Cognitive Impairment, Spontaneous Recovery and Environmental Enrichment Post Stroke

Presented by

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Declaration

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4. *The work in this thesis was carried out under the supervision of Associate Professor Frini Karayanidis, University of Newcastle and Dr. Karen Drysdale, University of Newcastle*

5. *The conduct of this research was approved by the Hunter New England Human Research Ethics Committee and the University of Newcastle Human Research Ethics Committee (approval number 09/09/16/5.08.)*

Signed:…… Date:…….

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Statement of Collaboration and Authorship

I hereby certify that I am joint author of the scholarly work embodied in this thesis *"Cognitive improvement during stroke rehabilitation: Spontaneous recovery or practice effects?"*

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Structured Abstract

Background: Cognitive impairment post stroke is common yet few studies have investigated cognitive deficits in the early stages post stroke. Spontaneous recovery of post stroke cognitive deficits has been reported. Studies assessing this phenomenon require the use of repeated neuropsychological assessments, however, the majority of this research fails to account for practice effects. The effects of intervention for cognitive deficits have also been explored. Stroke animal models reveal significant improvements in cognition following environmental enrichment, although human stroke studies are limited. Aims: The current study aims to 1) assess cognitive impairment in the early stages of stroke 2) assess spontaneous recovery of cognitive deficits while accounting for practice effects 3) assess the effects of enrichment on cognitive functioning post stroke. Method: Forty one stroke patients were assessed on memory, attention and executive functioning tasks on admission to and on discharge from a rehabilitative ward. Results were compared to 15 aged matched health controls. Cognitive performance was also compared between stroke participants allocated to a control or intervention (enrichment) group. Enrichment took place during the patient's rehabilitative stay and consisted of individual enrichment (books, music magazines) and communal enrichment (Nintendo Wii games, board games). Results: Stroke participants were impaired on all neuropsychological tasks compared to healthy controls. Stroke patients improved at the same rate as healthy controls on tasks of memory and attention therefore suggesting improvement was a result of practice effects, not spontaneous recovery. Stroke patients improved at a significantly greater rate than healthy controls on the executive functioning task therefore suggesting evidence of spontaneous recovery in

this particular cognitive domain. Enrichment did not enhance any of the cognitive deficits experienced by stroke patients. Conclusion: Cognitive impairment and spontaneous recovery in the early stages of stroke requires further attention. In particular, practice effects need to be accounted for. Further research on environmental enrichment should include increasing the duration of the enrichment period, and providing satisfactory methods for documenting patients' engagement in enrichment activities.

1. CRITICAL REVIEW OF THE LITERATURE

1.1 Stroke

Stroke is the second leading cause of death in Australia (Australian Institute of Health and Welfare 2011). In the last year alone, approximately 50,000 Australians suffered a stroke costing the Australian Government almost $50 billion (Australian Institute of Health and Welfare 2011). Approximately 80% of strokes are classified as ischemic strokes in which the brain is deprived of blood supply due to blockage of an artery (Hyman, 2002). The remaining 20% of strokes are classified as haemorrhagic strokes in which blood vessels either rupture within the brain (intracerebral haemorrhage) or rupture in the space surrounding the brain (subarachnoid haemorrhage; Hyman, 2002).

Stroke survivors often endure significant physical (Chen, Tang, Chen, Chung, & Wong, 2000), emotional (Dennis, O'Rourke, Lewis, Sharpe & Warlow 2000), and cognitive dysfunction (Rasquin, Lodder & Verhey, 2005) which ultimately leads to a substantial reduction in their quality of life (Nys, van Zandvoort, Van der Worp, Haan, Kort, Jansen, & Kappelle, 2006). There is a plethora of research investigating the assessment and intervention for motor impairment (Barreca, Wolf, Fasoli, Bohannon, 2003; Langhorne, Coupar & Pollock, 2009) and emotional problems (Hackett, Yapa, Parag & Anderson, 2005) of stroke individuals. However, the investigation of cognitive impairment and the development of rehabilitation programs for stroke individuals with cognitive deficits have been afforded less attention (Sarkamo, Tervaniemi, Laitinen, Forsblom, Soinila et al. 2008).

1.2 Cognitive Impairment Post Stroke

Initial research into the cognitive deficits experienced by stroke survivors focussed on the incidence and prevalence of dementia (Zhu, Fratiglioni, Guo, Aguero-Torres, Winblad, Viitanen, 1998; Desmond, Moroney, Sano & Stern, 2002; Khedr, Hamed, El-Shereef, Shawky, Mohamed, Awad, Ahmed, Shehata, Eltahtawy 2009). Research has revealed that stroke survivors, who were dementia free prior to injury, were four times more likely to develop progressive dementia than age-matched healthy controls (Desmond et al. 2002). Longitudinal studies have revealed that 12.2% to 26.5% of stroke individuals develop dementia by 1 year post-stroke (Tatemachi, Foulkes, Mohr, Hewitt, Hier, Price & Wolf, 1990; Rasquin, Lodder, Ponds, Winkens, Jolles, Verhey, 2003), whilst 21.3%, 23.2% and 32% of stroke survivors are classified as demented, three, four and five years post-stroke respectively (Henon, Durieu, Guerouaou, Lebert, Pasquier & Leys, 2001; Loeb, Gandolfo, Croce, Conti 1992; Bornstein, Gur Treves, Reider-Groswasser, Aronovich, Klimovitzky, Varssano, Korczyn, 1996).

Without doubt, it is evident that post stroke dementia significantly impacts on an individual's cognitive functioning (Desmond et al. 2002; Zhu et al. 1998;). However, stroke survivors need not necessarily suffer from post-stroke dementia in order to experience debilitating cognitive deficits (Stephens, Kenny, Rowan, Allan, Kalaria, Bradbury & Ballard, 2004). These type of stroke survivors who are referred to as Cognitively Impaired No Dementia (CIND; Stephens et al. 2004), Vascular Cognitively Impaired No Dementia (VCI-ND; Rockwood, Wentzel, Hachinski, Hogan, MacKnight, McDowell, 2000; Planton, Peiffer, Albucher, Barbeau, Tardy, Pastor, Januel, Bezy, Lemesle, Puel, Demonet, Chollet & Pariente, 2012) or Mildly Cognitively Impaired (MCI; Petersen 2004; Ballard, Rowan, Stephens, Kalaria &

Kenny, 2003), interchangeably throughout the literature, are arguably significantly affected by their cognitive deficits (Stephens et al. 1994; Planton et al. 2012). Certainly, the cognitive impairments experienced by stroke individuals are positively correlated with functional impairments and are negatively correlated with independent living at 3 months post stroke (Tatemachi et al. 1994). Cognitively impaired stroke individuals are at significant risk of experiencing further deterioration of their cognitive abilities (Rasquin et al. 2004) and of developing dementia 1 year post stroke (Tham, Auchus, Thong, Goh, Chang, Wong, & Chen, 2002) whilst institutionalization and mortality rates are significantly greater than stroke individuals without cognitive impairment at 1, 3 and 4 years post stroke (Patel, Coshall, Rudd & Wolfe, 2003).

Given the difficulties and poor outcomes that cognitively impaired stroke individuals face, recent research has focused on the need to assess cognitive impairment post stroke (Stephens et al. 2004; Tatemichi et al, 1994) The detection of cognitive impairment post stroke is considered vital in order to aid the development of intervention programs which may reverse or prevent further cognitive deterioration and subsequently improve patient outcomes (der Ser, Barba, Morin, Domingo, Cemillan, Pondal & Vivancos, 2005). However, understanding and defining the nature of cognitive impairment post stroke poses a number of challenges as there are no specific assessment or criteria to define this population (McDonnell, Bryan, Smith & Esterman, 2011)**.** Thus, research has used a variety of methods to detect cognitive impairment post stroke (McDonnell et al 2011).

Early studies commonly used the Mini-Mental State Exam (MMSE; Folstein, Folstein & McHugh, 1975) an 11-item standardised screening tool for cognitive impairment. Studies revealed that 15% to 38% of stroke patients were classified as

cognitively impaired at 3 months post stroke with the domains of learning, memory and attention most affected (Szatmari, Fekete, Csiba, Kollar, Sikula & Bereczki 1999; Patel et al. 2002). Longitudinal studies revealed that 35%, 30% and 32% of patients were classified as cognitively impaired at 1, 2 years and 3 years post stroke respectively (Patel & Coshall, 2003). These studies are supported by the Framingham study in which stroke patients' MMSE scores significantly declined, particularly in the areas of orientation and language, and to a lesser extent in the domains of attention and visuo-construction, compared to their MMSE scores pre stroke (Kase, Wolf, Hayes, Kannel, Beiser & D'Agostino, 1998).

The MMSE is widely accepted as a reliable, simple, quick and easy to use tool **(**Arciniegas, Kellermeyer, Bonifer, Anderson-Salvi & Anderson, 2011**)** which has allowed large co-hort studies (Kase et al. 1998) to provide a comparison between pre-morbid and post stroke cognitive functioning. Nevertheless, the MMSE presents a number of limitations: it only provides a vague estimate of an individual's overall cognitive impairment and its subdomains (Tombaugh & McIntyre, 1992), it fails to detect more mild cognitive impairment **(**Tombaugh & McIntyre, 1992) and it does not measure executive functioning (Pendlebury Mariz, Bull, Mehta & Rothwell, 2012). Consequently, it is argued that neuropsychological batteries should be used as the "golden standard" to provide more specific and detailed information regarding the cognitive impairments experienced by stroke patients (Cumming, Randolph, Marshall & Lazar, 2013).

Studies comparing hospital based stroke patients to aged matched healthy controls on a variety of neuropsychological batteries, have revealed that stroke individuals are significantly impaired in orientation, language, attention and memory (Tatemachi et al. 1994) 3 months post stroke. Subsequent hospital based studies also

report specific deficits in delayed verbal recall but not in immediate verbal recall, as measured by the Rey Auditory Verbal Learning Test (RAVLT; Rey 1964). Speed of information processing is also significantly affected (Hochstenbach, Mulder, Limbeek, Donders & Schoonderwaldt, 1998). More recent hospital-based control studies have highlighted the need to conduct neuropsychological assessments sooner than the 3 month period to provide further insight into the cognitive profiles of stroke patients (Nys, Zandvoort, Kort, Jansen, Haan & Kappelle, 2005). One of the few studies assessing patients as early as 3 weeks post stroke revealed that almost 40% of patients exhibited deficits in executive functioning and/or visual perception and construction, with approximately a quarter displaying impairments in visual and verbal memory, abstract reasoning and language (Nys et al. 2005). These results differ somewhat to that of Lesniak, Bak, Czepiel, Seniow, & Czlonkowska, (2008) who reported 48.5% and 24.5 % of patients displayed impairments in attention and memory respectively, although only 18.5% displayed executive functioning impairments 14 days post stroke.

Community-based control studies also report significant impairment in the areas of attention, language, perception and spatial ability, in addition to highlighting significant deficits in executive functioning 3 months post stroke (Stephens 1994 et al; Srikanth, Thrift, Saling, Anderson, Dewey, Macdonell & Donnan, 2003). This is supported by the findings of Planton et al. (2012), who reported significant impairment in memory (free recall, cued recall and recognition), verbal and visual working memory, attention and executive functioning deficits at 109 days post stroke. However, discrepancies in the literature are apparent. For example, Stephens et al. (1994) compared healthy controls to stroke individuals classed as cognitively unimpaired and stroke individuals classed as cognitively impaired no dementia

(CIND). Stephens et al. (1994) reported that stroke individuals who were classed as cognitively unimpaired (scored > 80 on the Cambridge Cognitive Examination; CAMCOG), still displayed deficits in attention and executive functioning, but not in memory. On the other hand, stroke individuals classed as CIND displayed deficits in all three areas of cognition.

Longitudinal studies have provided some understanding of the long-term impact of stroke on cognitive functioning (Serrano, Domingo, Rodriguez-Garcia, Castro & del Ser 2007). Serrano et al. (2007) reported that cognitive impairment was prevalent in 19-26% of stroke individuals at 3-24 months post stroke (Serrano et al. 2006) while del Ser et al. (2005) reported that approximately 20% of stroke patients showed deterioration in overall cognitive functioning from 3 months to 2 years post stroke. Although these studies provide evidence that cognitive impairment is persistent at least 2 years post stroke in a substantial proportion of patients, they do not specify the specific cognitive domains that are affected (Nys et al. 2005).

More recent longitudinal studies have focussed on this issue. Lesnizk et al. (2008) reported that attention and memory deficits are highly prevalent in stroke populations at 1 year post stroke while executive functioning deficits are less common. Furthermore, Nys et al. (2005) reported that a small proportion of patients with cognitive deficits at 3 weeks post stroke developed further impairments in the areas of abstract reasoning, language, visual and verbal memory and visual perception and construction by 6 to 10 months post stroke.

The above research provides substantial evidence of short term and long term cognitive impairments in stroke survivors. Nevertheless, there is inconsistent evidence regarding the specific cognitive domains that are affected. For example, while some studies have shown that stroke participants perform at similar levels to

controls on memory tasks (e.g. Stephens et al. 2004), other studies find significant memory impairment at 3 months (e.g. Hochstenbach et al. 1998; Lesniak, 2008) and 1 year post stroke (Lesniak et al. 2008). These discrepancies may be attributable to a number of factors, including differences in study design and patient characteristics, such asage, stroke type, stroke severity, and the number of prior strokes.

Moreover, as noted by McDonnell et al. (2011), another factor contributing to discrepancies between studies is that there is no standard neuropsychological battery to assess cognitive impairment post stroke. Consequently, researchers often use a wide range of tests to examine the same cognitive function and select "ad hoc cut-off points" to determine what constitutes cognitive impairment (Serrano et al. 2007). Furthermore, different studies use the same test to measure different cognitive functions. For example, while some studies use the Stroop and Trail Making Response Tests from the Delis-Kapln Executive Function System (Delis, Kaplan & Kramer 2001) to measure attention (e.g. Rasquin et al. 2004, Rasquin 2002 et al; Hochstenbach et al. 1998), other studies use these same tasks as a measure of executive functioning (e.g., McDonnell et al 2011). In addition, more recent studies have gone as far to include visual and verbal memory as part of executive functioning (e.g. Planton et al. 2012). Indeed, the wide variety of tests used to measure domains such as executive functioning may provide an explanation for the discrepant findings to date. Such an example is evident in the study by Lesniak et al. (2008). As previously mentioned, Lesniak et al. (2008) reported that executive function deficits are less common than attention and memory deficits. However, they do not use an established test of executive functioning. Specifically, Lesniak et al. (2008) measured executive functioning using a poorly characterised version of the "go, no go test", the Trail Making Test A&B from the D-KEFS, and the Verbal

Similarities test from the WAIS-IV, which is also used as a measure of verbal reasoning. Consequently, the finding that executive functioning is the least affected cognitive domain may be a result of the tests of executive functioning used rather than an absence of deficits in executive functioning per se.

This issue is further complicated by the argument that cognitive domains are not independent of one another, for example, the ability to remember and/or organise verbally or visually presented information will also be dependent on attentional skills (Cumming, et al. 2013). For this reason Cumming et al. (2013) highlight that an impairment in one domain may be partly attributable to impairment in another. Also, an individual's performance on tasks may be affected by deficits in processing speed. Consequently, individuals may appear particularly impaired on tests that are time limited (Cumming et al. 2013).

In conclusion, it is evident that the methods used to assess cognitive impairment in stroke survivors present with numerous complications. Thus, further research is required to provide more accurate information regarding the cognitive impairments in stroke survivors, particularly during their hospital admission. This is essential in order to develop future rehabilitation interventions that may alleviate or aid the recovery of cognitive impairments of stroke individuals.

1.3 Spontaneous Recovery

During the past two decades, neuroscience research has paid particular attention to the brain's ability to repair itself following insult (Cramner, 2008). This phenomenon, referred to as neuroplasticity, has sparked major interest in the area of stroke and has led to the emergence of numerous studies investigating the spontaneous recovery of stroke patients (Murphy & Corbett, 2009). The

understanding of spontaneous recovery in stroke is considered important in order to guide the development of future interventions (Hochstenbach, den Otter & Mulder, 2003) and to inform practitioners which patients may or may not require intervention (Rasquin et al. 2005).

Early studies conducted on cognitive spontaneous recovery reported significant improvements in language abilities of aphasic stroke patients with the most significant gains occurring between 4 to 10 weeks post stroke (Lendrem & Lincoln, 1985). More recent studies have reported one quarter of stroke patients fully recovered from aphasia 18 months post-stroke (Laska, Hellblom, Murray, Kahan & Von Arbin, 2001). While these studies provide evidence of spontaneous recovery, they focus primarily on only one cognitive domain such as language (Hochstenbach et al. 2003). Consequently, research has emphasised the need to examine possible global cognitive recovery, in addition to other specific cognitive domains (Hochstenbach et al. 2003).

Studies using screening tools to measure cognitive recovery have revealed spontaneous improvements from 3 to 15 months post stroke with up to 50% of patients displaying an increase of 2.2 points on the MMSE by the latter date (Ballard et al. 2003). Studies using neuropsychological batteries have also provided evidence of cognitive spontaneous recovery. Tham et al. (2002) reported that 31% of patients classed as CIND via neuropsychological assessment at 6 months were classed as cognitively intact 1 year after whilst Rasquin et al. (2004) reported that 33.1% of stroke patients assessed as mildly cognitively impaired at 1 month no longer met this criterion at 6, 12 or 24 months, due to cognitive improvement. However, informative as these studies are, they provide no information regarding the specific cognitive domains affected (Nys et al. 2005). Desmond, Moroney, Sano & Stern (1996)

reported that 19 out of 151 patients tested on a neuropsychological battery at 3 months baseline performed significantly better on assessment at 12 months post stroke, noting specific improvements in the areas of memory, orientation, visuospatial function and attention. These findings are somewhat supported by more recent studies which have reported significant improvements in the areas of attention, in addition to small improvement in the areas of working memory and verbal recognition at 2 years post stroke compared to baseline assessment performed at 2.3 months (Hochstenbach et al. 2003).

Although these studies provide evidence of cognitive spontaneous recovery post-stroke it has been argued that the level of spontaneous recovery taking place may be greater than initially thought. The tendency for studies to use the period of 3 months for baseline assessment may lead to an underestimation of the recovery arising as significant improvement maybe occurring in the first few months post stroke (Nys et al. 2005). Certainly, this argument is supported by the finding that the brain experiences a plethora of neurological changes following insult which are believed to be restorative and neuroprotective in nature (Cramner, 2008).

