Traumatic brain injury and post-acute decline: what role does environmental enrichment play? A scoping review

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Abstract

Objectives. While a number of studies provide evidence of neural and cognitive decline in traumatic brain injury (TBI) survivors during the post-acute stages of injury, there is a dearth of research on the possible mechanisms underlying this decline. The purposes of this paper, therefore, are to (1) examine evidence that environmental enrichment (EE) can influence long-term outcome following TBI, and (2) examine the nature of post-acute environments, whether they vary in degree of EE, and what impact these variations have on outcomes.

Methods. We conducted a scoping review to identify studies on EE in animals and humans, and post-discharge experiences that relate to barriers to recovery.

Results. Ninety-six articles that met inclusion criteria demonstrated the benefits of EE on brain and behaviour in healthy and brain-injured animals and humans. Nineteen papers on post-discharge experiences provided evidence that variables such as insurance coverage, financial and social support, home therapy, and transition from hospital to home, also play a vital role in regaining independence.

Conclusion. There is evidence to suggest that lack of EE, whether from lack of resources or limited ability to engage in such environments, may play a role in post-recovery cognitive and neural decline. Maximizing EE in the post-acute stages of TBI may improve long-term outcomes for the individual, their family and society.

Key Words Traumatic brain injury; environmental enrichment; post-recovery cognitive decline; neural decline; engagement; post-discharge environment; post-acute decline
**Introduction**

Moderate to severe TBI is a ubiquitous injury: studies suggest an annual incidence of upwards of 20-60 per 100,000 (Bruns and Hauser, 2003; C.I.H.I., 2006; Cassidy et al., 2004; Narayan et al., 2002). Many of these injuries are sustained in young adulthood (C.I.H.I., 2006; Faul et al., 2010) and result in significant impairment to cognitive, motor and emotional functioning. Predominant and persisting deficits to executive functioning, attention, memory and speed of processing compromise psychosocial functioning and quality of life (Hawthorne et al., 2009; Resch et al., 2009; Sander et al., 2001). Because these deficits prevent many TBI survivors from returning to pre-injury levels of activity and participation (Christensen et al., 2008; Dikmen et al., 1983; Dikmen et al., 1995; Lezak, 2004), successful community integration is now recognized as a primary goal of rehabilitation for persons with brain injury (Sander et al., 2010).

The consequences of brain injury are particularly concerning given the high incidence of TBI. Murray and Lopez (1997) predicted that by 2020, TBI will be the third leading cause of disability in the world. Given that males aged 15-24 years have the highest incidence of TBI (C.I.H.I., 2006; Faul et al., 2010; Pickett et al., 2004), this can mean decades of disability and lost productivity. Not surprisingly, the annual burden of acute care and rehabilitation in North America is estimated to be in the billions of dollars (Faul et al., 2010; SmartRisk, 2006).

A theoretically intriguing and clinically important question that is emerging from the literature is whether an impediment to recovery and a contributing factor to failed community integration after moderate to severe TBI is cognitive and brain deterioration in the post-acute stages of TBI. TBI recovery studies typically show an asymptotic pattern of recovery, with rapid improvement within the first weeks and months of injury, followed by a slower rate of improvement and then a plateau with limited measurable recovery thereafter (Basso, 1989; Blatter et al., 1997; Christodoulou et al., 2001; Farne et al., 2004; Heinemann et al., 1995; Holbrook et al., 1999). However, not only do many fail to return to pre-injury levels of function when they reach that plateau (Christensen et al., 2008), but there is growing evidence that a subset of TBI survivors show cognitive deterioration.

A number of studies that have examined post-acute cognitive changes in TBI survivors have demonstrated that across domains of functioning, a combination of maintenance, further recovery and frank declines are observed (Himanen et al., 2006; Millis et al., 2001; Ruff et al., 1991; Salmond et al., 2006; Sander et al., 2001; Till et al., 2008). For example, Till et al. (2008) showed that nearly 30% of their sample of moderate-severe TBI patients showed clinically significant decline (as measured by the reliable change index) in two or more domains of cognitive functioning.

In examining changes of the brain during the post-acute stages of TBI, imaging studies have also shown evidence of deterioration, including decreased cerebral blood flow (Kim et al., 2010), declines in whole brain volume (Blatter et al., 1997; Hudak et al., 2011; MacKenzie et al., 2002; Ng et al., 2008; Sidaros et al., 2009; Trivedi et al., 2007), atrophy of discrete grey and white matter structures including the hippocampus and
Correlations between brain and behavioural decline have also been observed. In one study, 24 TBI survivors underwent MRI scans at eight weeks and 12 months post-injury. The authors not only demonstrated increased atrophy during this time period, but also negatively correlated outcomes on the Glasgow Outcome Scale (Sidaros et al., 2009). In other studies, Hudak et al. (2011) found that decreases in brain volume correlated with depressive symptoms in the post-acute phase, and Farbota et al. (2012) demonstrated that diffusion tensor imaging findings (fractional anisotropy values) and neuropsychological task performance were positively correlated.

Given the weight of evidence revealing post-acute decline, we suggest that it is important at this stage of research to begin to consider what factors may hold the potential to influence, and in particular, offset this decline.

One factor that may play a role is “environmental enrichment” (EE). As we will discuss further in the next section, EE broadly refers to enhanced stimulation, associated with (1) environments that provide access to cognitive as well as physical and social stimulation, and (2) conditions that encourage maximal participation. An extensive body of literature shows positive correlations between EE and cognitive and neuronal status. (Dobrossy and Dunnett, 2001; 2004; Scarmeas and Stern, 2003; Will et al., 2004). There have also been some findings to suggest that EE influences post-acute decline. In Till et al.’s (2008) study of cognitive decline from 12 to 24 months post-injury, the authors found a relationship between hours of therapy at five months post-injury and degree of cognitive decline. They concluded that lack of access to complex and enriched environments, due in part to limited access to resources, may play a critical a role in decline. In another study, Miller et al. (this issue) found that greater hippocampal volume loss in the chronic stages of TBI was negatively correlated with degree of self-reported cognitive stimulation.

These important findings raise the question whether post-recovery decline seen in TBI survivors is influenced by the extent of enrichment, or lack thereof, in the post-discharge environment. A reduction in the level of enrichment in the later stages of recovery from TBI might occur when the number and hours of therapies are reduced or when patients move from in-patient neurorehabilitation back to the home environment. Additionally, TBI survivors may return to environments that are indeed complex and enriched, but without the expertise of therapists actively providing supports and adaptations to the environments, patients may be unable to engage due to cognitive, emotional and/or physical impairments that render the environments overwhelming or inaccessible.

The purposes of this paper, therefore, are to (1) examine evidence that EE can influence long-term outcome following TBI, and (2) examine the nature of post-acute
environments, whether they vary in degree of EE, and what impact these variations have on outcomes. To accomplish these aims, we will undertake a scoping review summarizing literature related to EE and post-acute environments.

**Scoping review methods**

This paper addresses two of the reasons for undertaking a scoping review identified by Arskey and O’Malley (2005): to summarize and disseminate research findings and to identify research gaps in the existing literature. The scoping review typically unfolds in five steps: (1) identify the research question; (2) identify all pertinent studies; (3) select the studies for detailed analysis; (4) chart the data according to key concepts; and (5) collate and summarize the findings of the selected studies (Arksey and O'Malley, 2005; Rumrill et al., 2010):

1. **Identify the research question.** The research questions addressed in this paper are whether (i) EE can influence long-term recovery, and in particular, whether the absence of EE can contribute to post-recovery decline and (ii) post-discharge environments vary in degree of EE, and whether such variations influence outcomes.

2. **Identify all pertinent studies.** The literature review aimed to identify a comprehensive set of articles detailing the effects of EE in animals and humans, and the post-discharge experiences related to recovery and regaining independence in the post-acute stages after TBI. Articles that addressed these topics were obtained through use of a traditional keyword-driven electronic search guided by the following terms: traumatic brain injury; recovery; environmental enrichment; environmental complexity; active lifestyle; stimulation; neuroplasticity; cognitive reserve; intervention; multi-disciplinary; multi-contextual; post-rehabilitation; transition home; barriers; community integration; re-engagement. Peer-reviewed journals were searched using the PubMed and Cochrane Collaboration research databases as well as the Google Scholar search engine, for articles published between 1987 and 2012. Additionally, hand searches were conducted of references from key articles to follow up on seminal work and promising literature that might not have been captured by the databases used.

3. **Select studies for detailed analysis.** To be considered for inclusion in the review, articles had to meet the following criteria: (1) describe EE (or components of EE) in animals or adult humans or (2) describe the post-discharge experience, and more specifically, the transition from hospital to home in adult brain-injury survivors; and (3) be available in English. No methodological limitations were applied to screen for levels of evidence.

4. **Chart data according to key concepts.** Articles that met the inclusion criteria were reviewed in detail and categorized based on population examined, methodology, and study objectives to discover commonalities and provide connections between the sets of literatures reviewed.
5. Collate and summarize findings. The results are presented to correspond with the objectives of this paper. A numerical summary of the articles included is followed by a summary of the literature.

Results

Database searches identified 2,020 articles. Of these, 115 were included in the review based on the selection criteria listed above. Table 1 provides a brief summary of the articles that were included. Tables 2 and 3 provide a more detailed summary of the papers that specifically addressed EE in brain-injured animals and humans, as well as EE and post-discharge experiences, respectively. Tables 2 and 3 detail the populations, methods, objectives, and main findings of the articles that were included.

