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Virtual enriched environments in paediatric neuropsychological rehabilitation following traumatic brain injury: Feasibility, benefits and challenges

P. R. PENN[1], F. D. ROSE[1], & D. A. JOHNSON[2]

[1]*School of Psychology, University of East London, Stratford, London, UK and* [2]*Clinical Psychologist, Child Life & Health, University of Edinburgh, Scotland, UK*

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Abstract

A frequent consequence of traumatic brain injury (TBI) is a significant reduction in patients' cerebral activation/arousal, which clinicians agree is not conducive to optimal rehabilitation outcomes. In the context of paediatric rehabilitation, sustained periods of inactivity are particularly undesirable, as contemporary research has increasingly called into question the Kennard principle that youth inherently promotes greater neural plasticity and functional recovery following TBI. Therefore, the onus to create rehabilitation conditions most conducive to harnessing plasticity falls squarely on the shoulders of clinicians. Having noted the efficacy of environmental enrichment in promoting neural plasticity and positive functional outcomes in the animal literature, some researchers have suggested that the emerging technology of Virtual Reality (VR) could provide the means to increase patients' cerebral activation levels via the use of enriched Virtual Environments (VEs). However, 10 years on, this intuitively appealing concept has received almost no attention from researchers and clinicians alike. This paper overviews recent research on the benefits of enriched environments in the injured brain and identifies the potential and challenges associated with implementing VR-based enrichment in paediatric neuropsychological rehabilitation.

Keywords: *Environmental enrichment, virtual reality, paediatric neuropsychological rehabilitation*

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Introduction

TBI has been acknowledged as the most common cause of death and disability in childhood [1]. The reported incidence of TBI in children varies between 1–300 per 100 000 of the population [2]. Establishing more precise figures is problematical owing to differences in the definition of TBI and the age ranges included in estimates. Hawley et al. [1] conducted a 10-year population-based study of children 0–15 years admitted to a UK hospital for a period of more than 24 hours with a TBI and arrived at an overall figure of 280 children per 100 000 of the UK population.

Uncertainty about the prevalence of brain injury in childhood is matched by uncertainty concerning the effect of age on recovery from TBI. Kennard [3] demonstrated superior initial recovery in neonate monkeys over adult monkeys following surgically-induced lesions to the motor and pre-motor cortex. This research is commonly cited as the watershed study informing the viewpoint that 'younger is better' in the recovery from brain injury. Proponents of the 'Kennard principle', as it became known, suggested that the developing nervous system has a greater capacity for plasticity than the fully developed nervous system. This principle received support from a number of lines of evidence, for example, studies of children who had undergone neurosurgery to relieve intractable epilepsy [4] in addition to a selection of clinical studies [5].

The Kennard principle remains a pervasive influence in the prognosis of medical practitioners [6], is a commonly held view by many lawyers dealing with cases of children with TBI and often influences the determination of the level of financial compensation [7]. However, research over the last two decades has increasingly failed to support the Kennard principle and, in many instances, indicated that brain injury in early life can be more damaging; increasing vulnerability to residual cognitive and

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Correspondence: P. R. Penn, School of Psychology, University of East London, Romford Road, Stratford, London, UK. Tel: +44 (0) 20 8223 4424. Fax: 44 (0) 20 8223 4937. E-mail: p.r.penn@uel.ac.uk

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functional deficits in both animals [8] and humans [9]. Developmental neuropsychologists argue that a prognosis based on the age of a child at the time of injury is too simplistic and does not take account of factors such as: cognitive development at the time of the injury; functional development of the site of the injury; and developmental milestones yet to be achieved. The interested reader is directed to Gil [10] for a comprehensive account of the shift from the Kennard principle to a developmental perspective. The implications of this shift for clinicians has been succinctly summarized by Anderson et al. [9]:

> Contrary to traditional views, young children who sustain severe TBI in early childhood or moderate or severe TBI in infancy may be particularly vulnerable to significant residual cognitive impairment. From a clinical perspective, results indicate that long-term follow-up monitoring and management should be targeted to this high-risk group (p. 1374).

Put simply, if youth alone cannot be relied upon as an aid to plasticity, then it is imperative that clinicians devise innovative and effective interventions that will promote optimal recovery from TBI in childhood. One such possible intervention involves the utilization of VR technology.

The use of VR in neuropsychological rehabilitation has been advocated on many occasions over the last decade [11, 12]. VR has been usefully defined as:

> An advanced form of human–computer interface that allows the user to interact with, and become immersed, in a computer-generated environment in a naturalistic fashion ([11], p. 299).

A decade ago, Rose et al. [13] identified a large body of literature on the positive effects of environmental enrichment on plasticity and functional recovery in the damaged animal brain. They pointed out that VR had the clear potential to provide enriched environments for humans following a brain injury, arguing that it could offset the severe reductions in the quantity and quality of environmental interactions and associated declines in cerebral arousal/activation that often result from hospitalization [14].

The intervening 10 years have been characterized by researchers expending considerable effort in identifying the characteristics or 'assets' of VR that make it particularly amenable to neuropsychological assessment and rehabilitation [11]. However, the use of virtual enriched environments has received no serious attention from researchers, despite an acceleration in the number of articles published on enrichment since 1999 [15]. The research community appears to have overlooked what might be VR's greatest asset for neuropsychological rehabilitation. This paper overviews contemporary research on the effects of environmental enrichment and examines the amenability of VR to generate enriched environments. The challenges facing the use of VR based enrichment for use in paediatric neuropsychological rehabilitation are then considered.

VR and neuropsychological rehabilitation

The last decade has been an enormously exciting time for neuropsychological VR applications. Research in the late 1990s began tentatively with attempts to establish whether the effects of interaction with real and virtual environments were functionally equivalent at a neuropsychological level, using evidence gained from brain imaging technology [16, 17]; electrophysiological studies [18] and transfer of training paradigms [19]. Research has now evolved to a point where VR is regarded as an invaluable tool in examining the neural correlates of everyday cognition in the injured and intact brain. Indeed, a variety of studies have used VR in conjunction with brain imaging technology to investigate topics as diverse as: spatial memory [20, 21]; postural responses to visual field motion [22]; VR-induced analgesia [23]; and cue-induced smoking craving [24]. Moreover, the combination of VR and fMRI generates the exciting possibility of monitoring the effects of exposure to rehabilitation in virtual environments on the injured brain [25, 26].

Research involving comparisons between virtual and real world based interventions and benchmarking the effectiveness of VR interventions in the real world has progressed significantly over the last 10 years. Some recent examples of domains of neuropsychological assessment and rehabilitation that have utilized VR are listed in Table I.

Yen and Wong [27] pointed out that rigorous research involving children and adolescents with TBI is still relatively scarce. The same is true to an even greater extent in VR-based research: applications of VR to paediatric neuropsychological rehabilitation have yet to address TBI. However, promising VR interventions have been reported for children

Table I. Domains of application of VR within neuropsychological assessment and rehabilitation.

Application of VR	References
Attention	[30, 67]
Visual neglect	[68, 69]
Memory	[70–72]
Spatial navigation	[73, 74]
Executive functioning	[75, 76]
Motor skills	[77, 78]
Instrumental activities of daily living (IADLs)	[79]

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with brain damage of a genetic, developmental or teratogenic origin. A full review of this research is beyond the scope of this paper. However, some contemporary examples are listed in Table II.