However, studies performing baseline assessments prior to 3 months are scarce (Nys et al. 2005). Whilst this may be attributable to practical difficulties, for example, obtaining informed consent from the patient and their family at an early date, researchers have primarily been reluctant to assess stroke in the acute phase due to possible confounding factors such as lethargy, labile mood and unstable arousal states (Nys et al. 2005). Nevertheless, studies assessing cognition in the early stages of stroke have provided invaluable information regarding the level of spontaneous recovery that can occur. Rasquin et al. (2004) assessed patients at 1 month baseline and reported that 12.9% of patients displayed an increase of at least 10 points in

global cognitive functioning at 6 months post stroke with 52.1%, 37.2% and 41.8% improving in memory and speed of mental processing, respectively.

However, the majority of studies on spontaneous recovery do not include a healthy control group. Arguably, this may lead to an incorrect interpretation of their findings (Nys et al. 2005). While many of these studies compare stroke patients' cognitive performance to a control group at baseline they fail to retest the control population at the specific time points at which their stroke counterparts are assessed (Nys et al. 2005). Consequently, it is possible that practice effects may account for the cognitive improvements observed **(**Lezak, Howieson & Loring 2004**;** Nys et al. 2005). While the occurrence of practice effects is discussed in more detail further on, it is worth noting at this point that the research on spontaneous recovery post stroke has failed to adequately account for the presence of practice effects. Consequently, improvement in cognitive tasks may erroneously be attributed to spontaneous recovery (Calamia, Markon & Tranel 2012; Heilbronner, Sweet, Attix, Krull, Henry & Hart, 2013). A clear example of this argument is evident in the study by Rasquin et al. (2004). Rasquin et al (2004) state that the spontaneous improvement of specific cognitive functions in stroke patients found in their study cannot be attributable to practice effects because otherwise one would expect improvement in all domains rather than improvement in specific domains. However, this can be strongly disputed as research has clearly revealed that certain neuropsychological tests may be more susceptible to practice effects than others (McCaffrey, Ortega & Haase, 1995; Basso, Bornstein & Lang, 1999; Estevis, Basso & Combs, 2012). It is therefore reasonable to suggest that, in order to eliminate the possibility of practice effects, control participants should be tested at the same points in time as their stroke counterparts (Calamia et al. 2012).

Few studies assessing patients in the early phase of stroke have addressed this methodological flaw. Nys et al (2005) compared a healthy control group to stroke patients who were impaired in at least one cognitive domain at 3 week baseline (initially impaired patients) and to stroke patients who performed within the normal range for all cognitive domains at baseline (initially unimpaired patients). Results revealed that at 6 to 10 months post stroke 83%, 78% 41% and 54% of initially impaired patients displayed significant improvements in the areas of visual perception/construction, visual memory, abstract reasoning and language respectively (Nys et al. 2005). What's more, this improvement was significantly greater than that found in healthy controls thus suggesting that the improvement could not be attributed to practice effects. Nys et al. (2005) conclude that the improvements observed are greater than those reported in other studies, (e.g. Rasquin et al. 2004) as the earlier baseline assessment of 3 weeks allows the detection of the spontaneous recovery that occurs prior to the 3 months post stroke.

1.4 Cognitive Rehabilitation for Memory, Attention and Executive Functioning Deficits

As previously mentioned stroke patients suffer significant cognitive deficits, particularly in the areas of memory, attention and executive functioning (Tatemachi et al 1994; Stephens 1994 et al; Srikanth et al. 2003). Such deficits have also been commonly documented in TBI populations (Hart, Whyte, Kim, Vaccaro, 2005). Consequently, a large proportion of cognitive rehabilitation research has focused on interventions to assist with memory, attention and executive functioning impairments.

The majority of research for cognitive rehabilitation in memory impaired patients has focused primarily on compensatory external memory aids and mnemonics (Harris, 1984). TBI patients given external memory aids, such as diaries and note books increase their use of these items to assist with memory performance (Evans & Wilson, 1992) whilst the use of electronic devices, that provide visual and auditory reminders, have proved to be subjectively beneficial (Kim, Burke, Dowds, Robinson, Park et al. 2000.). However, memory aids may not always be accessible nor practical (Evans & Wilson 1992). For example, motor impairments may hinder a patient's ability to use such tools (Evans & Wilson 1992). Furthermore, the use of electronic devices may be limited by the patient's cognitive capacity which may result in the patient being unable to learn how to use the equipment (Levine, Horstmann & Kirsch, 1992).

Research into mnemonics has focused on visual imagery techniques in which patients are taught to produce a visual image following the presentation of verbal information (Kashel, Sala, Cantagallo, Fahlbock, Laaksonen & Kazen, 2002). TBI patients trained in visual imagery techniques over a 10 week period performed significantly better on verbal memory tasks (immediate and delayed) compared to patients receiving pragmatic memory training (Kashel et al. 2002). Similar techniques to counteract prospective memory deficits of TBI patients have proved beneficial with reports of improved performances on prospective memory tasks post intervention, in addition to a reduction in prospective memory problems as reported by relatives (Potvin, Rouleau, Senechal & Giguere, 2011).

There is a paucity of research into the cognitive rehabilitation of memory impairments in stroke patients (Lincoln & Weyman, 2007). Indeed, the majority of studies conducted in stroke patients with memory problems are single case

experimental designs with only one control based study to date (Lincoln, Majid & Weyman, 2007). Doornhien & De Haan (1998) trained memory impaired stroke patients in both visual imagery techniques and in strategies designed to help "re-order and re-organise" incoming information. Training included the use of specific homework exercises intended to provide opportunities to practice these skills in real life situations. Moderate results were revealed as patient's performance on memory tests post training improved only on tests that had been specifically rehearsed throughout the intervention and not on tests where no practice had occurred (Doornhien & De Haan, 1998).

Cognitive rehabilitation for attention deficits has focused on specific skills training and direct attention training (Park & Ingles 2001). Specific skills training, which involves the practice of particular individual tasks to improve attention, has been shown to be effective (Mazer, Sofer, Korner-Bitensky & Gelinas, 2001). However, the use of such an intervention is arguably greatly limited as there is a lack of research to support its generalization to other tasks and to everyday life (Park & Ingles, 2001). Unlike specific skills training, direct attention training aims to improve the underlying cognitive deficit (Sohlberg & Mateer, 1987). Attention Process Training (ATP), the most common form of direct attention training, is designed to address specific areas of attention deficits, i.e. sustained, selective, alternating and dividing attention (Sohlberg & Mateer ,1987). ATP involves training on simple tasks such as pressing a button when hearing a particular number and more complex tasks such as semantic categorization (Sohlberg & Mateer, 1987). TBI patients undertaking 24 hours of APT over a period of 24 weeks performed significantly better on tasks on the Paced Auditory Serial Attention Test (PASAT; Gronwall, 1977) than a control support and education group (Sohlberg, McLaughlin,

Pavese, Heidrich & Posner, 2000). Few studies have investigated the role of ATP in stroke individuals alone (Majid, Lincoln & Weyman, 2008). In a randomised control trial stroke patients undertaking the APT program for 30 hours over a 4 week period performed significantly better on the Integrated Visual Auditory Continuous Performance Test (IVA-CPT; Sandford & Turner, 2000) than controls assigned to standard care. However, no significant differences were found on their performance on the PASAT (Barker-Collo, Feigin, Lawes, Parag, Senior, Rodgers, 2009).

Cognitive rehabilitation for executive functioning deficits has focussed on interventions such as Goal Management Training, (GMT; Levine et al. , 2000). GMT involves a stepwise process of instructions and specific tasks combined with discussion and feedback to assist the development of various processes including goal setting, encoding, performing, inhibiting and self-monitoring (Levine et al. 2000). TBI patients undertaking GMT training performed significantly better on two executive functioning tasks, i.e. paper and pencil task and grouping task post intervention than patients undertaking motor skills therapy. Nevertheless, no significant differences were found on other executive functioning tasks such as proof reading and room layout (Levine et al. 1999). These results are partly consistent with those of Novakovic-Agopian et al. (2010) who combined a modified version of GMT with attention and mindfulness training. TBI patients showed significant improvement in memory and executive functioning tasks (Novakovic-Agopian et al. 2010).

Few studies have investigated the benefits of GMT training in stroke (Levine, Schweizer, O'Connor, Turner, Gillingham, Stuss, Manly & Robertson, 2011). Levine et al. (2011) studied a group of 19 patients, 6 of whom had stroke. Patients who undertook the GMT training performed significantly better than patients

undertaking a Brain Health Workshop on the Sustained Attention to Response Test (SART; Robertson, Manly, Andrade, Baddeley, Yiend, 1997) and the D-KEFs Tower Test (Delis et al. 2001). However, there were no significant differences in the patients subjective reports of their executive functioning skills (Levine et al. 2011).

Cognitive rehabilitation has come under considerable criticism. Firstly, the treatment process only singles out specific domains i.e. attention, memory or executive functioning, rather than multiple domains (Sohlberg & Mateer, 1987; Kashel et al. 2002; Levine et al. 1999). Given that stroke leads to multiple cognitive deficits it would be unrealistic for a patient to undertake separate interventions for each cognitive domain, due to the amount of time and effort that would be required. Furthermore, interventions only improve a proportion of subdomains within the main cognitive domain. For example, Kashel et al. (2002) reported that patients who improved in verbal memory tasks, following visual imagery training, did not improve on general memory as measured by the Wechsler Memory Scale (WMS IV; Wechsler, 2008**).** Secondly, the notion that cognitive rehabilitation such as ATP addresses the underlying cognitive function has been rigorously challenged (Park, Proulx, Towers 1999). Park et al. (1999) argue that interventions such as ATP improve patients' performance on cognitive tasks merely due to the acquisition of specific skills that are required in these particular tasks and not as a result of restored underlying cognitive function. Indeed, the finding that TBI patients' improvement on the PASAT post APT was no greater than healthy controls suggests that improvement was a result of "learning and practice" (Park et al. 1999). In other words, the improvements observed on specific cognitive tasks are not generalized to other tasks. Thus, it is unlikely that participants would receive any substantial benefit in their every day life from engaging in cognitive rehabilitation. Thirdly, cognitive

rehabilitation involves considerable time and resources. In addition, it requires patients to commit to and undertake lengthy and mundane tasks which may contribute to fatigue and dropout. Finally, it is evident that cognitive rehabilitation often takes place years post injury (Potvin, Rouleau, Senechal, & Giguere, (2011) which arguably may not maximise the patient's recovery, given that restorative neurological changes take place following the first few weeks of insult (Cramner, 2008).

The criticism and limitations of cognitive rehabilitation emphasise the need for alternate interventions to assist and improve the cognitive functioning of stroke patients. Such an intervention is that of Environmental Enrichment (EE; Hebb, 1947). EE does not address a specific function via particular training or intervention, rather it simultaneously stimulates the use of a variety of cognitive functions through enjoyable activities such as puzzles, books and music, which the patient can engage in during times that are suited to them. It provides a more realistic approach to interventions for cognitive deficits as it is arguably more ecologically valid than cognitive rehabilitation. In addition, EE may be implemented soon after stroke, thus optimizing the "golden window" of brain repair (Cramner, 2008).

1.5 Current Trends in Stroke Rehabilitation.

If EE is to be implemented within weeks of stroke it is most likely that such an intervention will need to take place within the hospital ward. However, in order to determine whether this is feasible an understanding of the activity levels of hospital based stroke patients is needed.

A European based study, observing the behaviours of patients in both a Swiss and Belgian rehabilitation unit, reported that stroke patients engaged in therapeutic activities for 4 hours and 2.5 hours respectively (De Weerdt et al. 2000) whilst a Canadian study reported patients spent on average only 1hr and 15 minutes with physiotherapists, occupational therapists and speech pathologists combined (Foley, McClure, Meyer, Salter, Bureau, Teasell, 2012). Furthermore, only 67% to 74% of the time that patients spend with rehabilitation professionals was based in therapeutic activities (Foley et al. 2012).

Australian based studies have revealed more concerning results regarding the daily activities and rehabilitation schedules of stroke patients. Patients in Australian Rehabilitation units spend approximately 43% of the day alone (King, McCluskey, Schurr, 2011). Indeed, patient activity levels are low with 75% of the time spent in passive activities, such as watching T.V, (King et al. 2011) up to 60.4% of the time spent resting in bed (Bernhardt, Dewey, Thrift, & Donnan, 2004) and only 27% and 23% of the day devoted to social and physical activity respectively (Jansen et al. 2012). Furthermore, only 5.2% (Bernhardt et al. 2004) to 15% (King et al. 2011) of the day is devoted to therapeutic activities with allied health professionals; Bernhardt et al. (2004) report that, on average, patients spent 32.5 minutes, 24 minutes and 22.8 minutes with speech pathologists, occupational therapists and physical therapists respectively.

There is a paucity of research that has focused on the cognitive activities of stroke patients in rehabilitation units (Jansen, Ada, Bernhardt, McElduff, Pollack, Nilsson & Spratt, 2013; Jansen et al. 2012), thus again emphasising the lack of attention that has been paid to cognitive rehabilitation post stroke. In one of the few studies assessing cognitive activities in rehabilitation units Jansen et al. (2013)

reported that patients were engaged in cognitive activities, such as reading, listening to music, puzzles and games, for only 5% of the day.

Jansen et al. (2012) highlight that engagement in activities may be hindered by the way in which the rehabilitation unit functions, for example, to minimise staff workload patients may be kept by their bedsides, where they have little or no access to stimulating and communal activities. Nevertheless, such barriers to patient participation in activities may be overcome by enriching the patient's environment. Indeed, patients provided with communal activities, such as Nintendo Wii and bingo, in addition to individual activities such as bedside audio books and music were 1.7 times more likely to engage in cognitive activities than patients exposed to standard care (Jansen et al. 2013).

Thus, given the lack of activity that stroke patients engage in, it is arguable that stroke patients would have the time to engage in EE activities whilst they are in hospital. The finding that the presence of EE materials increases the likelihood of patients engaging in cognitive activities provides additional evidence that EE can be implemented within the hospital environment.

1.6 Environmental Enrichment – Intact, Brain Injured and Stroke Animal Models

EE in animal models refers to housing conditions in which rats are exposed to a novel environment containing various "toys", such as wheels, tubes, ropes, chains, platforms and ramps (Hebb1947; Ruscher & Wieloch, 2010). Objects within the cages are regularly changed thus encouraging inquisitiveness and exploration. Rats are housed in groups of 5 to 8 to aid social interaction. Unlike previous forms of rehabilitation EE allows the animals to explore and play within their environment at their own leisure and pace, ultimately serving to enhance their motor, social and

cognitive functions. Standard conditions (SC) usually consist of animals housed, individually or in groups, in smaller cages with no access to toys. EE and SC rats have equal accessibility to food and water (Ruscher & Wieloch, 2010).

A variety of tests have been used to establish the functional and cognitive abilities of rats housed in EE and SC. Motor tasks include pole rotation, ladder climbing, paw reaching and rearing which test the rats' forelimb, hindlimb and movement abilities (Ohlsson & Johansson, 1995). Cognitive tasks include the Williams - Hebb Maze (Hebb & Williams, 1946) which measures acquisition and learning, the Morris Water Maze task (MWM; Morris 1981) a measure of spatial memory ability, conditioning tasks which measure contextual fear memory (Duffy, Craddock, Abel, Nguyen, 2001) and novelty/object recognition tasks which measure exploration and habituation (Rampon, Tan, Goodhouse, Shimizu, Kyin & Tsien, 2000).

Such studies have revealed that EE conditions are of significant benefit in uninjured rats (Leggio et al. 2000). Healthy rats housed in EE conditions for a period of 2 to 2.5 months displayed significant improvements in spatial memory (Leggio et al. 2000), contextual fear memory (Duffy, Craddock, Abel & Nguyen, 2001) and exploration (Rampon et al. 2000), compared to age matched healthy rats housed in SC.

Further research has provided promising results for the mitigating effects of EE on age related cognitive deficits (Kobayashi, Ohashi & Ando, 2002). Aged rats housed in EE for a duration of 2.5 months or more displayed increased learning capacity on the Hebb Williams Maze task, comparative to aged rats housed in SC. The finding that increased exposure time to EE was positively correlated with improved learning capacity further provides support for such a therapeutic invention

(Kobayashi et al. 2002). Nevertheless, in order for such positive effects to occur, such lengthy intervention periods are not always required (Frick & Fernandez, 2002). Aged female rats housed in EE conditions for as little as 14 days displayed significant improvement in spatial memory compared to aged females housed in SC and also revealed similar results to young rats housed in SC (Frick & Fernandez, 2003).

Studies have revealed that EE is also beneficial in aiding the cognitive deficits experienced in genetic disorders. Ts65Dn knockout mice, a model of Down Syndrome, displayed significant improvements in exploratory behaviours following 15 days in EE conditions (Martinez-Cue et al. 2002), whilst FMR1 knockout mice, a model of fragile X syndrome, showed significant improvements in exploration and habituation behaviours, in addition to revealing a reduction in anxiety related behaviours following 60 days of EE exposure (Restivo et al. 2004). Furthermore, olfactory discrimination and habituation behaviours are significantly improved in EE CA 1 hippocampal knockout mice, whilst their performance in a contextual freezing task, measuring fear memory, matched that of non-injured mice (Rampton et al. 2000).

More importantly, for the past two decades studies have been providing evidence for the ameliorating effects of EE on motor and cognitive deficits sustained from acquired brain injuries. Female rats with sensorimotor cortex lesions exposed to EE showed significant improvement in beam walking skills compared to rats housed in SC (Christie & Dalrymple-Alford, 1995). Male rats with bilateral hippocampal lesions, housed in EE conditions for a period of 30 days, show significant improvements in working memory than rats housed in SC (Galani, Jarrard, Will & Kelche, 1997). Further studies have revealed that brain injured rats need only be

exposed to EE conditions for a period of two weeks in order for cognitive improvements to be observed, for example EE rats experiencing neural tissue damage, via fluid percussion, perform significantly better on the MWM than their counterparts housed in SC, after 14 to 15 days of EE exposure (Hicks, Zhang, Atkinson, Stevenon, Veneracion &Seroogy 2002) with some studies reporting that performance was almost equivalent to that of sham injured rats (Hamm, Temple, O'Dell, Pike & Lyeth, 1996).