Table 1. Numerical summary of articles reviewed

<table>
<thead>
<tr>
<th>Literature topic</th>
<th>Number of studies</th>
<th>Methodology</th>
<th>Population</th>
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<tr>
<td>Post-discharge experiences</td>
<td>19</td>
<td>qualitative, observational, correlational, reviews, case study</td>
<td>Brain-injured humans</td>
</tr>
</tbody>
</table>

Table 2. Detailed summary of articles included in ‘Brain-injured animals and EE’ and ‘Brain-injured humans and EE’ scoping review

<table>
<thead>
<tr>
<th>Brain-injured animals and EE</th>
<th>Authors</th>
<th>Methods</th>
<th>(1) Main Objectives &amp; (2) Findings</th>
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<tr>
<td></td>
<td>Hamm et al., 1996</td>
<td>Brain-injured and sham-injured rats in EE and standard environment</td>
<td>(1) Determine whether exposure to EE would promote recovery of cognitive function; (2) Brain-injured rates in EE vs. SE: EE rats more improvement Morris Water Maze; Brain-injured rats in vs. sham-injured: performed at same level</td>
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<td></td>
<td>Johansson &amp; Ohlsson, 1996</td>
<td>Brain-injured rats randomly assigned to EE, social-stimulation only or physical-stimulation only environment</td>
<td>(1) Determine relative importance of social and physical activity to EE; (2) No difference in infarct size between groups. EE group performed better than physical group in all tests, better than social group on rotating pole. With time EE group performed better than social group in limb placement, climbing, inclined plane. Social group performed better than physical group on inclined plane and in climbing at all times, by 13 weeks also in limb placement test and on beam.</td>
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<td></td>
<td>Passineau et al., 2001</td>
<td>Brain-injured and sham-injured rats randomly assigned to EE and standard environments (SE)</td>
<td>(1) Examine effect of EE on behaviour and on histological integrity of brain tissue selectively vulnerable to brain trauma; (2) Injured animals in EE showed shorter latencies to find platform in Morris Water Maze task vs. injured/standard animals on day 12 post-TBI. Both injured groups showed deficits vs. sham groups. At 14 days post-TBI, EE animals had approximately 2x smaller lesion areas in regions of cerebral cortex posterior to injury epicenter compared to injured/standard animals. Overall lesion volume for entire injured cortical hemisphere was smaller in animals recovering in EE.</td>
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<td></td>
<td>Dobrossy &amp; Dunnett, 2001</td>
<td>Brain-injured rodents; review</td>
<td>(1) Review degree to which housing conditions or behavioural training can modify survival, integration or function of transplanted tissue; (2) Behavioural training, experience promote behavioural, functional compensation, influence neuroplasticity at cellular, systems levels of neuronal reorganization.</td>
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<td></td>
<td>Johansson, 2003</td>
<td>Brain-injured rats; review</td>
<td>(1) Review influence of post-ischemic environmental factors, possible clinical implications; (2) EE increases functional outcome, increases dendrite branching, number of dendritic spines in contralateral cortex, influences expression of many genes, modifies lesion-induced stem cell differentiation in hippocampus</td>
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<td></td>
<td>Dobrossy &amp; Dunnett, 2004</td>
<td></td>
<td>(1) Examine effects of differential housing conditions on striatal graft morphology and functional recovery; (2) Functional recovery accompanied by reduction in infarct size &amp; more afferent connections</td>
</tr>
<tr>
<td></td>
<td>Will et al., 2004</td>
<td>Brain-injured rats; review</td>
<td>(1) Compare three main non-invasive therapeutic strategies for achieving rehabilitation after brain damage: EE, physical exercise, specific formal training; (2) EE increased neurogenesis in hippocampus and up-regulation of neurotropic factors (e.g., NGF) that result in decreased spontaneous apoptosis and increased neuronal survival</td>
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<tr>
<td>Reference</td>
<td>Setting</td>
<td>Objective</td>
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<tr>
<td>Gobbo &amp; O’Mara, 2004</td>
<td>Brain-injured rats housed under EE or standard conditions, 6 weeks before, 4 weeks after surgery</td>
<td>(1) Investigate if EE can protect rats against the cognitive and neurological consequences of transient ischemia; (2) EE improved learning and memory; does not protect against actual loss of CA1 pyramidal cells. Brain-derived neurotrophic factor levels were increased</td>
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<tr>
<td>Pereira et al., 2007</td>
<td>Brain-injured and sham-injured rats randomly assigned to EE and SE</td>
<td>(1) Examine effects of daily EE on memory deficits in water maze and cerebral damage; (2) Spatial reference, working memory impairments were completely reversed by EE; Reduction of both hippocampal volume and cortical area, ipsilateral to arterial occlusion, no EE effect on morphological measurements</td>
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<tr>
<td>Hoffmann et al., 2008</td>
<td>Brain-injured and sham-injured rats randomly assigned to early EE, delayed EE, continuous EE or no EE</td>
<td>(1) Examine whether EE-mediated benefits are dependent on exposure to EE during neurobehavioral training; (2) A3 cell loss significantly attenuated in TBI + continuous EE group vs. TBI + no EE group. Beam-walking was facilitated in TBI groups that received early or continuous EE vs. those receiving delayed or no EE. Cognitive training enhanced in TBI groups that received continuous or delayed EE vs. early or no EE groups.</td>
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<td>Matter et al., 2011</td>
<td>Brain-injured or sham-injured rats randomly assigned to 8 groups receiving continuous or early and delayed EE with either 1 or 2 weeks of exposure.</td>
<td>(1) Further assess effects of time of initiation and duration of EE on neurobehavioral recovery by evaluating and directly comparing all the temporal permutations; (2) Motor ability was enhanced in TBI groups that received early EE (i.e., during testing) vs. standard housing. Acquisition of spatial learning facilitated in groups receiving delayed EE (i.e., during training).</td>
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<tr>
<td>De Witt et al., 2011</td>
<td>Brain-injured and sham-injured rats randomly assigned to EE, EE (2 hours), EE (4 hours), EE (6 hours), or SE</td>
<td>(1) Determine whether abbreviated EE (i.e., rehab-relevant dose response) confers benefits similar to typical EE; (2) TBI + EE (2 hours) and TBI + EE (4 hours) groups not different from TBI + STD group in behavioral assessment. TBI + EE (6 hours) group exhibited enhancement of motor and cognitive performance when compared with TBI + STD group, TBI + EE (2 hours) and TBI + EE (4 hours) groups, and did not differ from TBI + EE (typical) group.</td>
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<td>Cheng et al., 2012</td>
<td>Brain-injured and sham-injured rats randomly assigned to 3 weeks of EE SE. In phase 2: half of rats in EE transferred to SE conditions (TBI + EE + SE and sham + EE + SE); re-assessed 1/month for 6 months</td>
<td>(1) Determine whether EE-mediated motor and cognitive benefits persist after its withdrawal; (2) TBI + EE and TBI + EE + STD groups performed better in the water maze than the TBI + STD group, did not differ from one another. Data replicate several studies showing that EE enhances recovery after brain injury, and extend by demonstrating that cognitive benefits are maintained for at least 6 months post-rehab.</td>
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**Brain-injured humans and EE**

