An investigation into the use of Addenbrooke's Cognitive Examination – revised (ACE-R) as a means of predicting rehabilitation outcomes in adults aged 16 or over.

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Volume I

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Chapter 1: Systematic literature review

The role of cognition in predicting functional outcomes in stroke rehabilitation: A systematic review

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Abstract

Objectives: To review the literature on inpatient stroke rehabilitation where cognition has been an independent variable. These data were used to establish how much variance in relation to functional outcome can be explained by cognition compared to potential covariates.

Data Source: A systematic search of electronic databases (Ovid databases, EMBSE. PsychInfo, CINAHL, Web of Knowledge, Cochrane) was conducted between the years 2000 – May 2012 and reference lists of relevant articles were hand searched.

Design: Articles thought to be appropriate for review were compared against an inclusion/exclusion criteria. Articles included were reviewed using a methodological rating scale based on the STROBE cohort guidelines. All articles were subject to inter-rater assessment.

Results: Thirteen papers were initially identified for review. However, it was not possible to obtain the relevant data for two of these articles. Therefore, a total of 11 articles were subject to review and analyses. Papers were categorised into three categories for the purpose of methodological rating; Bivariate analysis, Multivariate analysis using part/partial correlations, R^2 change multivariate analysis.

Conclusion: A general consensus in the literature indicates that cognition has an influential role to play in regards to functional outcomes post inpatient rehabilitation. However, it is not possible to state how much variance this explains given the methodological differences between articles. The process of synthesising these data has highlighted a need for more formal guidelines and recommendations to be published advising authors on how best to report correlational studies, in particular multiple regression analyses.

Introduction

Stroke is a neurological event defined as the sudden onset of disturbance of cerebral function that is vascular in origin and lasts more than 24 hours without any other apparent cause.[1]It is estimated that 150,000 people per year in the UK have a stroke.[2] The consequence of stroke is widely documented[3,4,5] and it is estimated that 450,000 stroke patients at any one time in the UK are living with serious physical and cognitive impairments.[6]

It is common for post stroke patients to enter inpatient rehabilitation and it has long been reported that the time spent in initial acute rehabilitation is the period where maximum post stroke functional recovery happens.[7]The importance of such rehabilitation has been highlighted in a number of studies.[8] It has been found that when early versus delayed inpatient stroke rehabilitation was compared, early intervention was associated with better functional outcomes. Findings such as these emphasise the importance of and support the theoretical grounds for acute rehabilitation in recovery from stroke. However, it has only been in the last decade that guidelines have existed to inform professionals of what acute, inpatient rehabilitation should consist. One of the most frequently referenced guidelines is the Royal College of Physicians National Clinical Guidelines for Stroke,[9] which provide a unified and formal recommendation for the process and content of programmes within inpatient rehabilitation units.

As inpatient rehabilitation is time limited, it is important that a patient's duration of stay in such facilities is productive and that the client's potential is maximised. To achieve this, it is important to understand what facilitates and what hinders the rehabilitative process. It is estimated that cognitive impairment occurs in 12-56% of post stroke patients[10] and includes difficulties with memory, attention, perception, reasoning and speech.[4]

As cognitive impairment is a common consequence of stroke, it has been extensively explored in the literature and the impact of this on functional recovery during rehabilitation has created some debate. There are some reports that state that effective stroke rehabilitation is not influenced by cognitive factors[11] and others have found cognitive variables to have only a weak correlation with functional outcomes[12]. However, some studies argue the opposite[13] and postulate that cognition, second to baseline functional ability, is the most prominent factor determining outcome post stroke rehabilitation.[14]In rehabilitative settings, there are certain demands placed upon a person's cognitive capacity as they need to be able to attend to, process and learn new information. Therefore, it would appear logical that impairment in these areas, in particular memory and executive functioning (an umbrella term used to describe higher order cognitive abilities such as planning, organising and mental flexibility), would negatively impact on rehabilitative progress. Rabadi et al.[5] cautioned that often stroke patients who have cognitive impairment have restricted access to rehabilitative facilities suggesting that they may be under represented in research which might explain the lack of relationship with outcome in some studies.

Cognition is only one variable that has been explored in relation to outcome post stroke.[3,4,10,15,16,17]Other variables that have received attention include age,[3,18] gender,[19] and mood disorders.[20] There is agreement in the literature that patients who are in better functional condition on admission benefit more from inpatient rehabilitation.[3,21,22]However, beyond this there does not seem to be a consensus regarding other prominent factors. Ones et al.[3] reflected that the difficulty in drawing any clear conclusion can be understood in terms of studies adopting different inclusion/exclusion criteria, methodologies and measurement tools.

There are a number of reviews looking at stroke and the various factors influencing outcome.[23,24,25]However, some of these are not systematic reviews and those that are do not specifically explore the role of cognition or are over 10 years old, which will not capture recent publications. A review of relevant stroke literature exploring the role of neuropsychological deficits on functional stroke outcomes has been carried out.[26] Even though where possible, data relating to the variance explained by cognition was presented, it was not a systematic review (with no evidence of a systematic search of the literature and no methodological review allowing the reader to establish the methodological strength of the papers included). In addition to this, it has only been in the last decade that guidelines on stroke rehabilitation have been made available.[9] As such, this review sets out to systematically explore predictors of acute inpatient rehabilitation outcome in post- stroke patients with a special emphasis on the role of cognition.

Systematic Review Objectives

This review evaluated the recent literature available on inpatient stroke rehabilitation where cognition was considered as a variable influencing outcome and sets out to achieve the following objectives:

1. To examine whether cognition is related to outcome after stroke rehabilitation
2. To examine how much variance in outcome is explained by cognition compared to potential covariates.

Method

Search strategy

A search of the Cochrane database demonstrated that in the last decade there has been no systematic review in this specific area and no protocols posted. Papers in this review have been limited to the years 2000- May 2012 because a previous systematic review[25] included papers published between 1986-1999. This time scale also coincides with the emergence of stroke rehabilitation guidelines,[9] which may have influenced the content of inpatient rehabilitation. As a systematic review[23] looking at the role of visual neglect on stroke rehabilitation already existed it was decided that reviewing papers that specifically looked at this would add little to the already existing literature and have been excluded from this study. In a similar vein, a separate evidence base exists exploring aphasia after stroke and it was decided that a review of this literature goes beyond the scope of this systematic review and it is often an exclusion criteria for many of the studies identified in this review.

The following electronic bibliographic databases were searched: Ovid databases, EMBASE, PsychINFO, CINAHL, Web of Knowledge and Cochrane. The databases were searched using keywords, Mesh headings and Boolean terms such as; "stroke*", "cognition*", "rehab*". "recovery of function", and "outcomes research" (see Appendix 1.2, p84) for full search terms). Electronic database functions were also used to find similar articles and articles that cited included studies. Reference lists of relevant articles were also checked to identify further papers. Titles and abstracts of papers identified were examined to identify articles featuring stroke rehabilitation, cognition and outcome.

Inclusion and exclusion criteria

Relevant articles that were identified as featuring stroke rehabilitation, cognition and

outcome were screened against the following inclusion and exclusion criteria.

Inclusion Criteria:

- Studies that involved acute inpatient stroke rehabilitation
- Studies that were prospective in nature
- Studies where cognition was a variable explored in relation to rehab outcomes
- Studies that provided admission and discharge data

Exclusion Criteria

- Prevalence/incidence studies
- Studies that explored rehabilitative methods/strategies
- Retrospective studies
- Pharmacological studies
- Longitudinal follow up studies where rehab admission and discharge data were not provided
- Community based studies
- Studies that were not in English
- Studies that only assessed sensitivity of cognitive screening tools within a stroke population
- Lesion/imaging studies
- Studies where cognition was not included as a variable

Following this search strategy, a total of 11 papers were identified for this systematic review (See Figure 1).

INSERT FIGURE 1 HERE

Assessment of methodological quality

To rate the methodological quality of the included papers a rating checklist was devised based on the STROBE Statement checklist for cohort studies.[27] Additional items were added or removed to ensure transparent reporting of the methodology of the outcomes studies included in this review. The rating checklist had a maximum score of 54 (see Appendix 1.3, p85) and both the author and a second rater scored all papers as a means of examining the inter-rater reliability of the checklist (Appendix 1.4 p87). There was a 90% agreement between the raters. Any discrepancies that occurred throughout the scoring process were resolved through discussions.

Management of data

Whilst the studies included have in common a focus on inpatient stroke rehabilitation and cognition, there is an element of heterogeneity between the studies. To address the objectives of the study, where possible, the coefficient value and percentage of variance explained by each variable in each study has been reported in addition to the method of assessment for each variable. A summary of data regarding variables measured, preferred tools, variance and demographics is available in Table 2 (p88) whilst inclusion/exclusion criteria's across the studies are provided in Appendix 1.5 (p91).

A meta-analytical approach was considered as a means of combining relevant data. However, this was not appropriate given the heterogeneity in the management of data, the

measurement tools used and the inclusion of selected variables and outcomes. Of the papers identified for inclusion in this review, three papers presented data using beta values which was not compatible or comparable with the remaining papers that presented coefficient values. Attempts were made to contact the authors,[28,29,]but only Leung et al.[30] were able to supply the relevant data necessary for this review.

