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# *Reorganizing Therapy: Changing the clinical approach to upper limb recovery post-stroke*

*Short title*

## *Reorganizing upper limb therapy post-stroke*

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## *Abstract*

Stroke is the leading cause of adult disability and, as a consequence, most therapists will provide healthcare to patients with stroke during their professional careers. An increasing number of studies are investigating the association between upper limb recovery and changes in brain activation patterns following stroke. In this review we explore the translational implications of this research for health professionals working in stroke recovery. We argue that in light of the most recent evidence, therapists should consider how best to take full advantage of the brain's natural ability to reorganize, when prescribing and applying interventions to those with a stroke-affected upper limb. The authors propose that stroke is a brain-based problem that needs a brain-based solution. This review addresses two topics, anticipating recovery and maximizing recovery. It proposes five practice-ready recommendations that are based on the evidence reviewed. The over-riding aim of this review and discussion is to challenge therapists to reconsider the healthcare they prescribe and apply to people with a stroke-affected upper limb.

## *Introduction*

Stroke is the leading cause of adult disability and, as a consequence, most therapists will provide healthcare to patients with stroke during their professional careers. An increasing number of studies have investigated associations between upper limb (UL) recovery and changes in brain activation post-stroke (Buma et al, 2010; Hodics et al 2006; Hubbard et al 2012a; Kokotilo et al 2010; Rehme & Grefkes, 2013; Richards et al 2008). Evidence indicates that the mechanisms supporting the brain's learning processes are recruitment (reorganisation) of spared regions (Carey et al., 2013; Rehme & Grefkes, 2013; Ward, 2011) and growth of new nerve cells (neurogenesis) (Li et al., 2010). Both processes, when combined, define what is now referred to as neuroplasticity (Dobkin & Carmichael, 2005; Johansen-Berg et al., 2004). In this paper, the authors will focus on the capacity of the brain to reorganise regions that support particular functions, and seek to answer the following question as reviewers of the evidence, researchers in the field and

academic educators: What are the translational implications of this research for therapists working in stroke recovery?

Stroke is a brain-based problem that needs a brain-based solution. To apply an evidence-based approach in our management of patients with a stroke-affected UL, we must be conversant with the research-generated knowledge, and be able to evaluate its influence on clinical practice (Grol & Grimshaw, 2003). Applying an evidence-based approach means that we use scientific principles in our clinical decision-making, including our selection of stroke recovery assessments (Heart and Stroke Foundation of Ontario and Registered Nurses' Association of Ontario, 2005; Kitsos et al 2011), interventions (De Wit et al., 2006; French et al., 2007) and strategies (Hubbard et al, 2009). This approach requires us to continually translate new knowledge that has been generated by research, into everyday clinical practice. Following discussion about a particular issue, this review will make practice-ready recommendations for therapists prescribing and applying healthcare to people with a stroke-affected UL.

## *Anticipating Recovery*

In the past 15 years, evidence has demonstrated that the human brain has a natural and life-long capacity to reorganize in response to changes in behavioural demands (Cramer et al., 2011; Dobkin & Carmichael, 2005; Pascual-Leone et al, 2005). Whereas just over a decade ago, therapists believed that the adult brain was relatively static, we now know this to be entirely untrue! Therefore, as a result of this evidence, we should anticipate some recovery in most people diagnosed with stroke. Not only should this be our expectation in the acute and sub-acute phases post-stroke, it should also be our expectation in the chronic phase post-stroke (Hakkennes & Keating, 2005; Richards, et al., 2008). This is an excellent example of how new knowledge can challenge long-held beliefs, and it reinforces the benefits of applying a scientifically rigorous and evidence-based approach to healthcare (Hubbard et al., 2012). As Hankey (2002) stated, fortunately the days of “ignorance, nihilism and negativity” (preface) in stroke are fast disappearing.

In healthy adults, Elbert et al (1995) demonstrated that as a person learned to play the violin, the cortical representation of the non-dominant hand, (the hand that takes the lead role in violin playing,) increased over the learning period. Following stroke, evidence indicates that the non-lesioned areas of the brain, or those that have been “spared” from the impact of the stroke and are therefore still essentially healthy, reorganise (Buma, et al., 2010; Hubbard et al., 2012a; Kerr et al, 2013). This reorganisation capacity is the theoretical mechanism supporting acute, sub-acute and long-term recovery (Carey & Seitz, 2007), and the basis on which we argue that therapists should anticipate recovery in most people with a stroke-affected UL. The brain’s natural ability gives new hope and impetus to therapists and stroke survivors alike.