Research into the effects of EE on animal stroke models initially focused on the recovery of motor abilities (Ruscher & Wieloch, 2010). Rats with a cerebral infarction housed in EE post stroke performed significantly better on various motor tests than rats housed in SC (Ohlsson & Johansson, 1994). Furthermore, EE still significantly increases functional recovery even if it is not implemented immediately following stroke (Johansson, 1996). Johansson (1996) found that rats who were housed in EE conditions 15 days after focal brain ischemia performed significantly better on motor tests than rats who were housed in SC post stroke. These results are supported by the review and meta-analysis of 21 studies in which the effects of EE were significantly associated with motor recovery in ischemic stroke animal models (Jansen et al. 2010).

Few studies document the effects of EE on ICH stroke animal models (MacLellan, Plummer, Silasi, Auriat & Colbourne 2011). MacLellan et al. (2011) express caution in generalizing the results of ischemic based studies to those of ICH based studies given the differing neurological basis of these two stroke subtypes (MacLellan et al. 2011). However, studies assessing the effects of EE, combined with skill reach training, on motor recovery in ICH models have revealed significant improvements in the motor abilities of rats (MacLellan et al. 2011). Consequently,

the effects of EE may be beneficial for both ischemic and ICH models of stroke (MacLellan et al. 2011).

More recent research has focussed on the effects of EE on cognitive functions in stroke animal models. Male ischemic rats housed in EE conditions for a period of 31 to 34 days performed significantly better on the MWM than rats housed in SC (Dahlqvist, Ronnback, Bergstrom, Soderstrom & Olsson, 2004). Soderstrom, Strand, Ingridsson, Nasic & Olsson (2009) reported significant improvements in ischemic rats in spatial learning and memory tasks following 6 weeks of EE exposure, combined with 17b estradiol. What's more, aged female rats need only be housed in EE conditions for as little as 4 days for significant improvement in spatial working memory to occur (Briones, Therrien &Metzger, 2000). In addition, rats exposed to EE conditions, combined with exposure to a labyrinth, for 7 days showed significant enhancements in their learning abilities (Puurunen, Jolkkonen, Sirvio, Haapalinna & Sivenius, 1997).

The effects of EE on healthy and brain injured animals are further supported by the neurological changes that take place following its implementation (Frick & Fernandez, 2003). Intact, brain injured and stroke animal models have revealed significant changes in the hippocampus following EE exposure (Frick & Fernandez 2003; Rampton et al. 2001). Healthy rats exposed to EE have shown increased synaptophsyin immunoreactivity in the hippocampus (Frick & Fernandez, 2003) and increased LTP in the CA1 region of the hippocampus (Duffy et al. 2001). Furthermore, the dentate gyrus (DG) of the hippocampus in EE rats has a greater proportion of neurons and granual cell neurons, in addition to a larger granule cell layer compared to SC rats (Kemperman, Kuhn & Gage, 1997). These findings have been replicated in brain injured and stroke animal models (Rampton et al. 2001).

Indeed, rats with damage to the CA1 hippocampus show significantly higher synaptic density (Rampton et al. 2001), and increased synaptogenesis (Morroni, Kitazawa, Drago, Cheng, Medeiros & LaFerla, 2011) in the CA1 region following exposure to EE compared to their counterparts housed in SC (Rampton et al. 2001, Moronni et al. 2011). The DG of the CA1 hippocampus impaired rat further benefits from EE exposure with reports of enhanced neurogenesis in its subgranular zone (Morooni et al. 2011), whilst ischemic models have revealed EE plus spatial learning tasks result in significantly greater neuronal differentiation and neurogenesis in the DG (Matsumori, Hong, Fan, Kayama, Hsu, Weinstein & Liu, 2006). Other brain regions benefiting from the effects of EE in ischemic stroke models include the unharmed motor cortex; Biernaskie & Corbett (2001) found that EE combined with skill reach training in rats resulted in greater dendritic complexity and dendritic length in the undamaged motor cortex.

EE conditions have also been shown to alter levels of trophic factors that are associated with neuronal plasticity (Zhao, Risedal, Wojcik, Hejzlar, Johansson & Kokaia, 2001). Rats housed in EE conditions showed significantly higher levels of NGFI-A mRNA (Dahlqvist, Zhao, Johansson, Mattsson, Johansson, Seckl & Olsson, 1999) and altered levels of Brain Derived Neurotropic Factor protein (BDNF; Zhao et al. 2001) compared to those rats housed in standard conditions.

Additional biological changes influenced by EE include that of cholesterol transporters which play a protective role in the ischemic brain. Levels of Apolipoprotein D (apo D; Rickhag, Deierbor, Patel, Ruscher & Wieloch, 2008) and Apolipoprotein E (apo E; Ruscher, Johannesson, Brugiere, Erickson, Rickhag, Wieloch, 2009) are significantly affected following EE exposure.

Subsequent research has further examined the specific nature of EE (Sozda, Hoffman, Olsen, Cheng, Zafonte, Kline, 2010). Research has questioned whether one particular component of EE, social, explorative or sensory may be more beneficial than the other (Sozda et al. 2010). Animal models of healthy rats have revealed that the absence of socialisation does not affect the acquisition of spatial navigation, as measured by the MWM, or discriminatory behaviours but does, however, result in deficits of reversal learning in the latter skills (Schrijver, Pallier, Brown & Wurbel, 2004). Opposite effects are found when rats are exposed to socialisation but are devoid of objects and sensory stimulation, with significant impairment found in the acquisition of the MWM (Schrijver et al. 2004). These results suggest that different parts of enrichment may positively affect different aspects of recovery. In turn, one may argue that EE as a whole rather than its counterparts would be more effective in the overall recovery of cognitive deficits (Schrijver et al. 2004).

Certainly, evidence suggests that it is the combination of EE activities, including socialisation,that provides the most beneficial outcome (Johnson & Ohlsson, 1996). Indeed, ischemic rats housed in EE plus social conditions performed significantly better on various motor tasks than rats housed in EE minus social conditions and rats housed individually with access to physical activities (Johnson & Ohlsson, 1996). These results are supported by Sozda et al. (2010), who reported that TBI rats housed in typical EE activities were significantly better in the acquisition on tasks of spatial learning and memory retention than that of TBI rats housed in environments which gave access to either toys or social activities but not both (Sozda et al. 2001).

In summary, the evidence for the effects of EE on cognitive improvement and recovery in the intact and brain injured/stroke animals is strong. However, some researchers express caution when assessing the effects of EE on such models. Duffy et al. (2001) note that other factors such as gender may influence the effects of EE on the recovery of cognitive abilities. For example, recovery of spatial memory as observed in brain injured male rats following 14 days in EE did not occur in brain injured EE female rats (Wagner, Kline, Sokoloski, Zafonte, Capulong & Dixon, 2002). Conversely, improvement of spatial memory witnessed in non injured female rats housed in EE for 15 days was not observed in intact EE males (Martinez-Cue et al. 2002). Wagner et al. (2002) argue that such gender differences may be due to differing time spans of neurological changes within the male and female brain, thus suggesting that the time and duration of EE maybe crucial in determining its effectiveness.

Given that early rehabilitation of motor impairment following stroke may exacerbate injury (Risedal, Zeng & Johansson, 1997) researchers have also queried whether EE may exacerbate cognitive impairments (Jansen et al. 2010). Indeed, in a meta-analysis of 21 studies assessing the efficacy of EE on motor recovery in stroke, Jansen et al. (2010) reported that on average an 8% increase in infarct volume was apparent following exposure to EE. Such findings have been related to a combination of late tissue loss and the stress associated with a novel environment (Jansen et al. 2010). However, currently there is little to suggest that this increase in infarct volume results in increased motor impairment (Jansen et al. 2010). Jansen et al. (2010) argue that the significant gains observed in EE animal models provide overwhelming evidence for the effectiveness of EE. Given the absence of research suggesting exacerbation of cognitive deficits following EE and the plethora of

research documenting its positive effect on cognitive impairment in animal models, it would seem highly reasonable to pursue this intervention without concerns of any significant detrimental effects.

Criticism of the EE research also raises the variations and inconsistencies of the enriched environment. Indeed, Sodaz et al. (2010) note that there is considerable variability in the size of EE cages and the number of rats and toys per EE cage, which ultimately may lead to differing results. Consequently, research calls upon future studies to regulate the components of EE (Sodaz et al. 2010). Furthermore, research has questioned whether animal models are in any way comparative to human models, for example, researchers have argued that standard conditions in animal models do not represent that of a "normal" environment, rather it characterizes that of a deprived environment (Jansen et al. 2010). However, Jansen et al. (2010) argue that, even if this is the case, the set up and nature of rehabilitation wards do not provide the stimulation that one would experience outside of the hospital in everyday life. Thus, in effect hospital based stroke patients are in an "environmentally deprived" setting. Consequently, EE animal model based research is, as much as practically possible, representative of hospital rehabilitation environments (Jansen et al. 2010).

1.7 Environmental Enrichment – Human Studies

Despite the promising evidence of the mitigating effects of EE on cognitive deficits there has been a paucity of research examining the effects of EE in humans (Sarkamo et al. 2008). Perhaps the closest example of EE in human populations is that of Snoezelen, also known as Multi Sensory Stimulation (MMS; Botts, Hershfeldt & Christensen-Sandford, 2008), in which subjects are guided in a non

directive manner through a room of auditory, tactile and visual stimulation. MMS improves attentiveness to the environment and improves the recollection of memories in dementia patients (Baker et al. 2001), as well as improving cognitive abilities in children with TBI (Hotz, Castelblanco, Lara, Weiss, Duncan, Kuluz, 2006). However, these cognitive improvements were assessed only by brief subjective measures completed by staff and not by detailed neuropsychological assessments. Furthermore, the MMS approach focuses on providing sensory stimulation only, whereas typical EE incorporates other aspects such as social, cognitive and physical factors (Hotz et al. 2006).

In terms of typical EE, to our knowledge, there has only been one study to date that has examined its effects on the human stroke population. Sarkamo et al. (2008) randomly assigned 60 ischemic stroke patients to a music group, language group or control group. Patients in the music group were provided with CDs of their favourite music whilst the language group were given audio cassettes. Patients were asked to listen to the CDs or audio cassettes for at least 1 hour a day, for a period of 2 months post stroke. Patients used these devices at their own leisure with gentle reminders and encouragement from staff and family members. Patients were tested on a battery of neuropsychological assessments 1 week, 3 months and 6 months post stroke. Results revealed that patients within the music group performed significantly better on verbal memory and focused attention tasks 3 months post stroke compared to the language and control groups. Furthermore, these results were sustained at 6 months post stroke (Sarkamo et al. 2008). However, the enrichment condition was delivered in both the hospital and home environment. There are no current studies that assess the effects of enrichment solely in a rehabilitative ward. Developing an

understanding of the effects of enrichment during a patients rehabilitative stay may provide a foundation for future hospital based interventions.

1.8 Practice Effects

In order to determine whether there has been a change of cognitive functioning over a precise period of time, whether it be due to cognitive decline, spontaneous recovery or an intervention such as EE, the most efficient and common method is to repeat a battery of neuropsychological assessments at specific intervals. (Heilbronner, Sweet, Attix, Krull, Henry & Hart, 2010). However, if repetition of neuropsychological assessments is to take place, practice effects must be accounted for (Lezak et al. 2004). Indeed, in the absence of any intervention, improvement in test scores may inhibit the detection of possible cognitive decline or provide inaccurate assumptions that spontaneous recovery has occurred when in truth no such process has taken place (Calamia et al. 2012). Secondly, in the presence of an intervention, enhanced performance may be wrongly attributed to therapeutic factors thus providing false evidence for future rehabilitative programs (Calamia et al. 2012).

Practice effects can occur for a variety of reasons. Calamia et al. (2012) emphasise three main factors. First, is that of the differing features of the tests used. Certain aspects of neuropsychological tests can lead to improved performance either via memorization of the tasks presented (McCaffrey, Ortega & Haase, 1995) or as a result of learnt procedural strategies (Basso et al. 1999). The former can occur when tests require the recall of identical definite information in each of the assessments. For example, practice effects are evident at 6 months post baseline assessment on Logical Memory I and II of the WMS (Wechsler, 2008; McCaffrey et al. 1995). The

latter can occur in tests of executive function which require the presence of problem solving skills. Once the individual has learnt the problem solving method required to successfully complete the task, they need only recall this strategy upon repeated assessments. Indeed, healthy subjects display significant gains in scores on the Wisconsin Card Sorting Test, the Ruff Figural Fluency Tests and the Verbal Concept Attainment Test when retested at 12 months (Basso et al. 1999). Tests of processing speed or those that require a timed component, such as Symbol Search and Coding from the Wechsler Adult Intelligence Scale (WAIS IV; Wechsler, 2008) are also particularly susceptible to practice effects as the examinee becomes quicker at completing the task at hand (Estevis, et al. 2012).

The second factor influencing the presence of practice effects is that of the various aspects of the examinee. Younger adults show greater gains at reassessment than older individuals (Horton, 1992) while healthy adults with an average or high average IQ display significantly greater improvement from the first to second assessment than individuals with a low average IQ (Rapport, Brines, Theisen & Axelrod, 1997). Furthermore, researchers should abstain from making assumptions that clinical populations display the same pattern of practice effects as non-clinical populations (Zehnder, Blasi, Berres, Spiegel & Monsch, 1997) Indeed, Zehnder et al. (1997) reported Alzheimer sufferers failed to show any improvement in a variety of tests form the Consortium to Establish a Registry on Alzheimer's Disease-Neuropsychological Assessment Battery (CERAD-NAB; Monsch & Monsch, 1997) at 1 year testing post baseline, where as healthy controls showed significant improvements in the majority of the CERAD-NAB subtests at 2.4 years post baseline. Lastly, when considering aspects associated with the examinee, researchers

should be aware that enhanced performance may be a result of reduced anxiety levels as repeated assessments allows the subject to become familiarised and thus more relaxed with the testing environment (Anastasi, 1988).

The final factor influencing the presence of practice effects is that of study design. (Calamia et al. 2012) Research has revealed that practice effects may diminish with increasing time between assessments (Falleti, Maruff, Collie & Darby, 2006). Furthermore, practice effects are usually most apparent from the first to second assessment, with a plateau effect occurring by the third and fourth assessments (McCaffrey, Ortega, Orsillo, Nelles & Haase, 1992, Rapport et al. 1997, Falleti et al. 2007). Other studies have shown that practice effects may take a cubic or quadratic pattern over multiple assessments (McCaffrey et al. 1993).

Researchers have emphasized the need to account for or minimise the occurrence of practice effects through a variety of methods. Calamia et al. (2012) highlight a variety of methods. Based on the finding that practice effects are most prominent from the first to second assessment researchers have proposed a dual baseline approach in which the subject's second assessment, rather than the first, is used as a baseline to compare subsequent tests to (McCaffrey et al. 1992). However, this approach may not always be practical. Consider for example the neuropsychological assessment of a stroke individual. Testing is often lengthy (approx. 1 to 2 hours) which arguably may result in significant fatigue and frustration, ultimately leading to future refusal to take part in any further testing. For this reason, one should aim to keep the number of neuropsychological assessments to a minimum, particularly when intervals between assessments are short.

Other researchers have argued for the use of alternate forms of neuropsychological assessments, for example, using the TMRT A and TMRT B

from the D-KEFS (Delis et al. 2001) at the first and second assessment respectively (Benedict & Zgaljardic, 1998). The use of alternate forms can be effective in reducing the occurrence of practice effects, specifically in tasks such as the Hopkins Verbal Learning Test HVLT-R word learning test (Benedict & Zgaljardic, 1998). However, not all alternate forms are robust to practice effects with the visuospatial learning task of the Brief Visuo-spatial Memory Test – Revised (BVMT; Benedict, Schretlen, Groinger, Dubraski & Sphritz, 1996) showing some evidence of performance gain (Benedict & Zgaljardic 1998). Furthermore, alternate forms may differ in their level of difficulty and in other cases may not be available at all. For example, Calamia et al. (2012) highlight that there is no current alternate forms for the WAIS-IV (Wechsler, 2008), a commonly used neuropsychological assessment. In addition, tests such as the D-KEFS trails (Delis et al. 2001), require motor skills, which would not be suitable for motor impaired stroke patients.

Arguably, study design could be another method to manage the occurrence of practice effects. As previously mentioned it is evident that many studies on cognitive impairment and spontaneous recovery fail to include a control group. Calamia et al. (2012) argue that while the use of a clinical control group in intervention studies may be beneficial, it may also be unethical. Nevertheless, clinical control groups are regularly used throughout research and with good clinical care, ethical dilemmas can be managed. Healthy controls may also provide useful information when determining the presence of practice effects. Thus, arguably the combination of a healthy control group and a clinical control group would provide a robust method to account for practice effects.

1.9 The Current Study

The current study focuses on a number of issues that have not been addressed in the literature to date. Firstly, to our knowledge there is no current research that has assessed memory, attention and executive functioning deficits in the early stages of stroke during patients' rehabilitative admission. Secondly, there is no current research that has investigated the level of cognitive spontaneous recovery that occurs during patients' rehabilitative stay, while also accounting for practice effects. Thirdly, the only study to date assessing enrichment on post stroke cognitive deficits focuses on one specific activity (Sarkamo et al. 2008). To date, there is no research that assesses an enriched environment that is representative of those found in stroke animal models, i.e. an environment that provides multiple individual and communal activities.

Thus, the first aim of the current study is to investigate the cognitive profiles of stroke survivors during their rehabilitative stay. The second aim is to investigate the level of cognitive spontaneous recovery that occurs between admission to and on discharge from a standard rehabilitative ward, while accounting for the occurrence of practice effects. In order to achieve these first two aims stroke patients will be tested on memory, attention and executive functioning neuropsychological tasks upon admission to and prior to discharge from a rehabilitative ward. Their performance will be compared to that of aged matched healthy controls who will complete the same neuropsychological test battery on two occasions, separated by a similar time window. Thirdly, the study aims to investigate the effects of an enriched environment on stroke patients' attention, memory and executive functioning deficits. In order to do so a sub group of stroke patients will be exposed to an enrichment condition. Their performance on the neuropsychological tasks will be

compared to stroke patients who have been exposed to standard rehabilitative conditions.