Review of findings

The systematic review of 11 correlational studies exploring the relationship between cognition and discharge functional outcome was conducted and each paper in turn was rated for methodological robustness. Five of these papers used only bivariate correlations therefore it was not possible to comment on the spread of variance between the variables influencing outcomes. Within the six papers that employ multivariate analysis, there was some variation in how the regression models were reported. Three of the articles report R^2 change allowing the reader to see the accumulated effects of the adjusted models. However, the other three articles report individual *r* values from the regression model making it possible to see the individual variance contributed to the model by each significant variable.

This variation in ways of reporting correlations and regression based analyses meant that it was not possible to directly compare findings from different approaches of analyses with each other in a systematic fashion. In an attempt to synthesise the data and review like with like, the papers were divided in to three categories for review of methodological robustness; bivariate analysis, multivariate analysis using part/partial correlations, R^2 change multivariate analysis. Reference will be made to all three categories when drawing out the methodological strengths and weaknesses in this area of research.

Results

Overall quality of papers

No paper in the review scored full marks on the quality rating scale (Appendix 1.4) indicating that within this area of literature there is scope for improvement. The highest score achieved was 47/54[30, 35] with the remaining papers obtaining a wide range of scores from 24-46. A clear distinction in scores arose between multivariate and bivariate papers as the latter group lost points in their methodology because they did not control for potential confounding variables. No paper received a score for justification of sample size, something that is important for studies to ensure appropriate power. For articles that employ multivariate analysis[15,30,34,35,36,37] this raises some questions as to whether they had enough power to detect significant findings at differing levels of effect size. A difference between higher and lower scoring articles is also attributable to the scientific rationale given for their research with some articles[31,32, 33, 37] failing to make a solid and distinctive argument. The discussions in some articles[4,31,33] are somewhat weakened by a lack of acknowledgement of the limitations to their own studies with reduced referencing as to how their findings fit within the existing literature, including areas for future research. Another area of weakness within the literature relates to the reduced transparency of some articles[3,4,31, 32, 34] in their methodology. The recruitment process for participants was not always clear and the reliability and validity of the measurement tools used within the studies was rarely reported in detail. This makes it difficult for readers to be certain whether the tools utilised by the various authors' measure what they intend to.

Bivariate analysis

All of these papers achieved a low score on the methodological rating scale (see Table 1) as there was no consideration for confounding variables and no attempt to control for shared variance between variables. At a bivariate level, two articles[3,4] found that baseline cognition was significantly correlated with discharge functional ability but it was not possible to speculate how much overlap there was between the variables in relation to the variance they each explained. The third paper[31] explored only cognition as a variable as measured by the Cognitive Functional Independence Measure and found it to have a non-significant correlation with their main dependent variable, the Chedoke Assessment. Cognition did correlate with discharge motor FIM, however as discussed below this may be an expected outcome given the high correlation between these two subscales of the FIM.

Ozdemir et al.[32] and Zwecker et al.[33] are slightly harder to categorise as both papers use regression models however, they only report *r* values for bivariate analysis and only include cognition as a variable. Ozdemir et al.'s regression model did not add any further information to what was already established by their bivariate analysis and no additional co-variates were included. Their score on the rating scale reflects this but also appreciates their attempt to carry out a regression model and their transparency in their methodology. Zwecker et al.[33] assess the ability of three different cognitive measures to predict functional outcome against some additional covariates but they make no explicit reference to their regression model in the results section and again only report bivariate coefficients. It is for this reason, among others, that this paper scored the lowest on the methodological rating scale.

Multivariate analysis using part/partial correlations

A limitation to these papers is the failure of the authors to state whether the individual *r* values they report in relation to their multiple regression models are derived from the part (i.e semi-partial) or partial correlations. This has an impact in regard to understanding the strength of the relationship between variables and outcomes as the coefficient value may reflect either only unique variance explained by the variable or both shared and unique variance, directly impacting the size of the correlation. Attempts were made to contact authors to establish what correlations were used but this was unsuccessful and subsequently, the data provided in these articles may have to be interpreted with some caution. This weakens the methodological robustness of these articles and may explain why the variance explained by cognition between papers varies (see Table 2). Although Skidmore et al.[15]did not score the highest in methodological rating, this paper reports the highest level of variance for a specific component of cognition compared to other articles, even when baseline ability is controlled for. They report a combined R^2 of 54% for executive functions and baseline ability, and reported individual bivariate correlations that indicate an equal strength of relationship (r= -0.55, 0.56 respectively).

Leung et al.[30] jointly scored the highest on the methodological rating scale. This article only reported individual beta values within their article but through personal correspondence with the author the coefficients from their regression models were obtained (see Table 2). Reporting their part correlations, they found that whilst a significant independent variable, cognition as measured by digit span backwards explained only small positive correlation contributing 1.3% to the total variance of their model. As with much of the literature in this area, baseline abilities were found to be the strongest predictor of discharge total FIM scores

and discharge Motor FIM scores.[30] Fang et al.[34] scored the lowest in this category on the methodological rating(see Table 1). They found that cognition as measured by the MMSE was an independent predictor of functional outcome as measured by an array of outcome measures (see Table 2).

INSERT TABLE 1 HERE

R^2 change multivariate analysis

Both Lin et al.[35] and Denti et al.[36] score highly on the rating scale (see Table 1) as they attempt to control for confounding variables, are transparent in their methodology, and tie their findings in with current literature. They recognise the role of cognition and found this variable to be an independent significant predictor of outcome. Despite Denti et al.[36]also using the Montebello Rehabilitation Factor Score (MRFS) to control for ceiling effects on the FIM, both papers demonstrate that whilst cognition plays a role, it seems that this may be small or non significant when discharge FIM total scores are the dependent variable. Most of the variance in their model appears to be explained primarily from baseline ability and the change in the variance explained by their models only increases slightly when cognition is included (see Table 2). However, the nature of reporting the R^2 change means that it is not possible to see how much shared variance there may be between variables. Although Denti et al.[36]take their data a step further and explore domain specific components of the FIM and the MRFS, Lin et al.[35] do not meaning the comparison between the two papers ends there. By looking at discharge FIM domain scores and the MRFS scores it can be seen that cognition appears to play a more prominent role in explaining outcomes[36] (see Table 2). There is an article that uses the R^2 change model that scores similarly on the methodological rating scale[37] and that found when admission variables were correlated with discharge motor

FIM, cognition was *not* an independent predictor and did not contribute to their overall R^2 value. This contradicts the findings of Denti et al.[36] and Lin et al.[35] findings and makes it difficult to draw conclusions around the role of cognition when regression data is reported as accumulative R^2 change.

The variance explained by cognition is similar in a number of articles[30,35,36] and even though the way the regression models have been reported varies between these articles, they score the highest on the methodological rating suggesting that these articles carry the most weight due to robust methodology, clear reporting of results and sound scientific rationale.

INSERT TABLE 2

Discussion

The majority of papers found that cognition was an independent predictor of functional outcome regardless of which statistical analysis was applied. However, the articles that employ multivariate analysis should be viewed as carrying more weight. As indicated in, the variance amongst these studies varied significantly (see Table 2). As noted in the literature[26] the studies that found cognition to be a significant independent predictor of outcomes can be divided into those that measure general cognition (i.e. multiple areas of brain functioning) and others that measure a specific component of cognition (e.g memory, executive functioning).

Two of the articles, [30,15] one of which was rated the highest, look at specific components of cognition and both report high levels of variance explained by these factors (see Table 2). These papers are also similar in how they handle the regression data. Of the three cognitive domains assessed by Skidmore et al[15] (attention, executive functioning and memory), a

regression model found only executive functioning to be predictive of functional outcomes. There is a more common trend in the papers which show that general cognition also correlates with functional outcome in a more consistent fashion although often at a smaller level.[34,35,36]

There were two studies that found no significant relationship to exist between cognition and functional outcome. Nas et al.[31,] a bivariate study, scored low on the methodological rating scale. However, their findings were supported by Fong et al.[37], a multivariate study, that obtained a higher score. Fong et al.[37] failed to find a significant relationship between baseline measures of cognition and discharge motor levels but they did find that cognition became more relevant as rehabilitation progressed and cognition and functional ability did correlate at later time points.

The process of synthesising the data from the literature was a difficult process because the management of the data varied greatly making direct comparisons problematic. As such, it is difficult to present a clear answer to the question regarding the amount of variance that cognition explains in regards to functional outcomes. Aside from the difference in the statistics applied and the way that regression models are reported, there are other factors that make the papers heterogeneous further complicating the synthesis of the data.

Methodological Limitations

There are a number of additional issues that should be considered in turn when trying to tease out the reasoning in regards to the range of variance between papers in this review. Aside from the regression models, this may be further understood by looking at how each paper

measured cognition, classified functional outcome and exploration of the inclusion criteria and sample size.

Measurement of cognition

Measuring specific components of cognition allows for the researcher to explore in more detail the key cognitive abilities necessary for successful rehabilitation. This is reflected well in the literature[15] and it is feasible that dysexecutive symptoms would negatively impact on functional outcomes as being able to initiate and sustain levels of engagement in rehabilitation activities is essential. Executive functions are neuro-anatomically linked with attention and aspects of memory so there may be an overlap between these variables. Skidmore et al.[15] found memory to be a non-significant predictor but it may be that there are more compensatory tactics that can be employed to support memory and as such reduce the impact that memory impairments have on overall rehabilitation outcomes. They also found executive functions to explain a larger portion of variance and this was equalled only by baseline disability levels (see Table 2), a finding replicated by a number of other studies.[35]

Executive functioning may have been pinpointed as an element of cognition central to functional outcome during inpatient rehabilitation but only one paper[15]specifically assesses this cognitive domain. Most of the studies in this review utilise the MMSE and cognitive FIM which place little or no emphasis on executive functioning and it may be that subsequent studies have neglected to consider this potentially important aspect of cognition.