<table>
<thead>
<tr>
<th>Reference</th>
<th>Setting</th>
<th>Objective</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blackerby, 1990</td>
<td>Acute moderate-severe TBI (n=145); retrospective; quantitative</td>
<td>(1) Investigate effects of different levels of rehabilitation intensity on length of stay in two hospital-based coma and acute rehabilitation populations; (2) After increasing treatment intensity and changes in case management, patients were discharged an average of 1.5 months earlier than before changes</td>
</tr>
<tr>
<td>Toglia, 1991</td>
<td>Brain injury; concept paper</td>
<td>(1) Review literature on learning and generalization and direct applications to treatment; (2) Five components identified in cognitive psychology literature as critical to process of generalization: (a) use of multiple environments, (b) identification of criteria for transfer, (c) meta-cognitive training, (d) emphasis on processing strategies, and (e) use of meaningful activities</td>
</tr>
<tr>
<td>Spivack et al., 1992</td>
<td>Acute moderate-severe TBI (n=95); prospective; quantitative: repeated measures</td>
<td>(1) Examine effects of intensity of treatment and length of stay during inpatient rehabilitation hospitalization; (2) Patients with longer length of stay (LOS) made more progress across all outcome variables than patients with shorter LOS. In long LOS group, two treatment-intensity groups initially equivalent, and at discharge high-intensity treatment group surpassed low-intensity treatment group.</td>
</tr>
<tr>
<td>Willer et al., 1999</td>
<td>Post-acute/chronic severe TBI (n=46); prospective; quantitative: case control matched design, repeated measures</td>
<td>(1) Compare outcomes of a post-acute residential rehabilitation program with a matched sample receiving limited services in their homes or on an outpatient basis; (2) Individuals who received intensive rehabilitation services in community-based residential program exhibited considerable improvement in functional abilities (cognitive skills, motor skills). Treatment group showed greater improvement in community integration.</td>
</tr>
<tr>
<td>Sohlberg et al., 2000</td>
<td>Chronic moderate-severe TBI, ABI (n=14); prospective; quantitative: repeated measures</td>
<td>(1) Compare attention processing training with an educational and support method; (2) 10 weeks of brain injury education seemed most effective in improving self-reports of psychosocial function. Attention process training influenced self-reports of cognitive function, had stronger influence on performance of executive attention tasks. Vigilance, orienting networks showed little specific improvement</td>
</tr>
<tr>
<td>Cicerone et al., 2000</td>
<td>TBI /Stroke, review</td>
<td>(1) Establish evidence-based recommendations for clinical practice of cognitive rehabilitation from methodical review of scientific literature concerning effectiveness of cognitive rehab; (2) Attention deficits: limited evidence exists for generalization of benefits attributable to attention remediation, tendency to observe gains on tasks most closely related to training tasks; Multi-modal interventions: can significantly improve neuropsychological performance in many skill areas. Maintenance, generalization of benefits from cognitive rehabilitation greatest when treatment is provided for appropriately long periods of time, when efforts are made by clinician and patient to identify and apply interventions to</td>
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<tr>
<td>Study Authors</td>
<td>Design</td>
<td>Sample</td>
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<td>DeWeerdt et al., 2000</td>
<td>Acute stroke (n=56); prospective; quantitative: observational</td>
<td>(1) Observe how stroke patients spend their time in a rehabilitation unit; (2) Patients most frequently involved in therapeutic activities, Belgium: 28% of day, Switzerland: 45%. Belgian patients: 27% of day in own room, Swiss: 49% of day. Swiss patients spent nearly 1.5 hours per day more in therapy. Differences between two settings could only partially be explained by more favourable patient-staff ratios in Swiss setting.</td>
</tr>
<tr>
<td>Fasotti et al., 2000</td>
<td>Post-acute/chronic severe TBI (n=22); prospective; quantitative: repeated measures</td>
<td>(1) Compare the effectiveness of TPM training with concentration training in which verbal instruction was the key element; (2) TPM produces greater gains than concentration training and appears to generalise to other measures of speed and memory function.</td>
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<tr>
<td>Zhu et al., 2001</td>
<td>Post-acute moderate-severe TBI (n=36); prospective; quantitative: repeated measures</td>
<td>(1) Evaluate effects of different levels of intensive rehabilitation treatment on functional outcome; (2) Increasing amount of rehabilitation from conventional 2 to 4 hours/day improved functional outcome as measured by GOS. More patients in intensive group returned to gainful work, either original or modified job. Improvement most significant in early post-injury period at 2–3 months.</td>
</tr>
<tr>
<td>Shiel et al., 2001</td>
<td>Moderate-Severe TBI (n=56); prospective; quantitative: repeated measures</td>
<td>(1) Investigate effect of increased intensity of rehabilitation on rate at which independence was regained and duration of hospital admission; (2) Increasing hours per week of therapy can accelerate rate of recovery of personal independence and result in being discharged from hospital sooner. No evidence of ceiling effect of therapeutic intensity beyond which no further response observed.</td>
</tr>
<tr>
<td>Park &amp; Ingles, 2001</td>
<td>ABI; meta-analysis</td>
<td>(1) Examine the efficacy of attention rehab; (2) Direct-retraining methods produced only small non-significant improvements in performance. Few studies that attempted to rehabilitate specific skills requiring attention showed statistically significant improvements after training and had considerably larger effect sizes. Results suggest learning that occurs as function of training is specific, does not tend to generalize or transfer to tasks that differ considerably from those used in training.</td>
</tr>
<tr>
<td>Powell et al., 2002</td>
<td>Post-acute/chronic severe TBI (n=94); prospective; quantitative: RCT</td>
<td>(1) Evaluation of multidisciplinary community based outreach rehabilitation; (2) Outreach participants significantly more likely to show gains on Barthel Index, BICRO-39 total score, self organisation, psychological wellbeing subscales. Strong trends for BICRO personal care and mobility, on FIM+FAM for personal care and cognitive functions.</td>
</tr>
<tr>
<td>Cifu et al., 2003</td>
<td>Moderate-Severe TBI (n=491); prospective; quantitative: RCT</td>
<td>(1) Identify factors relating to intensity of rehabilitation services received and to ascertain relation between injury outcomes, demographics, types of therapy, and intensity of rehabilitation services provided; (2) Findings support assertions that increased therapy intensity, particularly physical and psychological therapies, enhances functional outcomes.</td>
</tr>
<tr>
<td>Rath et al., 2003</td>
<td>Chronic mild-severe TBI (n=60); prospective; quantitative: repeated measures</td>
<td>(1) Compare efficacy of a group-treatment protocol using a remedial programme that aims to reduce difficulties in emotional self-regulation, and (2) Increasing amount of rehabilitation from conventional neuropsychological rehabilitation programme; (2) Participants in innovative group improved in problem solving as assessed using a variety of measures, including (1) executive function, (2) problem-solving self-appraisal, (3) self-appraised emotional self-regulation and clear thinking, (4) objective observer ratings of role-played scenarios. Improvements were maintained at follow-up.</td>
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<tr>
<td>Boman et al., 2004</td>
<td>Mild-Moderate TBI (n=10); prospective; experimental: repeated measures</td>
<td>(1) Examine efficacy of cognitive rehabilitation in the patient's home or vocational environment; (2) positive effect on some measures on impairment level, no differences on activity or participation levels at follow-up; indicates home-based cognitive training improves some attentional and memory functions and facilitates learning of strategies.</td>
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<tr>
<td>Ciccone et al., 2004</td>
<td>Post-acute/chronic moderate-severe TBI (n=56); prospective; quantitative: repeated measures</td>
<td>(1) Evaluate effectiveness of an intensive cognitive rehabilitation program (ICRP) compared with standard neurorehabilitation (SRP); (2) ICRP participants over twice as likely to show clinical benefit on Community Integration Questionnaire. ICRP participants showed improvement in overall neuropsychological functioning; participants with clinically significant improvement on Community Integration Questionnaire showed greater improvement of neuropsychological functioning. Satisfaction with cognitive functioning made significant contribution to post-treatment community integration.</td>
</tr>
<tr>
<td>De Wit et al., 2005</td>
<td>Stroke (n=60); prospective; quantitative: observational</td>
<td>(1) Identify differences in use of time by stroke patients in 4 rehabilitation centers in 4 countries; (2) Patients in Belgium and UK spent more time in passive behaviour, in rooms, without any interaction compared with patients in Germany and Switzerland. Latter centers had more structured rehabilitation program. May have resulted in more therapy time, more challenging environment for patients, physically and mentally.</td>
</tr>
<tr>
<td>Authors</td>
<td>Scoping review Details</td>
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<tr>
<td>Till et al., 2007</td>
<td>Review 10 principles of experience-dependent neural plasticity and considerations in applying them to the damaged brain; (2) optimism that the knowledge nature of brain plasticity can be capitalized upon to improve rehabilitation efforts and to optimize functional outcome</td>
<td></td>
</tr>
<tr>
<td>Cicerone et al., 2005</td>
<td>Review studies that focused on executive functions of problem solving, planning, organising and multitasking; (2) Compelling evidence from 10 intervention studies that using step-by-step meta-cognitive strategy instruction improves problem solving, etc. for personally relevant activities or problem situations; Changes more likely to be observed at level of activities and participation in daily living than on standardised tests (i.e., impairment outcomes)</td>
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<tr>
<td>Zhu et al., 2007</td>
<td>Evaluate the effects of an increase in the intensity of rehabilitation on the functional outcome; (2) more patients in the high intensity group than in the control group who achieved a maximum FIM total score at the third month and a maximum Glasgow Outcome Scale (GOS) score at the second and third months</td>
<td></td>
</tr>
<tr>
<td>Kleim &amp; Jones, 2008</td>
<td>(1) Explore the course and timing of functional recovery in patients who have emerged from coma; (2) To achieve a good response and outcome nearing normalcy, a patient needs over 300 hours of intensive rehabilitation</td>
<td></td>
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<tr>
<td>Kennedy et al., 2008</td>
<td>(1) Review studies that focused on executive functions of problem solving, planning, organising and multitasking; (2) Compelling evidence from 10 intervention studies that using step-by-step meta-cognitive strategy instruction improves problem solving, etc. for personally relevant activities or problem situations; Changes more likely to be observed at level of activities and participation in daily living than on standardised tests (i.e., impairment outcomes)</td>
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<td>Spikman et al., 2009</td>
<td>(1) Evaluate the effects of a treatment for dysexecutive problems on daily life functioning; (2) Experimental patients resumed previous roles significantly more than before treatment. From post-treatment to follow-up, only experimental group showed further improvement over time; DEX showed decrease of executive complaints similar for both groups. On DEX-therapist, significantly less executive problems after treatment for experimental group. Executive abilities observed by professionals improved more in experimental group</td>
<td></td>
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<tr>
<td>Toglia et al., 2010</td>
<td>(1) Define, explore and provide preliminary testing of the multi-context approach in promoting strategy use across situations and increasing self-regulation, awareness and functional performance; (2) Participants demonstrated positive changes in self-regulatory skills and strategy use across tasks. Examination of individual participants revealed important, varying patterns of change in strategy use, learning transfer and self-awareness across intervention</td>
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<tr>
<td>Leon-Carrion, 2012</td>
<td>(1) Explore the course and timing of functional recovery in patients who have emerged from coma; (2) To achieve a good response and outcome nearing normalcy, a patient needs over 300 hours of intensive rehabilitation</td>
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### Table 3. Detailed summary of articles included in ‘Post-discharge experiences and EE’ scoping review

