Current issues and challenges in research on virtual reality therapy for children with neurodisability

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ABSTRACT

A PICO (population, intervention, comparison, outcome) approach is adopted to discuss issues and challenges in virtual reality therapy research in community health settings. Widespread variation within and between populations, e.g. co-morbid conditions, complicates treatment fidelity and applicability. Interventions require flexible dose and frequency to fit into children's family circumstances, with clearly employed specialist paediatric research staff. Comparisons require adaptation to digital technology, and keep pace with development. Outcomes may overstate the impact of virtual reality therapy and technological novelty, while not fully unpacking hidden digital effects. A wide set of agreed, flexible, and patient-centred outcome measures are required to establish positive clinical baseline.

1. INTRODUCTION

"As a parent I know that my child, along with others, is keen to engage with modern technology in most aspects of life, from assisting with school work, communicating with others and as a form of entertainment. If physiotherapy was delivered using a "computer games" format, I feel that my child would be much keener to engage in undertaking necessary tasks and exercises" (parent of child with cerebral palsy).

Virtual reality therapy (VRT) has required a massive investment from academic and clinical researchers, from time taken to develop technology, getting clearance for using technology that may be commercially produced, piloting the work, grant applications, analysis of results and to rollout of interventions. There are a vast number of pitfalls that can affect the outcome and quality of intervention. There are a number of patterns that continually re-appear, and here we present those, in relation to children with neurodisability, so as to help future research. These issues – perhaps unsurprisingly – fit into problems associated with the population (including within this individual variation), intervention, comparison, and outcome (PICO). Problems occur because of the population we are studying, the intervention we employ, the way we try and compare groups, and the outcomes we are seeking. This paper will therefore look at:

1. Population, and variation that occurs across individuals within groups e.g. co-morbidity, as well as between groups (e.g. Autism versus Cerebral Palsy).
2. Intervention – dose, frequency and therapist delivery
3. Comparison issues within method construction – e.g. placebo, novelty effect
4. Issues with outcome measures; their consistency, and how these are shaped by interaction with patient and public involvement (PPI) groups e.g. what parents tell us.

We use our own nationally (UK) funded feasibility study that looked at using the Nintendo Wii with children with Cerebral Palsy, outlined below, to ground our examples. We conclude with some pointers to tackle these problems.

2. A FEASIBILITY STUDY OF VIRTUAL REALITY AS A THERAPEUTIC INTERVENTION IN CHILDREN WITH AMBULATORY CEREBRAL PALSY

This study (National Institute of Health Research for Patient Benefit Programme PB-PG-0613-31046, approved by National Health Service Research and Ethics Committee) looked at the feasibility of running a large-scale multi-centre study using the Nintendo Wii Fit to deliver regular home-based physiotherapy. Participating families completed a questionnaire regarding children's current use of computer games such as Nintendo Wii Fit within the home. Participating children were randomised into either a supported or unsupported (control) participant group. Supported participants followed a physiotherapist (PT) prescribed schedule over a 12-week period, utilising only specified Nintendo Wii Fit games for designated amounts of time per session. Sessions were recommended to last 30 minutes, three times a week with games selected for specific physiotherapy purposes, such as core stability or balance. During this 12-week period, fortnightly telephone contact to families oversaw the child's progress, updated game selection and responded to any queries in the PT supported group. The unsupported (control) participants were also asked to use the Nintendo Wii Fit for 30-minute sessions, 3 times a week, over a 12-week period. However, they had free choice over which games they chose and duration each game was to be played within the session. Scheduled phone contact was minimal to this group during the 12-week period, unless specific physiotherapy advice was required. Carers and children of both groups were required to keep a simple daily diary to rate the sessions. Assessments of balance and functional mobility were taken before commencing the trial, halfway through, and on completion. An exit questionnaire asked parents and children to report on factors such as engagement, ease of use and effects of fatigue. Factors that impacted on the choice of method are discussed in section 3.