Research involving VR and paediatric populations to date has indicated that the characteristics of VR that have empowered research in impaired adult populations have equal, if not greater, utility in the brain-injured child. For example, VEs can be orientated to provide gaming elements to increase patient motivation and compliance. Padgett et al. [28] reported positive results when using a VR game to teach children with Foetal Alcohol Syndrome (FAS) fire safety skills. Research has also pointed to VR's capacity to ameliorate children's experience of aversive stimuli and reduce anxiety levels [29]. The degree of stimulus control and sensitivity of monitoring afforded by VR is also a significant advantage when examining subtle behaviours, such as head movements in children with ADHD [30].

However, despite the valuable contributions made by the above research, a more fundamental problem with conventional neuropsychological rehabilitation remains unresolved. Following a brain injury, patients experience significant reductions in cerebral activation/arousal. De Wit et al. [14] reviewed the amount of time spent by stroke patients in formal therapy across four rehabilitation centres within Europe and concluded:

> Patients spent a large amount of the day in their rooms, inactive, and without any interaction (p. 1983).

The UK fared particularly badly, with patients spending, on average, only 1 hour per day in rehabilitation and, despite an open access environment, less than 11 minutes per day interacting with other patients. This is broadly in line with earlier European research [31–33]. The resultant lack of cerebral arousal/activation is far from a trivial issue: Grealy and Heffernan [34] commented that many patients with a brain injury have levels of cerebral activation so low that their ability to concentrate is impaired and their threshold for fatigue is diminished. Low levels of cerebral activation have also been associated with impaired allocation of attentional resources, which Schmitter-Edgecombe [35] suggested may be a principle cause of cognitive deficits following a brain injury. Grealy and Heffernan [34] argue that:

> Improving levels of cerebral activation is likely to be fundamental challenge in any rehabilitation programme (p. 43).

Their argument resonates with that of Von Steinbuchel and Poppel [36], who identified four domains of rehabilitation: restitution, substitution, activation and integration. In respect of the activation domain, Steinbuchel and Poppel pointed to the deleterious effects of low levels of activation on motivation, fatigue and mental processing speed. They went on to suggest that appropriate levels of cerebral activation are likely to be a prerequisite of successful therapeutic interventions. Both Grealy and Heffernan [34] and Von Steinbuchel and Poppel [36] identify environmental enrichment as a means of improving levels of activation.

Table II. Examples of research involving VR in paediatric neuropsychological rehabilitation.

Application of VR	References
Autism	[80, 81]
Cerebral Palsy	[25, 82]
Downs Syndrome	[83]
FAS	[28]

Environmental enrichment: Effects on the intact and injured brain

At this point, it is prudent to define what is meant by the term 'environmental enrichment' within the scope of this paper. The research of Hebb [37] is often cited as the genesis of contemporary work on environmental enrichment. Will et al. [38] adapted the definition provided by Hebb, describing environmental enrichment as:

> Environmental conditions (EC) which, in comparison to standard housing conditions (SC), provide enhanced possibilities of physical and social stimulation and/or interaction (p. 168).

The majority of the enrichment research has been conducted on laboratory rats; this is reflected in the focus of the studies reviewed here. Furthermore, with a few exceptions for works of historical significance, the following will focus exclusively on research conducted after the publication of Rose et al. [13], i.e. in the last decade.

The research of Rosenzweig et al. [39] is frequently credited as the template for the environmental enrichment conditions that have been adopted in subsequent research involving rats. Typically, enriched environments will consist of a group of rats occupying large containers featuring items that provide multi-sensory stimulation, e.g. blocks of wood, plastic tubes, table tennis balls, tin cans and so forth. Furthermore, the experimenter will often manipulate the presence and position of such stimuli according to a pre-determined agenda. In contrast, standard housing conditions usually involve a smaller group of rats being kept in smaller cages without such items. Impoverished conditions generally involve rats being housed individually in

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even smaller cages that also feature no stimulating items. There is, however, no generally adopted standardized protocol for enriched, standard and impoverished housing conditions, nor general agreement as to what environmental enrichment protocol is most conducive with enhancing brain function and promoting recovery from injury. However, some authors have offered guidelines [40].

The debate concerning what constitutes an enriched environment was precipitated by research indicating that rats housed in standard laboratory conditions sometimes exhibited abnormal behaviours [41, 42]. This led some researchers to question whether standard housing conditions were not, in point of fact, more akin to conditions of environmental impoverishment. Obviously, were this to be the case, it would render comparisons of animals kept in such conditions with animals kept in enriched conditions problematical. Würbel and Garner [43] have argued for the distinction between:

> Enrichment as an experimental variable (meaning adding inanimate and/or social stimuli to the environment) and beneficial enrichment for cases where enrichment results in improved animal welfare. This distinction is also relevant with respect to the effects of environmental enrichment on the validity of animal experiments. It is clear that a putative enrichment that induces chronic stress is not only detrimental to animal welfare, but also to the validity of experiments with these animals (p. 4).

Wolfer et al. [44] conducted a study to examine whether beneficial enrichment could be performed without a deleterious effect on the standardization of enrichment protocols. They found that it produced neither significant variation in behavioural test measures over the 6-week period that the enrichment was implemented, nor increased the risk of conflicting results obtained from three replicate studies from three different laboratories.

A further issue is that the concept of enrichment is a composite of a number of elements, e.g. increased exercise, sensory stimulation, learning/training and social interaction. Relatively few studies have attempted to elucidate the importance of each of these components [45,46]. Broadly speaking, the results of such investigations, whilst highlighting the importance of learning, i.e. cognitive engagement with the environment, have pointed to no one single component being sufficient, but rather that:

> The specific efficacy of EC, as compared to exercise or training, may be induced not only by an additive effect of its components, but also by the interaction of their effects ([38], p. 177).

Putting the above conceptual and methodological issues aside for a moment, what is clear is that from its commencement in the 1960s [47, 48] research has consistently demonstrated marked beneficial effects of environmental enrichment on the intact cerebral cortex. Some examples of contemporary research are provided in Table III.

During the last four decades, a large body of research has also pointed to the increasing generality of the effectiveness of environmental enrichment in ameliorating the impairments associated with a diverse range of different types of CNS injury. Some examples of contemporary work are provided in Table IV.

There is, therefore, copious evidence for the potential benefits of environmental enrichment. Indeed, commenting on the rehabilitation of brain damage in human populations, Will et al. [38] state that environmental enrichment is increasingly looking like 'a potential therapeutic tool of high efficacy and low risk' (p. 177).

Unfortunately, creating enriched enrichments for humans in a clinical setting is highly problematic

Table III. Selection of research concerning the effect of environmental enrichment at neurological and behavioural levels.

Effect of enrichment	References
Neurological	
Volume and length of dendritic spines	[84, 85]
Synaptic strength, including long-term potentiation	[86]
Neurogenesis	[87, 88]
Neurotrophin levels, e.g. NGF, BDNF and NT-3	[89]
Modulation of the expression of glutamate receptors and transporters, e.g. the AMPA receptors and EAAC1 transporter	[90, 91]
Behavioural	
Learning and memory	[84, 92–94]
Exploratory activity	[95, 96]
Socio-positive and play behaviour	[97]
Emotional behaviour and anxiety levels	[54]

Table IV. Research concerning the effect of environmental enrichment on the recovery from different types on CNS damage*.