<table>
<thead>
<tr>
<th>Authors</th>
<th>Methods</th>
<th>(1) Main Objectives &amp; (2) Findings</th>
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<tr>
<td>Corrigan et al., 2004</td>
<td>Chronic mild-severe TBI (n=1802); prospective; quantitative</td>
<td>(1) Provide population-based estimates of perceived needs following TBI and the prevalence of unmet needs; (2) Many reported still requiring help managing money</td>
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<td>Staudenmayer et al., 2007</td>
<td>Post-acute severe TBI (n=211); prospective; quantitative</td>
<td>(1) Determine whether there are specific types of functional deficits that disproportionately affect ethnic minorities after TBI. (2) Minorities demonstrated worse long-term functional outcome, less social and financial resources suggested as related/causal variables</td>
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<td>Shafi et al., 2007</td>
<td>Post-acute severe TBI (n=344); prospective; quantitative</td>
<td>(1) Analyze whether racial or ethnic disparities exist in trauma care, specifically related to access to rehabilitation services and functional outcomes of patients with TBI. (2) Ethnic minorities less likely to be insured; more likely to have moderate-severe disability at follow-up. Data suggest insured patients less likely to be disabled, relationship strongest for private insurance</td>
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<tr>
<td>Till et al., 2008</td>
<td>Post-acute moderate-severe TBI (n=33); quantitative:</td>
<td>(1) Assess prospectively degree of post-recovery long-term cognitive decline after TBI. (2) Amount of therapy received at 5 months post-injury significantly higher in group of non-decliners versus decliners; individuals who were insured received more hours of</td>
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Lack of awareness, education and resources acknowledged as key challenges to successful transitioning by clients and healthcare providers. Other key elements: establishing routines or schedules and occupying one's time. Participation in meaningful occupations was fundamental element of recovery gains. Other occupations was source of stress and frustration. Many family caregivers reported lack of awareness, education and resources as contributing to decreased participation in the community. People's lived experiences of reengagement in meaningful occupations during hospital-to-home transition phase after ABI. Not being able to participate in desired occupations was source of stress and frustration. Many family caregivers reported participation in meaningful occupations was fundamental element of recovery gains. Other key elements: establishing routines or schedules and occupying one's time. Participation in meaningful occupations perceived to enhance functional recovery during transition.

### Post-discharge factors that influence engagement

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<td>Freeman, 1997</td>
<td>Severe TBI; Concept paper</td>
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<td>(1) Explore methods used to establish a rehabilitation program in the home, the initial moves, the family dynamics, the advantages, and some of the programs required for the restoration of function of sensory, cognitive and motor abilities. (2) Family environment provides wide variety of activities, which are inclusive of person, guarantees provision of stimulation over a wide spectrum of inputs and activities</td>
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<td>Rotondi et al., 2007</td>
<td>Chronic moderate-severe TBI + caregivers(n=185); qualitative</td>
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<td>(1) Determine expressed needs of persons with TBI and their primary family caregivers. (2) Inadequate preparation of primary support persons and persons who experienced TBI for personality and behavioural sequelae prior to discharge from the hospital appeared to be a common complaint</td>
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<td>McCormack &amp; Lilliard, 2009</td>
<td>Chronic severe TBI (n=1); case study</td>
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<td>(1) Examines a model of community rehab; (2) Supportive and effective familial care system and specialist community interdisciplinary rehabilitation was effective in facilitating recovery</td>
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<td>Keightley et al., 2011</td>
<td>TBI, ABI + caregivers(n=17); qualitative</td>
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<td>(1) Explore barriers and enablers surrounding transition from health care to home community settings for Aboriginal clients recovering from ABI in north western Ontario. (2) Lack of awareness, education and resources acknowledged as key challenges to successful transitioning by clients and healthcare providers</td>
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<td>Sander et al., 2011</td>
<td>Post-acute mild-severe TBI (n=167); prospective; mixed methods</td>
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<td>(1) Investigate meaning of community integration in an ethnically diverse sample. (2) Financial issues, such as home ownership and insufficient funds, were perceived as contributing to decreased participation in the community</td>
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<td>Turner et al., 2011b</td>
<td>Post-acute mild-severe TBI, ABI + caregivers(n=38); qualitative; pre-discharge, 1, 3 months post-discharge</td>
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<td>(1) Explore service and support needs of individuals with ABI and family caregivers during transition phase from hospital to home (2) Individuals with ABI experience a range of service and support needs during the early transition phase, many of which are currently unmet. Findings also indicated that support for family caregivers and access to early community rehabilitation were the two areas in which participants most commonly reported experiencing unmet needs</td>
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<td>Rusconi &amp; Turner-Stokes, 2003</td>
<td>Post-acute/chronic TBI, ABI, SCI (n=53); quantitative; cross-sectional cohort survey</td>
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<td>(1) Evaluate aftercare of patients discharged from specialist rehabilitation unit with respect to use of equipment and follow-up by therapy and care services and to assess change in dependency and care needs. (2) Many patients observed they were ill-prepared for sudden change from an intensive therapy programme on unit to a much less frequent and more self-reliant programme in community</td>
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<td>Rittman et al., 2004</td>
<td>Post-acute stroke + caregivers(n=51); qualitative</td>
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<td>(1) Evaluate the aftercare of patients discharged from specialist rehabilitation unit with respect to use of equipment and follow-up by therapy and care services and to assess change in dependency and care needs. (2) When routines are not re-established, survivors and caregivers experience more chaos, disruption during the transition. When talking about ways days are spent, most survivors describe problems with boredom and not having meaningful activities in their lives</td>
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<tr>
<td>Turner et al., 2007</td>
<td>Chronic TBI, ABI + caregivers(n=24); qualitative</td>
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<td>(1) Explore transition experiences from hospital to home of a purposive sample of individuals with ABI. (2) Many participants found it difficult to locate and access suitable post-discharge therapy services. Friendship and social networks played important role during transition process. Post-discharge boredom, particularly during first 1–2 months at home, commonly expressed by participants</td>
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<tr>
<td>Turner et al., 2011</td>
<td>Post-acute mild-severe TBI, ABI + caregivers(n=17); qualitative</td>
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<td>(1) Explore people's lived experiences of reengagement in meaningful occupations during hospital-to-home transition phase after ABI. (2) Not being able to participate in desired occupations was source of stress and frustration. Many family caregivers reported participation in meaningful occupations was fundamental element of recovery gains. Other key elements: establishing routines or schedules and occupying one's time. Participation in meaningful occupations perceived to enhance functional recovery during transition</td>
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<td>Year</td>
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<td>2009b</td>
<td>Severe TBI, ABI + caregivers (n=38); qualitative pre-discharge, 1, 3 months post-discharge</td>
<td>Hospital-to-home transition phase after ABI. (2) Not being able to participate in desired occupations was source of stress, frustration for many participants. Many family caregivers reported participation in meaningful occupations was fundamental element of recovery gains. Other key elements of transition success include establishing routines or schedules and occupying one's time. Results demonstrated participation in meaningful occupations was perceived to enhance functional recovery during transition; underscores importance of encouraging and facilitating participation in meaningful occupations.</td>
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<td>Hoogerdijk et al, 2011</td>
<td>Chronic mild-severe TBI (n=4); qualitative</td>
<td>(1) Better understand how individuals with TBI make sense of adaptation process and their performance of occupations within this process. (2) Results indicate adaptation process following TBI is a necessary struggle to gain new identity; facilitated by engagement in familiar occupations in familiar environments; a protracted learning process that continues long after rehabilitation ends; individual, situated.</td>
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<tr>
<td>Turner et al., 2011a</td>
<td>Post-acute mild-severe TBI, ABI + caregivers (n=38); qualitative pre-discharge, 1, 3 months post-discharge</td>
<td>(1) Explore perspectives of individuals with ABI and their family caregivers concerning recovery and adjustment during the early transition phase from hospital to home. (2) Findings highlight that while returning home was typically perceived to facilitate ongoing recovery, process of adjusting emotionally to life at home posed significant challenge for many participants during transition phase.</td>
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<tr>
<td>Nalder et al., 2012a</td>
<td>Post-acute moderate-severe TBI + caregivers (n=210); prospective quantitative repeated measures discharge, 1, 3, 6 months post-discharge</td>
<td>(1) Identify factors associated with perceived success of transition from hospital to home after TBI. (2) Greater perceived success of transition associated with higher levels of health-related quality of life, level of community integration, more severe injury. Sentinel events (e.g., returning to work, independent community access, changing living situation) associated with greater perceived success; financial strain, difficulty accessing therapy services associated with less success.</td>
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<tr>
<td>Nalder et al., 2012b</td>
<td>Post-acute moderate-severe TBI + caregivers (n=210); prospective quantitative repeated measures discharge, 1, 3, 6 months post-discharge</td>
<td>(1) Describe timing and factors associated with occurrence of sentinel events (financial strain, difficulty accessing therapy, return to work, accommodation change and independent transport use) during transition to community for individuals with TBI. (2) General positive sentinel events (e.g., regaining independence, returning to work) more likely experienced by individuals with higher levels of global functioning and psychosocial integration. Individuals with lower levels of functioning at greater risk of experiencing more negative sentinel events (e.g., financial strain). Individuals with more severe injury and poorer adjustment more likely to report difficulty accessing therapy.</td>
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Acute = 0-3 months post-injury, post-acute = 3-12 months post-injury, chronic = greater than 12 months post-injury

1. **EE has beneficial effects on the brain and behaviour, in animals and humans.**

1.1. **Defining EE**

A number of different definitions have been proposed for the concept of EE, and it is often defined in relative terms. In animals, enriched environments (e.g., cages with running wheels, novel toys, several animals) are typically contrasted with standard environments (e.g., cages with a single animal, and only the basic necessities for living). In these studies, researchers stress the importance of having cognitive, social and physical stimulation for environments to be considered enriched and a key property is the maintenance of novelty, for example through regularly changing toys and food (Diamond, 2001).