It is hypothesised that stroke individuals will show significant impairment in memory, attention and executive functioning compared to age matched healthy controls. It is further hypothesised that stroke participants will show a level of spontaneous recovery that is above and beyond the effect of practice. It is also hypothesised that stroke individuals exposed to enriched conditions will show superior performance on memory, attention and executive functioning tests than to stroke patients exposed to standard conditions.

2. RESEARCH MANUSCRIPT

Cognitive improvement during stroke rehabilitation: Spontaneous recovery or practice effects?

2.1 Abstract

Background: Cognitive functioning is significantly impaired after stroke and improves in the short to medium post-stroke period. However, existing studies do

not differentiate between spontaneous recovery and practice effects arising from repeated testing with the same instruments.

Aims The current study examines whether changes in cognitive functioning during the early stages of stroke can be attributed to spontaneous recovery or to practice with the specific neuropsychological tests. We also examine whether an environmental enrichment intervention improves the rate of cognitive recovery at this early post-stroke period.

Method: Forty one stroke patients were assessed on tests of memory, attention and executive functioning upon admission to and prior to discharge from a rehabilitative ward. Twenty seven stroke patients experienced standard rehabilitation conditions, whereas 14 were exposed to an environmental enrichment program. Fifteen aged-matched healthy controls completed the same neuropsychological test battery on two occasions, separated by a similar time window.

Results: Compared to healthy controls, stroke patients performed poorly on all neuropsychological tasks. Both stroke patients and healthy controls showed improved performance at re-test. The rate of improvement did not differ between groups on memory and attention tests, but stroke patients improved more than healthy controls on executive functioning. The enriched rehabilitation stroke subgroup showed a tendency for greater rate of improvement on working memory tasks than the standard rehabilitation group, but the effect failed to reach statistical significance.

Conclusion: Stroke was associated with significant decline in memory, attention and executive functioning, in the early post-stroke period. During their rehabilitation

stay, stroke patients showed no evidence for spontaneous recovery of memory and attention, over and above effects of task practice. However, executive functions showed spontaneous recovery, reaching healthy control levels at 4-6 weeks post-stroke. While enrichment intervention showed a trend for improved working memory performance, the effect was weak and requires further investigation with a larger sample size.

2.2 Introduction

Cognitive impairment after stroke is common (1), with over a quarter of stroke survivors showing significant cognitive impairment 1-3 years post stroke (2) in areas including attention (3), memory (4) and executive functioning (3). However, few studies have assessed cognitive impairment in the early stages of stroke (4). Despite some evidence that cognitive functioning improves spontaneously after stroke (e.g., 5, 6), the factors that promote spontaneous recovery and the critical timeframe for this recovery remain to be defined.

Improvement in cognitive functioning has been shown in the period of 1-2 years post-stroke. For example, a third of stroke patients showed significant cognitive improvement from 6 to 12 months (5). A similar percentage of patients diagnosed with mild cognitive impairment one month post-stroke no longer met this criterion at 6-24 months (6). Although these studies suggest spontaneous recovery of cognitive functioning in a significant proportion of stroke patients, they do not control for practice-related performance improvement (7). Yet, significant practice effects have been reported on tests of memory and executive functioning extending over 6-12 months post-baseline assessment (8-9). It is therefore not clear whether

any improvement in neuropsychological test performance in stroke patients can be attributed to spontaneous recovery or task practice.

There is some evidence that cognitive interventions may improve cognitive performance in stroke survivors. Task-specific training has moderate effects on cognitive deficits post-stroke (10). For instance, visual imagery was shown to reduce memory impairments (11), and attention training tasks to alleviate attentional deficits (12). However, these improvements were specific to the training tasks themselves and did not generalise to other tasks or domains (12).

In animal models of stroke, environmental enrichment has been found to improve cognitive and motor recovery (13). Environmental enrichment involves housing animals in group cages with exposure to novel environments that encourage exploration and social interaction (14-15). A meta-analysis of 21 studies revealed that enrichment was significantly associated with motor recovery in ischemic stroke animal models (16). For instance, male ischemic rats housed in enriched conditions for a period of one month performed significantly better on the Morris Water Maze task than rats housed in standard conditions (17). Even after only four days of housing in enriched conditions, female ischemic rats showed significant improvement in spatial working memory compared to rats housed in standard conditions (18). Environmental enrichment also promotes neurological recovery. Enrichment significantly increased synaptic density (19) and synaptogenesis (20) in the damaged CA1 region, as well as facilitated neurogenesis and neuronal differentiation in the dentate gyrus (21), when compared to standard housing.

Only two studies have assessed enrichment interventions on cognitive functioning in stroke patients. Sarkamo et al. (22) compared music and audio-book enrichment programs to a no-enrichment condition. Stroke patients exposed to music

showed significantly greater improvements on attention and memory tasks at 3 and 6 months post stroke, when compared to either audio-book or control conditions. In a pilot study, Janssen et al. (2014; 23) applied a broad environmental enrichment program in a stroke rehabilitation ward (for protocol see Janssen et al., 2012; 24) that was modelled after that used in animal stroke models. Exposure to an enriched environment that included both personal and group activities resulted in an increase in overall activity, with the strongest effect on engagement in cognitive activities.

In summary, while stroke is associated with long-lasting residual cognitive deficits, there is evidence for both spontaneous recovery of cognitive functions and effectiveness of enrichment programs in improving cognitive outcomes. However, despite evidence for high neuroplasticity of motor functions in the 1-2 month post-stroke period (25) during which in-patient rehabilitation services are usually offered, little is known about the level of cognitive functioning, the rate of spontaneous recovery or the effectiveness of environmental enrichment in this period.

This study examines attention, memory and executive functioning in stroke patients over a 2-3wk period while in a rehabilitative ward, and compares their performance to healthy age-matched controls tested over the same period. The first aim was to examine whether memory, attention and executive functions are affected in the early stages post-stroke, i.e., at admission to rehabilitation. The second aim was to assess spontaneous recovery in these cognitive domains and determine whether stroke participants showed improvement above and beyond the expected improvement with task practice. Over the period of this study, a subgroup of our stroke patients participated in a trial environmental enrichment program (24). Hence, the third aim was to explore whether exposure to environmental enrichment during

rehabilitation improved cognitive function relative to stroke patients recovering in standard rehabilitation conditions.

2.3 Method

2.3.1. Design

A non-randomized controlled trial was conducted in a 20-bed mixed rehabilitation unit at the Rankin Park Centre, John Hunter Hospital. Patients who were admitted during two recruitment periods (April-August, 2010, November 2011 - September 2012) were exposed to a standard rehabilitation environment (i.e. control condition). Patients admitted from April - July 2011 were exposed to the enrichment protocol.

The enrichment protocol is outlined in Janssen et al. (24). Briefly, participants were provided with individual and communal activities. Individual activities included audio and print books, music, magazines and puzzles placed in a satchel at the patient's bedside for easy access. Communal activities were available in the dining room and included Nintendo Wii games and board games. The communal area also provided access to the internet, newspapers and social interaction with other patients. Participation in all of these activities was encouraged by staff and family members. The stroke control group was exposed to a standard rehabilitation environment (see Janssen et al., 2014; 23). Both groups undertook standard rehabilitative therapies such as physiotherapy and speech therapy.

2.3.2 Stroke Participants

Forty one stroke participants were recruited into the study. Of the 27 stroke control participants, six did not undertake the second assessment. Of the 14 stroke patients recruited into the enrichment condition, only nine completed both testing

sessions. Drop-outs were due to patient refusal to continue participation, patient discharge prior to the second assessment or deterioration in patient's physical health.

Stroke patients were included in the study if they were above 18 years and had suffered a recent ischemic stroke, an intracerebral or a subarachnoid haemorrhage. Patients were included regardless of level of global cognitive functioning. Patients with motor problems were not excluded from the study; however, they received a modified testing protocol that excluded subtests requiring complex motor skills. Patients were excluded from the study if they were medically unstable or had significant communication and or visual impairments which prevented their ability to participate in the testing. The date of onset, type, side and location of the stroke, as well as patients' gender, age and ethnicity were obtained from their medical file.

2.3.3 Healthy Control Participants

Sixteen aged-matched healthy controls were recruited from the Hunter Medical Institute (HMRI) Volunteer Database. Fifteen of these completed both test sessions.

2.3.4 Ethics Approval & Consent

Ethics approval was obtained from the Hunter New England Human Research Ethics Committee (HNEHRE) and the University of Newcastle Human Research Ethics Committee (UoN - HREC). If medical staff deemed patients to be capable of providing informed consent, agreement to take part in the study was obtained from the participant only. Consent from family members was also obtained if there was concern regarding the individual's capacity to provide informed consent.

2.3.5 Assessments

Patients were tested on a set of neuropsychological assessments as soon as practically possible after admission to the rehabilitation centre and 2-3wks later depending on discharge. The assessment process took approximately 1-1.5 hours. All controls were tested in a single sitting, whereas for patients, where necessary, testing was administered in two 30-minute sessions scheduled no more than 3 days apart. For patients, stroke severity was measured upon admission and at discharge using the Functional Independence Measure (FIM; 26).

At baseline, the test battery included assessment of current global level of cognitive functioning (MoCA; 27) and premorbid functioning (WTAR; 28). At both baseline and retest, the neuropsychological battery consisted of eight tests. Immediate and delayed verbal and visual memory were measured using the Logical Memory I and II and the Visual Reproduction I and II subtests from the Wechsler Memory Scale – IV, respectively (29). Visual and auditory working memory were measured using the Symbol Search from the WMS IV (29) and the Digit Span from the Wechsler Adult Intelligence Scale – IV (30), respectively.

The remaining four tests were administered from the Cambridge Neuropsychological Test Automated Battery (31). The CANTAB tests were performed on a 1.6Hz Paceblade SlimBook P120 PC. Sustained and selective attention were measured using the Simple Reaction Time (SRT) and the Choice Reaction Time (CRT) tests, respectively. Responses for SRT and CRT were made using a button press response with their dominant hand. Visual Recognition was measured using the Pattern Recognition Memory (PRM) test. Executive functioning, and specifically attentional set switching was assessed using the Intra/Extra Dimensional (IED) shifting test. Responses to PRM and IED were made via touch screen responses with their dominant hand.

2.3.6 Data Analysis

Changes from baseline to retest were analysed using Session (baseline, retest) as a factor. Effects of group were examined using two orthogonal planned contrasts. One compared stroke patients to the healthy control group (Stroke vs. Healthy Control) to examine stroke-related effects. The other compared the two stroke subgroups (Stroke Enriched vs. Stroke Control) to examine any effects of environmental enrichment. Level of significance was set at a=0.05. Practice effects are represented by a main effect of Session. Spontaneous recovery is represented by a Group (Healthy Control vs. Stroke) x Session interaction. Enrichment effects are represented by a Group (Stroke Enriched vs. Stroke Control) x Session interaction.

2.4 Results

2.4.1 Demographics and general cognitive functioning

Table 1 shows mean demographic information for each of the three groups. The three groups did not differ significantly in age, both $F < 1$. Gender and education distribution did not differ between healthy control and stroke groups, but the stroke control group had significantly more males and more people with >12y education than the stroke enrichment group, $X^2 = 5.39$, $p < 0.05$, $X^2 = 6.90$, $p < 0.05$, respectively. The healthy control group had higher WTAR and MoCA scores than the stroke group, $t(50) = 3.87$, $p < 0.05$, $t(49), = 5.74$, $p < 0.001$, respectively. Although the stroke control group had higher WTAR and MoCA scores than the stroke enriched group, these differences were not significant, $t(50) = 3.58$ $p > 0.05$, $t(49) = -0.63$, $p > 0.05$, respectively. The number of days between test and re-test was marginally longer for the healthy control than the stroke group ($t(37)=-2.04$, $p<.05$), but did not differ between enriched and control stroke groups.

2.4.2 Stroke patient characteristics

Table 2 compares stroke characteristics across the two groups of patients. While the stroke enrichment group had lower FIM scores at admission and at discharge, as well as longer length of stay at rehabilitation, these differences were not statistically significant, all $p > 0.05$. Stroke patients showed a significant improvement on the Functional Independence Measure (FIM) from admission to discharge, $F(1,36) = 110.10$, $p < 0.05$, but there was no difference in the rate of improvement between stroke control and stroke enrichment, $p > 0.05$.

2.4.3 Neuropsychological Test Performance

Logical Memory

Figure 1A shows immediate and delayed recall scores on the Logical Memory test. Averaged across all groups, there was no significant difference between immediate and delayed recall, $p>.05$, but recall performance improved significantly from baseline to retest, $F(1,37) = 56.58$, $p < 0.001$. Verbal memory recall was significantly better for healthy controls than stroke participants, $F(1,38) = 26.20$, $p < 0.001$, and for enriched than standard rehabilitation groups, $F(1,23) = 3.92$, $p < 0.05$. However, there was no significant interaction with session (all $F<1$), indicating that all groups improved equally with task practice.

Visual Reproduction

Visual memory results are shown in Figure 1B. Again, recall performance did not differ between immediate and delayed recall but improved from baseline to retest, $F(1,35) = 18.92$, $p < 0.001$. Visual memory recall was better for healthy controls than for stroke participants $F(1,36) = 36.67$, $p < 0.001$, but the two groups

did not differ in the rate of improvement with practice. While there was no main effect of stroke group, $F(1,21) < 1$, there was a significant stroke group by session interaction, $F(1,21) = 7.98$, $p < 0.05$. However, as seen in Figure 1B, this arose because the stroke control group showed some improvement from baseline to retest, whereas the stroke enrichment group did not.

Digit Span

Digit span improved from baseline to retest, $F(1, 41) = 13.46$ $p < 0.001$ (Figure 1C, left). The healthy control group had higher digit span scores than the stroke group, $F(1,42) = 32.62$, $p < 0.001$. Although the latter improved at a greater rate from baseline to retest, the group x session interaction was not significant, $F(1,42) = 1.65$, $p > 0.05$. There was no difference in mean digit span between the two stroke groups, $F(1,27) = 2.71$, $p > 0.05$, however the stroke enrichment group showed a marginally significant trend for greater improvement from baseline to retest than the stroke control group, $F(1, 27) = 2.88$, $p = 0.10$.

Symbol Search

Visual working memory also improved from baseline to retest, $F(1,27) = 5.26$, $p = < 0.05$ (Figure 1C, right). Stroke participants had poorer visual working memory compared to healthy controls, $F(1, 36) = 13.71$, $p < 0.01$, but the two stroke groups did not differ significantly, nor was there any difference in the rate of improvement over session between the groups.

Pattern Recognition Memory (PRM)

As shown in Figure 1D, mean RT reduced from baseline to retest, $F(1,32) = 16.80$, $p < 0.001$, but the increase in accuracy was not significant, $F(1,32) = 1.16$, $p > 0.05$. Healthy controls responded significantly faster and more accurately than stroke

participants, $F(1,33) = 9.75$, $p < 0.01$, $F(1,33) = 5.11$, $p < 0.05$, but the rate of improvement from baseline to retest did not differ between the two groups. Stroke control and stroke enriched groups did not differ in mean RT, however, the stroke enriched group showed greater improvement from baseline to retest than stroke controls, $F(1,18) = 5.36$, $p < 0.05$. The two stroke groups did not differ in accuracy scores.

Simple Reaction Time (SRT)

As shown in Figure 1E, response time reduced and accuracy improved significantly from baseline to retest, $F(1,36) = 11.29$, $p < 0.01$, $F(1,36) = 6.27$, $p < 0.05$. The healthy control group responded significantly faster and more accurately than the stroke participants, $F(1,37) = 6.30$, $p < 0.05$, $F(1,37) = 5.18$, $p < 0.05$. Although the stroke participants showed significantly greater improvement in mean RT and accuracy scores from baseline to re-test, the interaction between group and session was not significant for either score. There was no difference in response speed or accuracy between stroke control and stroke enriched groups, both $F(1,22) < 1$.

Choice Reaction Time (CRT)

There was no effect of session on either response time or accuracy on the CRT task (both $F(1,30) < 1$, Figures 1F). Healthy controls were significantly faster and more accurate than stroke participants, $F(1,30) = 6.12$, $p < 0.05$, $F(1,31) = 8.24$, $p < 0.01$, but there was no interaction between session and group, both $F(1,31) < 1$.

Stroke control and stroke enrichment groups did not differ in response time or accuracy on the CRT (all $F(1,16) < 1$).

Intra-Extra Dimensional Shift (IED)

On the IED task, participants are required to identify the task rule and then use verbal response feedback to change task rules. A total of nine stages are available and include simple response reversals (Stages 3,5,7,9), shifting to a new exemplar of the same dimension (Stage 6: intradimensional shift) and to the dimension that was previously irrelevant (Stage 8: extradimensional shift). We focus on three scores. Number of completed stages is the number of stages in which participants completed six consecutive correct responses. Mean number of errors and mean number of trials correspond to the average number of error/trials made in achieving a stage. As many participants did not complete all nine stages, we use scores that adjust for non-completed stages by adding 25 trials per incomplete stage (31).

As shown in Figure 2, the healthy control group completed more stages , made significantly fewer errors and required significantly fewer trials than the stroke group, $F(1, 35) = 5.77$, $p < 0.05$, $F(1,35) = 5.61$, $p < 0.05$, $F(1,35) = 5.13$, $p < 0.05$. Moreover, the group x session interaction was significant for all three measures ($F(1,35) = 4.74$, $p < 0.05$, $F(1,35) = 4.21$, $p < 0.05$, $F(1,35) = 4.10$, $p = 0.051$). Figure 5 shows that the stroke participants performed significantly more poorly than healthy controls on all three scores of the IED task at baseline, $t(43) > 3.13$, $p<.003$), but there was no difference between groups at retest (all $p>.05$).

Analyses comparing the two stroke groups showed a significant improvement on all three measures from baseline to retest, $F(1,20) > 4.64$, $p < 0.05$, but no

difference between stroke enriched and control groups in overall level or rate of improvement.

2.5 Discussion

The present data show that, shortly after entry to rehabilitation, stroke patients showed significant impairment in performance relative to age-matched healthy controls on tests of episodic memory (Logical Memory, Visual Reproduction, Pattern Recognition Memory), working memory (Digit Span, Symbol Search), attention (Simple and Choice RT) and executive functioning (IED). These findings are consistent with prior evidence that stroke patients show significant deficits in verbal and visual memory, working memory, attention and executive functioning (3-4). However, these previous studies have tested stroke patients at least 6 months post-stroke.