Type of CNS damage	References
Brain damage of genetic/developmental origin	
Fragile X Syndrome	[98]
Huntingtons disease	[99, 100]
Focal/global ischemia	[57, 101]
Degenerative disease	
Alzheimer's disease	[45]
Parkinson's disease	[102, 103]
Pharmacological or teratogenic origin	[104, 105]
Spinal cord contusion	[106]

*In summarizing research indicative of the generality of environmental enrichment, the author classifies research by distinguishing between different types of CNS damage, based on the useful taxonomy of provided by Will et al. [38], but with emphasis on animal models of CNS disorders of particular concern to humans.

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owing to practical constraints such as clinician time, budgetary limitations and safety concerns. This is where VR could make a very significant contribution. In effect, if practical concerns mean that clinicians cannot provide an environment conducive with increased cerebral arousal/activation in the real world, VR technology could provide such an environment in the virtual world.

The initial challenge in devising enriched virtual environments for humans is elucidating relevant conceptual, methodological and practical issues from the animal literature. Essentially researchers need to ask: 'what principles of enrichment can be extracted from the animal literature and what are their implications for enrichment research in humans?'

Principles of enrichment and the assets of VR

Using the animal based literature, Kleim and Jones [49] outlined 10 principles that mediate the effectiveness of experience-induced plasticity. They then pointed to their implications for research involving humans. Using these principles, the current authors now elaborate on the practical issues associated with providing enriched environments in the real world and indicate how the assets of VR can overcome these problems. This information is summarized in Table V.

Enriched virtual environments: From principle to practice, challenges and research priorities

Table V indicates that VR is amenable to addressing the principles of enrichment-induced plasticity and clearly has the potential to produce enriched environments. However, research is needed to translate the potential into progress. In proposing such research, it is necessary to take account of the outcomes and conceptual/methodological issues that have emerged from both the environmental enrichment and VR literature. This information must inform the design, implementation and subsequent assessment of enriched virtual environments. The review of the literature thus far poses a number of challenges and suggests several priorities for enriched virtual environment research for both adult and paediatric populations.

First and foremost, there is the issue of what constitutes an enriched environment. Nithianantharajah and Hannan [50] point out that the features that identify an enriched environment in animal research have little to do with the richness of human environments. However, any meaningful research rests on the specification of parameters that differentiate an enriched environment from a standard rehabilitation environment. Such a specification, at this point in time, does not appear to be forthcoming; understandable perhaps, given that the animal literature has yet to reach an agreed definition or standardized specification for conditions of enrichment.

In identifying what might constitute an enriched environment for use with humans, it is appropriate to start by reiterating the nature of the reductions in environmental interaction that are likely to be experienced by a patient undergoing brain injury rehabilitation. Research suggests that patients often endure long periods of inactivity sitting in their beds or being asleep [14]. Indeed, it has been suggested that there may be parallels between such periods and conditions of environmental impoverishment in rodent research [13], i.e. a small immediate environment, lack of physical exercise, social interaction and stimulus conducive with multi-sensory engagement. As such, perhaps it is not stretching credulity too far to suggest that the factors that distinguish enriched and standard environments in rodents also constitute appropriate initial parameters for the manipulation of enrichment in humans. The significance of these factors within brain injury rehabilitation is not based on speculation. For example, research has pointed to the importance of: physical exercise and the utility of VR in this respect [51, 52]; social interaction [53]; and multi-sensory information on the recovery of both motor and cognitive functions [54, 55] in addition to cerebral reorganization [56]. As noted in Table V, the characteristics of VR are amenable to extensive manipulation of ecologically valid environments, can utilize several sensory modalities, provide automated rudimentary social interaction or provide a forum for real time social interaction (e.g. Second life) and exercise strict control over stimulus presentation. However, the manner in which these parameters are implemented will obviously require considerable thought from clinicians. It is, of course, likely that the specification of an enriched environment will be affected by the patients age; salience is a factor that mediates enrichment-induced plasticity—what is salient for adult populations may not be at all salient for paediatric populations. Additional specification changes may be required for different types of injury in order to accommodate different levels of motor function, for example.

In considering the specification of a virtual enriched environment, it may be useful to turn to the work of investigators who have already examined the effect of VR-based rehabilitation programmes on individuals with brain damage. You et al. [25] utilized an IREX VR system, consisting of a video

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Table V. Principles of enrichment with potential contributions of VR.

Principle of enrichment induced plasticity [49]	Examples of the problems associated with addressing the principle in the real world	The potential contribution of VR
Use It or Lose It—Failure to drive specific brain functions can lead to functional degradation [107]	Patients often spend a large part of their days in rehabilitation, 'in their rooms, inactive, and without any interaction' ([14], p. 1983).	VR has the capacity to simulate practically any real world environment, from entire cities [108] right down to a home environment [72]. It significantly reduces or completely negates many real world practical concerns.
Use It and Improve It—Training that drives a specific brain function can lead to an enhancement of that function [50]	Constraints on clinician time, budgetary limitations and safety concerns all contribute.	
Specificity—The nature of the training experience dictates the nature of the plasticity, e.g. self-taught compensatory strategies [109]	Not all self-taught compensatory behaviours are helpful, some may undermine the efficacy of rehabilitation efforts [110,111].	The control afforded by VR can constrain undesirable strategies, e.g. a patient relying on the use of an unaffected limb and refraining from attempting to regain the function of the affected limb.
Repetition—Induction of plasticity requires sufficient repetition [112]	Intensive repetition is both time and labour intensive for clinicians. Problems with procedural and stimulus consistency/reliability can occur [113] which is disruptive where intensive repetition is a requisite for learning.	Intensive repetition is not labour intensive in VR, as interaction can be automated. VR can precisely deliver stimuli under very controlled conditions without unintentional variations between task repetitions.
Intensity—Induction of plasticity requires sufficient training intensity [114]		
Time—Different forms of plasticity occur at different times during training [115]	Optimal rehabilitation outcomes may require early and protracted enrichment to secure significant and durable gains in functional outcomes [60,116]. Providing such an environment at short notice and for extended periods is problematical for practical reasons.	VR can be used in conjunction with brain scanning technology such as fMRI to facilitate timely assessment of injury and the effects of enrichment on plasticity. VR can also be used to provide tele-rehabilitation [117] which allows rehabilitation to continue after the patient has been discharged.
Salience—The training experience must be sufficiently salient to induce plasticity [118]	The most obvious way to increase saliency is to make rehabilitation activities relevant to the patients' everyday functioning, However, this is problematical for practical reasons.	VR can simulate situations and tasks characteristic of daily living, e.g. food preparation [119] and shopping [120].
Age—Training-induced plasticity occurs more readily in younger brains [121]	Not all research points to enrichment being beneficial to recovery from brain injury in developing nervous systems, e.g. Shieh et al. [58] found increases in neuronal growth were not accompanied by increases in functional connections.	The extensive control and monitoring afforded by VR could be critical in elucidating the relative weighting of the elements of an enriched environment in producing beneficial effects on recovery and the optimal level/intensity of these elements.
Transference—Plasticity in response to one training experience can enhance the acquisition of similar behaviours [122]	TMS can be used in conjunction with rehabilitation techniques to harness transference effects for specific functional gains [107]. However, TMS is not always practical in the rehabilitation of everyday aspects of cognition which are less amenable to being conducted in the same clinical setting as the TMS.	By creating virtual scenarios that reproduce conditions consistent with evoking an aspect of everyday cognition and integrating this with rehabilitation, VR can easily address the problems of using TMS in the rehabilitation of behaviours that would not be amenable to study in the laboratory.
Interference—Plasticity in response to one experience can interfere with the acquisition of other behaviours [107]	The timing of TMS appears to be critical. It can also reduce cortical excitability yielded by training.	The control afforded by VR could potentially make it easier to monitor for interference effects and, in conjunction with brain imaging technology, assist in identifying their neurological mechanism.

