CP as well as DCD.

Second, the use of VR means that off the shelf devices can be adapted and therefore, enable children with CP to compete with able bodied peers without feeling that they are being segregated. In line with this, the use of VR with children who have CP means that social interaction may increase and therefore the social integration may also have a knock on effect with regards to rehabilitation. Thirdly, many games can be adapted to allow individuals with CP to compete on an even basis with able bodied children, which means that covert MI training may occur without these children requiring special training.

There is a caveat to this, however, which is that, the skills that the children pick up during the VR activity must show far-transfer effects. Older children and adolescences are notoriously rebellious to employ training to everyday life activities; therefore, perhaps the use of mentors to encourage them to use this may be helpful. VR technology may be one option of making MI training more economically viable and more accessible in homes and schools. This will reduce the cost of intensive rehabilitation programs and may increase compliance with children who have CP.

4.5. Summary of MI Research

Finally, the use of robotics may be beneficial in rehabilitating children with CP. For example, Shire et al. (2016) showed how a haptic robotic arm benefitted children with DCD who were in the lowest 15th percentile for handwriting. This could be transferred to hemiplegic and quadriplegic children with CP to promote motor planning. In line with a combination of VR, MI and metacognition training, it is likely that this will improve the control pathway of metacognition in these patients. Further research is needed to explore this potential, but critically make the training more accessible and enjoyable for children with CP.

5. Summary and Conclusions

Cerebral palsy is the most common cause of lifelong disability in the UK, affecting roughly 1 in 400 live births. It is a lifelong condition and has direct and indirect costs to the NHS, social services, patients, parents/carers and the overall economy. In a recent focus group (Lewis et al, *unpublished*), patients with CP and their families/carers expressed concerns regarding the lack of communication between pharmaceutical corporations and academics in rehabilitation in terms of not addressing the everyday needs of those with CP.

This paper has commented on both outcome measures and methodologies of pharmaceutical companies and rehabilitation techniques that focus on CP. With regards to outcome measures, pharmaceutical research and rehabilitation approaches hand pick outcome measures that tend not to address the needs of many patients with CP. For example, pharmacological research has mainly focused on spasms and neglected dyskinesia and ataxia, which are a major hindrance for many individuals with certain types of CP. There is a need to investigate the area of GABA-a allosteric modulators in an attempt to counteract dyskinesia and ataxia. If these can be introduced at an early age then they could potentially provide a cure for CP. Regarding the rehabilitation techniques of physiotherapy, CE, Bobath/NDT, Vojta therapy and to some extent MI training, there needs to be a focus on far-transfer effects and not just near-transfer effects. One possibility for this reluctance for investigating far-transfer effects is that academic journals tend not to publish null findings.

The methodologies of pharmacological research are rigorous and tend to use randomised control trials or crossover designs. Sadly, this is not the case with alternative rehabilitation approaches which means that it is almost impossible to identify whether these theory driven interventions assume that the rehabilitation techniques work. There is a drastic need to adopt the randomised controlled trial and especially the crossover design to definitively show evidence that these rehabilitation techniques are making a significant difference in both children and adults with CP.

Finally, the role of MI training must incorporate a larger sample population and take into account executive functioning as well as the theory of metacognition. These techniques have developed with the use of VR, meaning that children with CP feel more included compared to their able bodied peers. The age and classification of CP should determine the type of MI training that is used. VR offers a promising opportunity to make MI training more accessible and more economical, thus, reducing the burden on the NHS, social services and patients/parents/carers that have CP.

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References

Almond, N.M. & Chakrabarty, S. (2017). A Review of Cerebral Palsy; Aetiology, Current Understanding and Treatment: A Call for Action. *Horizons in Neuroscience*. Chapter 1, NOVA Publishers.

Arnould, C., Penta, M., Renders, A. & Thonnard, J.L. (2004). ABILHAND-Kids: A Measure Of Manual Ability In Children With Cerebral Palsy. *Neurology,* 63(6), 1045-1052.