Despite showing that stroke patients performed more poorly than healthy controls, the present data are important in showing that, even as early as 18 days post-stroke, 63-83% of patients successfully completed most tests of the neuropsychological battery (mean completion of 6.4 +/-1.8 from a total of eight tests). The greatest dropout was on the choice RT and the IED tasks, which assess selective attention and set shifting. Number of tests completed did not correlate significantly with either functional independence score (FIM: $p>.14$) or premorbid intelligence (WTAR: $p>.36$). However, it did correlate with current global cognitive functioning (MoCA; $r(39)=.432$, $p<.003$). MoCA also did not correlate with functional independence score. Thus, level of global cognitive impairment was not associated with stroke recovery as assessed by the FIM. These findings point to the

importance of cognitive testing early post-stroke to identify areas of cognitive decline in need of rehabilitation.

For both stroke patients and healthy controls, performance improved from baseline to retest on both episodic memory and working memory tasks. Importantly, for most tests, the amount of baseline to retest improvement did not differ between stroke patients and healthy controls. Therefore, while cognitive function significantly improved during inpatient stroke rehabilitation, the degree of improvement is consistent with a task practice effect rather than spontaneous recovery.

Spontaneous recovery was evident in two tasks. On the Simple RT task, stroke patients showed greater rate of improvement in RT and accuracy from baseline to retest than healthy controls (Figure 1E), but the effect failed to reach statistical significance. The only test to show statistically significant differential improvement in stroke participants was the IED task, a task that was especially sensitive to stroke-related disruption at baseline. As shown in Figure 2, at baseline, stroke patients achieved fewer categories, made more errors and required more trials than healthy controls. Yet, at retest, they reached healthy control levels on all three measures. Therefore, these findings provide evidence for spontaneous recovery occurring specifically for set shifting, a process related to executive functioning. This is the first study to show specific spontaneous recovery of executive functioning over a 2-3 wk period in the immediate post-stroke period.

A subsidiary aim of this study was to explore whether exposure to a model of environmental enrichment program during rehabilitation has a positive effect on cognitive function. Janssen et al. (2014; 24) found that stroke patients exposed to enriched rehabilitation conditions were 1.7 times more likely to engage in cognitive activities over the 13 day enrichment period than stroke patients exposed to standard

rehabilitation conditions. The stroke patients included in the current study partly overlap Janssen's sample. Although the stroke patients exposed to the enriched environment model showed a tendency for greater improvement from baseline to retest on Digit Span and Pattern Recognition Memory tasks (Figure 1C and D), these effects were not statistically significant. Given the small sample size, it is highly likely that this is due to low statistical power.

In conclusion, the present study shows that neuropsychological testing is feasible in stroke patients as early as 2-3 weeks post-stroke and can provide information about the patient's cognitive functioning. There is strong evidence for cognitive improvement over the period of rehabilitation. However, in most fields, this improvement could be attributed to task practice. In contrast, executive functioning, and in particular set-shifting, was particularly sensitive to stroke and showed a rate of recovery well above that expected on the basis of task practice. Executive functions are central in enabling and supporting goal-directed behaviour, including ability to comply with treatment and adhere to training programs. Therefore, assessment of executive functioning in the early post-stroke period may be clinically useful in developing individualised rehabilitation programs that vary in level of clinician support, maximising allocation of resources. The environmental enrichment model produced promising results, indicating the need for future larger clinical trials to determine the efficacy of this paradigm in stroke rehabilitation.

Table 1. Patient and healthy control characteristics.

Group (n)	***Stroke Enrichment 14***	***Stroke Control 27***	***Healthy Control 15***
Mean age (years)	70.6 ± 15.22	70.1 ± 13.86	69.5 ± 7.25
Gender (M:F)	4:10	18:9	5: 10
Education > 12yrs (n)	1	13	9

WTAR Score	94.83 ± 14.40	97.85 ± 13.13	113.53 ± 11.13
MoCA (max 30)	16.23 ± 7.17	17.30 ± 4.66	26.41 ± 2.31
Baseline to Retest (days)	15.4 ± 5.7	16.7 ± 5.3	19.4 ± 4.7

Table 2. Stroke characteristics and assessment information

Group	***Stroke Enrichment***	***Stroke Control***
Mean FIM Admission Score	54.1 ± 22.8	68.2 ± 17.0
Mean FIM Discharge Score	93.4 ± 23.4	97.6 ± 22.2
Right Hemisphere (n)	8	13
Left Hemisphere (n)	6	11
Bilateral (n)	0	1
Previous Stroke (n)	5	4
Previous TIA (n)	2	2
Rehabilitation Length of Stay (days)	39.6 ± 25.1	30.8 ± 14.2
Stroke to Baseline (days)	18.0 ± 13.0	20.5 ± 18.9
Rehab Admission to Baseline (days)	8.8 ± 11.5	9.6 ± 15.9

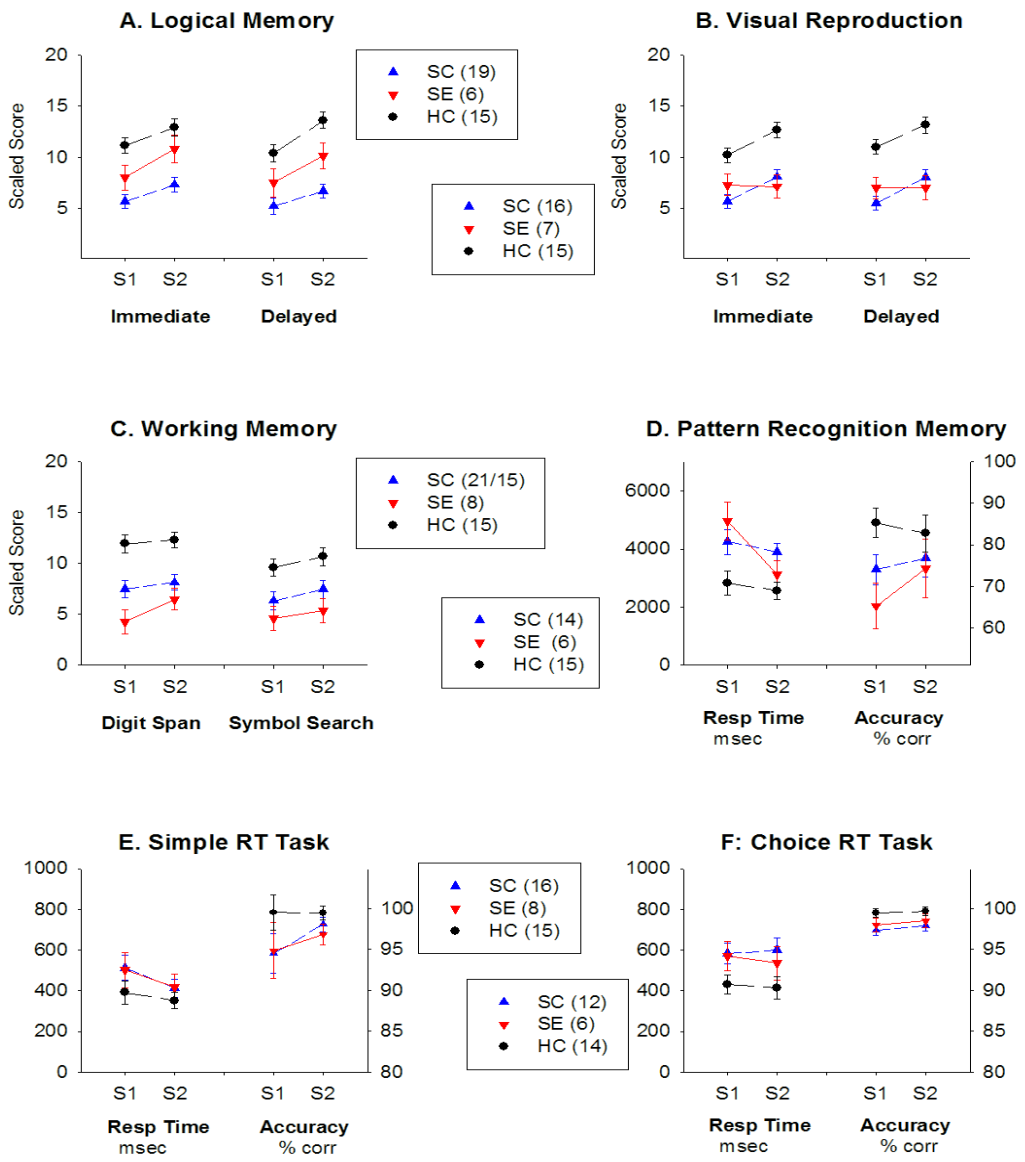

Figure 1. Mean and standard error for Healthy Control (HC), Stroke Control (SC) and Stroke Enriched (SE) groups on A. Logical Memory, B. Visual Reproduction, C. Digit Span and Symbol Search, D. Pattern Recognition Memory, E. Simple Reaction Time, and F. Choice Reaction Time tasks. Numbers in parentheses show number of participants who completed each task.

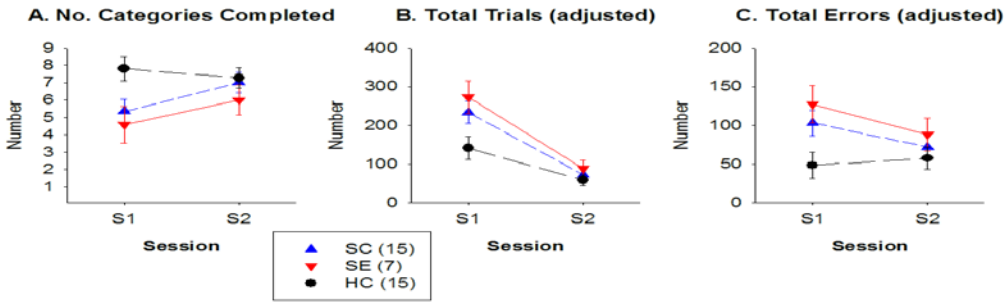

Figure 2. Mean and standard error for Intra/Extradimensional Task for for Healthy Control (HC), Stroke Control (SC) and Stroke Enriched (SE) groups on A. Number of stages completed, B. Total Trials (adjusted for stages completed), and C. Total Errors (adjusted for stages completed). Numbers in parentheses show number of participants who completed this task.

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3. Environmental Enrichment Post Stroke – Extended Discussion

3.1 Summary of Findings

There were three main aims of the study. Firstly, to determine areas of cognitive impairment experienced/shown by stroke patients admitted to a rehabilitative ward. Secondly, to assess the level of spontaneous recovery, while controlling for practice effects. Thirdly, to evaluate the effects of an enriched environment on cognitive performance after stroke.

The results revealed that stroke participants were significantly impaired in auditory and visual memory (immediate and delayed), auditory and visual working memory, sustained and selective attention, and executive functioning, when compared to aged matched healthy controls. Healthy controls and stroke participants displayed significant improvement from baseline to retest on all neuropsychological tasks apart from the Choice-RT task, a test of selective attention. Stroke participants improved at the same rate as healthy controls on tasks of memory and attention. However, stroke participants improved at a greater rate than healthy controls on the Intra-Extra Dimensional Shift task. Overall, there was no significant difference in the rate of cognitive improvement between the stroke control group and the stroke enrichment group.

3.2 Cognitive Impairment

The results support the initial hypothesis that stroke participants would be significantly impaired in the areas of memory, attention and executive functioning compared to aged matched healthy controls. These results are consistent with previous hospital-based studies which have reported significant impairment in verbal

memory, visual memory and executive functioning at 3 weeks post stroke (Nys et al. 2005), and in memory and attention at 3 months post stroke (Tatemachi et al. 1994). The results are also comparable to community-based stroke studies in which significant impairments have been reported in memory (free recall, cued recall and recognition), verbal and visual working memory, attention and executive functioning skills at 3 to 4 months post stroke (Planton et al. 2012) and in visual and verbal memory at 6 to 10 months post stroke (Nys et al. 2005).

However, certain differences between the current study and previous studies are notable. For example, Hochstenbach et al. (1998) reported that hospital-based stroke patients did not display significant deficits in immediate verbal recall, while Lesnizk et al. (2008) reported a low prevalence of executive functioning impairment 14 days post stroke. These findings differ to those of the current study in which immediate verbal memory impairment and executive functioning deficits were apparent. Such discrepancies may be accounted for by random variability, differing patient inclusion criteria and the use of different cognitive assessments. For example, Lesnizk et al. (2008) only included participants with first ever stroke, whereas the current study included participants with previous strokes and TIAs. Varying definitions of cognitive impairment may also account for the differences found. For example, in the current study stroke patients' performance on cognitive tasks were compared to healthy controls. In the current study controls were recruited from a research volunteer base. The results showed that overall these healthy controls had a higher IQ score, as measured by the WTAR, than stroke participants. It is thus possible that this particular control group was higher functioning than what would be expected of an average control group. In turn, the cognitive deficits observed in the stroke participants may be exaggerated.

Given the differences within the literature and, considering the results of the current study, it is evident that further investigation into cognitive impairment post stroke is required to further aid our understanding of its nature. Indeed, it is surprising that despite the growing amount of literature on cognitive impairment post stroke there is still no standard neuropsychological battery to assess the cognitive deficits for the stroke population. In turn, there still remains no specific criterion to define cognitive impairment post stroke (McDonnell et al. 2011). As a result, researchers use a selection of "ad hoc cut off points" to classify individuals as cognitively impaired (McDonnell et al. 2011). Researchers have argued that introducing a standard neuropsychological battery will further aid our understanding of cognitive impairment and may reduce the variability of results seen throughout the literature. However, such a task needs to be considered from a practical stance. Understandably, creating a standard neuropsychological battery for stroke patients could prove to be a difficult task. It would require considerable resources and would be a lengthy undertaking. Furthermore, if a specific neuropsychological battery was created, clinicians may not necessarily have access to them. As a consequence, it may be argued that brief screening tools such as the Mini-Mental State Exam (MMSE; Folstein, Folstein & McHugh, 1975) or the Montreal Cognitive Assessment MoCA (Nasreddine et al. 2005) should be used to detect cognitive impairment. Indeed, they are easy and quick to administer and thus they are more practical for a hospital or rehabilitation environment. However, as previously mentioned such measures only provide a general estimate of an individual's overall cognitive functioning (Tombaugh & McIntyre, 1992). Thus, if a deeper understanding of a patient's cognitive abilities is required a neuropsychological battery may need to be administered. In these cases, researchers and clinicians should pay particular

attention to the reliability and validity of the cognitive tests that they choose to use. In addition, they should consider the practical issues that arise from testing stroke patients. For example, stroke patients commonly suffer from motor impairments and can often become easily fatigued. Thus, clinicians and researchers should also choose tests that require minimal motor movements and can be administered either in a relatively short period of time or can allow for separate testing sessions.

At this point, one may question as to why cognitive impairment requires detection at all. There are numerous arguments as to why cognitive assessments should be conducted. As previously mentioned, stroke survivors with cognitive impairments are at significant risk of experiencing further deterioration of their cognitive abilities (Rasquin et al. 2004) and are at increased risk of developing dementia (Tham et al. 2002). Furthermore, institutionalization and mortality rates are significantly greater than stroke survivors without cognitive impairment (Patel & Coshall, 2003). In addition, the findings of the current study showed that there was no correlation between FIM scores (stroke severity) and cognitive impairment. This highlights an important issue that specific neuropsychological assessment is required to assess cognitive impairment rather than relying on stroke severity measures. As previously mentioned, the early detection of cognitive deficits is vital in order to be able to implement intervention at a crucial time. This is further supported by the plethora of neurological changes that takes place in the brain following insult (Cramner, 1998). Early intervention may result in a faster and/or greater improvement in acquired cognitive deficits. In turn, this may have significant outcomes for patients' cognitive functioning post hospital discharge and may improve their quality of life post stroke.

3.3 Spontaneous Recovery

At retest, stroke patients displayed significant improvements in the areas of memory and attention. However, the rate of improvement did not differ between stroke patients and healthy controls. Consequently, this suggests that the improvements observed in the stroke population were a result of practice, rather than spontaneous recovery. Conversely, stroke patients showed a greater rate of improvement than healthy controls on the IED task. This provides evidence for spontaneous recovery occurring specifically for executive functioning. It should be noted that while healthy controls had obtained high scores on the IED task at baseline they had not reached ceiling effects. Consequently, there was still room for them to improve. Furthermore, the healthy controls actually showed a decline in their performance on the IED task at retest. Thus, the greater rate of improvement observed in the stroke group cannot be attributed to ceiling effects in the healthy control group.The significant improvement displayed by stroke patients on this task is further highlighted through the analysis of the patients' individual scores on the IED task. Appendix 1 displays the individual results for each IED analysis. Figure 1a shows that stroke control patients 3, 6, 8, 13 and 15 completed at least four additional stages at retest. Furthermore, these patients displayed a reduction on the Total Errors Adjusted score (Figure 2a) and the Total Trials Adjusted score (Figure 3a). It is noticeable that the characteristics of these particular patients varied greatly. For example, their ages ranged from 42 years old to 82 years old, while their IQ scores ranged from a score of 87, average, to a score of 118, high average. Their MoCA scores also varied considerably from a score of 8 to 23. Their performance compares to that of the individual results of the healthy controls. As seen in Figure 1c, a large proportion of healthy controls (patients 2,4,5,6,7,9,11,12) showed decline

in their performance by at least one to two stages (Figure 1c). These patients also displayed an increase in the Total Errors Adjusted score (Figure3b) and Total Trials Adjusted score (Figure 3c). The characteristics of these patients also varied greatly. Their ages ranged from 61 years old to 77 years old, while their IQ scores ranged from 71, low average, to 123, superior. Their MoCA scores were less variable than the stroke controls, with scores ranging from 23 to 29.

The finding of the current study raises a complex issue; how do researchers differentiate between spontaneous recovery and practice effects? Various studies have reported spontaneous recovery in global cognitive functioning at 3 to 24 months post stroke (Ballard et al. 2003; Rasquin et al. 2004). More specifically, studies assessing individual cognitive domains have reported spontaneous improvements in the area of memory from 3 to 12 months post stroke (Desmond et al. 1996) and in the areas of working memory and visual recognition from 2.3 months to 2 years post stroke (Hochstenbach et al. 1998). However, these studies do not consider the presence of practice effects.