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camera and cyber gloves used to track users arm movements in real time and project them on a PC monitor, which also superimposes virtual objects on the display. Arm gestures in the real world are represented as corresponding gestures in the virtual world and such gestures are used to interact with virtual objects. For example, one such virtual environment involved placing the video footage of the user in front of a set of goalposts. Their task was to deflect oncoming footballs by making appropriate gestures with their arms. This method can be used to embellish what would otherwise be boring and repetitive rehabilitation exercises. You et al. found significant improvements in motor function in an 8-year old boy with hemiparetic cerebral palsy and evidence of cerebral reorganization (identified with fMRI) following a period of VR therapy using the above set-up. This type of VR arrangement could potentially be adapted for use as an enriched environment. Furthermore, the advent of commercially available video games hardware such as the motion-based Nintendo Wii system could be exploited to make such set-ups highly accessible and affordable.

A further challenge for virtual enriched environments concerns establishing an appropriate baseline against which their success can be meaningfully evaluated. Two issues are raised in this respect. Würbel and Garner [43] made the distinction between beneficial enrichment (i.e. enrichment that caters to animals' welfare) and enrichment as an experimental variable. They argued that what was commonly regarded as standard environmental conditions could be more accurately described as impoverished conditions, thus undermining the validity of the standard vs. enriched environment comparison. This point is particularly salient in the context of paediatric rehabilitation, since it has been argued that real world-based rehabilitation is often characterized by long periods of inactivity.

In view of the above criticism, the sole use of the conditions of real world rehabilitation as a baseline for the effectiveness of virtual enriched environments is inadvisable. This would likely generate doubts as to whether any observed beneficial effects of virtual enrichment represent more of a reflection on the long periods of inactivity between formal rehabilitation sessions in the real world than the effectiveness of virtual enrichment *per se*. Consequently, in specifying the parameters that characterize virtual enriched environments, it may be wise to adopt the distinction made by Würbel and Garner [43] and deliver a beneficial enrichment condition. This would constitute a standardized baseline level of enrichment and sit alongside a further optimal enrichment condition, in addition to a standard real world rehabilitation condition. This does, however, require clinicians to make further arbitrary judgements about what would differentiate beneficial enrichment from optimal enrichment.

In acknowledging the extent of the uncertainty as to the appropriate/optimal form of virtual enrichment, it should be noted that similar questions are far from resolved with respect to real world-based neuropsychological rehabilitation. In a review of the efficacy of brain injury rehabilitation, Cullen et al. [53] concluded that:

> The key questions that arise from these studies involve the ideal timing and intensity of the services provided and the types of therapy that are delivered (p. 129).

Further to specifying the form of an enriched virtual environment, the review of the animal literature yielded numerous factors that could be instrumental in determining its effectiveness [49]. However, starting to make progress in virtual enrichment research will necessarily involve prioritizing which of these factors merits attention first.

In respect of the use of virtual enriched environments for paediatric rehabilitation, the factor of age is, of course, of greatest intrinsic interest. Surprisingly, the interaction between age and the effectiveness of environmental enrichment on recovery from brain injury has received relatively little attention from researchers. Saucier et al. [57] indicated that enrichment reduced the volume of brain injury following an ischemic insult in young rats, compared to controls. However, research does not always indicate beneficial effects of enrichment following a brain injury in younger populations. Shieh et al. [58] noted that whilst environmental enrichment produced increased dendritic density in the occipital cortex of young rats subjected to a fluid percussion injury, there was no increase in dendritic branching (i.e. functional connections) and no significant behavioural improvement. The authors noted, however, that the percussion injury had damaged NMDA receptors which are implicated in the process of 'pruning' during the CNS development. This finding suggests that the factors that developmental neuropsychologists suggest mediate the relationship between age and brain injury generally (e.g. cognitive development at the time of the injury; functional development of the site of injury, etc.) are likely to also mediate the effectiveness of enrichment. The animal-based research does serve as a caution that the impact of virtual enrichment in humans should be carefully monitored at the neurological level, as well as cognitive/behavioural levels. Happily, the combination of VR and brain scanning technology makes such monitoring possible [25,26].

In terms of prioritizing the other factors that mediate the effectiveness of enrichment,

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the aforementioned quote from Cullen et al. [53] is useful, as the issues of timing and intensity of enrichment were also cited as critical in an evaluation of the lessons learned from the animal based enrichment research by Turkstra et al. [59]. The literature would seem to attest to the importance of a minimal delay in the instigation of enrichment and extended duration of enrichment post-injury [60, 61]. However, the evidence is not always without contradiction [62] and the factor of stimulus intensity can, if taken too far, exacerbate rather than ameliorate an injury [63]. Therefore, it would seem reasonable to argue that these factors are worthy of attention as a matter of priority in paediatric populations.

A further issue in establishing research priorities is determining which types of injury merit attention from research into virtual enrichment first. Turkstra et al. [59] have suggested that the domains of rehabilitation where animal research is not useful, for example those pertaining to language and higher level cognitive impairments, merit attention as a matter of priority. Data concerning the effect of real world-based rehabilitation on recovery from such impairments, with associated changes in patterns of brain activation demonstrated with FMRI, is available [64, 65]. Limited VR-based data is also available [25, 26]. Scrutinizing the methodology employed by existing studies will provide valuable information about the implementation of virtual enrichment and highlight conceptual/practical/methodological issues that may require attention or that may not be immediately apparent at this stage.

The introduction of virtual enrichment does raise some important ethical issues, a full review of which is well beyond the scope of this paper. The interested reader is directed to Behr et al. [66] for an exposition of some issues related to VR and neuropsychological rehabilitation generally. In respect of virtual enrichment, the most important considerations would appear to relate to the principles of beneficence and non-maleficence, i.e. safeguarding the welfare of the patients. For example, a principle benefit of virtual enrichment has been identified as the capacity for patients to engage with a VR system without the need for supervision from clinical staff. Engagement with VR can be as simple as a patient operating a laptop PC at their bedside and, as such, exposes them to very minimal physical risks. Also, as has already been stated, virtual environments can be configured to prevent undesirable behaviours, such as the acquisition of compensatory strategies detrimental to rehabilitation goals. However, clearly, any such system will need to implement a feature whereby a patient can alert the attention of staff should they, for example, begin to find interacting with the VR aversive in any way or if they begin to feel tired or unwell and wish to discontinue the interaction.