Kramer et al. (2004) have suggested that while numerous positive changes in cognitive functioning, neuroanatomy, and neurochemistry occur as a result of exposure to EE in animals, research must examine the degree to which these findings translate to humans, and they note that an operational definition of EE applicable to humans needs to be established. Whereas novel toys and food, running wheels, and housing several animals together maps well to cognitive, physical, and social stimulation in animals, providing concrete examples of these factors in humans has proven to be more difficult
because other subject factors, such as motivation, mental effort, and engagement play a large role in reaping the benefits of EE. Thus, critical factors that may influence engagement with environment include personality and earlier life experiences, such that what may be a stimulating and engaging environment for one person may not be for another (Johansson, 2003). Thus, for humans, the definition of EE is more complex, addressing both the nature of the environment and factors that influence engagement in the environment.

These ideas of Kramer et al. (2004) are consistent with earlier work by Schooler (1987), who defined environmental complexity as being determined by stimulus and demand characteristics. He theorized that greater diversity of stimuli in one’s environment could lead to more options/plans of action to consider and decisions to make. When cognitive efforts are reinforced and rewarded, people are motivated to continue engaging in complex environments, which in turn enhances cognitive functioning. Thus, enhancing cognitive functioning further promotes participation in complex environments, illustrating a dynamic facet of EE and its benefits. The enriched environment, therefore, reflects both its complexity (e.g., opportunity to participate in different sports, clubs or social networks, and to engage in intellectually demanding activities), one’s inclination to participate in the environment, and the frequency of participation.

It is important to note that given the methodological limitations in manipulating and controlling EE in humans (e.g., designing and tailoring EE to each individual), animal studies arguably provide the most compelling evidence for the causal effects of EE.

### 1.2. Benefits of environmental enrichment

#### 1.2.1. Environmental enrichment in healthy animals

In 1947, Hebb examined if rats exposed to EE would improve behaviourally on problem-solving tasks, compared to a control group (Hebb, 1947). EE rats were free to roam his home while control rats were housed in standard laboratory cages. Hebb found performance was superior in the EE group. Since then, more systematically controlled studies have had similar findings.

Exposure to EE has been shown to lead to increases in cognitive functioning, specifically improvements in response selectivity, learning ability, spatial and problem solving skills, memory, and processing speed (Kobayashi et al., 2002; Milgram, 2003; Mohammed et al., 1990; Nilsson et al., 1999; Rosenzweig and Bennett, 1996; Valero et al., 2011; van Praag et al., 2000). The benefits of EE are also observable at cellular and molecular levels. There is evidence of increased neurogenesis, synaptogenesis and dendritic spine density in parts of the brain associated with memory and learning (i.e., hippocampus, dentate gyrus and cerebellar Purkinje cells) in response to EE (Churchill et al., 2002; Eckert and Abraham, 2012; Johansson, 2000; 2002; Kempermann et al., 2002; Kolb and Whishaw, 1998; Valero et al., 2011; van Praag et al., 2000). Increases in brain weight and cortical thickness have also been demonstrated, as well as increases in the amount of nerve growth factor, brain derived neurotropic factor, acetylcholinesterase activity, neurotransmitters, glial proliferation, blood vessels, and protein synthesis.
In examining properties of EE that produce beneficial effects, factors such as intensity and duration emerge as critical for reaping the most benefits. Bennett and colleagues (2006) examined the effects of long-term continuous EE on memory performance in aged mice. Mice received a 10-week treatment of either five minutes of daily handling housed in impoverished environments (clear plastic shoe boxes), three hours of daily exposure to basic EE (small bin with fresh bedding, a running wheel, a plastic rodent dwelling, a plastic tube for climbing, a few toys), or continuous complex EE (larger bin to allow for more mice to be housed together, and for larger and more complex objects). Continuously enriched older mice performed significantly better than other groups of aged mice in spatial memory tasks, and were indistinguishable from younger control mice in their performance.

Amaral and colleagues (2008) examined durations of EE in mice and influences on behavioural changes (open field habituation and locomotion). They compared mice exposed to eight weeks, four weeks and one week of EE. While mice exposed to eight and four weeks of EE showed behavioural effects, the one-week group did not. Furthermore, mice in the four-week exposure group demonstrated effects lasting two months post-EE, but only mice in the eight-week EE exposure group demonstrated effects lasting six months. The authors suggest that these findings indicate (1) a minimum EE period is necessary to induce beneficial behavioural effects, (2) the effect of EE can persist at least partially for many months after its cessation, and (3) the degree of this persistence appears to be somewhat greater in animals exposed to longer durations of EE. Importantly, these findings indicate that the benefits of EE may be lost when animals are removed from such environments.

1.2.2. Environmental enrichment in healthy humans

Scarmeas and Stern (2003) undertook a review of the relationship between lifestyle and cognitive reserve, which they defined as the degree to which the brain can create and use networks or cognitive paradigms that are more efficient or flexible, and thus less susceptible to disruption. They examined whether exercise for the brain has the same healthy effect as exercise for the rest of the body. They concluded that greater participation in intellectual and social leisure activities is associated with less cognitive decline in healthy older adults and a lower incidence of dementia. These important “use it or lose it” findings are supportive of the supposition that in TBI, the absence of EE in the sub-acute and chronic stages of injury may result in decline. The authors also proposed mechanisms to explain how leisure activities and an active lifestyle might buffer against cognitive decline: (1) increasing synaptic density, which results in more efficient cognitive functioning of unaffected neurons; (2) more efficient use of the same brain networks; and (3) more efficient use of alternative brain networks. They also found that although it is a very active area of research, our understanding of the specific active ingredients that buffer against cognitive decline has not been fully elucidated.
In addition to studies examining how mentally active lifestyles confer cognitive benefits (Crowe et al., 2003; Fujiwara et al., 2009; Gribbin et al., 1980; Newson and Kemps, 2005; Pushkar et al., 1997; Verghese et al., 2003; Wang et al., 2002; Wilson et al., 2003; Wilson et al., 2002), studies have also illustrated the benefits of maintaining physically active (Clarkson-Smith and Hartley, 1989; Pignatti et al., 2002; Schuit et al., 2001; Voss et al., 2011) and socially active lifestyles (Bassuk et al., 1999; Fratiglioni et al., 2000; Mahoney et al., 2000; Seeman et al., 2001).

Maintaining an active lifestyle and living in stimulating environments has also shown to be essential for healthy older adults (Christensen and MacKinnon, 1993; Davidson and Bar-Yam, 2006; Huppert, 1991). For example, Winocur and Moscovitch (1990) compared cognitive functioning in community-dwelling and institutionalized older adults. After controlling for variables such as IQ, age, and health, they found that community-dwelling older adults had higher levels of cognitive functioning. They also identified a subgroup of high-functioning institutionalized older adults who performed similarly to the community-dwelling group. For this subgroup, they postulated that cognitive functioning may have been influenced by adjustment to institutional life, such that more social activity was correlated with better cognitive functioning, as was found in their prior study (Winocur et al., 1987). Winocur and Moscovitch suggested that lower cognitive functioning observed in the institutionalized group might be a result of an under-stimulating environment. This interpretation is also consistent with the position of Schooler and Mulatu (2001), who suggested that even if people have higher levels of education, it is the continued practice in complex activities that maintains their cognitive abilities – speaking directly to the thesis of this paper.

A number of studies have examined the benefits of continuous exposure (Blackerby, 1990; Cifu et al., 2003; De Weerdt et al., 2000; De Wit et al., 2005; Shiel et al., 2001; Spivack et al., 1992; Willer et al., 1999; Zhu et al., 2001), which is focused on the improvement or maintenance of global capacities. This research typically includes many different kinds of tasks (e.g., time pressure management, problem-solving, theatre arts, music-based exercises) and incorporates many elements of EE, such as cognitive, social and physical stimulation. These types of interventions can be contrasted with interventions administered over a discrete period of time that are designed to enhance a specific cognitive domain- or skill (Fasotti et al., 2000; Green et al., 2006; Gunther et al., 2003; Hayslip et al., 1995; Neely and Backman, 1995; Noice and Noice, 2004; Powell et al., 2002; Rath et al., 2003; Spikman et al., 2009; Stine-Morrow et al., 2007; Van de Winckel et al., 2004; Vance and Johns, 2002). The former have led to better functional gains, both cognitively and physically.

1.2.3. Brain-injured animals and EE

Brain-injured animals also show benefits from exposure to EE. Studies comparing recovery in brain-injured animals reared in enriched environments to those reared in standard environments demonstrate significant brain changes, including increased neurogenesis, upregulation of neurotrophic factors, increased neuronal survival, increased afferent innervation, as well as reductions in spontaneous apoptosis and infarct size.
Superior performance on tasks of learning and memory, and spatial reference has also been found in brain-injured animals exposed to EE as compared to animals exposed to standard and impoverished environments (Gobbo and O'Mara, 2004; Hamm et al., 1996; Hoffman et al., 2008; Johansson and Ohlsson, 1996; Passineau et al., 2001; Pereira et al., 2007; Will et al., 2004). For instance, Hamm et al. (1996) compared cognitive functioning in brain-injured and sham-brain-injured rats housed in enriched environments to those housed in standard environments. Rats housed in enriched environments were in social groups and had access to a variety of foods, novel toys, scented objects, and a running wheel. At 15 days post-injury, brain-injured rats exposed to EE performed significantly better than brain-injured rats in standard environments. Interestingly, they also found that brain-injured rats recovering in enriched environments performed just as well as non-brain injured animals.