3. ISSUES AND CHALLENGES WITH THE POPULATION

Children with neurodisability present in a number of ways, from disorders affecting movement, such as Cerebral Palsy (CP), Muscular Dystrophy and Developmental Coordination Disorder; to disorders of language and communication, including Autistic Spectrum Disorder; to broader disorders of global development, such as is seen in children with Downs syndrome. To further complicate matters these conditions can co-occur, for example children on the autistic spectrum will commonly also have Attention Deficit Hyperactivity Disorder and Developmental Coordination Disorder. Whilst for many children the cause of their disorder is uncertain, this is increasingly becoming identifiable, from known insults to the developing brain, including Fetal Alcohol Syndrome, Meningitis, extreme premature birth, Hypoxic Ischemic Encephalopathy, to genetic and chromosomal disorders such as Fragile X syndrome. In the UK most children with neurodisability are seen at community based Child Development Centres (CDCs), often utilising home or school based therapeutic interventions. More complex cases may be seen in a small number of specialist tertiary centres, which are often hospital based. Furthermore, there is a high level overlap between different diagnoses under the umbrella of neurodisability with children with CP at higher risk of social communication disorders and conversely, those on the autism spectrum at high risk of movement impairments (Green et al, 2009, Christensen et al, 2014). At present most neurodisability academics and research activity is based in the latter, begging the question of how to build a stronger research base in community centres focusing on how to improve practice in more common disorders (Morris et al, 2015).

Whilst there are pharmacological interventions that can help in some cases, for example the use of stimulant medication in Attention Deficit Hyperactivity Disorder, anticonvulsant medication in Epilepsy, or the emerging use of Gene splicing in Duchenne Muscular Dystrophy, it is rare for there to be a cure. Therefore, in most cases the mainstay of treatment is to ameliorate the impact of the condition through therapeutic intervention (Morris et al, 2015)**.** Whilst programs of physiotherapy, occupational therapy, speech therapy or behaviour modification can all help, they often rely on parents or school to deliver much of the program and from parental feedback can result in significant stress within the family (Coombe et al, 2012). Eventually this may well lead to the child refusing to complete their therapy. In the design stage of our study using the Wii Fit to determine whether it could improve balance and movement in children with cerebral palsy, parental input made it clear that as much as physical outcomes were important, for parents the primary measure of success of the intervention would be whether home based therapy could be delivered regularly without the levels of stress they associated with any attempt to deliver standard physiotherapy.

Each condition presents its own challenges to VRT research, although in many cases might be expected to respond to therapy developed through virtual reality technologies. For the current generation of children, virtual reality and information technology is a world they are very familiar and comfortable with, whether gaming, communicating, accessing information or working (Prensky, 2001). It would not be surprising therefore if therapies delivered through virtual reality technologies should prove motivating for modern children. This is no more so than for children on the autistic spectrum, particularly those considered "high functioning", or diagnosed

with Asperger's Syndrome, who are likely to be more comfortable interacting with technology than with their human peers, and indeed may well go on to work within the Information Technology industry (Murray et al, 2005). However, the challenges are very real.

Taking the example of Autistic Spectrum Disorder, there is an immediate issue over the breadth of the spectrum, from a child who may be non verbal with severe learning difficulties, to a "high functioning" child who may struggle understanding social interaction and be obsessive, yet at the same time have the genius to be a professor of maths, physics or computing, as portrayed in the TV character Sheldon Cooper (Big Bang Theory), or in Sherlock Holmes. As such designing a study for children with Autistic Spectrum Disorder immediately presents the question of which children within the spectrum the intervention is aimed at. For example we are currently developing a tool to support diagnostic assessment, incorporating a number of psychometric tests used in assessing school age children, into an App. We would anticipate that this is more likely to be helpful in children presenting at school age, and generally with a borderline to average academic ability, than those who are non verbal and with severe learning difficulties.

Similarly, interventions for children with cerebral palsy, need to take account that this "blanket" term, describing children with movement disorders resulting from a static brain insult occurring during early development, may present with different types of abnormal movement including spasticity and ataxia, and with a wide range of severity, from a child with a mild hemiplegia with minimal effect on movement, to a child with whole body involvement who is wheelchair dependent. With our Wii study this raised the question of which children to target. We chose to focus on children who are able to walk and therefore hopefully use the Wii Fit without having to use supportive technologies, e.g. standing frame, to even stand on the Wii Fit.