Arvio, M. & Merikanto, J. (2001) A Relief From Neural Pain - Gabapentin Helped Against Hip Ache In A Girl With Cerebral Palsy. *Duodecim; Laaketieteellinen Aikakauskirja*, 117(14), 1447-8.

Ashworth, B. (1964). Preliminary Trial Of Carisoprodal In Multiple Sclerosis. *Practitioner*, 192, 540-542.

Beukelman, D. R. & Mirenda, P. (1999). *Augmentative and Alternative Communication: Management of Severe Communication Disorders in Children and Adults* (2nd ed.). Baltimore: Paul H Brookes Publishing Co. pp. 246-249.

Braun, S.M., Beurskens, A.J., Brom, P.J., Schack, T. & Wade, D.T. (2006). The Effects Of Mental Practice In Stroke Rehabilitation: A Systematic Review. *Arch Phys Med Rehabil*, 87, 842-52.

Brunner, A.L., Rutz, E., Juenemann, S., & Brunner, R. (2014). Continuous vs. Blocks Of Physiotherapy For Motor Development In Children With Cerebral Palsy And Similar Syndromes: A Prospective Randomized Study. *Developmental Neurorehabilitation*, 17(6), 426-432.

Brunstrom, J.E., Bastian, A.J., Wong, M. & Mink, J.W. (2000) Motor Benefit from Levodopa in spastic quadriplegic Cerebral Palsy. *Annals of Neurology*. 47, 662-665.

Chinier, E., n'Guven, S., Lignon, G., Minassian, A.T., Richards, I. & Dinomais, M. (2014). Effects Of Motor Imagery In Children With Unilateral Cerebral Palsy: Fmri Study. *PLOS One*, 9(4), 1-9.

Christiansen, A.S. & Lange, C. (2008). Intermittent Versus Continuous Physiotherapy In Children With Cerebral Palsy. *Developmental Medicine & Child Neurology*. 50(4), 290-293.

Crajé, C., van der Graaf, C., Lem, F.C., Geurts, A.C. & Steenbergen, B. (2010). Determining Specificity Of Motor Imagery Training For Upper Limb Improvement In Chronic Stroke Patients: A Training Protocol And Pilot Results. *International Journal of Rehabilitation Research.* 33(4), 359-362.

Dalvand, H., Dehghan, L., Feizy, A., Amirsalai, S. & Bagheri, H. (2009). Effect of the Bobath Technique, Conductive Education and Education to Parents in Activities of Daily Living in Children with Cerebral Palsy in Iran. *Hong Kong Journal of Occupational Therapy*, 19(1), 14-19.

Deeken, J.F., Taylor, K.L., Mangan, P., Yabroff, K.R., Ingham, J.M. (2003) Care for the caregivers: a review of self-report instruments developed to measure the burden, needs, and quality of life of informal caregivers. *J Pain Symptom Manage*. 26(4), 922-53.

Ford, F., Bleck, E.E., Aptekar, R.G., Collins, F.J. & Stevick, D. (1976) Efficacy of Dantrolene Sodium in the Treatment of Spastic Cerebral Palsy. *Developmental Medicine & Child Neurology,* 18, 770–783.

Friel, K.M., Chakrabarty, S., Kuo, H.C. & Martin, J.H. (2012) Using Motor Behavior During An Early Critical Period To Restore Skilled Limb Movement After Damage To The Corticospinal System During Development. *J Neurosci,* 32, 9265-9276.

Friel, K.M., Williams, P.T., Serradj, N., Chakrabarty, S. & Martin, J.H. (2014) Activity-Based Therapies for Repair of the Corticospinal System Injured During Development. *Frontiers in Neurology,* 5, 229.

Gilmartin, R. et al. (2000) Intrathecal Baclofen For Management Of Spastic Cerebral Palsy: Multicenter Trial. *J Child Neurol*, 15(2), 71-7.