Research also needs to be wary of any unintended negative effects of exposure to virtual environments between formal rehabilitation sessions. For example, the authors have already alluded to the fact that stimulus intensity, if taken to far, may exacerbate rather than ameliorate an injury. Behr et al. [66] raise the issue of intensification of experience as a general issue in VR research. They advocate the importance of giving participants control over their exposure to VR environments, especially ones that feature vivid stimuli. Behr et al. also raise another concern with VR environments pertaining to re-entry to the real world after exposure to a virtual environment. As a hypothetical example of this concern, patients might enjoy the VR interactions between formal rehabilitation sessions so much that their compliance with these sessions declines on the basis that they don't find the formal activities as stimulating as those provided in VR.

The above issues will clearly not be resolved overnight and require close collaboration between researchers and clinicians. VR does, at least, make such collaboration easier by neatly side-stepping the issue of external validity. Variations in an enriched environment that might be unintentionally introduced between different locations in the real world would not occur; the VR environment would remain the same, irrespective of where it is utilized. This would be of great benefit to researchers when gathering data on the optimal specification of an enriched virtual environment from different rehabilitation centres, as it minimizes one significant source of confounding variables.

Conclusions

A decade on from Rose et al. [13] the evidence continues to point to the beneficial effects of enrichment on the recovery from brain injury in the animal literature. Meanwhile, data on human brain injury rehabilitation indicates patients spend a large portion of their rehabilitation time with low levels of cerebral activation. In the context of paediatric neuropsychological rehabilitation following a TBI, such extended periods of low cerebral activation are particularly unfortunate, as youth no longer appears to be the inherent facilitator of recovery that it had once seemed to be. The obvious way of negating low levels of cerebral activation/arousal is to increase the quantity and quality of patients' interaction with their immediate environment via environmental enrichment. Unfortunately, an array of significant practical and budgetary constraints makes real world-based environmental enrichment difficult.

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However, there is clear potential to provide enriched virtual environments that are not hampered by such concerns. Over the last decade VR has demonstrated its utility in the neuropsychological rehabilitation of predominantly adult populations. However, such research has failed to capitalize on the potential of VR-based environmental enrichment. The authors hope that this will not also be the case in the field of paediatric brain injury rehabilitation. Fundamental questions about the implementation of enrichment strategies in human brain injury rehabilitation still exist, some of which have been identified in this text. However, the technology and expertise to make virtual environmental enrichment a reality are readily available. The authors firmly believe that the arguments for rigorous empirical investigations into its effectiveness are now too compelling to ignore.

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References

1. Hawley CA, Ward AB, Long J, Owen DW, Magnay AR. Prevalence of traumatic brain injury amongst children admitted to hospital in one health district: A population-based study. Injury 2003;34:256–260.
2. McKinlay A, Grace RC, Horwood LJ, Fergusson DM, Ridder EM, MacFarlane MR. Prevalence of traumatic brain injury among children, adolescents and young adults: Prospective evidence from a birth cohort. Brain Injury 2008;22:175–181.
3. Kennard MA. Relation of age to motor impairment in man and in subhuman primates. Archives of Neurology and Psychiatry 1940;26:377–397.
4. Chugani HC, Shewmon D, Shields W. Surgery for intractable infantile spasms: Neuroimaging perspectives. Epilepsia 1993;34:764–771.
5. Aram D, Enkleman B. Cognitive profiles of children with early onset unilateral lesions. Developmental Neuropsychology 1986;2:155–172.
6. Hart K, Faust D. Prediction of the effects of mild head injury: A message about the Kennard principle. Journal of Clinical Psychology 2006;44:780–782.
7. Johnson DA, Rose FD, Brooks BM, Eyers S. Age and recovery from brain injury: Legal opinions, clinical beliefs and experimental evidence. Journal of Head Trauma Rehabilitation 2003;18:342–356.
8. Yager JY, Wright S, Armstrong EA, Jahraus CM, Saucier DM. The influence of aging on recovery following ischemic brain damage. Behavior and Brain Research 2006;173:171–180.
9. Anderson V, Catroppa C, Morse S, Haritou F, Rosenfeld J. Functional plasticity or vulnerability after early brain injury? Paediatrics 2005;116:1374–1382.
10. Gil AM. Neurocognitive outcomes following pediatric brain injury: A developmental approach. Journal of School Psychology 2003;41:337–353.
11. Rose FD, Brooks BM, Rizzo AA. Virtual reality in brain damage rehabilitation: Review. Cyberpsychology and Behaviour 2005;8:243–251.
12. Rizzo A, Schultheis M, Kerns K, Mateer C. Analysis of assets for virtual reality applications in neuropsychology. Neuropsychological Rehabilitation 2004;14:207–239.
13. Rose FD, Attree EA, Brooks BM, Johnson DA. Virtual environments in brain damage rehabilitation: A rationale from basic neuroscience. In: Riva G, Wiederhold BK, Molinari E, editors. Virtual environments in clinical psychology and neuroscience: Methods and techniques in advanced patient–therapist interaction. Amsterdam: IOS Press; 1998. pp 233–242.
14. De Wit L, Putman K, Dejaeger E, Baert I, Berman P, Bogaerts K, Brinkmann N, Connell L, Feys H, Jenni W, et al. Use of time by stroke patients: A comparison of four European rehabilitation centers. Journal of the American Heart Association 2005. Available online at: http://stroke.ahajournals.org/cgi/content/full/36/9/1977, Accessed on 23 January 2009.
15. de Azevedo C, Cipreste CF, Young R. Environmental enrichment: A GAP analysis. Applied Animal Behaviour Science 2007;102:329–343.
16. Aguirre GK, Detre JA, Alsop DC, D'Esposito M. The parahippocampus subserves topographical learning in man. Cerebral Cortex 1996;6:823–829.
17. Maguire EA, Frith CD, Burhess N, Donnett JG, O'Keefe J. Knowing where things are: Parahippocampal involvement in encoding object locations in virtual large scale space. Journal of Cognitive Science 1998;10:61–76.
18. Pugnetti L, Mendozzi L, Motta A, Cattaneo A, Barbieri E, Brancotti A. Evaluation and retraining of adults' cognitive impairments: Which role for virtual reality technology? Computers in Biology and Medicine 1995;25:213–227.
19. Rose FD, Attree EA, Brooks BM, Parslow DM, Penn PR, Ambihaipahan N. Training in virtual environments: Transfer to real world and equivalence to real task training. Ergonomics 2001;43(4):495–511.
20. Shipman SL, Astur RS. Factors affecting the hippocampal BOLD response during spatial memory. Behavior and Brain Research 2008;187:433–441.
21. Parslow DM, Rose FD, Brooks BM, Fleminger S, Gray JA, Giampietro V, Brammer MJ, Williams S, Gasston D, Andrew C, et al. Allocentric spatial memory activation of the hippocampal formation measured using MRI. Neuropsychology 2004;18:450–461.
22. Slobounov S, Hallett M, Wu T, Shibasaki H, Newell K. Neural underpinning of postural responses to visual field motion. Biological Psychology 2006;72:188–197.
23. Hoffman HG, Richards TL, Bills AR, Van Oostrom T, Magula J, Seibel EJ, Sharar SR. Using fMRI to study the neural correlates of virtual reality analgesia. CNS Spectrums: The International Journal of Neuropsychiatric Medicine 2006;11:45–50.
24. Lee J-H, Lim Y, Wiederhold BK. A functional magnetic resonance imaging (fMRI) study of cue-induced smoking craving in virtual environments. Applied Psychophysiology and Biofeedback 2005;30:195–204.
25. You SH, Jang SH, Kim Y-H, Kwon YH, Barrow I, Hallett M. Cortical reorganization induced by virtual reality therapy in a child with hemiparetic cerebral palsy. Developmental Medicine & Child Neurology 2005;47:628–635.
26. Jang S, You S, Hallett M, Cho Y, Park C, Cho S, Lee H, Kim T. Cortical reorganization and associated functional motor recovery after virtual reality in patients with chronic stroke: An experimenter-blind preliminary study. Archives of Physical Medicine and Rehabilitation 2005;86:2218–2223.
27. Yen H-L, Wong J. Rehabilitation for traumatic brain injury in children and adolescents. Rehabilitation Medicine 2007;36:62–66.