Regardless of diagnosis, engagement in therapeutic intervention may prove problematic (Coombe et al, 2012). In younger children, there may be issues over ability to access technologies, and to understand the research study enough to give assent. Teenagers by their nature may also choose to disengage, or may feel some Virtual Reality games are "no longer cool", and for younger children. The individual conditions present their own difficulties, for example offering a group intervention for children on the autistic spectrum may be doomed to failure. Research on intervention effects in paediatric neurodisability has been confounded by a number of differing behavioural approaches and defining outcomes. In the UK the James Lind Alliance - a leading charitable and academic think tank- recently determined the most important research questions in the field, helping set clearer agendas (Morris et al, 2015).

4. ISSUES AND CHALLENGES WITH THE INTERVENTION

Dose and frequency of an intervention employed in virtual rehabilitation is equally challenging, especially in community settings (James et al, 2015, Boyd et al, 2013). Community situations call for direct adaptations to family life, as emphasised in the International Classification of Functioning, Disability and Health – Children and Youth version (ICF-CY) where participation and activity performance across contexts is a key part of the framework (World_Health_Organisation, 2007). Acute settings e.g. hospitals are able to offer bespoke interventions but only in situ, whereas community settings are required to be more flexible in their approach to delivery of care. Therefore whilst variation in the amount of time spent on a therapy varies dramatically across the literature, those that have positive results are often lacking the sample size to justify clinically important differences (Tarakci et al, 2013), and those studies with a sufficient sample size sometimes show little clinically significant impact (Boyd et al, 2015), this is to be expected in a setting where social factors surrounding healthcare are equally as important as the treatment. A more personalised, adaptable, and consistent approach to treatment will only occur once VRT is adopted as regular care. Further, whilst VRT interventions are quite well classified (see Galvin and Levac, 2011), wider issues surrounding clinical research are more complex.

In our own present study, the intervention was developed using the Nintendo Wii Fit for use in the home for children with Cerebral Palsy. The Wii Fit was to be used three times a week, for thirty minutes, over a period of twelve weeks (following Chen et al, 2012) using the Wii Fit Plus set of games. Early results suggest that 12 weeks is possibly too long a period of time for the intervention as many families reported having struggled to "fit in" the intervention. Children were often ill, tired from school, away on holiday, having treatment such as botulinum toxin, or were busy with a full and active life. Many parents also pointed to a tipping point in motivation around the 8th week, a time-point echoed in the earlier work of Deutsch et al. (2008). After an active period of motivation it appears that interventions may lose novelty to the participant, and return to being just another form of physiotherapy. Future work may need to employ more flexible methods to allow for time points where children are ill, or away, and not become lost or missing data, allowing the current status of a participant to alter according to personal circumstance (Dempsey et al, 2015).

The intervention was dependent on delivery and monitoring by therapists. In the local community setting physiotherapists anecdotally had been using the Wii and the Wii Fit for many years, with focus groups

developing programmes that were believed to target different areas of the body e.g. core strength, balance. Many physiotherapists were keen to become involved with the study but once the study was underway external pressures changed the landscape of delivery. Pressures on retention and recruitment of therapy staff reduced the time available, especially with an increased emphasis on delivering established clinical services. To that end it seems imperative that specialist staff is employed where possible in a full-time research capacity to ensure clear protocol adherence, and ensure planned study recruitment and continuity. In England, research costs such as a research assessor measuring outcomes, are covered by the National Institute of Health Research (NIHR). Costs associated with delivering an intervention such as treatment are conversely met by local National Health Service (NHS) organisations. As a result the tax funded NHS organisations may resist research that would involve the testing of innovative methods, especially if they take staff away from clinical services. To test new treatment methods, resources are therefore needed to 'backfill' staff so that specialist staff can be freed up to take part in research. Expecting regular staff to fit in research on top of regular daily clinical work does not work well in practice. To fully explore the impact of interventions with VRT the intervention needs to be run as if it were regular care, with fully employed clinical staff.