Rather than assessing and managing stroke as a body-based problem, management should be focussed on what is happening in the brain. Thrombolysis is a contemporary example of a brain-based solution. It aims to salvage viable brain networks in the hyper-acute phase post-stroke (Parsons et al., 2010), and, to validate its evidence-based credentials, it has been scientifically tested so that the right dose is prescribed to the right patient, at the right time and in the right way. This approach should also be applied to post-stroke rehabilitation with the same scientific rigour. On the basis of the evidence related to brain activation patterns post-stroke, the interventions being prescribed and applied to people recovering from stroke should take full advantage of their influence on the brain (Khaleel et al, 2010; Lindenberg et al, 2010). Novel examples include imagery (Sharma et al., 2009), mirror therapy (Michielsen et al., 2011) and SENSe (Carey, 2012) (a clinically proven approach to recovery of sensation post-stroke). Today’s stroke rehabilitation should focus on challenging the brain’s capacity to learn new ways of achieving already-familiar tasks.

The research investigating brain activation indicates that the patterns associated with recovery of a stroke-affected UL primarily involve the recruitment of two types of regions (Allred et al, 2010; Buma, et al., 2010; Kokotilo et al, 2009; Richards, et al., 2008). The first is perilesional; this term refers to regions of the brain that are directly adjacent to the area permanently damaged by the stroke. The second is spared regions; this term refers to regions that have been spared from the

impact of the stroke and includes, but is not limited to, perilesional regions. In relation to UL recovery, these regions are often supplementary or secondary regions which, prior to the stroke, were not as actively involved in the UL task and/or behaviour, for example, the ipsilesional (same side as the lesion) supplementary motor area and premotor cortex (Buma, et al., 2010; Hubbard et al., 2012a; Rehme & Grefkes, 2013; Richards, et al., 2008). What is interesting is that in the first month post-stroke, other regions often recruited include the ipsilesional anterior cingulate area and the bilateral cerebellum (Carey et al, 2005; Tombari et al., 2004). This suggests that in the first few weeks post-stroke, the restoration of UL function needs additional support from regions more closely related to attention, learning and error detection (Allman et al, 2001; Forstmann et al, 2008; Patel et al, 2013).

### Recommendation 1: Anticipating recovery

*In most patients with a stroke-affected UL, therapists should anticipate recovery and default to restorative strategies that seek to apply an "upstairs" approach which purposefully targets the brain's natural ability to reorganise.*

There is compelling evidence that many stroke survivors can experience improvement months, and even years, post-event (French, et al., 2007; Page et al, 2004; Richards, et al., 2008). As Carey and Seitz (Carey & Seitz, 2007) point out, different mechanisms underlie recovery at difference phases post-stroke (Carey & Seitz, 2007; Kwakkel et al, 2004; Richards, et al., 2008). However, whilst there is more potential to experience recovery in the first few weeks post-stroke (Carey & Seitz, 2007), in the chronic phase, the evidence indicates that recovery is still possible in those who engage in targeted programs of behavioural UL training (Hodics, et al., 2006; Richards, et al., 2008). On the basis of this evidence, we recommend that people with stroke be offered ongoing access to 'Booster Clinics' that aim to improve, or at least maintain, long-term function, cardiovascular health and a sense of well-being (Jones, 2006). We base this on the notions that firstly, the brain's ability to reorganise is *not* dependent on just the early weeks post-stroke, and secondly, the evidence of recovery potential from the chronic, post-stroke literature is compelling. This could also overcome the sense of abandonment by health services, that patients can experience following discharge from hospital after a stroke (White et al., 2007). In contrast to the long-term structure of chronic cardiac rehabilitation programs however, the evidence indicates that patients in the chronic phase post-stroke, would benefit more from short bursts of intensive, recovery initiatives which target tasks that are of interest to the patient and use approaches based on motivated learning (Richards, et al., 2008; Sabini et al, 2013).

### Recommendation 2: Ongoing recovery

*During their survival years, people with a stroke-affected UL, who are able to comply, should be offered the opportunity to attend "Booster Clinics" that use an intensive, repetitive, task-specific approach that is based on motivated learning.*

## *Maximizing Recovery*

Current evidence indicates that to maximize recovery of a stroke-affected UL, therapists should apply intensive, repetitive task-specific training (French, et al., 2007; Richards, et al., 2008), using everyday tasks that are meaningful and already familiar to the person with stroke (Hubbard, et al., 2009). However, the evidence indicates that there are significant challenges to applying an adequate intensity of UL intervention (Lang et al., 2009). For the purposes of this paper, we define intensity as the amount of time patients with a stroke-affected UL are actively engaged in everyday activities at a level that will drive neuroplastic changes. The issue of intensity post-stroke has two distinct lines of emerging evidence; one line is 'active', indicating that intensity matters, whilst the other line is 'passive', indicating that patients in hospital with stroke are often inactive. Our ability to overcome this hot/cold clinical dilemma is crucial to maximizing UL recovery post-stroke.