Honey, E., Hastings, R.P. & McConachie, H. (2005) Use of the questionnaire on resources and stress (QRS-F) with parents of young children with autism. *Autism*. 9(3), 246-55.

Katz, S., Downs, T.D., Cash, H.R. & Grotz, R.C. (1970) Progress in development of the index of ADL. *Gerontologist,* 10(1), 20-30.

Knox, V. & Evans, A.L. (2002) Evaluation Of The Functional Effects Of A Course Of Bobath Therapy In Children With Cerebral Palsy: A Preliminary Study. *Dev Med Child Neurol*, 44(7), 447-60.

Kerem, M., Livanelioglu, A. & Topcu, M. (2001) Effects Of Johnstone Pressure Splints Combined With Neurodevelopmental Therapy On Spasticity And Cutaneous Sensory Inputs In Spastic Cerebral Palsy. *Dev Med Child Neurol*, 43(5), 307-13.

Kiresuk, T.J., Smith, A. & Cardillo, J.E. (1994) *Goal attainment scaling: Applications, theory, and measurement*. Hillsdale, NJ, England: Lawrence Erlbaum Associates, Inc.

Krumlinde-Sundholm, L. & Eliasson, A.C. (2003) Development of the Assisting Hand Assessment: A Rasch-built Measure intended for Children with Unilateral Upper Limb Impairments. *Scandinavian Journal of Occupational Therapy,* 10(1), 16-26.

Labaf, S., Shamsoddini, A., Hollisaz, M.T., Sobhani, V. & Shakibaee, A. (2015) Effects of Neurodevelopmental Therapy on Gross Motor Function in Children with Cerebral Palsy. *Iran J Child Neurol*. Spring, 9(1), 36-41.

Lewis, D., Almond, N.M., O'Connor, R.J., Chakrabarty, S. & Mon-Williams, M. (Unpublished)

Lust, J.M., Wilson, P.H. & Steenbergen, B. (2016) Motor Imagery Difficulties In Children With Cerebral Palsy: A Specific Or General Deficit? *Res Dev Disabil*, 57, 102-11.

Mann, R., Mushtaq, F., White, A., Cervantes, G., Pike, T., Coker, D., Murdoch, S., Hiles, T., Smith, C., Berridge, D., Hall, G., Hinchliffe, S., Smye, S., Wilkie, R.M., Lodge, P. &

Mon-Williams, M. (2016). The Problem with Big Data: Operating on Smaller Datasets to Bridge the Implementation Gap. *Front. Public Health*, 4(248), doi: 10.3389/fpubh.2016.00248.

Meghi, P. et al. (2012) Core Elements Of Physiotherapy In Cerebral Palsy Children: Proposal For A Trial Checklist. *Eur J Phys Rehabil Med,* 48(1), 123-33.

Milla, P.J. & Jackson, A.D. (1977) A Controlled Trial Of Baclofen In Children With Cerebral Palsy. *J Int Med Res,* 5(6), 398-404.

Molina, M. et al. (2015) Motor Imagery For Walking: A Comparison Between Cerebral Palsy Adolescents With Hemiplegia And Diplegia. *Res Dev Disabil*, 37, 95-101.

Morton, R.E., Gray, N. & Vloeberghs, M. (2011) Controlled Study Of The Effects Of Continuous Intrathecal Baclofen Infusion In Non-Ambulant Children With Cerebral Palsy. *Dev Med Child Neurol*, 53(8), 736-41.

Nasiri, J. & Kargar, M. (2014) Combination of Citicoline and Physiotherapy in Children with Cerebral Palsy, *Int J Prev Med*. 5(10), 1308-1313.

Nelson, T. O. & Narens L. (1990). Metamemory: A Theoretical Framework And New Findings. In Bower G. H. (Ed.), *The psychology of learning and motivation: Advances in research and theory*, 26, 125-140. San Diego: Academic Press.