5. ISSUES AND CHALLENGES WITH APPROPRIATE COMPARISONS

Virtual rehabilitation and the use of new technology come with challenges to the creation of appropriate method. A variety of models are already being attempted, such as 'micro-RCTs' (Dempsey et al, 2015), the use of standard controls (e.g. James et al, 2015), treatment as normal (e.g. Ferguson et al, 2013), reduced support in the intervention group (i.e. prescribed treatment versus freedom to use kit where appropriate) or even the use of computer controls such as delivery of an intervention via another modality such as a handheld device when an interactive console is being used in the experimental group (e.g. Hondori et al, 2015). However, the underlying problem with new technology is that we do not know the impact of any hidden effects of technology. Hidden effects are well documented in discussions of the placebo effect within medical interventions (Brissonnet, 2011, Brown, 1998, Moerman and Jonas, 2002) but there is yet to be a methodological discussion of the impact of digital technology on the participants - as well as researchers - behaviour (Farr et al, in submission). For example, what (if any) is the effect of the make or branding of technology and intuitive design if an iPhone is used compared to another standard smartphone? What technology, and what technological bias might already be present in the home? For example prior to our intervention in the home we conducted a survey of home use and presence of commercially available consoles. Parents and patients agreed that the most common, most useful tool, across all gradations of cerebral palsy, and especially for fine motor skills was the iPad (Farr et al, 2015). Therefore it is highly unlikely that individuals will have no experience of digital technology whatsoever, so there may be an impact of *prior experience*, plus an impact of *novelty* where an intervention uses a brand new piece of technology. Technological novelty may simply boost the interest in an intervention, thereby overstating its impact (Zaczynski, 2013). Ensuring health behaviour change, without lapses in the impact, is still relatively new and in development (Klasjna et al, 2011).

Furthermore, rate and pace at which research and development occurs is mismatched (Pagoto and Bennett, 2013). This would be in keeping with Moore's law that predicts ever increasing memory expansion in technology (Moore, 1965). But there is a large disjuncture between the time it takes for research using new technological devices to occur, and the pace at which new devices are being produced, which means that it is difficult to validate devices and applications (Pagoto and Bennett, 2013). In addition, a shortfall in the accuracy of sensors can further complicate technological use, reducing the reliability of clinically relevant information obtained from devices (Steinberg et al, 2015). Therefore it is imperative that any teams that use digital technology in clinical research keep abreast of the latest technological developments, with the right team in place. For example, the National Health Service in England sought to create and establish a database of smartphone applications in 2013 so that it could begin to ensure validity and compliance to local health ethics and ensure data protection. This pilot is currently no longer live whilst the data is being used to create a new endorsement model for patient focused healthcare applications, research found though that 89% of applications were transmitting patient information to online services and without encrypted personal information (Huckvale et al, 2015). It is possible that some technology may still be more hype than hope (Labrique et al, 2013)

During the creation of methods of intervention for digital technology use in clinical settings it is apparent that there are as yet many unanswered questions over the hidden impact of technology, and technology is set to become only ever more pervasive in our daily lives. Therefore the development of appropriate comparisons is still in its infancy. The lag from development to clinical research and validation is lengthy, as a result some authors have called for ever more close-knit research teams between the field of human-computer interaction and clinical research (Klasjna et al, 2011). In our own research, tensions existed between using technology that was fast becoming dated and used less by the general population (the Nintendo Wii has been surpassed by the Xbox in research), and establishing an effective and complex intervention that employed a technology when so little is known about hidden benefits and barriers. Agile, novel and new comparative methods will be needed as

community based populations take part in digitally based technological interventions. Micro-RCTs is one possible solution, as is the use of similar interventions in wings of studies, but with subtle variants (e.g. more versus less support as in our own study), until more is known about the direct benefits of digital usage.