In a study by Johansson and Ohlsson (1996), brain-injured rats recovering in an enriched environment (i.e., cognitive, social, physical enrichment) were compared to those recovering in either social environments (only) or exercise environments (only). Rats in the EE group were placed in one cage with several novel toys and objects that promoted exercise, whereas rats in the social-interaction group were caged with other rats without objects or toys, and rats in the exercise-activity group were individually caged with access to a running wheel. The social-interaction group improved more than the physical-activity group; however, the EE group improved more than either group. More recently, Hoffman and colleagues (2008) also demonstrated the advantages of EE, finding that brain-injured rats exposed to continuous EE [compared to early EE (immediately post-injury lasting one week), late EE (one week post-injury) and no EE] not only had significantly less hippocampal cell loss, but also performed better on motor and cognitive tests. Interestingly, they found an advantage of continuous and early EE for motor tasks, but an advantage of continuous and delayed EE for cognitive tasks. The benefits of increased EE-exposure in brain-injured rats have since been replicated (de Witt et al., 2011; Matter et al., 2010), and shown to be long-lasting (Cheng et al., 2012).

Animal studies provide evidence that enriched environments not only help recover functions after brain injury to levels that make them indistinguishable from healthy controls, but that continual EE is necessary to maintain both neural and cognitive improvements. The benefits of EE are substantial, but not permanent, thus highlighting the importance of ongoing stimulation. These findings are particularly relevant to questions about the post-discharge environment, and what factors may contribute to decline.

1.2.4. Brain-injured humans and EE

Similar to the distinction between use-it-or-lose-it studies versus discrete interventions above, EE interventions for brain-injured humans can be grouped into two types: those that provide increased hours and duration of therapy (without prescription of specific content of therapies) and those that address discrete impairments and focus on improvement of a specific skill. Note that in clinical practice, the latter might be referred
to as “training” rather than EE. However, we include them here as they entail an increase in cognitive stimulation relative to no treatment.

Human TBI EE studies have been less numerous than those in animals. While EE interventions, *per se*, have not been extensively examined using human TBI models, the effects of some properties of EE (identified in animal studies) that produce beneficial effects, such as novelty, intensity and duration, have been examined. Much like in healthy individuals, interventions for TBI survivors aimed at training specific skills often result in poor generalization to everyday performance (Boman et al., 2004; Cicerone et al., 2000; Cicerone et al., 2005; Kennedy et al., 2008; Park and Ingles, 2001; Ruff et al., 1991; Sohlberg et al., 2000). In their meta-analyses of cognitive rehabilitation for TBI survivors (Cicerone et al., 2000; Cicerone et al., 2005) Cicerone and colleagues suggested that cognitive rehabilitation should not focus exclusively on remediation of impairments, but should reduce disability and help restore social role functioning. Toglia (1991) provided information to guide therapists in directly addressing the generalization process, and proposed a multi-context treatment approach that uses varied stimulation and environments that are meaningful to the person to encourage participation, both critical factors for EE. Interventions that incorporate such components demonstrate better generalizability, as well as improvements in community integration (Fasotti et al., 2000; Leon-Carrion et al., 2012; Powell et al., 2002; Rath et al., 2003; Toglia et al., 2010; Van de Winckel et al., 2004; Vance and Johns, 2002).

Furthermore, interventions that are more intensive also result in better functional gains (Cicerone et al., 2004; Willer et al., 1999). Cicerone and colleagues (2004) compared the effectiveness of an intensive cognitive rehabilitation program to standard neurorehabilitation for persons with TBI. Participants in the intensive program not only demonstrated greater improvement in neurological function (composite score based on attention, speed of processing, memory and executive function test scores) but greater improvement in community integration. Increasing hours of therapy has also led to greater functional gains and faster recoveries (Blackerby, 1990; Cifu et al., 2003; De Weerdt et al., 2000; De Wit et al., 2005; Shiel et al., 2001; Spivack et al., 1992; Zhu et al., 2007; Zhu et al., 2001). Turner-Stokes et al.’s (2005) review of multi-disciplinary rehabilitation for brain injury concluded that “intensive intervention appears to lead to earlier gains.” Therefore, they concluded that “Patients discharged from in-patient rehabilitation should have access to out-patient or community-based services appropriate to their needs.”

1.3. What happens in the absence of environmental enrichment?

If exposure to EE is beneficial at both behavioural and neural levels, it logically follows that a dearth of it may lead to poorer behavioural and neural health. Experience-dependent plasticity refers to changes in the brain that result from new experiences, learning and/or practice. Certain actions will enhance or maintain neural pathways, whereas others will depress or weaken them (Blake and Merzenich, 2002; Blake et al., 2005; Kelly and Garavan, 2005). Where neural pathways are under-stimulated, it is possible to lose the function that was acquired or mastered (Robertson and Murre, 1999). In a recent paper, Kleim and Jones (2008) discuss the principles of experience-dependent
neural plasticity. Of particular relevance are the principles expressing not only the importance of active engagement to maintain neural networks, but that this engagement needs to be repeated and intensive to induce long lasting neural changes that may improve function and transfer to other tasks. As literature reviewed above suggests, continual and intensive cognitive, physical, and social stimulation results in improved behavioural and neural health, as well as maintenance of benefits. However, if this is stimulation and engagement is not maintained, as we suggest may be the case with TBI survivors transitioning from a rehabilitation setting to a home setting, we would postulate that a loss of benefits and a decline in function would follow.

1.3.1. Healthy animal models: Lack of EE

While studies provide evidence that animals exposed to enriched environments show gains in cognitive and motor performance, as well as at a neural level, they also demonstrate that those animals that are exposed to less stimulating or impoverished environments do not fare as well. Studies have shown that mice with less EE exposure have poorer performance on spatial memory tasks, as compared to continuously enriched mice, indicating lack of EE is associated with poorer cognitive functioning (Bennett et al., 2006), and that rats that receive less exposure may only maintain benefits for a shorter period of time (Amaral et al., 2008). Similarly, brain injured rats recovering in impoverished environments show poorer recovery of cognitive and motor functioning (de Witt et al., 2011; Hamm et al., 1996; Hoffman et al., 2008; Matter et al., 2010) and do not maintain benefits gained from short-term EE (Cheng et al., 2012; de Witt et al., 2011; Matter et al., 2010).

Furthermore, there is evidence that the benefits gained from EE are reversible (Bernstein, 1972; Winocur, 1998). Winocur (1998) demonstrated that older rats placed in impoverished environments performed worse on learning and memory tasks, compared to older and younger rats in enriched and standard environments. When transferring rats from impoverished to enriched environments, they improved significantly, whereas rats transferred from enriched and standard environments to impoverished ones declined. In accord with findings from Amaral et al. (2008), Bernstein (1972) and Winocur (1998) also provide evidence that the benefits of EE may be lost when animals are removed from such environments.

1.3.2. Healthy older adults: Use it or lose it

The adage ‘use it or lose’ as it applies to (older) adults and cognitive functioning has been studied extensively. Many studies have found that continued participation in stimulating environments maintains and promotes healthy aging and cognitive functioning, whereas more sedentary lifestyles have been linked to disease and disability, and overall poorer health (Huppert, 1991; Mackinnor et al., 2003; Pushkar et al., 1997; Salthouse, 2006; Shors et al., 2012). Likewise, Cabeza et al. (2002) examined brain activation in young and old people while performing cognitive tasks. They found that lower-functioning older adults showed less activation than younger adults. They also found that higher-functioning older adults showed similar levels of activation as young adults, albeit with more bilateral recruitment. The authors suggest that “high-performing older adults
counteracted age-related neural decline through a plastic reorganization of neurocognitive networks”.

Findings that provide support for the hypothesis that continued participation is necessary to maintain optimal functioning lend further support to the argument that environmental factors may influence post-recovery decline: returning to environments that do not encourage participation may not allow benefits gained while in the rehabilitation setting to be maintained, and therefore result in poorer functional outcome.

The types of interventions and intensity of stimulation provided during inpatient rehabilitation that demonstrate good functional outcomes are important to explore to examine which aspects of the environment change after TBI survivors are discharged home.

1.4. Environmental enrichment, post-recovery decline and sub-acute atrophy

As therapies diminish in frequency over time (e.g., when patients move from in-patient neurorehabilitation to the home or a chronic-care facility), the amount of EE exposure may also lessen. Turner and Green (2008) examined the principles of negative neuroplasticity (maladaptive changes to the brain with negative consequences) described by Mahncke et al. (2006a; 2006b), namely (1) reduced schedules of activity, (2) noisy processing in peripheral and central sensory systems, (3) alterations in neuromodulatory control, and (4) negative learning, in the context of TBI. They suggest that a similar process of negative neuroplastic change may undermine long-term outcome in TBI, particularly a reduction in schedules of activity.

As previously noted, in the case where neural pathways are under-stimulated, it is possible to lose the function that was acquired or mastered (Robertson and Murre, 1999; Rubinov et al., 2009). Findings of different neural recruitment in older and younger adults (Cabeza et al., 2002; Cabeza et al., 2004; Cirillo et al., 2011), increased neural representation after training (Cardinali et al., 2012; Cirillo et al., 2011) and different brain activation when comparing exposure versus deprivation of stimulation (Klinge et al., 2012) provide evidence for experience-dependent neuroplasticity. This raises the question whether under-stimulation of neural pathways, due to disuse, may be responsible for post-acute neural degeneration seen in TBI survivors. If so, EE exposure may play a role in minimizing, or averting, this problem.