A complicating factor when differentiating between spontaneous recovery and practice effects is that of differing baselines between clinical and non-clinical groups. For example, in the current study stroke survivors' baseline scores on all cognitive tasks were significantly lower than that of the healthy control group, yet both groups improved at a similar rate. Thus, one may question, whether the improvement observed by stroke controls can be interpreted simply as practice effects. In order to answer these questions, the current literature needs to be considered.

To date, there has been no specific investigation into the neuropsychological practice effects in stroke survivors. In addition, there is a paucity of research into the

relationship between practice effects and spontaneous recovery Furthermore, the few studies in this area have not addressed the issue of similar cognitive improvement across different baselines. Researchers have questioned the assumption that clinical populations are expected to improve at the same rate as healthy controls (Lezak et al. 2004). Zehnder et al. (1997) reported that Alzheimer patients failed to show any evidence of practice effects on the CERAD-NAB at 1 year post baseline assessment, compared to healthy controls who showed significant improvements at a retest interval of 2.4 years. Furthermore, practice effects found in healthy controls on the vocabulary subtest of the WAIS-R at 7 to 10 day retest, was not observed in HIV symptomatic and asymptomatic sufferers (McCaffrey et al. 1995). However, these diseases are neurodegenerative in nature and thus spontaneous deterioration of cognitive abilities would be expected. On the other hand, stroke does not follow the same trend as neurodegenerative diseases. Indeed, research has clearly provided evidence of cognitive improvement or at least preservation of post stroke cognitive functioning (Tham et al. 2002; Rasquin et al. 2005).

It is due to these complex issues that researchers need to control for the presence of practice effects when investigating improvements in cognition (Calamia et al. 2012). Perhaps the most informative research to date regarding spontaneous recovery and practice effects within the stroke population is that of Nys et al. (2005). Nys et al. (2005) reported that 54% to 83% of stroke patients displayed significant improvements in the areas of visual perception/construction, visual memory, abstract reasoning and language at 6 to 10 months post stroke. Importantly, these improvements were significantly greater than that found in healthy controls. This, along with the current study, provides evidence that stroke individuals can display

improvement above and beyond that of healthy controls, thus providing evidence of spontaneous recovery.

Given the current literature to date, there is not enough evidence to suggest that any improvement in cognitively impaired stroke individuals in the current study can be interpreted as spontaneous recovery, despite the lower baseline scores. However, it does highlight the need for future studies , as discussed later on, to address these issues.

It is questionable as to why the current study is not consistent with the results of Nys et al. (2005). Unlike, Nys et al. (2005) the current study did not find evidence of spontaneous recovery in the area of visual memory. There are a number of possibilities as to why the results of these two studies are not consistent. Differences in patient inclusion and exclusion criteria may have contributed to the difference in results. In the current study patients with previous strokes were included, whereas Nys et al. (2005) used first ever stroke patients only. As Nys et al. (2005) state, it is possible that patients with no prior stroke or cognitive impairment history may be more likely to experience spontaneous recovery than the general stroke population. Furthermore, Nys et al. (2005) compared stroke patients' performance to that of healthy controls who consisted of family/spouses of patients or volunteers from the community. As previously mentioned the controls of the current study were from a research volunteer base and displayed high IQ scores. Given that the level of spontaneous recovery was compared to healthy controls, it is possible that the differences within the control populations of each study may have accounted for the varying level of spontaneous recovery observed.

It is also possible that the difference in findings maybe attributable to the length of time between baseline assessment and retest. It is conceivable that spontaneous

recovery of visual memory requires a longer time period than 2.5 weeks. Indeed, one cannot conclude from the results of the current study that spontaneous recovery of memory and attention deficits does not occur at all. Rather, it may suggest that spontaneous recovery of these particular domains, unlike executive functioning deficits, does not occur within a short time frame. Perhaps, most notably, the results reveal that the time period for spontaneous recovery of cognitive domains may vary.

3.4 Practice Effects

The findings of the current study on practice effects are consistent with the literature to date. The presence of practice effects on memory and attention tasks is not surprising given that there was a short retest interval of 2.5 weeks. Indeed, practice effects are more likely to occur when assessments are repeated within a short time frame (Falleti et al. 2006).

The finding that practice effects were apparent on tasks of auditory and working memory are consistent with those of McCaffrey et al. (1993) who reported practice effects on logical memory (immediate and delayed) and visual memory based tasks when assessments were conducted 7 to 10 days apart. They are further consistent with the findings by Estevis et al. (2012) who reported a mean increase of .50 points in digit span at 3 and 6 months at retest.

It is possible that practice effects were observed in logical memory and visual memory due to memorization of the content of the tasks, for example, memorization of the stories or pictures presented (McCaffrey et al. 1995). One may argue that this presents a paradox as stroke patients are impaired in memory yet they retain a degree of memory that enables them to benefit from practice. However, memory impairment does not assume memory loss altogether. Indeed, it is possible that

practice effects do not necessarily rely on the particular type of memory that is affected during stroke.

Arguably, the contents of digit span and symbol span may be harder to remember over a 2.5 week period than the contents of logical memory and visual memory. For example, logical memory requires an individual to remember a story, whereas digit span requires an individual to remember a set of random numbers. It is thus possible, that practice effects occurred due to familiarisation with the task, rather than memory of specific details of the task.

Practice effects were also evident on the SRT task. This is consistent with the findings by Collie et al. (2003) who found evidence of practice effects on a similar SRT task when repeated four times in one day. Interestingly, no improvement was observed from baseline to retest on CRT in the current study. This contradicts the findings of Collie et al (2003) who found evidence of practice effects on a similar CRT task when repeated four times in a day. It may therefore be argued that CRT is susceptible to practice effects over very short periods of time, however, this task may be more robust to practice effects when the duration between test and retest is increased to 2.5 weeks. Yet, in the current study SRT preceded CRT. SRT and CRT tasks are very similar in nature. Thus, it is perhaps more plausible that by the time participants completed SRT their performance on these type of tasks had stabilised.

Perhaps most interestingly, the findings of the current study are not consistent with previous research on the presence of practice effects on executive functioning skills. As previously mentioned healthy controls showed little change in their performance on the IED task from baseline to retest. Researchers have argued that tests of executive functioning are particularly susceptible to practice effects as they require procedural learning; i.e. once the participant has learnt the problem

solving method required to successfully complete the task, they need only recall this strategy upon repeated assessments (Basso et al. 1999). Indeed, practice effects have been reported in healthy adult populations on the Wisconsin Card Sorting Test, the Ruff Figural Fluency test and the VCAT at 12 months retest (Basso et al 1999). Thus, the current findings suggest that IED is particularly robust to practice effects.

3.5 Enrichment

There was no significant difference in the rate of improvement between stroke control and stroke enrichment groups on memory, attention and/or executive functioning tasks, thus failing to support our final hypothesis. However, certain trends that occurred should be noted. The stroke control group displayed a greater rate of improvement than the stroke enrichment group on tests of visual memory (immediate and delayed). Yet, this is most likely due to the lack of improvement observed in the stroke enrichment group. The stroke enrichment group displayed a greater rate of improvement than the stroke control group on the test of auditory working memory. However, this is likely to be a result of a greater regression to the mean, given that the stroke enrichment group had lower scores at baseline.

There were no specific trends observed in the task of executive functioning. Both stroke groups showed an increase in the number of completed stages and a decline in the number of errors adjusted and trials adjusted scores at retest. Appendix 1 displays the individual analysis for stroke enrichment participants. Patients 5 and patient 7 completed an extra 5 and 7 stages respectively, at retest (Figure 1b). They further displayed a large reduction in the number of errors adjusted score (Figure 2b) and number of trials adjusted score (Figure 3b). Yet, despite this improvement, it does not differ greatly from the individual analysis of the stroke control group who

also showed improvements in the IED task. Furthermore, some enrichment participants showed a decline in performance on the IED task. In particular, patients 1 and 6 completed less stages at retest, made more errors and performed more trials. Consequently, this provides sound evidence to suggest that enrichment was not effective in alleviating executive functioning deficits in stroke individuals.

The finding of the current study is not consistent with animal research. Indeed, there is a plethora of animal studies to show that enrichment is effective for motor (Ohlsson & Johansson, 1994) and cognitive impairments (Leggio et al. 2000) in ischemic rats. In particular enrichment has been found to significantly improve cognitive impairment in ischemic rats, when housed in enriched conditions for as little as 4 days (Briones et al. 2000). These improvements observed in ischemic animal models are supported by the significant neurological changes that occur following enrichment, such as higher synaptic density and increased synaptogenesis in the CA1 hippocampal regions (Rampton et al. 2001; Morroni et al. 2011)

It is possible that the findings of the current study are not consistent with the results of animal enrichment studies due to the significant differences between the anatomical and cognitive abilities of humans and animals. Humans have a significantly more complex anatomical cognitive system than animals. Indeed, animal cognitive abilities are often singularly focussed, whereas human cognition is designed to serve numerous goals (Premack, 2007). Consequently, the enriched environment in the current study may not have been challenging enough to alleviate the cognitive deficits of stroke survivors.

Interestingly, the results are not consistent with those of Sarkamo et al. (2008), the only previous study to have assessed the effects of enrichment on acquired cognitive deficits post stroke. Sarkamo et al. (2008) allocated cognitively

impaired stroke patients to a music, language or control group. Results revealed that music listening significantly enhanced verbal memory and attentional skills at 3 and 6 months post stroke, compared to the language group and control group. As discussed below there may be a variety of reasons as to why the current results are not consistent with those of Sarkamo et al. (2008).

3.6 Factors affecting enrichment

There are a variety of factors that may account for why there was no significant effect of enrichment. In order to evaluate these factors consideration needs to be given to assessment and demographic variables, in addition to various aspects of the intervention.

Assessment variables in the current study were controlled for and thus the lack of effect of enrichment cannot be attributed to these. For example, there was no significant difference between the two stroke groups in the number of days spent in rehabilitation, the number of days between stroke and baseline assessment, or the number of days between rehabilitation admission and baseline assessment. Yet, there were differences between demographic variables. For example, there were significantly more males in the stroke control group than in the stroke enrichment group. Animal studies have revealed that gender differences may influence the effects of enrichment on the recovery of cognitive abilities. Intact female rats displayed significant improvement in spatial memory abilities following 15 days of enrichment exposure, unlike their non injured male rat counterparts. (Martinez-Cue et al. 2002). Conversely, brain injured male rats exposed to enrichment for 14 days displayed improved spatial memory abilities, although, this improvement was not observed in female injured rats (Wagner et al. 2002).

The two stroke groups also differed in the number of years of education. Stroke control participants had significantly more > 12 years education than the stroke enrichment group. Thus, it may be argued that stroke control participants were at a greater cognitive advantage than the stroke enrichment group. As a result, the stroke control participants may have been more likely to display improvements in cognition than the stroke enrichment group, i.e. stroke control participants may have shown a greater level of improvement in cognitive functioning, which ultimately may have matched the effect of enrichment displayed by the stroke enrichment participants. Nevertheless, there was no significant difference in premorbid IQ scores between the two stroke groups. Consequently, it is unlikely that the stroke participants were at any greater cognitive advantage at baseline. This argument is further supported by the finding that there were no significant differences between the stroke enrichment and stroke controls performance on the MoCA.

Perhaps a more reasonable explanation for the absence of enrichment may have been due to the wide variability between the cognitive performance of the enrichment group and the stroke group at baseline. Indeed, it is noticeable that the stroke enrichment group performed worse at baseline on tasks of working memory and executive functioning than the stroke control group. In contrast the stroke control enrichment group performed better than the stroke control group on tasks of auditory memory (immediate and delayed) and visual memory (immediate and delayed) at a baseline

There are a variety of factors regarding the intervention that may have influenced the effectiveness of enrichment. It is possible that the current study failed to show an effect of enrichment due to the time delay between stroke onset and exposure to enrichment. Indeed, Sarkamo et al. (2008) exposed individuals to

enrichment 1 week post stroke, whereas the current study implemented intervention at 18 days post stroke. However, animal studies have revealed that ischemic rats housed in enriched conditions 15 days post focal ischemic injury, performed significantly better on motor tests than their counterparts who were housed in standard conditions (Johansson 1996). No studies to date have assessed the effects of delayed exposure to enrichment on cognitive deficits in animals or humans. Thus it is still not known whether the timing in which enrichment is implemented moderates how effective it will be.

The duration of the enrichment period may also be a crucial factor in whether it is effective in alleviating cognitive deficits. The current study implemented enrichment for a period of 13 days. Sarkamo et al. (2008) implemented enrichment for a period of 2 months. It is therefore possible that the duration of enrichment in the current study was not of an adequate length to have an effect on the cognitive deficits tested. While animal studies have reported significant improvements in cognitive functioning in ischemic rats following 5 to 6 weeks of enrichment exposure (Dahlqvist et al. 2004; Soderstrom et al. 2009) they have also reported that ischemic rats need only be exposed to enrichment for a period of 4 days for significant effects to occur (Briones et al. 2000). Yet, as previously mentioned humans have a more complex anatomical cognitive system than animals. Consequently, it would seem reasonable to suggest that stroke patients may require exposure to enrichment for a longer period of time than animals. This may explain why Sarakmo et al. (2008) found positive effects on cognitive deficits, as they implemented enrichment for a period of 2 months.

On the other hand, it may not necessarily be the duration of enrichment that matters. It is possible that the frequency in which participants engage in enrichment

activities plays a significant role in its effectiveness. Indeed, the intervention implemented was passive, i.e. patients were regularly encouraged and reminded by staff and family members to take part in the activities but they were not required to engage in them for a specific amount of time. By using this method, it was found that the enriched participants were 1.7 times more likely to engage in cognitive activities than a sub group of the stroke controls (Jansen et al. 2014). It is thus possible that patients did not engage in activities at a high enough frequency for an effect of intervention to occur. It therefore remains unknown as to whether duration and/or frequency have a significant influence on the effects of enrichment on cognitive deficits in the human stroke population.

A further factor for consideration is the type of enriched environment that stroke patients are exposed to. The current study provided a range of cognitive activities. Interestingly, Sarkamo et al. (2008) focused on one specific activity, music. This may suggest that specific aspects of enriched environments are more beneficial than others. It is indeed possible that specific activities may enhance specific areas of cognition. Animal studies have reported that specific enriched conditions influence different areas of cognition (Schrijver et al. 2010). Healthy rats exposed to sensory and explorative enrichment but deprived of socialisation display intact spatial acquisition skills and impaired reverse learning skills. Conversely, healthy rats exposed to socialisation but devoid of objects and sensory stimulation display significant impairment in spatial acquisition skills (Johnson & Ohlsson 1996).

However, TBI animal studies have revealed that it is a combination of enrichment activities that are most effective in alleviating cognitive deficits (Johnson & Ohlsson 1996; Sozda et al. 2001). TBI rats housed in a typical enriched

environment perform significantly better in the acquisition of spatial learning tasks and memory retention tasks than TBI rats exposed to toys or social activities but not both (Sozda et al. 2001). There are no current stroke animal models that have assessed the effects of various aspects of enrichment on cognition, with studies focusing only on motor abilities. Johnson and Ohlsson (1996) reported that ischemic rats housed in enriched conditions plus social conditions performed significantly better on various motor tasks than both rats housed in enriched conditions minus social conditions and rats housed individually with access to physical activities.

Finally, it should be noted that there was only a small number of participants in the enriched condition. Thus, lack of effect of enrichment may be due to lack of statistical power.

3.7 Enrichment vs Cognitive Rehab

Cognitive rehabilitation has provided some evidence for the amelioration of cognitive deficits. Doornhien & De Hann (1998) reported that stroke patients displayed enhanced performance on memory tests post visual imagery training. Significant improvements in stroke patients' attentional deficits have also been reported post Attention Process Training (Barker – Collo et al. 2009). In addition, Goal Management Training has been shown to alleviate executive functioning deficits (GMT; Levine et al. 2000). However, there is strong evidence to suggest that these improvements are merely a result of practice, rather than intervention (Park & Ingles 2001). Indeed, improvements observed in memory function are specific to tests that have been practiced (Doornhien & De Hann, 1998; Park & Ingles, 2001), while improvements observed in attentional training are no greater

than that observed in healthy controls (Park et al. 1999). This highlights an important issue that the effects of cognitive rehabilitation fail to generalise to other tasks. Furthermore, cognitive rehabilitation focuses on one specific deficit e.g. memory, instead of addressing multiple cognitive deficits that are common in stroke survivors. It is possible that the dwindling research into cognitive rehabilitation may be attributed to the lack of significant effects of such an intervention. Indeed, the current findings on cognitive rehabilitation suggest that research into alternate interventions for post stroke cognitive deficits is urgently required.

However, this poses the question as to why research should specifically focus on environmental enrichment? As previously mentioned there is a plethora of research to show the positive effects of enrichment on motor and cognitive impaired deficits in ishemic animal models (Ohlsson & Johansson, 1994; Leggio et al. 2000). This alone, should provide motivation to continue to investigate the effectiveness of enrichment. In addition, more recent research has revealed that the use of computer games, such as the Nintendo Wii, has proved to be significantly effective on post stroke motor deficits. In particular, Mouawad, Doust, Max & McNulty (2011) reported significant improvement in functional upper extremity motor abilities following the implementation of Wii games over a 10 day period. What is particularly promising is that intervention was implemented 15.3 months post stroke. Given these findings it is important to consider how enrichment may positively affect post stroke cognitive deficits.

The outcome of an intervention is understandably the primary factor to consider when choosing how to address the cognitive deficits experienced by stroke survivors. However, when giving consideration to an intervention, such as cognitive rehabilitation or enrichment, within a rehabilitative setting, it is necessary to consider

other factors. Arguably, one particular factor to consider is that of the practical demands that is placed on both staff and patients.

Qualitative studies have revealed various barriers to enrichment in the stroke rehabilitative environment. The perception that enrichment increases staff workload, with a responsibility to prioritise daily care instead, affects staffs' ability to implement the activities (White et al. 2013). Staff are also less likely to encourage patients to engage in enrichment if patients are unmotivated, fatigued, agitated or are susceptible to mood disturbances (White, Alborough, Janssen, Jordan & Pollack, 2013). Furthermore, physical health problems may prevent participants from engaging in enrichment. For example, mobility problems affect the patient's ability to access the communal enrichment area while visual impairments prevent the patient from being able to engage in reading and computer activities.