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28. Padgett LS, Strickland D, Coles CD. Case study: Using a virtual reality computer game to teach fire safety skills to children diagnosed with foetal alcohol syndrome. Journal of Paediatric Psychology 2006;31:65–70.
29. Gold JI, Kim SH, Kant AJ. Effectiveness of virtual reality for pediatric pain distraction during IV placement. Special issue: Virtual and physical toys: Open-ended features for non-formal learning. CyberPsychology & Behavior 2006; 9:207–212.
30. Parsons TD, Bowerly T, Buckwalter JG, Rizzo A. A controlled clinical comparison of attention performance in children with ADHD in a virtual reality classroom compared to standard neuropsychological methods. Child Neuropsychology 2007;13:363–381.
31. De Weerdt W, Selz B, Nuyens G, Staes F, Swinnen D, Van de Winckel A. Time use of stroke patients in an intensive rehabilitation unit: A comparison between a Belgian and a Swiss setting. Disability and Rehabilitation 2000;22: 181–186.
32. Newall JT, Wood VA, Hewer RL, Tinson DJ. Development of a neurological rehabilitation environment: An observational study. Clinical Rehabilitation 1997;11:146–155.
33. Lincoln NB, Willis D, Philips SA, Juby LC, Berman P. Comparison of rehabilitation practice on hospital wards for stroke patients. Stroke 1997;28:543–549.
34. Grealy MA, Heffernan D. The rehabilitation of brain injured children: The case for including physical exercise and virtual reality. Developmental Neurorehabilitation 2001;4:41–49.
35. Schmitter-Edgecombe M. Effects of traumatic brain injury on cognitive performance: An attentional resource hypothesis in search of data. Journal of Head Trauma Rehabilitation 1996;11:17–30.
36. Von Steinbuchel N, Poppel E. Domains of rehabilitation a theoretical perspective. Behavioural Brain Research 1993;56:1–10.
37. Hebb DO. The effects of early experience on problem-solving at maturity. American Psychology 1947;2:306–307.
38. Will B, Galani R, Kelche C, Rosenzweig MR. Recovery from brain injury in animals: Relative efficacy of environmental enrichment, physical exercise or formal training (1990–2002). Progress in Neurobiology 2004;72:167–182.
39. Rosenzweig MR, Krech D, Bennett EL. Heredity, environment, brain biochemistry, and learning. In: Dennis W. Current trends in psychological theory. Pittsburgh: University of Pittsburgh Press; 1961. pp 87–110.
40. Tarou LR, Bashaw MJ. Maximizing the effectiveness of environmental enrichment: Suggestions from the experimental analysis of behaviour. Applied Animal Behaviour Science 2006;102:189–204.
41. Würbel H. Ideal homes? Housing effects on rodent brain and behaviour. Trends in Neuroscience 2001;24:207–211.
42. Garner JP. Stereotypes and other abnormal repetitive behaviours: Potential impact on validity, reliability, and replicability of scientific outcomes. ILAR Journal 2005; 46:106–117.
43. Würbel H, Garner JP. Refinement of rodent research through environmental enrichment and systematic randomization. National Centre for the Replacement, Refinement and Reduction of Animals in Research (NC3Rs) report; 2007. Available on-line at: www.nc3rs.org.uk, accessed February 2008.
44. Wolfer DP, Litvin O, Morf S, Nitsch RM, Lipp HP, Würbel H. Laboratory animal welfare: Cage enrichment and mouse behaviour. Nature 2004;432:821–822.
45. Cracchiolo JR, Mori T, Nazian SJ, Tan J, Potter H, Arendash GW. Enhanced cognitive activity—over and above social or physical activity—is required to protect Alzheimer's mice against cognitive impairment, reduce A β deposition, and increase synaptic immunoreactivity. Neurobiology of Learning and Memory 2007;88:277–294.
46. Dahlqvist P, Rönnbäck A, Risedal A, Nergardh R, Johansson IM, Seckl JR, Johansson BB, Olsson T. Effects of postischemic environment on transcription factor and serotonin receptor expression after permanent focal cortical ischemia in rats. Neuroscience 2003;119:643–652.
47. Diamond MC, Law F, Rhodes H, Lindner B, Rosenzweig MR, Krech D. Increases in cortical depth and glia numbers in rats subjected to enriched environment. Journal of Computational Neurology 1966;128:117–126.
48. Diamond MC, Lindner B, Raymond A. Extensive cortical depth measurements and neuron size increases in the cortex of environmentally enriched rats. Journal of Computational Neurology 1967;131:357–364.
49. Kleim JA, Jones TA. Principles of experience-dependent neural plasticity: Implications for rehabilitation after brain damage. Journal of Speech, Language & Hearing Research 2008;51:225–239.
50. Nithianantharajah J, Hannan AJ. Enriched environments, experience-dependent plasticity and disorders of the nervous system. Nature Reviews Neuroscience 2006; 7:697–709.
51. Mossberg K, Ayala D, Baker T, Heard J, Masel B. Aerobic capacity after traumatic brain injury: Comparison with a non-disabled cohort. Archives of Physical Medicine and Rehabilitation 2007;88:315–320.
52. Thornton M, Marshall S, McComas J, Finestone H, McCormick A, Sveistrup H. Benefits of activity and virtual reality based balance exercise programmes for adults with traumatic brain injury: Perceptions of participants and their caregivers. Brain Injury 2005;19:989–1000.
53. Cullen N, Chundamala J, Bayley M, Jutai J. The efficacy of acquired brain injury rehabilitation. Brain Injury 2007; 21:113–132.
54. Zhu SW, Yee BK, Nyffeler M, Winblad B, Feldon J, Mohammed AH. Influence of differential housing on emotional behaviour and neurotrophin levels in mice. Behavioral Brain Research 2006;169:10–20.
55. Lippert-Grüner M, Maegele M, Pokorný J, Angelov DN, Švestková O, Wittner M, Trojan S. Early rehabilitation model shows positive effects on neural degeneration and recovery from neuromotor deficits following traumatic brain injury. Physiology Research 2007;56:359–368.
56. Johansson BB. Functional and cellular effects of environmental enrichment after experimental brain infarcts. Research in Neurology and Neuroscience 2004;22:163–174.
57. Saucier DM, Yager JY, Armstrong EA, Keller A, Shultz S. Enriched environment and the effect of age on ischemic brain damage. Brain Research 2007;1170:31–38.
58. Shieh EY, Giza CG, Griesbach GS, Hovda DA. Lateral fluid percussion injury followed by rearing in enriched environment increases cortical dendritic density. Journal of Neurotrauma 2000;17 986.
59. Turkstra L, Holland A, Bays G. The neuroscience of recovery and rehabilitation: What have we learned from animal research? Archives of Physical Medicine and Rehabilitation 2003;84:604–612.
60. Amaral OB, Vargas RS, Hansel G, Izquierdo I, Souza DO. Duration of environmental enrichment influences the magnitude and persistence of its behavioural effects on mice. Physiology & Behavior 2008;93:388–394.
61. Kline S, Malena R, Olsen A, Zafonte R, Sozda C. Early versus delayed environmental enrichment differentially affects functional recovery after experimental traumatic brain injury. Archives of Physical Medicine and Rehabilitation 2006;87 2.