6. ISSUES AND CHALLENGES: RESULTS AND OUTCOME MEASURES

Our own systematic review of VRT for children with motor disorders confirmed the lack of fully powered studies to show if this is a valid direction of future travel, whether using off the shelf gaming technologies such as the Wii Fit, Xbox, iPad; or expensive, one off bespoke systems (Farr and Male, 2013). Of the available studies in children with cerebral palsy, a couple of which included 20-30 children, most suggested some improvement in motor measures, with effect sizes of 0.3 to 0.8 (Sharan et al, 2012, Jelsma et al, 2012) however there was little agreement over which outcome measures to use, even when focused on a specific skill such as balance. One study showed significant clinical improvement in dynamic balance and other motor outcomes in 10 children with Progressive Spinocerebellar Ataxia using the Xbox Kinect (Ilg et al, 2012). This intervention was considered highly motivational and cost-efficient. Two studies gave promising results for the Wii Fit in children with Developmental Coordination Disorder (Hammond et al, 2013, Ferguson et al, 2013) including our own randomised control crossover pilot study based in a school setting, involving 19 children. Bruininks Oseretsky Test of Motor Proficiency Short Form (BOT-2), used as the main outcome, as a measure of improvement in motor coordination, improved in both groups during period of intervention, but fell close to baseline once the intervention finished (see figure one below for group 1 who had intervention first, then control period). Further measures included CSQ, a measure of the child's perception of their motor ability that also improved during intervention, but continued to do so even after intervention finished. Given that low self-esteem is such a common problem in children with Developmental Coordination Disorder, this may be as important as any actual improvement in motor coordination. SDQ, a measure of emotional wellbeing, was also included but very few parents completed this following intervention. In those that did, scores improved significantly, often with improving category from abnormal, or borderline, towards normal. This was particularly noticeable for the hyperactivity subscale.

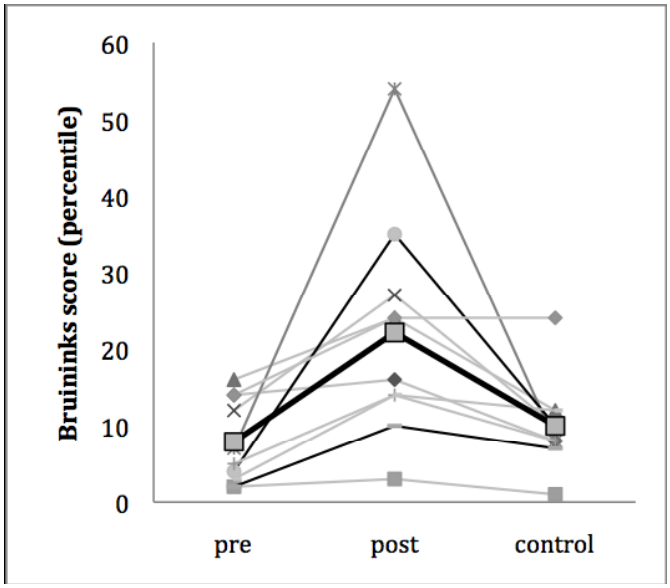

Figure 1. *Change in BOT-2 percentile for individual children using the Wii Fit as a treatment for DCD in a school setting; group A in a crossover study received intervention initially and then acted as controls. Mean result shown by thickened black line.*

Choice of outcome measure remains important, yet even in an area such as motor disability, where instinctively clinical measurement should be relatively straight forward, at least compared to measuring, for example, changes in social function in children with Autistic Spectrum disorder, there is no clear agreement over which measures to use. One of the key questions in our current Wii Fit feasibility study with children with Cerebral Palsy study has been to explore choice of outcome measure. From a motor perspective one would instinctively expect the Wii Fit, as a glorified balance board, to improve measures of balance, of which we chose the BOT-2 and Timed Up and Go Test. The former was developed for use in children with side of Developmental Coordination Disorder where poor balance is a frequent problem. In such children the better side is tested for example in testing fine motor coordination-whereas we have had to adapt this in children with unilateral Cerebral Palsy to

also test the affected side. The Gross Motor Function Measurement (GMFM), a specific measure of motor function for children with Cerebral Palsy has also been used. Although the study is still in progress, it is evident that for some children with very mild Cerebral Palsy that they reach 100% on GMFM before completing the intervention (ceiling effect), whilst we had concerns that BOT-2 might see the opposite (floor effect) with children scoring 0 pre intervention. Some measures therefore with virtual rehabilitation have ceiling or floor effects (e.g. Gross Motor Function Measure) when being used across a disorder that has a wide gradation, such as Cerebral Palsy as graded by the Gross Motor Function Classification System.