Nevertheless, it is arguable that these reported barriers may simply be "teething problems" during the preliminary implementation of enrichment. For example, while staff initially reported enrichment increased their work load, they paradoxically reported that patients were less likely to ring their buzzer, as they were engaged in activities. This ultimately reduced the demands on staff (White et al. 2013). White et al. (2013) also reported that as enrichment became part of the staff's routine, it became less of a burden.

On the other hand, cognitive rehabilitation arguably requires considerably more resources than enrichment. For example, cognitive rehabilitation requires the presence of a clinician to implement lengthy rehabilitative programs and classes at specific times during the day. What's more, the patients are often subjected to mundane tasks that are lengthy and time consuming. For example, attentional training as described by Westerberg et al. (1997) required patients to undertake

approximately 40 minutes of training per day for five days a week, for a period of five weeks. Barker-Collo et al. (2009) required patients to undertake 30 hours of Attention Process Training over four weeks. As a result, such lengthy and mundane interventions may result in patient refusal and drop out. Furthermore, it necessitates access to a computer and would further require motor skills, which are often commonly impaired after stroke.

Enrichment, on the other hand, provides a range of activities that the participant may engage in. Thus, if the patient is unable to take part in one activity due to specific deficits, e.g motor skills, there may be other activities that are more suited to them. In addition, if patients have a range of activities to choose from it is reasonable to suggest that they may find enjoyment in at least one of the activities on offer. As a result, patients may be less likely to drop out of such an intervention. Indeed, qualitative studies have revealed that enrichment is greatly valued by stroke participants with patients reporting enjoyment in the activities and social opportunities that enrichment presents them with (Bartley, White, Janssen & Spratt, 2011). For example, patients reported benefits of the communal area in which they could meet other stroke patients with whom they could share their experiences.

What's more, enrichment may reduce the amount of time that patients spend on their own. Indeed, stroke patients in Australian rehabilitation units spend approximately 43% of the day alone (King et al. 2011) and up to 60.4% of their time spent resting in bed (Bernhardt et al. 2004). Notably Jansen et al. (2012) reported that patients' activity levels are significantly increased when exposed to an enrichment environment. Specifically, stroke patients are 1.7 times more likely to engage in cognitive activities when provided with an enriched environment.

A further factor that makes enrichment more favourable is the location where it can be implemented. Cognitive rehabilitation may require patients to remain in hospital or to attend clinics to take part in the specific programs designed for them. Enrichment, however, may not require the patient to remain in hospital. Given that enrichment is designed to encompass a range of activities, patients may be able to take part in these activities at home. Thus, while patients may initially attend enrichment activities in the rehabilitation ward, they may continue with these activities while they are at home.

Consequently, given the advantages of enrichment it can be strongly argued that further research should be conducted into this area, to determine the critical parameters that may increase its effectiveness in alleviating the cognitive deficits of stroke individuals. The fine tuning of enrichment, such as increasing its duration and frequency, may result in more promising outcomes than those found in the current study.

3.8 Strengths of Current Study

The study aimed to assess the presence of cognitive impairment and spontaneous recovery on a stroke population that was representative of those found in hospital rehabilitation environments. Thus, the study encompassed stroke individuals who had either ischemic or subarachnoid haemorrhages, in addition to including patients who had previously experienced strokes and/or TIAs. To date, the majority of studies assessing cognitive impairment and spontaneous recovery have used stringent participant inclusion criteria. Arguably, these studies do not represent the average stroke population and thus limit generalization of their results.

The study was the first to assess the effects of a typical enriched environment on the cognitive abilities of a human stroke population. To date, no previous study has attempted to replicate the stroke animal enrichment research in human stroke. The only study to date on enrichment in humans focused on one specific activity (Sarakamo et al. 2008), rather than providing an enriched environment that is representative of those found in stroke animal models. The current study recruited patients from only one hospital, thus reducing the variability in the environment that both the stroke control and stroke enrichment were exposed to. Furthermore, access to enrichment was made as easy as possible. Although access to communal enrichment relied on transporting the patient to a communal area, individual enrichment was made available to the patient at all times.

The current study provided a robust method to account for practice effects. The use of a healthy control group and a stroke control group was essential in determining whether improvement observed in the stroke population and the enrichment group were a result of practice, spontaneous recovery, or intervention. Numerous studies investigating the spontaneous recovery of stroke individuals have failed to assess control participants at retest, thereby reducing the validity of their findings. The results of the current study, however, emphasise the need to account for practice and highlights the complex relationship between spontaneous recovery and practice effects.

Considerable care was taken to use appropriate tests to assess memory, attention and executive functioning. The tests used in the current study had good reliability and validity and they accommodated for the physical impairments that stroke survivors' experience. For example, stroke patients with motor impairments were able to complete all auditory memory, working memory, attention and

executive functioning tasks, as each of these assessments required minimal hand movements. Visual Reproduction I and II were the only tasks that motor impaired patients were unable to attempt.

3.9 Limitations & Future Research

Despite the best efforts of the researchers the current study presents with a number of limitations. The sample sizes of each group were small; there was a total of 41 stroke participants (27 control and 14 enrichment) and 15 healthy controls. Due to fatigue, boredom and refusal to participate not all participants took part in every neuropsychological subtest.

Due to resource limitations, such as availability of research assistants, the allocation of stroke patients to the standard or enrichment conditions occurred in a consecutive, rather than alternating manner; i.e. the delivery of the two different conditions occurred over two different time periods. As a result, there may have been a number of confounding variables that could have affected the outcome of the results. Such confounding variables may have included differences in rehabilitation staff, care provided by nurses and interactions with other patients.

The current study did not use the National Institutes of Health Stroke Scale (NIHSS 2003), a common measure of stroke severity which assesses levels of consciousness, orientation, visual fields, motor functioning and language (2003). Unfortunately, there were not the staffing resources to be able to conduct this particular assessment. Nevertheless, as part of the patients' hospital care, the Functional Independence Measure (Wright, 2000) was administered on admission to and on discharge from hospital by staff. The FIM is an estimate an individual's

functional independence in a rehabilitative setting. Thus, arguably the FIM score provided adequate information on stroke severity.

The assessments were administered in the same order for each patient. Therefore, it is possible that participants' performance on later tasks were affected by fatigue. However, due to the nature of the tasks, it was not feasible to change their order of presentation. For example, Logical Memory II requires a participant to recall a story twenty to thirty minutes after it has been presented. Consequently, it must be administered in a timely fashion that allows for the appropriate amount of time delay to occur. What's more, tasks involving presentation of visual stimuli, such as Symbol Search, could not occur between the administration of Visual Reproduction I and II, in order to prevent the occurrence of interference effects.

The current research did not administer any psychiatric measures at baseline or retest. Previous studies investigating cognitive impairment and recovery in stroke have paid attention to the assessment of depressive symptoms. However, the current study did not include any psychiatric measures, primarily due to time limitations. The delivery of the neuropsychological battery was lengthy and thus it was not deemed feasible or ethical to include additional assessments. Nevertheless, the investigation of depression in the current stroke population may have provided a further insight into the results obtained. In a systematic review Hackett, Yapa, Parag & Anderson (2005) reported that almost one third of patients will experience symptoms of depression post stroke. Most notably, studies assessing post stroke depression in hospital patients have revealed that 16% to 36% of stroke patients present with depression on admission to a rehabilitation unit (Diamond, Holroyd, Macciocchi & Felsenthal, 1985; Daily et al. 1983). Furthermore, 25% of stroke patients are classified as depressed 7 days post hospital admission while 29% of

patients are diagnosed as depressed on discharge (Daily et al. 1983). Thus, it is likely that a proportion of the patients in the current study may have been experiencing depressive symptoms. There is a plethora of research reporting the effects of depression on cognition. Depressed individuals show significant impairments in non verbal memory (Behnken et al. 2010), working memory (Rose et al. 2006), attention and executive functioning (Yvonne et al. 20). Consequently, patients' performance on the cognitive tasks at test and retest, may have been affected by their psychological state.

Finally, there was no specific measure to record the amount of time that participants engaged in enrichment activities. In the enrichment study conducted by Sarkamo et al (2008) patients were encouraged to keep a diary of the activities that they participated in. While this may be considered a reasonable method of activity recording it is possible that patients' ability to comply with this process may be hindered by their physical and cognitive deficits. For example, patients with motor difficulties may not be able to write, while patients with memory impairments may require constant prompting to use their diaries. Alternatively, staff or family members could be responsible for activity recording.

Consequently, the current study provides important implications for future research. Research into the cognitive deficits of stroke survivors requires further investigation. In particular, careful consideration needs to be given to the type of tests used in order to further assist our understanding of cognitive impairment post stroke. Secondly, future research should focus on the relationship between spontaneous recovery and practice effects in the stroke population. A future study comparing cognitively impaired stroke survivors to other cognitively impaired clinical populations that may not show cognitive improvement over time, such as

individuals with neurodegernative disorders, may help to aid our understanding of the relationship between spontaneous recovery and practice effects in clinical populations. Thirdly, research should focus on increasing the duration and frequency of enrichment in stroke rehabilitative wards using larger sample sizes, in order to determine whether enrichment may be effective. Indeed, focusing on improving such interventions could potentially alleviate the cognitive deficits experienced by stroke survivors, and in turn, improve their quality of life post stroke.

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Appendix 1.