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62. DeBow SB, McKenna JE, Kolb B, Colbourne F. Immediate constraint-induced movement therapy causes local hyperthermia that exacerbates cerebral cortical injury in rats. Canadian Journal of Physiology and Pharmacology 2004; 82:231–237.
63. Humm JL, Kozlowski DA, Bland ST, James DC, Schallert T. Use-dependent exaggeration of brain injury: Is glutamate involved? Experimental Neurology 1999;157:349–358.
64. Meinzer M, Obleser J, Flaisch T, Eulitz C, Rockstroh B. Recovery from aphasia as a function of language therapy in an early bilingual patient demonstrated by fMRI. Neuropsychologia 2007;45:1247–1256.
65. Laatsch L, Krisky C. Changes in fMRI activation following rehabilitation of reading and visual processing deficits in subjects with traumatic brain injury. Brain Injury 2006;20:1367–1375.
66. Behr KM, Nosper A, Klimmt C, Hartmann T. Some practical considerations of ethical issues in VR research. Presence Teleoperators and Virtual Environments 2005; 14:668–676.
67. Rizzo AA, Klimchuk D, Mitura R, Bowerly T, Shahabi C, Buckwalter JG. Diagnosing attention disorders in a virtual classroom. IEEE Computer 2004;37:87–89.
68. Broeren J, Samuelsson H, Stibrant-Sunnerhagen K. Neglect assessment as an application of virtual reality. Acta Neurologica Scandinavica 2007;116:157–163.
69. Glover S, Castiello U. Recovering space in unilateral neglect: A neurological dissociation revealed by virtual reality. Journal of Cognitive Neuroscience 2006;18:833–843.
70. Matheis RJ, Schultheis MT, Tiersky LA. Is learning and memory different in a virtual environment? Clinical Neuropsychologist 2007;21:146–161.
71. Penn PR, Rose FD, Brooks BM. Virtual reality in everyday memory assessment and rehabilitation: Progress to date and future potential. In: Wiederhold BK, Riva G, Bullinger AH, editors. Annual review of cybertherapy and telemedicine. 2005;3:31–38.
72. Brooks BM, Rose FD, Potter J, Jayawardena S, Morling A. Assessing stroke patients' prospective memory using virtual reality. Brain Injury 2004;18:391–401.
73. Livingstone SA, Skelton RW. Virtual environment navigation tasks and the assessment of cognitive deficits in individuals with brain injury. Behavioural Brain Research 2007;185:21–31.
74. Gramann K, Müller HJ, Eick E-M. Evidence of separable spatial representations in a virtual navigation task. Journal of Experimental Psychology: Human Perception and Performance 2005;31:1199–1223.
75. Penn PR, Rose FD, Johnson DA. The use of virtual reality in the assessment and rehabilitation of executive dysfunction. In: Oddy M, Worthington AW, editors. Brain injury and executive dysfunction. Oxford: Oxford University Press; 2008. pp 255–283.
76. Titov N, Knight RG. A computer-based procedure for assessing functional cognitive skills in patients with neurological injuries: The virtual street. Brain Injury 2005; 19:315–322.
77. Henderson A, Korner-Bitensky N, Levin M, Roth EJ. Virtual reality in stroke rehabilitation: A systematic review of its effectiveness for upper limb motor recovery. Topics in Stroke Rehabilitation 2007;14:52–61.
78. Holden MK. Virtual environments for motor rehabilitation: Review. Special issue: Use of virtual environments in training and rehabilitation: International perspectives. CyberPsychology & Behaviour 2005;8:187–211.
79. Lee J-H, Ku J, Cho W. A virtual reality system for the assessment and rehabilitation of the activities of daily living. CyberPsychology & Behaviour 2003;6:383–388.
80. Herrera G, Alcantud F, Jordan R, Blanquer A, Labajo G, De Pablo C. Development of symbolic play through the use of virtual reality tools in children with autistic spectrum disorders: Two case studies. Preview Autism: The International Journal of Research & Practice 2008; 12:143–157.
81. Jung K-E, Lee H-J, Lee Y-S, Lee J-H. Efficacy of sensory integration treatment based on virtual reality—tangible interaction for children with autism. Annual Review of CyberTherapy and Telemedicine 2006;4:45–49.
82. Bryanton C, Bossé J, Brien M. Feasibility, motivation, and selective motor control: Virtual reality compared to conventional home exercise in children with cerebral palsy. CyberPsychology & Behavior 2006;9:123–128.
83. Hovorka RM, Virji-Babul N. A preliminary investigation into the efficacy of virtual reality as a tool for rehabilitation for children with Down syndrome. International Journal on Disability and Human Development 2006;5:351–355.
84. Leggio MG, Mandolesi L, Federico F, Spirito F, Ricci B, Gelfo F, Petrosini L. Environmental enrichment promotes improved spatial abilities and enhanced dendritic growth in the rat. Behavioural Brain Research 2005;163:78–90.
85. Faherty CJ, Kerley D, Smeyne RJ. A Golgi-Cox morphological analysis of neuronal changes induced by environmental enrichment. Developmental Brain Research 2003;141:55–61.
86. Duffy SN, Craddock KJ, Abel T, Nguyen PV. Environmental enrichment modifies the PKA-dependence of hippocampal LTP and improves hippocampus-dependent memory. Learning and Memory 2001;8:26–34.
87. Kempermann G, Gast D, Gage FH. Neuroplasticity in old age: Sustained fivefold induction of hippocampal neurogenesis by long-term environmental enrichment. Annals of Neurology 2002;52:135–143.
88. Bruel-Jungerman E, Laroche S, Rampon C. New neurons in the dentate gyrus are involved in the expression of enhanced long-term memory following environmental enrichment. European Journal of Neuroscience 2005;21:513–521.
89. Ickes BR, Pham TM, Sanders LA, Albeck DS, Mohammed AH, Granholm A-C. Long-term environmental enrichment leads to regional increases in neurotrophin levels in rat brain. Experimental Neurology 2000;164: 45–52.
90. Naka F, Narita N, Okado N, Narita M. Modification of AMPA receptor properties following environmental enrichment. Brain Development 2005;27:275–278.
91. Andin J, Hallbeck M, Mohammed AH, Marcusson J. Influence of environmental enrichment on steady-state mRNA levels for EAAC1, AMPA1 and NMDA2A receptor subunits in rat hippocampus. Brain Research 2007; 1174:18–27.
92. Rampon C, Tang Y-P, Goodhouse J, Shimizu E, Kyin M, Tsien JZ. Enrichment induces structural changes and recovery from nonspatial memory deficits in CA1 NMDAR1-knockout mice. Nature Neuroscience 2000; 3:238–244.
93. Tang YP, Wang H, Feng R, Kyin M, Tsien JZ. Differential effects of enrichment on learning and memory function in NR2B transgenic mice. Neuropharmacology 2001;41: 779–790.
94. Bennett JC, McRae PA, Levy LJ, Frick KM. Long-term continuous, but not daily, environmental enrichment reduces spatial memory decline in aged male mice. Neurobiology of Learning and Memory 2006;85:139–152.
95. Zimmermann A, Stauffacher M, Langhans W, Wurbel H. Enrichment dependent differences in novelty exploration in rats can be explained by habituation. Behavioural Brain Research 2001;121:11–20.