There are a small number additional papers in the review that looked at specific components of cognition[30,32] however as can be seen in Table 2, the variance explained in these studies in relation to cognition was smaller.

Even though Ozdemir et al.[32] used the MMSE, they entered each sub-score into a correlation matrix to test out certain components of cognition. Different aspects of cognition independently predicted functional outcome depending on what aspect of functional outcome was being assessed. Only the MMSE total score significantly predicted discharge motor FIM scores and only baseline orientation MMSE scores predicted functional ambulation improvement. However, the coefficient of both variables was small (see Table 2) highlighting that other important variables need to be considered in this context. Whilst most of the MMSE subsections individually did not explain functional gain the total MMSE score did suggesting that as a whole, all cognitive abilities assessed by the MMSE subsections were important for rehabilitation. For ambulation, it seems that orientation alone is important as an individual needs to have self-awareness to engage in their environment efficiently, a finding that adds to the already existing evidence base[15].

In the remainder of the papers supporting the role of cognition, a more general measure of cognition is used and on some occasions both the MMSE and the Cognitive FIM are jointly utilised. By using a measure of more general cognition, the variance explained takes on a wider range of 2%-59%. This may be partly explained by how comprehensive the tool used for assessing cognition was. For example, Lin et al.[35] showed only a small accumulative effect of cognition in their model, however, their measure of cognition was the Canadian Neurological Status which is limited, assessing only speech, orientation and consciousness. The studies reporting the largest variance are those where the Cognitive FIM was used as the main measure of cognition. There is evidence to indicate that Cognitive FIM and MMSE correlate well together (r=0.66),[33] suggesting that they are both reliable and valid measures

of cognition. Yet, when the cognitive FIM and MMSE compete against each other,[33,36] the cognitive FIM consistently explains more variance (see Table 2).

This must be interpreted with some caution as there is a question over the extent to which these findings simply reflect the correlation between a subtest and its parent test. Given the high internal consistency of the FIM,[38]it would be predictable and expected that the cognitive FIM would have a stronger correlation with its parent test. With these points in mind it may be questioned that the 59% variance explained Denti et al.[36] in relation to functional outcome is affected this way. This may be further supported when the dependent variable changes to the MRFS, an efficacy indicator reflecting functional *gain* as the dependent variable. In this instance, the variance explained by cognitive FIM drops to 28 % supporting the argument that the degree to which cognition is an independent predictor of outcome is inflated when the FIM and its subsets of the FIM are used as both the independent and dependent variables.

The cognitive FIM requires the clinician to have a degree of familiarity with the patient and it is a more subjective measure which can result in subsequent errors of over/under estimating a person's cognitive ability and biases. The MMSE attempts to strip away strategies or techniques employed by an individual to mask cognitive impairment and there may be an argument that studies which employ the MMSE obtain a clearer snapshot of an individual's cognitive capacity. Nevertheless, it continues to remain that even at 28%, cognition is likely to be an influencing factor during their rehabilitation.[36]

Support for the MMSE is also reported by Fang et al.[34], although this paper scored the lowest rating in its category. They entered only admission and discharge data into their multivariate model and used the Clinical Neurological Deficit-Scale (CNDS) and Fugl Meyer Assessment

(FMA), both measures of stroke severity and motor function, and the Modified Barthel Index (MBI) to measure activities of daily living. The MMSE was the sole measure of cognition and they found that only severe cognitive impairment as determined by an MMSE score of <17, was significantly correlated with descending CNDS scores and change in upper limb FMA scores both representing 10.1 and 12.6% respectively. General cognition(MMSE > 17)correlated only to change in MBI explaining 15.9% of the variance in the model. It is unclear whether the *r* values they report are derived from the part or partial coefficient values however, compared to the accumulative R^2 articles. This way of reporting regression modelling means that insight can be gained in to the role of each variable. In this instance the Barthel Index was used to measure functional outcomes and this is the only dependent variable to which cognition does not correlate. What Fang et al.[34] report is a correlation between cognition and neurological and physical ability measures. This supports the hypothesis postulated by Hajek et al.[12] that performance on cognitive tests alone cannot predict functional outcomes because measures of functional ability under represent the role of cognition.

Overall, there seems to be a strong argument that cognition is an important factor that may influence outcomes, although the extent to which varies. Even though only beta coefficients were reported by Heruti et al.[28]andMutai et al.[29],they present additional findings strongly supportive of this consensus. Heruti et al.[28]compared the most cognitively intact and impaired patients with each other and established that those in the lowest quartile displayed the least amount of gain in their rehabilitation as well as the lowest FIM admission and discharge scores. Logistic regression analysis also found that MMSE scores were strongly associated with successful rehabilitation. In particular, they found successful rehabilitation as

determined by a 0.5 increase in relative functional gain was increased by 2 fold with every 5 unit increase in MMSE scores.

Measurement of functional outcome

The most commonly used functional ability tool is the Functional Independence Measure (FIM).[39]This is an 18-item scale made up of two components; motor functions (13 items) and cognitive functions (5 items).

A portion of the articles in this review chose to examine correlations between predictors of outcome with the discharge FIM motor score, FIM efficacy (discharge FIM-admission FIM), efficiency (efficacy/length of stay)or the MRFS, a method of working out relative gain. The latter is often viewed as a methodological strength as it provides a way of controlling for baseline disability and also the limited gain of patients who have higher baseline FIM scores compared to those who have lower baseline scores. When the total FIM at discharge was used as the main dependent variable, the overall variance explained by cognition was either relatively small or non-significant, regardless of the way the regression model was handled.[30,35,36] This may support the aforementioned argument that the total FIM scores do not control for ceiling effects of the FIM. It seems that more variance is explained when discharge motor FIM or the MRFS scores are utilised as the main dependent variable. Zwecker et al.[33]demonstrate that cognition was a particular predictor of MRFS efficacy, which reflects FIM gain during rehabilitation. Even though particular coefficient values were unattainable for Heruti et al.[28] they also explored relative gains and found that cognition was a stronger predictor for outcome when correlated to MRFS scores. It could be said that studies who do not establish the MRFS fail to account for the extreme variation often seen in baseline functional status between patients making it difficult to detect meaning change.

Skidmore et al.[15] is the only article to deviate from this traditional method of measuring functional outcome. They employed the FIM to measure baseline ability but choose to explore patients overall level of participation with the justification that less participation equates to poorer functional outcomes. It is in this context that executive functioning and baseline ability together explained equal proportions of variance that accounted for over 50% of the variance in outcome measures.

In summary, it can be said that where studies have used the MRFS as a dependent variable, compared to the total FIM discharge score, cognition explains more of the variance.

Additional Variables

The consideration of covariates is another factor creating a degree of heterogeneity amongst the literature and makes direct comparisons of findings difficult. There is a consensus in the literature that baseline functional ability is influential in predicting discharge functional ability however this was not considered by every author. Studies that do measure this variable[15,30,3,36,37]show that, when entered in to a regression model, this variable consistently predicts the most variance ranging from 30-74%. Where measured, baseline ability accounts for more variance in all studies when compared to cognition suggesting that functional ability at admission is the best predictor of overall functional gain and ability at discharge. However, it appears that of the 74% of variance explained by admission total FIM scores in the Denti et al.[36] paper, cognitive FIM domain scores provide the largest contribution (59%).

It could be construed as a limitation that a number of studies did not measure or control for baseline ability. A number of studies in the review[32,33]considered only cognition as a variable

and whilst others[34,35,36] measure a larger number of potential predictors, there was no clear measure of overall baseline functional ability. Where baseline ability was measured, it is often done so through the use of the FIM that contains a cognitive subscale. As such, baseline ability may not be a true independent variable as it is likely to encompass additional variables that are assessed in their own right e.g. cognition.

Given that cognition is a factor affected by age it is important to consider the impact of the wide age range seen is the literature (53.8yrs-80.8yrs, see Table 2). On the whole, age was found to make a relatively small contribution to functional outcomes at discharge. Only two papers[35,36] found age to be significant, albeit at a low level with this variable adding little to the variance explained by their models. Denti et al.[36] also found age to correlate with total FIM discharge but not efficacy MRFS scores suggesting that elderly stroke patients are still able to gain from rehabilitation. This is supported elsewhere[3] with findings indicating that whilst elderly participants tended to have a lower baseline functional ability, there was no significant differences in regards to functional gain when those above and below 65 years were compared. Others remain cautious postulating that cognition may still be a modifying variable as elderly patients who are more cognitively intact do tend to progress better in their rehabilitation.[28] Researchers may find it challenging to tease out the specific impact of age given that an increase in age is often associated with other co morbid difficulties e.g. reduced cognitive capacity.

A general consensus from this review is that gender, type of stroke, educational status, admission from onset and length of stay are not significant (see Table 2). Even though one article[34] found variables such as aphasia, double incontinence, muscular tension and site of lesion to be significant predictors for improvement of specific components of functional

ability this was not supported by other studies that gathered data on side of lesions (see Table 2).

Inclusion Criteria

The inclusion and exclusion criteria applied to journal articles can heavily influence the outcome of studies and the nature of these criteria varies greatly between papers in this review.