## *The active evidence*

This evidence indicates that to maximize recovery, patients with stroke should engage in intensive, task-specific programs as early as possible post-event (Dobkin & Carmichael, 2005), as recommended in nationally agreed clinical guidelines (Heart and Stroke Foundation of Ontario, 2007). In our randomised controlled trial, patients in the intensive-training group, who were within one month of experiencing a first-ischaemic stroke, all complied with the demands of a combined program of standard care and an additional two hours of intensive, task-specific UL training, for 5 days a week over 3 weeks (Hubbard et al, 2012b). We found this intensity to be clinically feasible and safe on the basis that no participants withdrew, and no adverse events were recorded. All those in the intensive-training group were compliant with what some therapists may perceive as a fairly demanding UL regime for patients so soon after a stroke. Perhaps this is one of the problems; as therapists we may need to re-think our perceptions about what is 'too demanding', if we are to adhere to nationally agreed clinical recommendations concerning intensity. Additionally, studies that have increased the intensity of early intervention post-stroke, including our own, rarely report adverse events related to post-stroke fatigue (Blennerhassett & Dite, 2004; French, et al., 2007; Lum et al., 2009; Scrivener et al, 2012). However, because there is also evidence indicating motor practice that is too intense in the very acute phase and disuse followed by intensive use in the post-acute and chronic phases may enlarge the lesion or result in less motor recovery than a more moderate intensity of practice (Leasure & Schallert, 2004; Lum, et al., 2009), more research is needed to clarify future approaches. In our experience, fatigue is an issue that is often raised as a potential barrier when therapists discuss increasing the early intensity of training. We may need to challenge long-held assumptions about the impediment of post-stroke fatigue to early intervention. As therapists, our perceptions, beliefs and concerns may hinder our ability to bridge the evidence-practice gap (Bayona et al, 2005; Dobkin & Carmichael, 2005; Heart and Stroke Foundation of Ontario, 2007). There are differing ways of defining intensity, for example, Scrivener et al (2012) prescribed 'intensity' in terms of the number of repetitions; therefore, further research and discussion is required before this can be adequately described. However, in the interests of providing a 'starting point' when it comes to UL recovery, the authors make the following recommendation on the basis of the protocol which they found to be clinically safe and feasible.

### Recommendation 3: Maximizing intensity

*In patients with a stroke-affected UL, strategies should be set in place that increase the intensity of UL behavioural training to at least 2 hours a day, 5 days a week for 3 weeks during the first month post-event.*

## *The passive evidence*

Whilst calls are made to increase the intensity of task-specific training, evidence is revealing that patients are doing very little in hospital (Bernhardt et al, 2007; Hubbard & Parsons, 2007), which brings us to the "cold" line of evidence. It seems that the average hospital ward admitting patients with stroke is environmentally bereft and occupationally non-challenging (Janssen et al., 2012). This evidence is not only cold, but grim, if you add issues such as a traditional reliance by most therapists on individual face-to-face sessions (De Wit, et al., 2006; Hubbard & Parsons, 2007) and 'risk averse' protocols to patients mobilising around the ward (New South Wales Health, 2011). Animal modelling studies initially demonstrated the clinical significance of an enriched environment to improving recovery outcomes following an ischemic stroke (Janssen et al., 2010; Ohlsson & Johansson, 1995) and researchers such as Janssen et al (2010) have investigated this further in studies involving patients undergoing stroke rehabilitation (Janssen, et al., 2012). All indications are that patients with stroke are often cared for in environments that actively discourage high levels of participation in everyday tasks. Could it be that today's average hospital ward is contraindicated for patients recovering from stroke?

We believe this active/passive clinical dilemma is currently the most pressing problem for those working to maximise recovery in patients with stroke. Unless it is resolved, these patients may not be able to achieve maximal UL recovery in the first month post-stroke, irrespective of the brain's ability to reorganize.

## Recommendation 4: Structuring the environment

*In patients with a stroke-affected UL, therapists should consider programs where the patients' environment is structured in a way that stimulates them to participate in everyday tasks at a level and intensity that is aimed at maximizing recovery.*

### *A multi-modal approach*

Maximizing recovery is the 'core business' of therapist who provide healthcare to people with a stroke-affected UL.