Ödman, P. & Öberg, B. (2005) Effectiveness Of Intensive Training For Children With Cerebral Palsy - A Comparison Between Child And Youth Rehabilitation And Conductive Education. *J Rehabil Med,* 37(4), 263-70

Palisano, R. et al., (1997) Development And Reliability Of A System To Classify Gross Motor Function In Children With Cerebral Palsy. *Dev Med Child Neurol*, 39, 214-223.

Priebe, M.M., Sherwood, A.M., Thornby, J.I., Kharas N.F. & Markowski, J. (1996) Clinical assessment of spasticity in spinal cord injury: A multidimensional problem, Archives of *Physical Medicine and Rehabilitation*, 77(7), 713-716.

Reitman, D., Currier, R.O. & Stickle, T.R. (2002) A critical evaluation of the Parenting Stress Index-Short Form (PSI-SF) in a head start population. *J Clin Child Adolesc Psychol.* 31(3), 384-92.

Rosenbaum, P. et al. (2007) A Report: The Definition And Classification Of Cerebral Palsy. *Dev Med Child Neurol Suppl*, 109, 8-14.

Russell, D.J. et al. (1989) The Gross Motor Function Measure: A Means To Evaluate The Effects Of Physical Therapy. *Dev Med Child Neurol,* 31, 341-52.

Sharma, N., Pomeroy, V.M. & Baron, J.C. (2006). Motor Imagery: A Backdoor To The Motor System After Stroke? *Stroke*, 37, 1941-52.

Souchay, C. & Isingrini, M. (2004). Age Related Differences In Metacognitive Control: Role Of Executive Functioning. *Brain Cogn*, 56, 89-99.

Spruijt, S., Jongsma, M.L., van der Kamp, J. & Steenbergen, B. (2015) Predictive Models To Determine Imagery Strategies Employed By Children To Judge Hand Laterality. *PLoS One*, 10(5), e0126568.

Spruijt, S., van der Kamp, J. & Steenbergen, S. (2015) The Ability Of 6- To 8-Year-Old Children To Use Motor Imagery In A Goal-Directed Pointing Task. *J Exp Child Psychol*, 139, 221-33.

Steenbergen, B., Crajé, C., Nilsen, D.M. & Gordon, A.M. (2009) Motor Imagery Training In Hemiplegic Cerebral Palsy: A Potentially Useful Therapeutic Tool For Rehabilitation. *Dev Med Child Neurol*, 51(9), 690-6.

Steenbergen, B., Meulenbroek, R.G. & Rosenbaum, D.A. (2004) Constraints On Grip Selection In Hemiparetic Cerebral Palsy: Effects Of Lesional Side, End-Point Accuracy, And Context. *Brain Res Cogn Brain Res*, 19(2), 145-59.

Trahan, J. & Malouin, F. (2002) Intermittent Intensive Physiotherapy In Children With Cerebral Palsy: A Pilot Study. *Dev Med Child Neurol*, 44(4), 233-9.

Tsorlakis, N., Evaggelinou, C., Grouios, G. & Tsorbatzoudis, C. (2004) Effect Of Intensive Neurodevelopmental Treatment In Gross Motor Function Of Children With Cerebral Palsy. *Dev Med Child Neurol*, 46(11), 740-5.

Wilson, P.H., Green, D., Caeyenberghs, K. Steenbergen, B. & Duckworth, J. (2016) Integrating New Technologies into the Treatment of CP and DCD. *Current Developmental Disorders Reports*, 3(2), 138-151.

Wilson, R.A., Kolobe, T.H., Arnold, S.H. & McEwen, I.R. (2015) Concurrent validity of the School Outcomes Measure (SOM) and Pediatric Evaluation of Disability Inventory (PEDI) in preschool-age Children. *Phys Occup Ther Pediatr*, 35(1), 40-53.

World Health Organization (2001) *International classification of functioning, disability and health*. Geneva: WHO.

Yarnell, J. & O'Reiley, D. (2013). Epidemiology and Disease Prevention: A Global Approach (02 ed.). Oxford University Press. p. 190.