It is noticeable that some papers only include first time stroke patients where others do not stipulate this to be an inclusion criteria (Appendix 1.5). Review of the literature suggests that this does not overly assist in explaining the variance in data but there is a possibility that cognition may have a larger role to play where previous strokes potentially result in accumulative cognitive impairment.

Only Skidmore et al.[15] included a measure of mood in their analysis, and whilst it did not survive their regression model, depression was strongly correlated with executive functioning. An overlap may exist between these two variables as affect can negatively impact performance on cognitive measures as well as affecting motivation to engage in rehabilitation.[15]As this variable was not included in any other study, no conclusions can be drawn regarding this. It has been well documented earlier in this review that one paper[15] reported a strong finding for executive functioning, a component of cognition. However one limitation to this paper is that the prerequisite for inclusion in their study was for a cognitive impairment in either attention, memory or executive function to be present. This is the only study to have such an inclusion criteria and as such, their findings may not be generalizable to the more general stroke population where cognitive impairment is not always a definite

consequence. This is further supported by other authors[33,36] who respectively report cognitive impairment in only 41 % and 51% of their samples and as such there is a question around whether Skidmore et al.[15] results are somewhat inflated due to this.

A common exclusion criteria within the literature are communication disorders. A general justification for this exclusion is that for rehabilitation to be most effective the individual must be able to comprehend instructions by therapy staff. If individuals are being asked to engage in activities that lack meaning then there is a risk that this will lead to reduced motivation and participation which in turn will negatively impact on functional outcomes. It may then be argued that discharge functional outcome measures would not reflect the true ability of the individual. It could also be argued that language disorders may make it difficult for such patients to complete the MMSE and for staff member to accurately complete the cognitive component of the FIM. Although not rated in this review, Heruti et al.[28] did not exclude aphasia from their review and noted that as the FIM and the MMSE have been validated and found appropriate for use in stroke patients,[12,40] including those with left hemispheric infarcts,[28] that exclusion of such individuals is not necessary. Certainly, looking at the variance explained by cognition in papers where such individuals were included and where they were excluded, no clear pattern can be seen in regards to what impact this has on the data and outcomes.

A prerequisite in many articles was for the patient to have 'rehabilitation potential'. Much of the research in this area appears to be undertaken in countries where the health care is often dictated by medical insurance. For someone to be accepted for rehabilitation, the insurance companies would want evidence that the individual will benefit from this. A limitation of available literature on stroke rehabilitation is that often the most impaired individuals are not

represented. It may also explain why FIM efficacy and MRFS scores are not always employed as there may not be as much variation in baseline FIM scores to start with so the need to control for this is not as prominent.

Sample Size

The sample size of the studies included in this review varies greatly from 25-359 (see Table 2). This raises the possibility that some studies were underpowered and cognition may have been more likely to have displayed a larger significant association with outcome had more participants been recruited.

Conclusion

The general theme in the literature is that cognition is an important variable to consider when trying to predict functional outcomes in inpatient stroke rehabilitation. In many instances cognition can explain a significant amount of variance seen in outcomes second only to baseline functional ability. Even though this finding is consistent within the literature, the heterogeneity in methodology and wide range of variance explained by cognition makes it difficult for conclusive decisions to be formed in relation to the strength of this relationship. Where this variance exists it seems that use of the MRFS is a more robust method of assessment and is a strength amongst this literature. From a clinical perspective, the current evidence base from which services can draw upon can be confusing given the wide range of cognitive and functional outcome measuring tools used. There is no clear consensus in the literature on whether specific cognitive abilities such as executive functioning or more general measures of multiple cognitive domains are more predictive of functional outcome. If patients who are cognitively impaired are not appropriately supported during their rehabilitation then there is some evidence to suggest that this may adversely affect their

recovery and over all outcome. This has implications for routine clinical practice within rehabilitation units as there is a need for appropriate resources to be accessible for both patients and clinicians to ensure that rehabilitation potential within these patients is maximised.

The need for participants in the reviewed literature to have 'rehabilitation potential' excludes the most impaired patients and the strength of relationship between cognition and functional outcome may be weakened when participants who are not as able or less likely to make rehab gains are included in analysis. However, it is also important to consider the idea that perhaps the ideal situation is that baseline cognitive functions do not affect functional outcome, or indeed gain, as if appropriate management of cognitive function is in place then ideally, the patient should benefit from rehabilitation despite the presence of cognitive impairment. More attention to how levels of baseline ability can be controlled must be considered in countries where medical care is not influenced by insurance. The limited attention to affective variables is a weakness and given the influence affect can have on cognitive performance and motivation it seems that this is an area that would benefit from further research.

At a more fundamental level, there appears to be no clear, distinct guidelines and consensus on how papers should handle and report multiple regression data. This is perhaps the main methodological limitation to this area of literature. It makes it difficult to answer the question set out in this review and draw parallels between papers in a clear and confident manner. Reviewers are unable to compare like with like and whilst it is possible to synthesise the overall methodological limitations to this area of literature, it is difficult to draw out strengths and make direct comparisons to achieve a strong conclusion in regards to the role of cognition in stroke rehabilitation.

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Figure 1- Search strategy

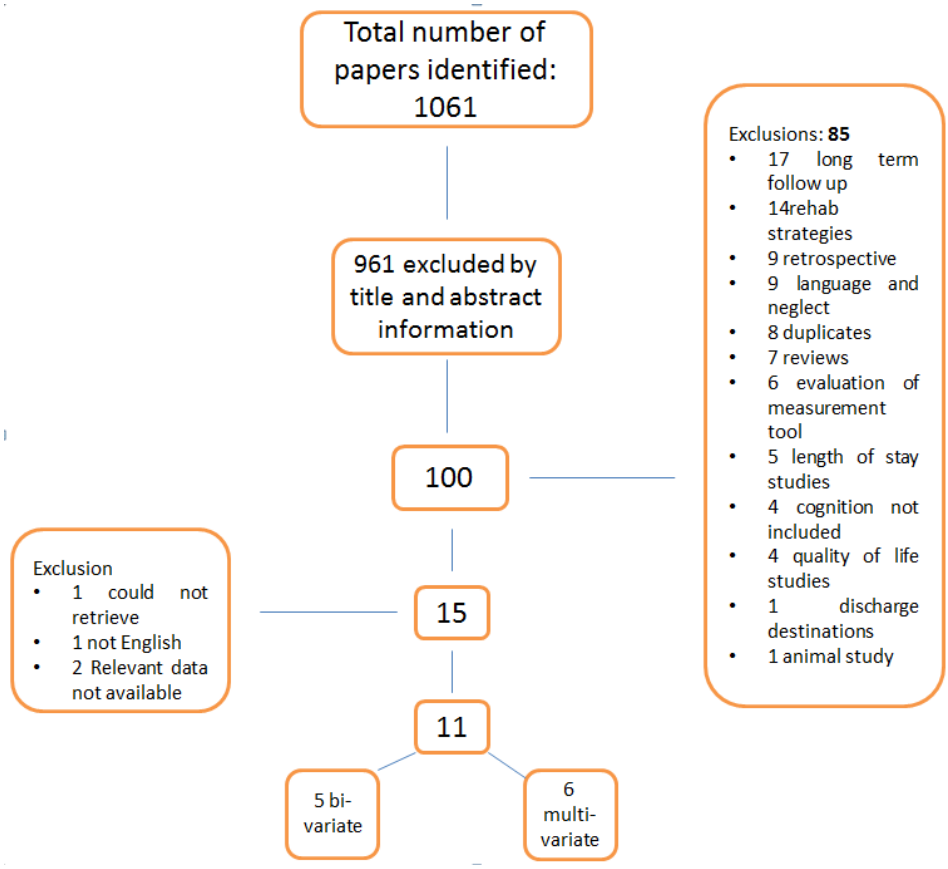

Table 1- Methodological Rating Scale Scores

	Author	**Rating Scale**
Bivariate Papers		
	Ones et al.[3]	32/54
	Ozdemir et al.[32]	31/54
	Man et al.[4]	26/54
	Zwecker et al.[33]	25/54
	Nas et al.[31]	24/54
Multivariate Analysis : part/partial correlations		
	Leung et al.[30]	47/54
	Skidmore et al.[15]	39/54
	Fang et al.[34]	38/54
Multivariate Analysis : R^2 change		
	Lin et al.[35]	47/54
	Denti et al.[36]	46/54
	Fong et al.[37]	40/54

Table 2– Summary of demographics, variables, measurement tools and coefficient values.