With respect to neural degeneration, mechanisms of apoptosis have been modelled in animals to understand the cascade of events that takes place after TBI (Keane et al., 2001; Raghupathi, 2004; Raghupathi et al., 2000). Coulson et al. (2004) provided support for their hypothesis that synaptic input may be the key to regulating neuronal survival and death pathways following neurotrauma. Synaptic activity regulates expression levels of neurotrophins and facilitates growth factor signalling. There is evidence that EE exposure enhances nerve growth factor and brain-derived neurotropic factor in animals (Bassuk et al., 1999; Blackerby, 1990; Cifu et al., 2003; Clarkson-Smith and Hartley, 1989; De Weerdt et al., 2000; Johansson, 2003; Mahoney et al., 2000; Rath et al., 2003; Spikman et al., 2009; Wang et al., 2002; Wilson et al., 2002). As well, animal studies have demonstrated that EE can enhance neurogenesis and attenuate apoptosis in the injured
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brain (Dobrossy and Dunnett, 2001; 2004; Gobbo and O'Mara, 2004; Hoffman et al.,
2008; Passineau et al., 2001; Pereira et al., 2007; van Praag et al., 2000; Will et al., 2004).
Lastly, neurons deprived of synaptic input can be rescued from death by an increased
supply of growth factors (Coulson et al., 2004). Taken together, these findings offer the
possibility that EE can help to prevent neuronal death,

The relation between changes in brain structure and neuropsychological performance
has also been recently explored (Farbota et al., 2012), providing further evidence that as
we see declines at a neural levels, we also see parallel declines in cognitive functioning.
Recent work from our laboratory has demonstrated that in TBI survivors, more
engagement in enriched environments, defined as participation in activities involving
cognitive, physical, and social demands, is correlated with less hippocampal volume loss
in the post-acute stages (Miller, this issue). While these findings are correlational, they
provide preliminary evidence of the positive impact that an enriched environment can
have in TBI survivors.

The research reviewed within this section of the scoping review supports that EE
improves outcomes and that a dearth of EE results in poorer outcomes. Studies
demonstrate continued and repeated EE exposure (Amaral et al., 2008; Blackerby, 1990;
Cifu et al., 2003; De Weerdt et al., 2000; De Wit et al., 2005; Schooler and Mulatu, 2001;
Shiel et al., 2001; Spivack et al., 1992; Zhu et al., 2007; Zhu et al., 2001), which provides
intensive cognitive, social and physical stimulation is necessary to induce beneficial
effects (Bennett et al., 2006; Cicerone et al., 2004; Willer et al., 1999). Furthermore, if
this exposure is reduced or removed, the benefits will not be maintained and may
diminish (Bernstein, 1972; Cheng et al., 2012; Winocur, 1998). Synaptic input may be
necessary to maintain and strengthen neural pathways and connections, particularly those
at risk after brain injury (Coulson et al., 2004; Turner and Green, 2008). Moreover, this
research supports our contention that for the subset of people with moderate-severe TBI
that show post-recovery cognitive decline and neural deterioration in the post-acute
phase, there may be some environmental variables that contribute to their negative
outcomes.

2. Post-discharge experiences and EE

In the first section, we discussed findings revealing that the brain atrophies and that
cognitive abilities decline in the post-acute stages of brain injury. In the second section,
we discussed findings that demonstrate that EE can alter the brain (both healthy and
damaged), and perhaps most importantly that it has the potential to minimize atrophy
after brain injury. Moreover, a mechanism of disuse-mediated atrophy has been proposed
(i.e., synaptic input and neuronal survival) (Coulson et al., 2004).

A critical question, then, is to what extent do post-discharge factors reflect EE? This
is important because it is possible that the post-discharge environment may be
functionally un-enriched, and this may exacerbate/lead to post-recovery cognitive and
neural declines. Thus, it is critical to explore the factors that influence the environments
in which people with brain injuries return with respect to level of enrichment, so that
factors can be adjusted to provide optimal levels of EE. In the current section, we will
discuss how post-discharge variables map onto EE and we will also discuss findings that show how these examples of EE (or lack thereof) correspond to human TBI outcomes.

2.1. What is EE in the post-discharge environment?
Continued participation in environments that are challenging, yet at levels that allow people to participate and remain motivated to do so, is the crux of EE. In section 2, we summarized findings demonstrating that people who (1) attend more social events, (2) are more physically active, and (3) engage in novel tasks (e.g., learning a new language, playing bridge) are mentally healthier. For TBI survivors, without continued support to foster recovery, community re-integration will continue to be a major obstacle. While demographic variables (i.e., age, pre-morbid intelligence, level of education) are important after brain injury (Green et al., 2008; Ruff et al., 1991), environmental variables (e.g., access to insurance coverage) also play a vital role in recovery, as will be discussed. These variables map onto EE in that they provide cognitive, social and physical stimulation through access to therapy, community resources, returning to meaningful occupations, and encouraging engagement in their environments.

2.2. Post-discharge factors that influence stimulation
A number of factors influence the degree of cognitive, social and physical stimulation either directly (e.g., presence of community resources such as a support groups or fitness centres) or indirectly (e.g., by influencing access to therapy, which provides stimulation). These include insurance, financial support, social support and community resources.

2.2.1. Insurance
As recommended by Turner-Stokes et al. (2005), after discharge from in-patient rehabilitation, TBI survivors should have access to out-patient or community-based services appropriate to their needs to facilitate the recovery process. Till and colleagues (2008) demonstrated that post-recovery cognitive decline was negatively correlated with the hours of therapy (i.e., more hours of therapy correlated with less decline). It has been widely demonstrated that individuals who have insurance, receive more access to therapy after discharge than those who do not (Chen et al., 2012; Heffernan et al., 2011; Lundqvist and Samuelsson, 2012; Pressman, 2007). Those that are insured have better access to post-acute medical care, which includes physical, occupational, and cognitive therapies, as well as home health and nursing needs, modification of living environment, vocational training, and job retraining (Shafi et al., 2007). In line with these findings, Shafi et al. (2007) found that ethnic minorities were less likely to be insured and more likely to have moderate to severe disability at follow-up.

2.2.2. Financial support
Similar to Shafi et al. (2007), Staudenmayer and colleagues (2007) examined ethnic disparities in long-term functional outcomes after TBI. They concluded that a possible explanation for their findings that minorities demonstrated worse long-term functional outcome was that they had less social and financial resources to support them. Additionally, in a study examining perceived needs after brain injury, many TBI survivors reported still requiring help managing money one year post-injury (Corrigan et al., 2004). Sander et al. (2009) reported that after controlling for age, education, injury
severity, and race/ethnicity, income made a significant contribution to the variance in social integration and in a more recent study, Sander et al. (2011) reported that TBI survivors perceived financial issues (e.g., home ownership, insufficient funds), as contributing to decreased participation in the community. Increased financial burden can mean less access to expensive resources (e.g., therapy, participating in social activities, transportation) and increased workload, as well as stress, to be meet costs of living.

2.2.3. Social support

Logically, a supportive social network influences participation in therapy, for example by providing transportation, accompaniment to therapies, supervision for recommended regimens for which safety is of concern (e.g., a gym program), and would thereby directly influence the amount of cognitive, social, physical exercise TBI survivors can receive. Turner et al. (2007) also showed that those who had more supportive and closer networks at home had better transitions from the hospital setting to the home environment, as this was related to more access to social activities and transportation outside the home. Support for this assumption are studies that have demonstrated that those with less social support often have less access to therapies (Keightley et al., 2011; Sander et al., 2009; Turner et al., 2009b).

2.3. Post-discharge factors that influence engagement

Without private insurance, and with less social and financial resources, TBI survivors may be less able to engage in stimulating activities to facilitate recovery. However, there are also factors that influence the level of engagement in the post-discharge environment, such as the amount of family support and patient education provided, as well as the structure and routine present in their home environment.

2.3.1. Family support

In Freeman’s (1997) review of community-based rehabilitation for TBI survivors, he suggested that the level of care in the home setting, with a strong support network, can play a major role in successful rehabilitation. The family environment may provide a wide variety of activities that are inclusive, stimulating and meaningful to the individual. This has been suggested as essential for experience-dependent neural plasticity (i.e., active engagement to improve function and transfer of skills)(Kleim and Jones, 2008) and generalization of skills (i.e., Toglia’s guidelines to use meaningful activities in therapy)(Toglia, 1991). In a case study by McCormack and Lilliard (2009), a TBI survivor receiving community rehabilitation was followed for three years. The authors reported that the supportive and effective care system in his family facilitated his recovery following severe TBI. His progress was attributed to active familial involvement, helping him with goal setting and carry-over between sessions. Furthermore, learning took place in his environment, increasing his ability to generalize skills. They concluded that these findings “add further weight … to the thesis that, with the right support, there is no place like home.”

2.3.2. Education

Corrigan et al. (2004) reported that TBI survivors who initially reported requiring help participating in recreation still did not have their perceived needs (viewed as a measure of
quality of life) met one year post-injury. Likewise, Sander et al. (2011) reported that for TBI survivors, feeling more integrated into the community was related to greater participation in their environments. Several studies have indicated that the most often-reported barrier is adequate preparation prior to discharge (Keightley et al., 2011; Rotondi et al., 2007; Sander et al., 2011; Sander et al., 2009; Turner et al., 2011b). Many TBI survivors and their care-givers report that they were not given enough information regarding brain injuries (e.g., behavioural sequelae), how to access community resources (e.g., rehabilitation, emotional support, respite services), or how to access or implement home therapies.