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96. Elliott BM, Grunberg NE. Effects of social and physical enrichment on open field activity differ in male and female Sprague–Dawley rats. Behavioural Brain Research 2005;165:187–196.
97. Marashi V, Barnekow A, Ossendorf E, Sachser N. Effects of different forms of environmental enrichment on behavioral, endocrinological, and immunological parameters in male mice. Hormone Behavior 2003;43:281–292.
98. Restivo L, Ferrari F, Passino E, Sgobio C, Bock J, Oostra BA, Bagni C, Ammassari-Teule M. Enriched environment promotes behavioral and morphological recovery in a mouse model for the fragile X syndrome. Proceedings of the National Academy of Sciences (USA) 2005;102:11557–11562.
99. Glass M, van Dellen A, Blakemore C, Hannan AJ, Faull RL. Delayed onset of Huntington's disease in mice in an enriched environment correlates with delayed loss of cannabinoid CB1 receptors. Neuroscience 2005;123: 207–212.
100. Lazic SE, Grote HE, Blakemore C, Hannan AJ, van Dellen A, Phillips W, Barke RA. Neurogenesis in the R6/1 transgenic mouse model of Huntington's disease: Effects of environmental enrichment. European Journal of Neuroscience 2006;23:1829–1838.
101. Gobbo OL, O'Mara SM. Impact of enriched-environment housing on brain-derived neurotrophic factor and on cognitive performance after a transient global ischemia. Behavioural Brain Research 2004;152:231–241.
102. Faherty CJ, Raviie Shepherd K, Herasimtschuk A, Smeyne RJ. Environmental enrichment in adulthood eliminates neuronal death in experimental Parkinsonism. Brain Research: Molecular Brain Research 2005;134:170–179.
103. Jadavji NM, Kolb B, Metz GA. Enriched environment improves motor function in intact and unilateral dopamine-depleted rats. Neuroscience 2006;140:1127–1138.
104. Koh S, Magid R, Chung H, Stine CD, Wilson DN. Depressive behaviour and selective down regulation of serotonin receptor expression after early-life seizures: Reversal by environmental enrichment. Epilepsy & Behaviour 2007;10:26–31.
105. Hannigan JH, O'Leary-Moore SK, Berman RF. Postnatal environmental or experiential amelioration of neurobehavioral effects of perinatal alcohol exposure in rats. Neuroscience & Biobehavioral Reviews 2007;31:202–211.
106. Lankhorst AJ, ter Laak MP, van Laar TJ, van Meeteren NL, de Groot JC, Schrama LH, Hamers FP, Gispen WH. Effects of enriched housing on functional recovery after spinal cord contusive injury in the adult rat. Journal of Neurotrauma 2001;18:203–215.
107. Robbins JA, Butler SG, Daniels S, Gross RD, Langmore S, Lazarus C, Martin-Harris B, McCabe D, Musson N, Rosenbek J. Neural plasticity, swallowing and dysphagia rehabilitation: Translating principles of neural plasticity into clinically oriented evidence. Journal of Speech, Language, and Hearing Research 2007;50:276–300.
108. Shopland N, Lewis J, Brown DJ, Dattani-Pitt K. Design and evaluation of a flexible travel training environment for use in a supported employment setting. Proceedings of the 5th International Conference on Disability, Virtual Reality and Associated Technology. Oxford; 2004. pp 69–76.
109. Kwakkel G, Kollen B, Lindeman E. Understanding the pattern of functional recovery after stroke: Facts and theories. Restorative Neurology and Neuroscience 2004;22:281–299.
110. Celnik PA, Cohen LG. Modulation of motor function and cortical plasticity in health and disease. Restorative Neurology and Neuroscience 2004;22:261–268.
111. Allred RP, Maldonado MA, Hsu JE, Jones TA. Training the 'less-affected' forelimb after unilateral cortical infarcts interferes with functional recovery of the impaired forelimb in rats. Restorative Neurology and Neuroscience 2005; 23:297–302.
112. Kleim JA, Bruneau R, VandenBerg P, MacDonald E, Mulrooney R, Pocock D. Motor cortex stimulation enhances motor recovery and reduces peri-infarct dysfunction following ischemic insult. Neurology Research 2003;25:789–793.
113. Morganti F. Virtual interaction in cognitive neuropsychology. Studies in Health Technology and Informatics 2004;99:55–70.
114. Monfils MH, Teskey GC. Skilled-learning induced potentiation in rat sensorimotor cortex: A transient form of behavioural long-term potentiation. Neuroscience 2004;125:329–336.
115. Biernaskie J, Chernenko G, Corbett D. Efficacy of rehabilitative experience declines with time after focal ischemic brain injury. Journal of Neuroscience 2004;24:1245–1254.
116. Kline AE, Wagner AK, Westergom BP, Malena RR, Zafonte RD, Olsen AS, Sozda CN, Luthra P, Panda M, Cheng JP, Aslam HA. Acute treatment with the 5-HT1A receptor agonist 8-OH-DPAT and chronic environmental enrichment confer neurobehavioral benefit after experimental brain trauma. Behavioural Brain Research 2007; 177:186–194.
117. Deutsch JE, Lewis JA, Burdea G. Virtual reality-integrated telerehabilitation system: Patient and technical performance. Proceedings of the International Workshop on Virtual Rehabilitation; 2006. pp 140–144.
118. Weinberger NM. Specific long-term memory traces in primary auditory cortex. Nature Reviews Neuroscience 2004;5:279–290.
119. Brooks BM, Rose FD, Attree EA, Elliot-Square A. An evaluation of the efficacy of training people with learning disabilities in a virtual environment. Disability and Rehabilitation 2002;24:11–12.
120. Lo Priore C, Castelnuovo G, Liccione D, Liccione D. Experience with V-STORE: Considerations on presence in virtual environments for effective neuropsychological rehabilitation of executive functions. Cyberpsychology and Behaviour 2003;6:281–287.
121. Burke SN, Barnes CA. Neural plasticity in the ageing brain. Nature Reviews Neuroscience 2006;7:30–40.
122. Hummel FC, Cohen LG. Non-invasive brain stimulation: A new strategy to improve neurorehabilitation after stroke? Lancet Neurology 2006;5:708–712.
123. Schultheis MT, Rizzo AA. The application of virtual reality technology in rehabilitation. Rehabilitation Psychology 2001;46:296–311.