	Author	N	Mean age	Methodological rating Scale	Dependent variables	Independent variables	Measure	r value	P value	Variance
Multivariate analysis – part and partial										
	Leung et al 2010	85	53.8yrs	47/54	Discharge total FIM	Cognition	Digit Span Forwards Digit Span Backwards CAVLT Cognition FIM	-0.114	0.48	1.3%
						Baseline ability Age	FIM	-0.661 -0.183	0.001 0.002	43.7% 3.3%
	Skidmore et al 2010*	44	73.6yrs	39/54	PRPS score	Executive Function Baseline Ability	EXIT FIM	-0.55 0.56	0.005 0.02	54% combined
	Fang et al 2003*	156	63.65 yrs	38/54	CNDS change	Aphasia		-0.329	0.05	10.8%
					Decrease CNDS score	Serious cognitive function	MMSE <17	0.318	0.05	10.1%
					Change in FMA upper limbs	Serious cognitive function	MMSE <17	-0.355	0.05	12.6%
					Change in FMA lower limbs	Incontinence		-0.467	0.01	21.8%
					Increase FMA score upper limbs	Sensory impairment		-0.252 -0.515	0.01 0.01	6.3% 26.5%
					Change in MBI	Incontinence		-0.435	0.01	18.9%
						Site of lesion Incontinence Baseline cognition	 MMSE	-0.482 0.399	0.01 0.01	23.20% 15.9%
Multivariate Analysis- Accumulative R^2										

	Lin et al 2003*	105	63.2yrs	47/54	Discharge total FIM	Baseline ability Cognition Age	FIM CNS		0.001 0.012 0.007	61% 2% 3%
	Denti et al 2008	359	80.8 yrs	46/54	Discharge FIM total	Admission ability Age Trunk control LOS	FIM Trunk control test	0.86 0.11	0.000 0.001 0.003 0.01	74 % 1.3% 0.4% 0.6%
					Discharge FIM domain	Cognition Motor ability Trunk control Age LOS	Cognitive FIM Motor FIM Trunk control test	0.76	0.000 0.000 0.000 0.002 0.03	59% 17.9% 0.11% 0.1% 0.03%
					MRFS total	Admission ability Age Daily activities	FIM Rankin Scale	0.54	0.000 0.000 0.000	30.2% 3.6% 1.2%
					MRFS domain	Cognition Trunk control Age	Cognitive FIM Trunk control test		0.000 0.000 0.001	28.1% 6.1% 0.26%
	Fong et al 2001	25	63.2yrs	40/54	Discharge motor FIM	Motor ability Cognition Baseline ability	FMA NCSE FIM	NS NS 0.686	 0.000	 47%
Bivariate Analysis										
	Ones et al 2009	88	63.14yrs	32/54	Discharge FIM total	Age Motor upper limbs Motor lower limbs Motor hands Spasticity Cognition	 BMES BMES BMES Ashworth Scale MMSE	0.49 0.50 0.41 0.12 0.35 0.66	0.001 0.001 0.01 NS 0.01 0.000	24% 25% 16% 12% 43%
					Discharge FIM motor	Baseline ability Age Motor upper limbs Motor lower limds Motor hands Spasticity Cognition	Cognitive FIM FIM BMES BMES BMES Ashworth Scale MMSE Cognitive FIM	0.54 0.65 0.48 0.62 0.55 0.30 0.28 0.69 0.51 0.69	0.001 0.000	29% 42%

						Baseline Ability	FIM	0.60		
	Ozdemir et al 2001*	43	60.49YRS	31/54	APECS	Orientation	MMSE	0.31	0.03	9%
					Discharge Motor FIM	Cognition total	MMSE	031	0.04	9%
	Man et al 2006	148	70.38yrs	26/54	Discharge FIM self care	Cognition	NCSE Factor 1	0.310	0.01	9.6%
						Cognition	NCSE Factor 2	0.256	0.01	6.6%
						Age		-0.142	0.05	2%
						Years of education		Ns		
						length of stay		-0.179	0.05	
					Discharge FIM mobility	Cognition	NCSE Factor 1	0.146	0.05	2%
						Cognition	NCSE Factor 2	0.177	0.05	3%
						Age		Ns		
						Years of education		Ns		
						length of stay		Ns		
	Zwecker et al 2002	148	70.38yrs	26/54	Discharge FIM self care	Cognition	NCSE Factor 1	0.310	0.01	9.6%
						Cognition	NCSE Factor 2	0.256	0.01	6.6%
						Age		-0.142	0.05	2%
						Years of education		Ns		
						length of stay		-0.179	0.05	
					Discharge FIM mobility	Cognition	NCSE Factor 1	0.146	0.05	2%
						Cognition	NCSE Factor 2	0.177	0.05	3%
						Age		Ns		
						Years of education		Ns		
						length of stay		Ns		
	Nas et al 2004	40	57.1yrs	24/54		Cognition	Cognitive FIM	Ns		
					Chedoke Assessment	Motor ability	Motor FIM	0.733	0.001	54%

Abbrv(FIM= functional independence measure, MRFS= Montebello Rehabilitation Factor Score, CNDS=Clinical Neurological Deficits Scale, FMA- Fugl-Meyer Assessment, MBI= Modified Barthel Index, MSME= Mini Mental State Examination, NCSE- Neuro-behavioural Cognitive Status Examination, CNS=Canadian Neurological Status, APCES= Adapted Patient Evaluation and Conference System , PRPS= Pittsburgh Rehabilitation and Participation Scale , EXIT= Executive Interview, LOTCA= Lowenstien Occupational therapy Cognitive Assessment , BMES= Brunnstrom Motor Evaluation Scale

Chapter 2: Major Research Project

An investigation in to the use of Addenbrooke's Cognitive Examination – revised (ACE-R) as a means of predicting rehabilitation outcomes in adults aged 16 or over

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Lay Summary

Patients who have a physical disability often spend a period of time in an inpatient rehabilitation unit where therapy staff assist them in getting better. It is common for patients with such difficulties to also have problems with cognition (e.g language, memory, concentration). It is important for therapy staff to have a way of identifying patients with these problems as cognitive difficulties can stop patients from progressing in their rehabilitation if support is not given to them. This study explores how useful a cognitive screening tool called the ACE-R is in allowing staff to predict how well the person will do in their rehabilitation. It was also of interest to see whether patient scores on the ACE-R identified those who required extra help from staff during their rehabilitation. A total of 65 adult patients filled out the ACE-R and some extra clinical information was also gathered. Patient ACE-R scores were compared to their individual Functional Independence Measure (FIM) scores, a way of measuring improvement during rehabilitation. The FIM was completed by staff at the point of admission and discharge from the unit. There was no relationship between ACE-R and FIM scores suggesting that the ACE-R is not helpful in predicting rehabilitation outcomes. However, patients who had the lowest score on the ACE-R did require extra help from therapy staff and men needed more help than women. These findings are helpful for rehabilitation units to ensure that they are able to offer the right support to patients so their time in rehab is maximised.

Abstract

Objectives: To investigate (1) the use of the ACE-R in predicting functional gain during inpatient rehabilitation, and (2) whether ACE-R scores identify patients who will require additional therapy support during their rehabilitation.

Design: Prospective cohort study.

Setting: UK inpatient physically disabled rehabilitation unit.

Participants: Of the 100 adult participants approached, 65 had baseline assessments. Complete data sets were available for 60 (92.3%) participants and included for analysis. Mean age was 49.847 yrs (SD=12.01.

Main Outcome measures: Functional gain during rehabilitation was measured using the Functional Independence Measure (FIM). To control for baseline ability, the FIM change (FIM Discharge – FIM admission) was used as the main outcome measure.

Results: There were no significant correlations between ACE-R total (rho=.104, P=0.43), Memory (rho=.02, p=0.89) or Fluency (rho=.15, p=0.25) scores and FIM change. There were no significant correlations between FIM change and MMSE, mood, age, medical co-morbidities, number of medications, medication type, gender, continence and catheterisation, or social deprivation. There was a significant difference in the ACE-R Total ($p<0.014$), Memory (p=0.039) and Fluency (p=0.012) scores between those who did and did not require additional therapy support. A significant difference was also found between men and women in their ACE-R scores and need for additional support. Only ACE-R fluency and gender survived Logistic Regression Analysis.

Conclusion: ACE-R scores were not predictive of FIM change scores. The tool appeared more sensitive in identifying patients who required additional support with ACE-R fluency and gender appearing to be independent predictors. The study may have been underpowered to detect significant associations.

Introduction

Inpatient rehabilitation has a large role to play in determining long-term functional outcomes and it accounts for 60-75% of overall long-term functional gain after a significant medical event.[1] However, outcomes after rehabilitation nevertheless vary and it is therefore important to understand what factors impact on outcomes and the extent to which patients benefit from rehabilitation. This is particularly important as some variables may be open to intervention.

In some neurological conditions such as stroke, research suggests that medical co-morbidities[2], demographics[3,4] and affect[5] all predict functional outcomes. Another important factor that has received attention in this field is cognition. In rehabilitation settings, there are demands placed upon a person's cognitive capacity with the need to attend to, process and learn new information. If patients have attention difficulties and subsequently struggle to concentrate in the busy setting of a rehab unit or have memory problems where they are unable to learn new techniques, then it would be reasonable to assume that they may face more difficulties in achieving their rehabilitation goals compared to those without cognitive impairment. There are studies supporting the idea that cognitive impairment is a valuable predictor for rehabilitative outcomes. Studies looking at prosthetics use and frequency of power wheel chair use reported negative correlations between cognitive impairment and functional outcomes.[6,7,8] Many of these studies report that cognitive impairment, specifically memory, account for a large portion of variance in rehab outcomes. O'Neill and Evans[9] found that prosthesis use at 6 months follow up was predicted by verbal fluency and mobility by memory. This adds to the evidence from other studies[10] which have found that sustained attention deficits, which is a frontal lobe function, two months post stroke predicted motor recovery at a two year follow up. However, there may be some inconsistency in findings

relating to this as elsewhere, [11]as only an indirect relationship between attention and function has been found.