2.3.3. Routine& schedules

The above adage that ‘there is no place like home’ may stand true when TBI survivors return to an environment that is well-equipped and has sufficient support; greater access to therapy and rehabilitation services (i.e., via insurance coverage), strong social support networks and continued support in the home environment map onto EE post-discharge in that they allow for and encourage participation in cognitively, physically and socially stimulating activities.

However, many studies document that TBI survivors report feeling ill-prepared for the transition from hospital to home (Rusconi and Turner-Stokes, 2003). Several qualitative studies have explored the transition home, and the barriers or difficulties that TBI survivors experience (Rittman et al., 2004; Turner et al., 2007; Turner et al., 2011a; Turner et al., 2009b). Rittman and colleagues (2004) found that, post-discharge, commonly reported problems were increased idle time, boredom, and little-to-no engagement in meaningful activities. Survivors often reported, “finding something new every day that they couldn’t do.” When routines were not re-established, survivors and caregivers experienced more chaos and disruption to the transition home. Turner et al. (2011a) examined perspectives concerning recovery and adjustment during the transition phase from hospital to home, and found that the process of adjusting emotionally to life at home posed significant challenges for many brain-injury survivors during this phase.

Turner et al.’s (2007) qualitative study of brain injury survivors’ experiences with the transition from hospital to home reported similar findings in terms of difficulty re-engaging in meaningful activities and occupations. Survivors and caregivers reported difficulty finding appropriate services post-discharge, as well as services that were of suitable intensity and duration. However, those who were able to create a routine or structure once at home had better transitions. Essentially, this facilitated participation in their environments by providing organization in their daily schedules, which had been previously often provided for them in the rehabilitation setting. Turner et al. (2009b) also examined re-engagement in meaningful occupations during the transition from hospital to home in brain-injury survivors. Many survivors reported that recovery sped up at home, and caregivers frequently attributed this to key elements such as creating routines and schedules, which enabled participation in meaningful activities. However, for those that did not have such experiences, not being able to participate in desired occupations led to stress and frustration. Turner et al. (2009b) found that “for some participants, the impact of this change in environment, coupled with the reality of not being able to engage in
their desired occupations, led to a relatively unproductive lifestyle in which the main activity of their day involved little more than watching television or playing computer games.” In Hoogerdijk et al.’s (2011) study of identity after TBI, the authors suggested that the adaptation process is a necessary struggle to gain new identity and it is facilitated by engagement in familiar occupations in familiar environments. In line with this finding, Nalder et al. (2012a; 2012b) reported that TBI survivors that were able to reengage in meaningful occupations had greater perceived success of the transition from hospital to home. Reengagement in meaningful occupations was often experienced by individuals with higher levels of global functioning and psychosocial integration.

The research presented in this section of the scoping review provides evidence that there are variables in the post-discharge environment that influence the amount of stimulation available and other variables that influence the level of engagement in EE. Largely, evidence suggests that those with better access and resources that map onto EE (i.e., insurance coverage, financial and social support) and those that are in environments that encourage participation (i.e., strong familial support, access to educational resources, more structure) have better functional outcomes.

Discussion

Perhaps the most compelling (preliminary) evidence of the benefits of EE in the post-acute stages of recovery comes from work by Miller et al. (this issue), where more engagement in enriched environments, defined as participation in activities involving cognitive, physical, and social demands, is correlated with less hippocampal volume loss. Further evidence comes from Till et al.’s (2008) finding of a relationship between hours of therapy at five months post-injury and degree of cognitive decline, which they hypothesized may be due in part to lack of access to complex and enriched environments.

As we have discussed, a large corpus of studies have demonstrated the benefits of EE in healthy and brain-injured animals. There is evidence of neuroplastic change after EE exposure, with beneficial changes to neuroanatomy and neurochemistry (Kramer et al., 2004). These studies further support Coulson et al.’s (2004) hypothesis that synaptic input is critical to offset atrophy, in that increased input regulates neuronal survival, and prevents or attenuates apoptosis. This is of particular relevance to the neural decline observed in the post-acute stages after TBI. Turner and Green’s (2008) proposition that negative neuroplasticity (i.e., reduced activity schedules) may undermine long-term outcome in TBI, is also in accord with the hypothesis that EE may indeed play an important role in recovery.

In humans, engaging in cognitively, socially, and physically stimulating activities is related to better cognitive functioning in younger and older adults. Studies have also demonstrated that therapies for TBI survivors delivering continuous and intensified interventions result in better recovery at all levels of analysis, as well as better functional gains. These therapies have critical elements of EE, such as novelty, intensity and prolonged periods of engagement in meaningful activities.

According to Schooler’s (1987) model of environmental complexity, when cognitive efforts are reinforced and rewarded, people are motivated to continue engaging in
complex environments, which in turn enhances cognitive functioning. However, when
TBI survivors cannot participate in complex environments, whether due to cognitive
impairment or lack of resources, there is no reward and little motivation to continue to do
so. Animal literature examining EE has provided critical evidence for maintaining high
levels of enrichment and stimulation post-discharge (Amaral et al., 2008; Bennett et al.,
2006; Hamm et al., 1996; Hoffman et al., 2008). Findings that support the ‘Use it or Lose
it’ theory also suggest that continued engagement in mentally effortful activities is
necessary to maintain cognitive functioning (Huppert, 1991; Mackinnor et al., 2003;
Pushkar et al., 1997; Salthouse, 2006; Shors et al., 2012), and that an individual’s
environment can influence level of activity (Winocur, 1998; Winocur and Moscovitch,
1990). While TBI survivors may benefit from capacity-enhancing and intensified
therapies provided in hospital, animal models have demonstrated that the effects of this
enrichment will only continue to persist with longer exposure periods (Amaral et al.,
2008). Furthermore, transitioning from a more stimulating/complex environment to a
lesser one may result in a loss of benefits (Winocur, 1998).

The aim of this paper was to examine the question whether EE in the sub-acute and
chronic stages of injury can influence progressive neural and cognitive decline. The aim
of the first section was to establish the role of EE in long-term outcomes, and in
particular, in offsetting decline; the aim of the second section was to illustrate that in the
post-acute stages of injury, a number of factors influence the degree of EE. We have
argued that post-discharge environments map onto conventional variables considered to
create EE in that access to rehabilitative, social and community resources, as well as a
strong support networks, provides essential cognitive, social and physical stimulation.
Moreover, these factors have shown to influence outcomes.

While there is strong evidence to suggest that TBI may be a progressive injury,
more research needs to be conducted to further elucidate the role of EE in recovery. It is
important to note that the exact active ingredients of current interventions that incorporate
multi-context environments and higher intensity therapies are still unclear, and how they
compare to therapies that incorporate all elements of EE is still unknown. Furthermore,
studies are needed that examine whether there is a correlation between post-acute brain
changes and declines in function, as well as the type of environments that TBI survivors
return to post-discharge. Turner et al. (2008) recommended that research is needed to
explore the transition home after brain injury in order to “(i) Develop a comprehensive
theoretical framework of the transition phase; and (ii) facilitate both the validation of
current intervention strategies and the development of innovative/tailored intervention
approaches.”

As reported by caregivers and TBI survivors, creating a routine and structure around
daily activities facilitated engagement. Furthermore, activities that are meaningful and at
an appropriate level (e.g., tailored to the individuals specific impairments) to facilitate
participation are critical. Researchers that have examined the needs of TBI survivors and
their caregivers in the post-acute phase have recommended increased education provided
by health care institutions would be beneficial to ease the transition from hospital to
home (Arango-Lasprilla et al., 2011; Turner et al., 2009a; Turner et al., 2007; Turner et
al., 2011b). More resources and guidelines on how to create structure and daily routines,
as well as information regarding self-administered therapies and activities for the individual and their caregiver, would be beneficial. Further rehabilitation support during the post-acute stages of recovery, such as home assessments or on-going therapy maintenance, would also be optimal. Gan and colleagues (2010) examined the support needs after brain injury and made several recommendations for support services. They suggested that family systems-based services should be accessible, life-long, individualized and flexible, as well as efficient, and that support system-based services should include proper diagnoses, incorporate a multi-component approach, provide brain-injury-specific services that are responsive to needs with proactive follow-ups, and importantly, provide continuous education. The benefits of social peer-mentoring programs as an intervention to enhance improvements in social integration for TBI survivors has also shown promise in recent studies and is currently being further investigated (Hanks et al., 2012; Struchen et al., 2011).

TBI survivors often fail to return to pre-injury levels of cognitive functioning, as well as employment and income, and these factors have been shown to be related with life satisfaction, perceived quality of life, depression and social isolation (Christensen et al., 2008; Eriksson et al., 2009; Hawthorne et al., 2009; Resch et al., 2009; Shigaki et al., 2009; Strandberg, 2009; Tsouaousides et al., 2009). Assuming that post-acute atrophy contributes to the failure to return to pre-injury levels of cognitive function and thus successful community integration, then the clinical consequences are notable.

While the elements that comprise an enriched environment may be different from one person to another, it is evident that engagement in such environments is beneficial at both the cognitive and neural level, and thus it is plausible that EE can offset post-acute decline that has recently been documented in TBI survivors. Providing information and support to ease the transition home, information about the benefits of an enriched environment and guidelines on how to successfully participate in enriched settings, may be key elements in improving recovery. Most importantly, it may be a critical factor to facilitate successful community integration.

References