The Goal Attainment Scale (GAS) has also demonstrated improvement in participating children, and mirrors clinical practice in therapeutic goal setting by personalising targets. However, goals set by each child will differ, so it is difficult to compare the degree of improvement in each child. Nevertheless, some of the individual stories of functional improvement are almost more persuasive of the benefits offered by VRT, than overall statistical analysis. For example, in this study one 12 year old boy improved from being unable to stand on one leg at all at the start of the study, to doing so successfully for 10 seconds by the end. Another 10-year old girl with hemiplegic Cerebral Palsy, involved in a one-week intensive pilot study using the Xbox Kinect for an hour a day for five days, focussing on upper limb function, reported with great excitement being able to do up her seatbelt for the first time in her life. As noted previously, measures of motor outcome are important to us as clinicians. However, for the family, impact of therapy on family life is an equally, or indeed, a more important outcome. For this study families have been encouraged to keep a diary exploring compliance with the protocol, but also to report difficulties in persuading the child to "do their exercises". Strengths and difficulties questionnaire (SDQ) has also been used as a measure of emotional wellbeing for the child. Hopefully by the end of the study it will be clearer which measures are most useful, to inform future study design, with the need for larger, probably multi-centre RCTs, needed to finally confirm whether VRT has a valid role within the therapeutic armoury for children with motor neurodisability. There is equal need for similar feasibility studies in other areas of neurodisability, for example to explore the potential of collaborative play when using the Xbox Kinect adventure games to improve social skills in children with Autistic Spectrum Disorder.

The issue of individual variation – discussed in section 2 – results in a wide spread of scores which could be due to co-morbidity or wide gradation across a developmental disorder. One solution for evaluation is through multiple case studies analysis, thereby highlighting individual variation but isolating the impact on personal health (e.g. Green and Wilson, 2011). For example during a study week where we assessed the potential benefits of the Xbox Kinect for upper limb function, one patient struggled following instructions due to his additional learning needs, and Attention Deficit Disorder. For example, whilst playing virtual bowling the child struggled to comprehend where the bowling ball went in space when the ball was virtually 'picked up'. On other tasks the child understood what to do but the notion of a 'virtual' ball was tricky to comprehend. Interestingly when the child was playing bowling on the Wii, demanding he hold and move the controller, it was much easier for him to grasp and use the ball with more proprioceptive feedback. His results therefore were not complete for the Xbox, but the outcome was useful in terms of what he was capable of doing. Another child with Cerebral Palsy and Autism, with oppositional defiant disorder, in the Wii Fit study, struggled to even get through any of the measurements with the physiotherapist. For the physiotherapist to be able to take any measurements a large amount of adaptation was used such as integrating other games into the session to ease the pressure on taking measurements. The child's parent eventually dropped out of that study due to stress when coming to clinic for measurements. Again, this child presented without results at the end of the 12-week Wii fit study, but there was a result in terms of study feasibility, in relation to age group, and the impact of co-morbid developmental disorders on the child's ability to adhere to measurement and study protocol.

7. CONCLUSIONS

We used a PICO (population, intervention, comparison, outcome) approach to discuss issues and challenges in virtual reality therapy research in community health settings. Future studies will need to be designed with sufficient power to prove, or disprove the effectiveness of VRT, and allow for children not completing studies, or consider excluding them from the onset if they are unlikely to complete. Therefore unexpected results and outcomes are to be somewhat expected in the process of community research, and are ultimately more naturalistic to how interventions would be employed in day-to-day life. But also, widespread variation exists within and between populations, complicating treatment fidelity and applicability, therefore necessitating care in sufficiently surveying populations with regards to technology before any intervention or experimentation takes place. Whilst traditional research methodologies such as the Gold Standard Double Blind Randomised Placebo Controlled Trial work well for example in studying a new medicine, the nature of Virtual Reality interventions makes this much harder to achieve. It will be important to learn the lessons of feasibility research such as described in this paper to enable studies that truly validate and hopefully justify the use of Virtual Reality Therapies in the future. Importantly, this would increase the evidence base underlying current practice in Paediatric Neurodisability.

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