A full, comprehensive neuropsychological assessment is one method by which a person's cognitive ability can be assessed. Such an assessment highlights in detail an individual's cognitive strengths and weaknesses and it allows for a more accurate inference to be made about the severity of cognitive impairment.[12]Whilst it is acknowledged that this method allows for a more thorough and reliable measure of ability, there are various factors which would make this impractical. Batteries of assessment are often lengthy and taxing. Furthermore, many services have no access to specialist staff for a full assessment making it important to have some method of briefly and quickly screening for cognitive deficits.[13] Access to cognitive screening tools may allow staff to identify patients who require additional needs, or trigger a referral to another professional. There is still some debate about the suitability of screening tools as often their use has not been validated for the clinical population for which they are used.[14] However, some literature validating the use of certain screening tools in a population of younger clients with neurological conditions has been positive.[15-17] More importantly, there is evidence in older adult populations suggesting that cognitive screening tools (e.g. MMSE) are a reliable method of predicting functional outcomes in post stroke and hip fracture rehabilitation settings.[4,18,19]

Within dementia research the use of the ACE-R as a brief cognitive screening tool is widely acknowledged and its appropriateness of use has been recognised in Government Guidelines[20, 21]. The ACE-R[22] was developed following on from the already existing ACE [23] and it incorporates the Mini Mental Sate Examination (MMSE)[24] allowing for the assessment

of the following cognitive domains; attention and orientation, verbal fluency, language, visuospatial and memory.

Within dementia literature, the ACE-R has been found to be sensitive and specific in identifying those with and without cognitive impairment.[22,25,26] Despite this, studies examining the use of the ACE-R in non-dementia client groups are scarce. There is one study to date that has examined the sensitivity of the ACE-R in post acute brain injury, with encouraging results.[13] However, there is no published research on the use of the ACE-R in other neurological conditions that affect younger adults such as multiple sclerosis and stroke Therefore, the present study: examined the predictive power of the ACE-R in relation to rehabilitation outcomes in adults aged 16 or over with neurological conditions in an in-patient physical disability rehabilitation unit. The following hypotheses were tested:

1) Patients with lower ACE-R scores on admission will show less change on the Functional Independence Measure between admission and discharge, compared with patients who have higher ACE-R scores. More specifically, lower memory and verbal fluency sub scores will predict poorer rehabilitative outcomes.

2) Patients who were reported by staff to require additional input to achieve rehabilitation goals will have lower ACE-R total, verbal fluency and memory scores.

Methods

This was a prospective correlational study between cognition as measured by the ACE-R, other key baseline independent variables and a primary outcome measure, the Functional Independence Measure (FIM) change and discharge scores. The West of Scotland Research and Ethics Committee gave ethical approval (Appendix 2.1p92) and written informed consent

was obtained from all participants. A witness signed on behalf of participants who were only able to give informed verbal consent. All participants were able to withdraw their consent at any stage of study.

Participants

Participants were all consecutively admitted patients to the Physically Disabled Rehabilitation Unit at the Southern General Hospital in Glasgow and recruitment was conducted between September 2011 – May 2012. All patients were deemed suitable to participate unless they had a severe language disorder, current substance abuse, a lack of capacity to consent to research, where there was evidence of a learning disability or they were under the age of 16 years.

Assessment of Variables

Functional Outcome

Functional status, the primary outcome variable, was measured using the Functional Independence Measure (FIM),[27]upon admission and discharge. The FIM was the routine outcome measure used within the rehabilitation unit. The FIM is an 18 item instrument that measures mobility, self care and social interaction. Each item is rated on a scale that has 7 levels with 1 point indicating total dependence to 7 indicating total independence. The FIM has good inter reliability (r=0.92),[28]internal consistency (0.88-0.91)[29] and concurrent validity (0.74-0.92).[29] The FIM change score was calculated (FIM Discharge minus FIM Admission) for each participant, making this the main dependent variable for the study. As there was likely to be a wide variation in FIM scores, it was felt that basing functional outcome on FIM change allowed for baseline levels of disability to be controlled for and

ensure that rehabilitation gain was emphasised. This method of measuring change is supported by Linacre et al.[30] who established that comparison of admission and discharge scores indicated that the instrument measure the same variables at both time points so comparison of the two scores is valid.

Cognition

The Addenbrooke's Cognitive Examination – Revised (ACE-R)[22] was used to assess cognition and was administered with all participants upon admission. The ACE-R is a well established brief cognitive screening tool that is widely used in clinical settings, in particular with older adults. It takes approximately 20 minutes to complete and the maximum total score of 100 is made up of 5 subsections with 18 points available for attention and orientation, 26 for memory, 14 for verbal fluency, 26 for language and 16 for visuo-spatial skills. There is no normed data for its use in younger adults and subsequently there are no available cut off scores to indicate cognitive impairment in this age group. Mioshi et al. [22] provide two cut off scores of 88 (possibility of cognitive impairment) and 82 (cognitive impairment) based on three age ranges of 50-59yrs, 60-69yrs and 70-75 yrs. This was derived from sensitivity and specificity data. Gaber[13] has set a precedent of applying these cut offs to a younger brain injured population (mean age 37.2yrs) and found that the sensitivity remained acceptable. The lower end cut offs were applied to the current data.[22]

Scores for all subtests were recorded but only the total, memory and fluency scores were included in the analysis as supported by the literature.

Additional Needs

An 'Additional Rehabilitative Needs Questionnaire' (ARNQ; Appendix 2.2, p98-99) was constructed to act as the secondary outcome measure as it provided a way for staff opinions and predictions of the need for additional support to be collated. The ARNQ was constructed collaboratively with senior members of each discipline of the rehabilitation team, with specific examples of additional support being generated by team members. This ensured that all staff members were clear about the operational definition of what additional support meant in this context. Staff members were asked before each participant's goal planning meeting (approximately 7-10 days in to admission) to state whether they thought the individual would require additional support above the typical level expected given their degree of physical disability and if so, was this due to cognitive difficulties. Examples of additional support included extra prompting, one-to-one therapy sessions etc. At the point of discharge staff were asked the same questions to see if their predictions came to fruition and at that point it was also noted if the participants required psychological input for either treatment or additional assessment.

Additional variables

Additional clinical and socio-demographic data that could also have an impact on functional outcome as indicated in the literature were also collected. Mood state was assessed using the Hospital Depression and Anxiety Scale (HADS)[31]and data on diagnosis, age, gender, co morbidities, medication, continence status and socio-demographics were obtained from medical notes.

Once postcodes were obtained, the Scottish Government's Scottish Index of Multiple Deprivation (SIMD) website was used to determine relative deprivation status by quintile

(1 = most, 5 = least).

(http://www.scotland.gov.uk/Topics/Statistics/SIMD/SIMDPostcodeLookup).

Although length of stay is a variable which is commonly measured in rehabilitation outcome studies, this was not included as either a predictor or an outcome variable in the present study because interest lay specifically in predictors which were measurable at point of admission, and in outcome variables related to functional gain and therapy input only.

Procedure

Every consecutively admitted patient to the unit was screened against the inclusion and exclusion criteria and if they were deemed eligible to participate, a member of staff from the clinical team in the unit who was not clinically involved with that particular patient handed them an information sheet regarding the study (Appendix 2.3, p100-101). With their consent, one of the researchers approached the potential participants to discuss the study and obtain either written or verbal consent (Appendix 2.4, p102-103). The ACE-R was then administered along with the HADS. These were administered by either a Trainee Clinical Psychologist or a Clinical Neuropsychologist, both of whom were experienced in administering and scoring both measurement tools.

These baseline data were gathered within one week of admission to the unit in all instances. Additional information (as detailed above) from each participant's medical file was also gathered at this time point. Prior to goal planning meetings, a second researcher approached clinical staff to complete the ARNQ. The second researcher and the clinical team remained blind to the ACE-R score throughout the admission.

At the end of each participant's stay within the unit their discharge FIM score was obtained from their medical notes by researcher 1, and researcher 2 asked clinical staff members to complete the second part of the ARNQ. In line with normal clinical practice, members of the multi-disciplinary team completed the parts of the FIM which were relevant to their profession and these scores were recorded in the patients' medical file. For the participants who agreed for their GP to be contacted, a letter was sent detailing their scores on the ACE-R, FIM and HADS.

Justification of sample size

Available literature which looks at the use of cognitive screening tools, cognition as a predictor of rehabilitation and those which employ a similar design,[5,7,8,9,16] report medium to large effect sizes (f^2= 0.27-4.26) and provide evidence to suggest that a large portion of variance is explained by cognitive variables (24% - 81%). Preliminary studies looking at the ACE-R in different clinical populations[13] suggest that it is sensitive in detecting cognitive impairment. We therefore predicted at least a medium effect size in our study and this would be required for the ACE-R to have real clinical utility for the purpose of predicting outcome.

G*Power,[32] a general power analysis programme, was used to conduct a power calculation for the main hypothesis to inform sample size and number of predictor variables that could be included in a linear regression model, with power set at 0.80 and alpha set at 0.05. Aside from the effect size based method used by G*Power, there are other traditional rules of thumb[33] which have been used to obtain more conservative power estimates for linear regression modelling. In recognition of this, the present study used the more conservative estimate produced by G*Power. It is therefore expected that in a sample size of 60 and using

an f^2 value of 0.27, 8 predictor variables can be included in a linear regression model to achieve a power of 0.80.

Data Analysis.

Baseline demographic and clinical characteristics are presented with frequency and descriptive statistics. A Wilcoxon signed ranks test was applied to assess the difference between FIM admission and discharge scores. Continuous variables were checked for normality and transformed as appropriate. Group analyses (using correlations, *t* tests, Mann-Whitney U tests or chi square) were performed in the first instance to identify any relationships among baseline variables. Where appropriate, effect sizes are reported and described in relation to Cohen's[34] recommendations of small (r=0.1), medium (r=0.3) and large (r=0.5). The Predictive Analytics Software 18 (PASW – 18) package was used for all analyses.