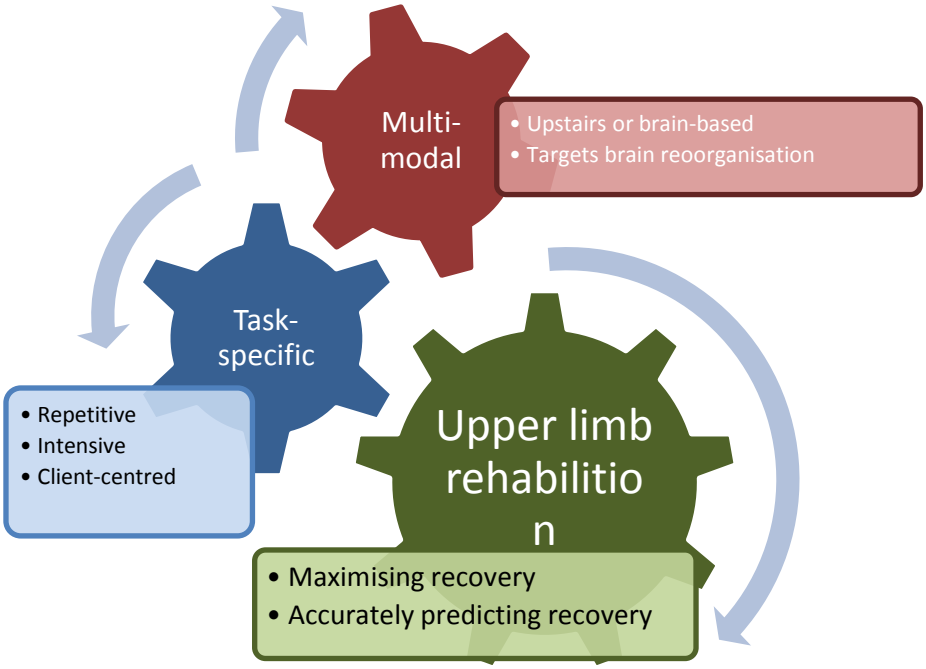


**Figure 1: Graphic depicting a potential hierarchy of restorative approaches in post-stroke rehabilitation that targets recovery of an affected upper limb**

In applying a task-specific approach, the evidence relating to brain reorganisation post-stroke indicates that consideration must be also given to the fact that these tasks are now more complex (Johnson & Prigatano, 2000; Riecker et al., 2010), and may require the brain to recruit regions that were not previously as engaged in undertaking the task, prior to the stroke. With this in mind, the authors propose that therapists apply strategies that purposefully build upon the task-specific approach (French, et al., 2007) (Figure 1). An approach that targets brain reorganisation by value-adding to repetitive, task-specific training, will be referred to as a 'multi-modal' approach (Johansson, 2012). Some example of strategies that fall under a multi-modal approach include those that aim to prime the brain (Carey, 2012; Stinear et al, 2008), those that include mental practice (Page, Szaflarski, Eliassen, Pan, & Cramer, 2009), and those that aim to overcome problems specific to UL recovery, for example, overcoming learned non-use by applying constraint-based interventions (Hakkennes & Keating, 2005; Page et al, 2005). Another approach that could be identified as multi-modal is one that purposefully uses tasks that require patients to use both arms bilaterally (Stinear et al., 2008). Bimanual or bilateral UL movement is usually smooth, responsive, accurate and reliable, relying on mastered cooperation between the dominant, more controlling limb and the non-dominant, more supportive limb. Both can work together in free-flowing, exquisite unison, achieving everyday tasks with high levels of accuracy and reliability, time and time again. Animal modelling studies have demonstrated that following injury to the brain, bilateral training can improve functional outcomes (Kerr et al., 2013), and in humans, bilateral skill learning has been shown to elicit changes in areas associated with 'attention-demanding task performance, processing of sensory information and corrective action-planning' (Debaere et al., 2004). A multi-modal approach is recommended on the basis that it seeks to apply a brain-based

solution to stroke recovery that drives the brain to use its natural ability to reorganize in response to changes in behavioural demands.

### Recommendation 5: Applying multi-modal strategies

*Therapists prescribing and applying healthcare to people with a stroke-affected UL, should consider strategies that apply a multi-modal approach that seeks to take full advantage of the brain's natural ability to reorganise.*

## *Conclusion*

Stroke is a brain-based problem that needs a brain-based solution. Following stroke, it is time to reconsider the evidence related to anticipating recovery and maximizing recovery, and time to reorganise how this is best applied in clinical practice. It is time to consider strategies that aim to ensure that the rehabilitation prescribed to patients recovering from, or living with stroke, meets the intensity requirements of an effective task-specific approach. It is time to consider strategies and approaches that take full advantage of the brain's natural ability to reorganise throughout a person's lifetime.

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