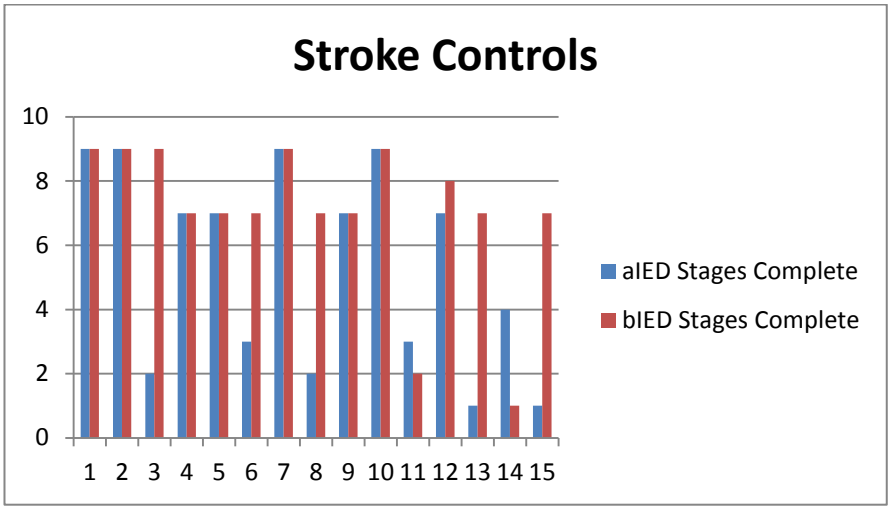

Figure 1a. Stroke Controls – No. of Stages Completed

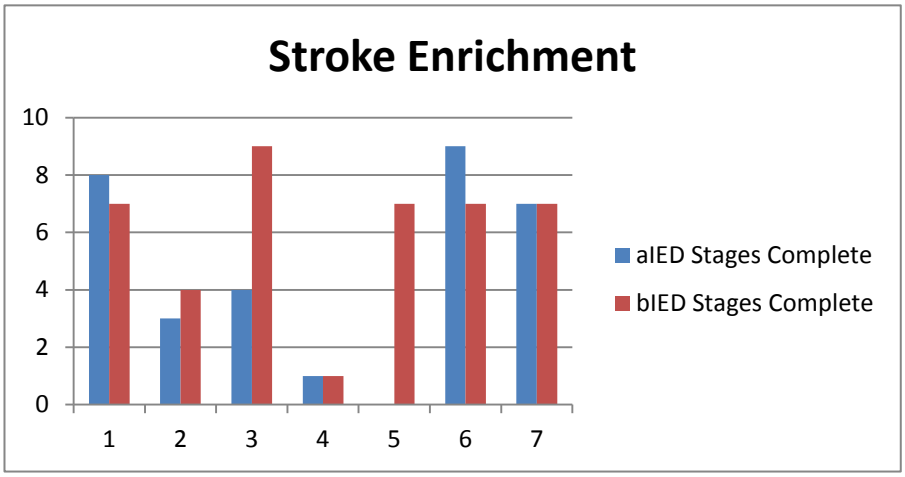

Figure 1b. Stroke Enrichment – No. of Stages Completed

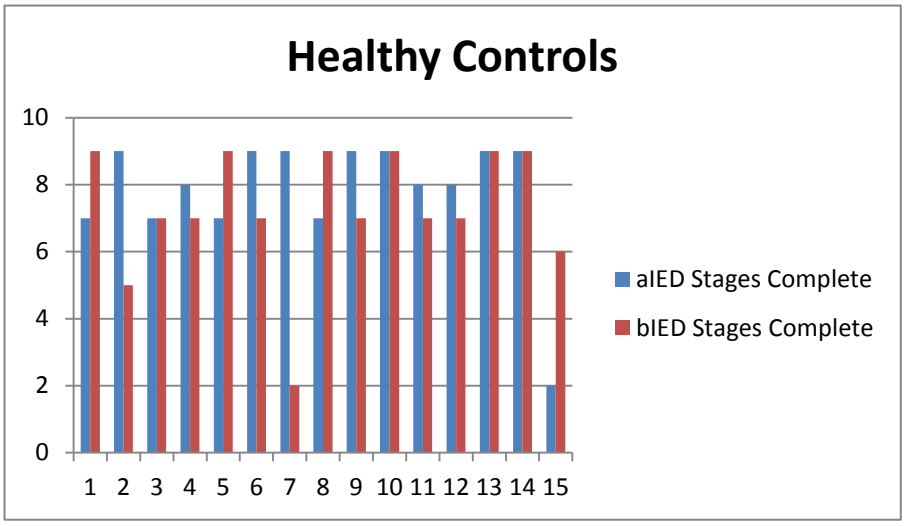

Figure 1c. Healthy Controls – No. of Stages Completed

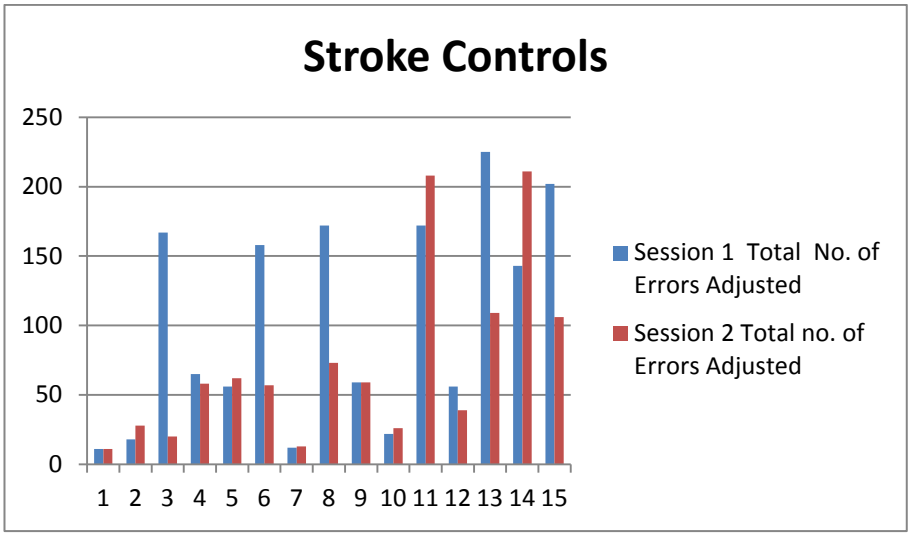

Figure 2a. Stroke Controls – No. of Errors Adjusted

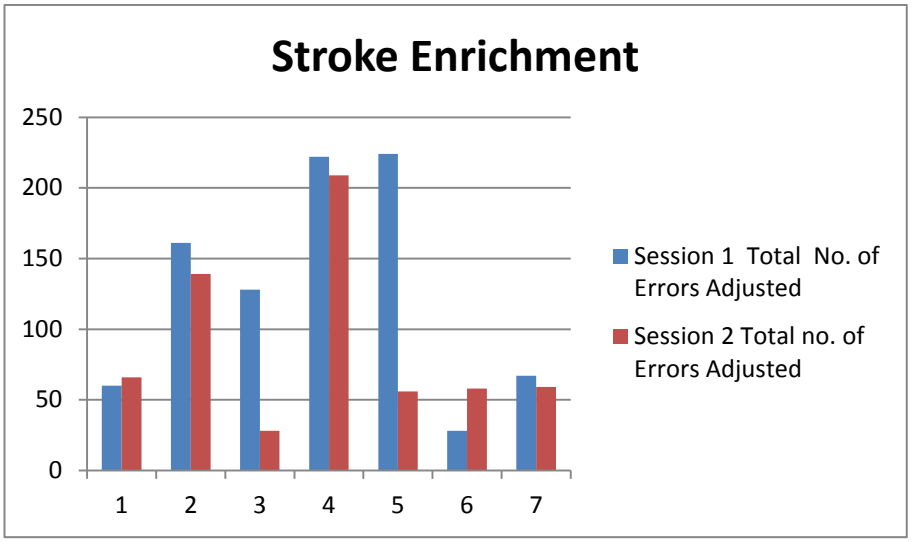

Figure 2b. Stroke Enrichment - No of Errors adjusted

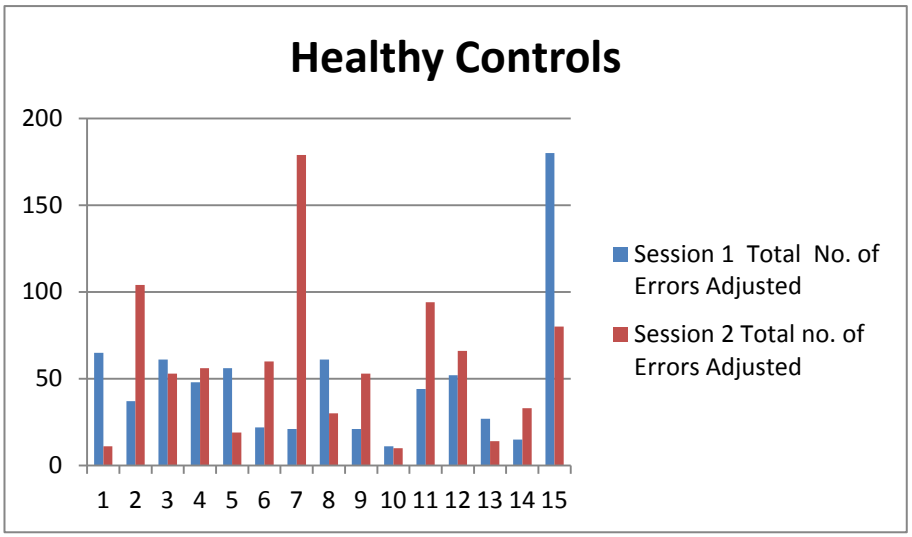

Figure 2c. Healthy Controls – No. of Errors Adjusted

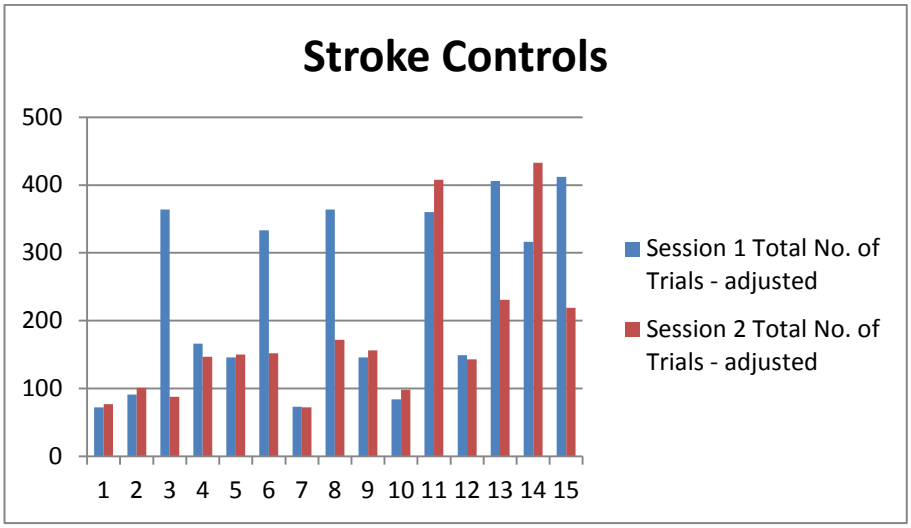

Figure 3a. Stroke Controls – No. of Trials Adjusted

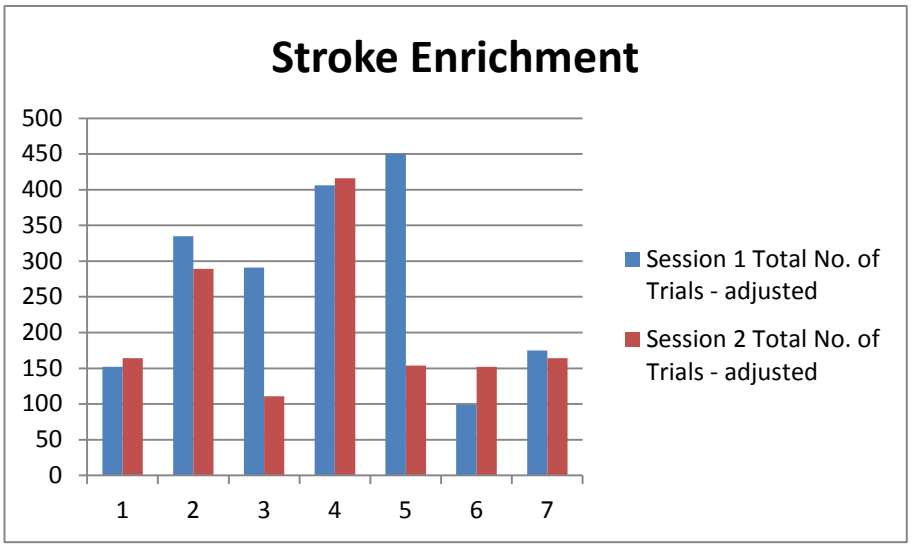

Figure 3b. Stroke Enrichment – No. of Trials Adjusted

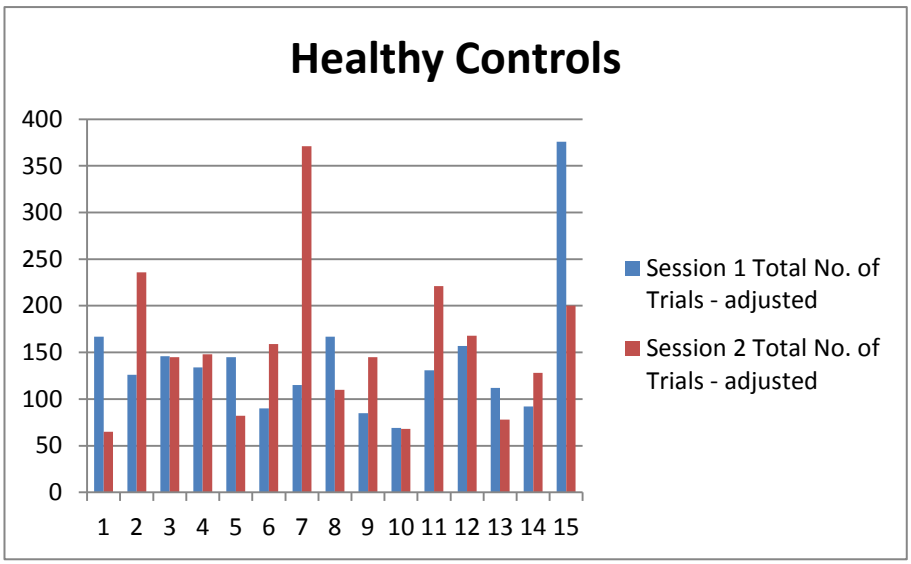

Figure 3c. Healthy Controls – No. of Trials Adjusted

Appendix 2.

15 November 2011

HUNTER NEW ENGLAND
NSW HEALTH

Dr Neil Spratt
Neurology Dept
John Hunter Hospital

Dear Dr Spratt

Re: Environmental Enrichment Post Stroke (09/09/16/5.08)

HNEHREC Reference No: 09/09/16/5.08
NSW HREC Reference No: HREC/09/HNE/299
SSA Reference No: SSA/09/HNE/338

Thank you for submitting a request for an amendment to the above project. This amendment was reviewed by the Hunter New England Human Research Ethics Committee. This Human Research Ethics Committee is constituted and operates in accordance with the National Health and Medical Research Council's *National Statement on Ethical Conduct in Human Research (2007)* (National Statement) and the *CPMP/ICH Note for Guidance on Good Clinical Practice*. Further, this Committee has been accredited by the NSW Department of Health as a lead HREC under the model for single ethical and scientific review.

I am pleased to advise that the Hunter New England Human Research Ethics Committee has granted ethical approval for the following amendment requests:

- For the addition of Ms Helen Andrews as co-researcher;
- For the removal of Ms Ruby Hooke as student researcher;
- For the removal of Ms Jennifer White as co-researcher;
- For the removal of Ms Emma Bartley as co-researcher;
- For the Participant Information Statement ((Version 9 dated 1 November 2011);
- For the Guardian/Person Responsible Consent Form (Version 8 dated 1 November 2011);
- For the Participant Consent Form (Version 8 dated 1 November 2011);
- To no longer involve the observation of patients in their surroundings; and
- To no longer include the administration of an interview about the patient's hospital experience

For the protocol: **Environmental Enrichment Post Stroke**

Approval from the Hunter New England Human Research Ethics Committee for the above protocol is given for a maximum of **3** years from the date of the approval letter of your initial application, after which a renewal application will be required if the protocol has not been completed. The above protocol is approved until **October 2012.**

Hunter New England Human Research Ethics Committee
(Locked Bag No 1)
(New Lambton NSW 2305)
Telephone (02) 49214 950 Facsimile (02) 49214 818
Email:hnehrec@hnehealth.nsw.gov.au
http://www.hnehealth.nsw.gov.au/research_ethics_and_governance_unit

Appendix 3.

Dr Neil Spratt
Neurologist, Hunter New England Health, and
Conjoint Senior Lecturer,
School of Biomedical Sciences and Pharmacy
MS502 Biomedical Sciences Building
University of Newcastle
Callaghan Drive, Callaghan
NSW. 2308

Information Statement for the Research Project:

Environmental Enrichment Post Stroke

You are **invited** to take part in a research project, which is being **carried out** by the **Hunter Stroke Service** (Hunter New England Health), the **University of Newcastle** and the **University of Sydney**. Dr Neil Spratt, a neurologist from the Department of Neurology, John Hunter Hospital, is leading the study as Chief Investigator.

Why is the research being done?

The **purpose** of the research is to gather information to further understand how the rehabilitation surroundings of a stroke survivor affects their **stay in hospital,** and their **recovery**.

Who can take part in the research?

We are seeking **stroke survivors** who are **receiving treatment** within **Rankin Park Centre**.

What choice do you have?

Taking part in this research is **entirely your choice**. Only those people who give their **informed consent** will be included in the project. Whether or not you decide to take part, your decision will **not disadvantage** you in any way and will **not affect** any part of your **rehabilitation** program.

If you do decide to take part you may **withdraw** from the research project at **any time** without giving a reason. If you do decide to withdraw from the research project, you have the option of withdrawing all information relating to you.

In the event of a serious incident we are obliged to report all information to the Human Research Ethics Committee that has reviewed and approved this research.

What would you have to do?

You will be asked to consent to:

- performing **tests** which help measure your current level of **mood**
- complete a **set of tests** which help determine your **ability to concentrate** and **remember** things. This set of tests will be conducted at the **beginning of the project** and then again **two to three weeks later**. The tests will take approximately **1 hour** to complete with an option to complete the tests over **two separate 30 minute sessions** and with as many **breaks** as you may **need**
- a researcher **visiting you** at **your home** to allow the completion of tests should you be **unable** to complete them at the Rankin Park Centre (e.g. due to discharge or transfer, or due to other commitments).

- a researcher **reviewing your inpatient medical file** to gain **information** about:
  - your **background** (such as age, country of birth, living arrangements, occupation and how well you functioned prior to your stroke)
  - **other conditions** or **diseases** you may have
  - details about your **stroke** (such as **date**, **where** in the brain your stroke occurred, how it has **affected your abilities**)
  - details about your **hospital stay** (like how **long** you have been in hospital and how much **help** you need currently).

If you take part in this research program, you will **not miss out** on any **treatments**. There is **no cost** to you for taking part in this program. You are required to **do nothing** else other than go about your **normal** daily **activities**.

What are the risks and benefits of taking part?

There are **no known risks** of participating. If you feel uncomfortable at any stage, you are free to **alert the researcher and testing will cease immediately.** There will be **no immediate individual benefit** to you from participating in this research; however information gained may **contribute** to the development of intervention programs for future stroke survivors.

How will your privacy be protected?

All the **information** you give will be **confidential**. To keep your records confidential, they are identified by a **code instead** of your **name**. All personal health information will be accessed, used and stored in accordance with Commonwealth Privacy Laws and the NSW Health Records and Information Privacy Act 2002. All study records will be **kept in a secure place** to which no one but the researchers has access.

Information from all the people in the study is **combined** and **summarised** and **no individually identified data** will be **reported**.

How will the information collected be used?

All information will be kept in a database. Individual participants will not be able to be identified from the database. These results **may** be **published** in a **scientific journal** or at health **education forums** but your name will not be used at any time. Information obtained throughout the project will be retained at the University of Newcastle for **five years**, after which it will be **destroyed**.

What do you need to do to take part?

Please **read** this Information Statement and be sure you **understand** its content **before** you **consent** to take part.

If you would **like** to **take part**, please **complete** the **consent form** and **return** it to a staff member.

Questions or further information?

You **may wish** to **consult** with your **doctor, a relative or friend before agreeing** to take part in this study.

If you need any **more information** you can contact a **member of the research team**. The researchers responsible for this study are:

Principal Investigator: Dr Neil Spratt (**Phone: 4921 3491**)

Co-investigators:

University of Newcastle		**Hunter New England Health**	
Heidi Janssen	Ph: **0411 114995**	Dr Michael Pollack	Ph: **02 49 21 4840**
Dr Frini Karayanidis	Ph: **02 49 21 5457**		
Dr Karen Drysdale	Ph: **02 49 21 7120**		
Helen Andrews	Ph: 0447 291 964		
University of Sydney		**National Stroke Research Institute**	
Assoc.Prof. Louise Ada	Ph: **02 93 519544**	Assoc. Prof. Julie Bernhardt	Ph: 03 94 962783

Thank you for considering the invitation to take part in this research project.

Yours sincerely,

Dr Neil Spratt

This project has been approved by the Hunter New England Human Research Ethics Committee of Hunter New England Health, Reference 09/09/16/5.08 .
Should you have concerns about your rights as a participant in this research, or you have a complaint about the manner in which the research is conducted, it may be given to the researcher, or, if an independent person is preferred, to **Dr Nicole Gerrand**, Manager, Research Ethic and Governance,, Hunter New England Human Research Ethics Committee, Hunter New England Health, Locked Bag 1, New Lambton NSW 2305, **telephone (02) 4921 4950**, email Nicole.Gerrand@hnehealth.nsw.gov.au

Dr Neil Spratt
Neurologist, Hunter New England Health, and
Conjoint Senior Lecturer,
School of Biomedical Sciences and Pharmacy
MS502 Biomedical Sciences Building
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Callaghan Drive, Callaghan
NSW. 2308

University of Newcastle		*Hunter New England Health*	
Dr Neil Spratt	**Ph: 02 49 213491**	**Dr Michael Pollack**	**Ph: 02 49 21 4840**
Heidi Janssen	**Ph: 0411 114995**		
Helen Andrews	**Ph: 0447 291 964**		
Dr Frini Karayanidis	**Ph: 02 49 21 5457**		
Dr Karen Drysdale	**Ph: 02 49 21 7120**		
University of Sydney		**National Stroke Research Institute**	
Assoc Prof. Louise Ada	**Ph: 02 93 519544**	**Assoc Prof. Julie Bernhardt**	**Ph: 03 94 962783**

I **agree to take part** in the above research project and give my **consent freely**.

I have been **given a copy** of the **Information Statement** and I understand that the **project** will be **carried out** as **explained**.

I understand that I can **withdraw** from the program **at any time**. I **do not have to give any reason** for withdrawing.
As outlined in the Information Statement I **consent** to:

- a **research team** member **reviewing my medical record**
- taking part in **tests** as described in the information statement
- a researcher visiting me at **my home** at a mutually agreeable time in the event that testing cannot be completed at the Rankin Park Centre

I **understand** that **my personal information** will remain **confidential** to the researchers.
I have had the **opportunity** to **ask questions** and have them **answered** to my **satisfaction.**

Participant
Signature:_____

Print name: _____

Date: _____

Witness
Signature:_____

Print name: _____

Date: _____

Dr Neil Spratt
Neurologist, Hunter New England Health, and
Conjoint Senior Lecturer,
School of Biomedical Sciences and Pharmacy
MS502 Biomedical Sciences Building
University of Newcastle
Callaghan Drive, Callaghan
NSW. 2308

Guardian/ Person Responsible Consent Form for the Research Project:

Environmental Enrichment Post Stroke

Version 8 – 01/11/2011

Research Team

University of Newcastle

Dr Neil Spratt	**Ph: 4921 3491**	**Dr Michael Pollack**	**Ph: 4921 4840**
Heidi Janssen	**Ph: 0411 114995**		
Dr Frini Karayanidis	**Ph: 49 21 5457**		
Dr Karen Drysdale	**Ph: 49 21 7120**		

Hunter New England Health

University of Sydney

A. Prof. Louise Ada	**Ph: 02 93 519544**	**A.Prof. Julie Bernhardt**	**Ph: 02 94962783**

National Stroke Research Institute

I am the Guardian/ person responsible for: *(print name of stroke survivor)*

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and I agree for them to participate in the above research project and give my consent freely.

I have been given a copy of the Information Statement and I understand that the project will be carried out as explained.

I understand _____ can withdraw from the program at any time. No reason needs to be given for withdrawing.

As outlined in the Information Statement, on behalf of_____ I consent to:

-
- a research team member reviewing their medical record
- taking part in all tests as described in the Information Statement
- a researcher visiting _____ _____at their home to allow the completion of tests should they be unable to complete them at the Rankin Park Centre (e.g. due to discharge or transfer, or due to other commitments).

I understand that all personal information will remain confidential to the researchers.

I have had the opportunity to ask questions and have them answered to my satisfaction.

Signature:_____ Print name: _____

Date: _____ Phone Number: _____

Appendix 4.

Journal Article

International Journal of Stroke - Author Guidelines

3000-4000 words, including references and tables.

Abstract
Please provide a structured abstract according to the following headings:
• Background
• Aims and/or hypothesis
• Methods
• Results
• Conclusions

Text
Introduction
Aims and/or hypothesis
Methods
Results
Discussion
References

Figures and Illustrations
Illustrations are encouraged for their educational value. Diagrams, line drawings, photographs or flow charts are valuable but their use will be subject to editorial judgment. Photographic illustrations and diagnostic imaging media must be supplied in electronic form. The only acceptable format is Tiff or JPEG file, at 300 dpi.

Go to http://0-authorservices.wiley.com.library.newcastle.edu.au/bauthor/illustration.asp for author guidelines on electronic artwork.

*Tables must supplement the text without duplicating it. Each should be numbered, typed on a separate electronic sheet, and have an appropriate title, all manuscripts must be in basic Word format, **PDF files cannot be accepted**. Please do not create tables as a JPEG file if it can be avoided. They need to be in word format for editing purposes.*

References
These must be limited to the work cited in the paper and should not be a bibliography of the subject. Personal communications and unpublished material are not acceptable as references.

*Each reference should conform to the **Vancouver style**, (http://en.wikipedia.org/wiki/Vancouver_system) and references should be numbered*

consecutively in the order in which they are first mentioned in the text.

List all authors (include all initials) when there are six or fewer; when seven or more, list the first three and add 'et al'.

Give the title of the paper in full; the title of the journal abbreviated according to Index Medicus or on PubMed (if not listed by Index Medicus spell in full); the year; the volume number and the first and last page numbers of the article.