To test the hypotheses, the following analyses were carried out:

Hypothesis 1

To test whether patients with lower ACE-R scores had lower outcome scores, Spearmans rho correlations were carried out between the ACE-R total, memory and fluency scores, and the FIM change and discharge scores.

As other covariates may influence outcomes, additional correlations were run between the remaining continuous variables, and Mann Whitney U tests between pairs of continuous and categorical data. As the ACE-R incorporates the MMSE, individual MMSE scores were

obtainable for each participant and these were also entered into the analysis. This enabled the identification of significant variables for a multivariate analysis, if required.

If more than one baseline variable was found to be significantly associated with either of the FIM outcome variables, and after checking for multicollinearity, then it was planned that multivariate statistics (e.g. linear regression or ANOVA) were carried out. If the ACE-R scores were found to significantly predict FIM outcomes, then a ROC analysis was planned to establish what the suggested cut off score should be on the ACE-R in order to identify clients who are likely to make less rehabilitative gains.

Hypothesis 2

The sample was grouped dichotomously into those who needed additional input during the rehabilitation process (according to the second administration of the ARNQ) and those who did not, so that a comparison of ACE-R score distributions could be calculated between these groups using a series of Mann Whitney U tests. Further Mann Whitney U tests and Chi Square analyses were run to investigate the possible relationship between other baseline co-variates and whether additional support was required.

If more than one baseline variable was found to be significantly associated with the need for extra support, and after checking for multi-collinearity, then it was planned that multivariate statistics (e.g. logistic regression) were carried out. If the ACE-R scores were found to significantly predict need for additional support, a ROC analysis was planned to establish what the suggested cut off score should be on the ACE-R in order to identify clients who may require additional support to achieve rehab goals.

Additional Analysis

To investigate the accuracy of the clinical team's initial prediction of the need for additional support, a Chi Square analysis between predicted and actual support was conducted.

Results

Participants

As can be seen in Figure 1, of the 100 patients admitted to the unit during the study period, 25 did not meet the eligibility criteria and 10 declined to participate, meaning 65 patients met inclusion criteria and gave consent for participation.

Of the 65 participants who agreed to take part in the study, 5 did not have goal planning meetings and as such, no FIM data could be gathered resulting in incomplete data sets. As the data missing was related to the main outcome measure, all their data was excluded from further analysis. There was no other data missing for any other variables.

Therefore, a total of 60 participants (mean age 49.84yrs, males=23, females=37) took part in the study with complete data sets available for all.

INSERT FIGURE 1 HERE

As the participants all had some degree of physical disability, some were unable to complete the written sentence and drawing components of the ACE-R, meaning that they were unable to achieve a score above 91. As complete fluency and memory scores were obtainable for these participants, it was not desirable to exclude their data from the analysis. Therefore, all total ACE-R scores were converted in to a percentage, largely un-affecting the majority of the

data whilst levelling out the discrepancy between participants who were able to provide complete data on this measure and those who were not.

Baseline assessment

Table 1 summarises the characteristics of the sample and their performance on the baseline assessments.

INSERT TABLE 1 HERE

The most common diagnosis in the sample was Multiple Sclerosis reflecting the most common physically disabling disease in adults in the local geographical area. Other prominent diagnostic categories were stroke, Guillain Barre Syndrome, medically unexplained disability, and TBI, with the remainder of the sample having a range of other medical conditions such as Parkinson's disease, subarachnoid haemorrhage, encephalopathies and spinal cord compressions. The median scores on the ACE- R total, memory and fluency were 87 (IQR=14), 20 (IQR= 5) and 10 (IQR=4) respectively. In relation to existing clinical cut off scores, 29 patients had an ACE-R score of ≥88, 10 received a score between 82-87 inclusive, and 21 had a score ≤81 indicating that just over half the sample had evidence of cognitive impairment. Mean scores on the HADS indicated that most of the participants were in the sub-clinical range for anxiety and depression. Most participants were continent, and most were on some form of medication that could potentially impact on cognitive performance.

There were some significant associations among baseline continuous variables; age was associated with both anxiety (r=-.42, p=0.001, n=60) and depression scores (r=-.37, p=0.004, n=60) suggesting that as age increases anxiety and depression scores decrease. The ACE-R total scores were significantly correlated with memory (r=.77, p<0.001, n=60) and fluency (r=.78, p<0.001, n=60) sub-scores as expected. Admission FIM scores were not correlated with any measures of cognition indicating that these two constructs were independent of each other at baseline.

With regard to the relationship between the ACE-R scores and categorical baseline variables, women tended to score significantly higher (see Table 2) on ACE-R total, memory and fluency scores than men. Admission FIM scores were not affected by gender with no significant differences existing between men and women. Participants who were on hypnotic medications (see Table 3) tended to have significantly lower ACE-R Total, memory and fluency scores than those who were not on this medication. Only ACE-R total scores were affected by painkillers as those who were on this medication had significantly higher scores (Mdn=90) than those who were not (Mdn=84), U=275, z=-2.53, p=0.01, r=-0.33.

INSERT TABLE 2 HERE

INSERT TABLE 3 HERE

There were no other significant relationships between ACE-R scores and other baseline variables.

Outcome data

Discharge data was available for 60 participants. A Wilcoxon Signed Rank Test showed a significant difference between admission *(Mdn=90)* and discharge FIM *(Mdn=108)*, T=0, p<0.001, r=-0.54. Significant improvement in functional ability characterised by a median gain of 6.5 points (min=0, max=60) was achieved by all but 14 participants, whose FIM score remained the same. There was also a significant negative correlation between admission FIM and FIM change, perhaps reflecting a ceiling effect (r=-0.27, p=0.038, n=60). Within the sample, 14 participants (23.3%) required additional support from therapy staff, with the other 46 participants able to carry out their rehabilitation without additional support over and above normal clinical practice.

Hypothesis 1

As many variables were non-normally distributed and could not be transformed successfully, a series of Spearman's Rho correlations and Mann Whitney U tests were conducted in the first instance to identify significant relationships between baseline variables, specifically ACE-R scores, and the main outcome variable of FIM change. There was no significant correlation between FIM change and the main independent variables of cognition as measured by the ACE-R (ACE-R total: rho=.104, p=0.43 n=60; ACE-R memory: rho=.02, p=0.89, n=60; ACE-R fluency: rho=.15, p=0.25, n=60). Similarly, there was no significant relationship between FIM change and MMSE, HADS scores, age, number of medical co-morbidities, total number of medications, type of medication, gender, continence and catheterisation, or social deprivation. A Mann Whitney U test showed a significant difference with a small effect size between discharge FIM scores in patients with (n=20) and without (n=32) a catheter at baseline (U=197, z= -2.316, p=0.021, r=0.30), indicating that

those who were catheterised at baseline had a lower discharge FIM. There were no other significant relationships between FIM discharge and the aforementioned variables.

To further explore the possible relationship between baseline cognitive impairment and FIM change, the sample was divided in to those with possible and probable cognitive impairment (ACE-R total <88, n=31, Mdn=6, IQR=18) and those without cognitive impairment (ACE-R total ≥ 88, n=29, Mdn=7, IQR=19). A Mann Whitney U test indicated that there was no significant difference (U=391, z=-0.872, p=.383) in median FIM change scores between these two groups. This further indicates a lack of relationship between cognition and subsequent degrees of functional outcome as measured by the FIM.

It was not appropriate to carry out a multivariate statistics or ROC analysis as there was no significant relationship between ACE-R scores and FIM change or discharge scores. Hypothesis 1 is therefore not supported.

Hypothesis 2

A series of Mann-Whitney tests were conducted to test the hypothesis that there would be a significant difference in the ACE-R score distributions of those who required additional support during the rehabilitation process and those who did not.

It was found that those who required additional support had a significantly lower ACE-R total score (Mdn= 78, U=181, z=-2.25, p<0.014 r=-0.30), fluency score (Mdn=7.5, U=179.5, z=-2.51, p=0.012, r=-0.32) and memory score (Mdn=17.5, U=204.5 ,z=-2.06, p=.039, r=0.27) than those who did not require support (Mdn=88, Mdn=10 and Mdn= 21 respectively.) These

findings indicate that lower cognitive performance, is predictive of requiring extra support from staff during the rehabilitation process.

In regards to additional covariates, a significant association between gender and the need for additional support was found (Fisher's exact test p=0.005). It appeared that, based on the odds ratio, men were 6 times more likely to require additional support from therapy staff than women. No other baseline co-variates were found to be significantly associated with additional therapy support.

These four variables (ACE-R Total, ACE-R Memory, ACE-R Fluency and gender) were examined for multicollinearity, and diagnostic statistics indicated that the pairing of Total and Fluency ACE-R scores caused the Tolerance value to drop below 0.3. The variables were then grouped to avoid this pairing, and two separate Forward Stepwise Logistic Regression models were constructed. In Model 1 (gender, Total and Memory ACE-R scores), gender was the only significant independent predictor of additional therapy support (see Table 4). In Model 2 (gender, Fluency and Memory ACE-R scores), only ACE-R fluency was a significant independent predictor (see Table 4); however, gender reached borderline significance of p=0.053. As gender remained prominent in Model 2, this was taken as converging evidence that, overall, both gender and fluency were important independent predictors of additional therapy support.

INSERT TABLE 4 HERE

Odds ratio indicated that, in this sample, men were approximately 6 times more likely than women to require additional support from therapy staff during inpatient rehabilitation. With

regard to ACE-R fluency, ROC curve analysis established that a score of 10.5 or below on this subtest was the optimum indicator of a likely need for additional support (sensitivity=0.79, specificity=0.48). A cut-off score of 11.5 or below raised sensitivity to 0.93, but caused specificity to drop to 0.22. Area under the curve was 0.721 (95% CI = 0.553–0.889, SE=0.086, p=0.013).

Additional Analysis

The results of a Chi Square analysis indicated that therapy staff tended to significantly over estimate the need for additional support at point of admission (Fisher's exact test $p<0.001$). In total, 31.3% of participants who were predicted on admission to be likely to require additional supported turned out not to need this. However, only 6.8% of patients who were predicted by staff to not need additional support turned out to require it.

Discussion

This study set out to explore the relationship between cognition as measured by the ACE-R, and functional outcomes in an in-patient rehabilitation setting. It also aimed to establish whether individuals with lower scores on the ACE-R required additional support from therapy staff in order to achieve their rehabilitation goals.

In regards to hypothesis one, initial analyses suggested that there was no significant relationship between ACE-R scores and functional outcome as measured by both FIM change and discharge scores. There was sufficient power in this study for bivariate analyses however, only the ACE-R fluency score approached a significant relationship with the discharge FIM score. This was not a strong finding displaying only a borderline small effect size. These findings differ from the majority of the literature that found cognition to be an important

factor in regards to functional outcome in a variety of medical conditions[5,8,9,18,35,36] but, there are also a number of studies more congruent with the present findings.

Diamond et al.[37] found that within a sample of geriatric patients undergoing inpatient rehabilitation, cognitive status as measured by the MMSE had no relationship (on its own or combined with age) with functional gains. In particular they found that patients continued to make similar levels of gains regardless of cognitive ability. The properties of the FIM as a discharge measure should also be taken into account. It has been noted that within a spinal injury population the sensitivity of the FIM can be reduced as there is often a ceiling effect for the FIM cognitive subscale[38]. Reduced sensitivity is also supported by Dodds et al.[39] who found that the FIM failed to highlight the differences in functional ability in individuals with various levels of amputation.

It may be helpful to consider more broadly the relationship between cognition and functional ability when trying to interpret the current findings and Hajek et al.[40] offer some helpful insights into this. Within this current study the FIM was used as a way to detect meaningful change within patients between admission and discharge. However, as highlighted by Hajek et al.[40], some authors[41,42] have suggested that the FIM does not have sufficient sensitivity to predict discharge levels of functional ability and is not predicted by patient performance on cognitive tests.[43] Hajek et al.[40] make an important distinction in their study between neurological and cognitive tests, the first providing a way for professionals to establish the severity of a neurological event whilst cognitive tests allow actual brain functioning to be measured. They found that when correlated to functional outcome as measured by a number of tools including the FIM, no cognitive tests measuring either general or specific components of cognition demonstrated a significant relationship with functional ability.

The FIM is heavily weighted to physical functions. However, functional ability is not solely defined by physical ability and as such, trying to understand the relationship between cognition and functional ability may be complex. It is feasible that someone who is extremely physically impaired will obtain a low score on the FIM but have the cognitive capacity to function well day-to-day in other ways. The opposite is also true as someone may score high on the physical ability but have poor cognition hindering their ability to truly function independently but this will not be identified readily by the FIM. This was further supported by the lack of relationship between ACE-R scores and baseline FIM. This may be helpful for explaining the findings from our main analysis as the fact that cognition is under represented in the FIM may imply that it was less likely that a strong correlation would have existed between these two measures. There is recognition that the FIM is not sensitive to cognitive abilities and there is a sister measure called the Functional Assessment Measure (FAM) that is recommended to be used in conjunction with the FIM.[27] It was not routine clinical practice to use the FIM plus the FAM within the rehabilitation unit in which this study was conducted, and future research using the FAM as a joint outcome measure may yield more significant results.

However, the above points do not negate the fact that there are a large number of studies that have found measures of cognition to significantly correlate with either total FIM discharge scores or FIM change scores. Much support for this exists within the stroke literature but differences in methodology and measurement tools make it difficult for these findings to be compared. The strongest relationships are found in studies where the FIM cognitive subscale is used as the independent variable measuring cognition[44,45] and the total or motor FIM is used as the dependent variable assessing functional ability. Given the data reporting the

FIM's internal consistency[29]it would be expected that the subscales of this test would correlate together since they belong to the same parent test leading to questions about the true relationship of cognition and functional measures in these studies. Stroke studies that have used separate measures of cognition such as the MMSE[45,46,47] or the NCSE[48] find either non significant or a much weaker correlation than the studies that have used the FIM cognitive scale as the independent variable. Fang et al.[46] found one of the strongest relationships between the MMSE and outcomes post stroke rehabilitation, but in this instance outcomes were measured via a series of neurological and physical ability assessment tools, not the FIM. It may be that the weaker correlations in other studies are partly attributable to the use of the FIM as the main dependent variable, which does not always correlate with cognitive measures as postulated by Hajek et al.[40]

There is a distinct lack of literature exploring the usefulness of the ACE-R as a means of predicting rehabilitation outcomes in adults and as such, no direct comparison of findings in this paper can be made to an existing evidence base that looks specifically at the ACE-R. This was recognised by Gaber[13] who attempted to validate the ACE-R in a brain injury rehabilitation centre. However, those with extensive physical disabilities and who were unable to complete all components of the ACE-R were excluded, meaning his results may have limited comparability to the present study. Gaber[13] also sought to test only the ACE-R's sensitivity for use outside a dementia population, not its ability to predict rehabilitation outcomes.

There were more significant findings to tentatively support hypothesis two, which was that cognitive status would predict the requirement for additional support for patients during the rehabilitation process. This highlights the potential importance of general cognition and intact

memory and executive functions, in successful engagement in intensive rehabilitation. It also suggests that the ACE-R has value in identifying at the point of admission those patients who will require additional support.

The importance of executive functioning in relation to rehabilitation has been widely acknowledged. Skidmore et al.[35] measured three separate components of cognition (memory, attention and executive functions) whilst exploring the relationship between cognitive and affective predictors of rehabilitation participation after stroke. They found that only executive functions independently predicted outcome explaining 27% of the variance, matched only by baseline ability. It makes sense that intact executive functions are necessary for successful rehabilitation as a person must be able to sustain and focus attention on tasks at hand and initiate and sequence actions in an appropriate fashion.

O'Neill & Evans[9] also recognised the role of executive function in relation to mobility rehabilitation after lower limb amputation. The majority of their participants had vascular disorders presenting with subcortical difficulties primarily characterised by executive impairment as such this may reflect the high portion of variance explained by this particular cognitive domain in their study. The most common diagnostic category in the current sample was MS and patients with this diagnosis often present with sub-cortical difficulties such as slowed information processing and executive impairments. The ACE-R appears to be sensitive to this type of impairment in an MS population and even though it has been recognised that often such cognitive impairment is subtle[17], there is additional evidence that the fluency component of the ACE-R allows for a rapid screening of deficits in this area.[49] This is an important finding given that our results indicate that deficits in this area have

implications for the adaptations therapy staff may need to make to try and facilitate rehabilitative gains, and the additional time and resource needs that follow from this.

It is more difficult to explain the non significant relationship between the ACE-R memory scores and functional outcome, and the smaller significant relationship between memory scores and additional support compared to ACE-R total and fluency scores. O'Neill & Evans[9] report that memory alone, in particular immediate verbal memory, explained most variance in their study (24.8%). Both O'Neill & Evan[9] and Cullen et al.[8] recruited participants from outpatient clinics where less control and input would have been given in regards to aids to compensate for cognitive impairment, including memory deficits. Whilst the role of memory was not supported by other studies,[35] it seems logical that a relationship would exist between memory and functional outcome as it is necessary to retain and recall rehabilitation advice to achieve rehab gains. Within the rehabilitation unit in which this study was conducted, memory impairments are a common consequence of the neurological conditions that patients often present with. It may be that normal clinical practice is set up in such a way where this is naturally supported, perhaps not overtly, and as such, the provision of incidental support for memory deficits may not be defined by staff as 'additional support' over and above normal clinical practice in this setting. Also, in both Cullen et al.[8] and O'Neill & Evans,[9] memory functions were assessed using subcomponents of the RBANS, a more detailed tool than the ACE-R. Therefore this raises the question that even though the ACE-R gives more weight to memory than the MMSE, it may not be sensitive enough to capture and identify the memory impairments in patients with more subtle difficulties, possibly explaining the small effect size of memory and additional support, which diverges from other existing literature.

Gender also significantly predicted additional therapy support, with men reportedly requiring most assistance. The fact that males in this sample required more additional support than females may reflect the fact that men tended to perform significantly worse on the ACE-R, suggesting that therapy staff were responding to their increased cognitive impairment. This difference in gender and the need for additional support cannot be explained by level of overall disability because no significant associations were found between gender and baseline FIM scores. This raises some questions as to why a significant effect was found with the ACE-R but not the FIM. It is important to recall that the FIM is not designed to measure cognition in the way the ACE-R does, perhaps explaining why there was no relationship between the FIM and ACE-R and also between FIM and gender. This has implications for rehabilitation units in regards to their awareness of the limitations of commonly used assessment tools such as the FIM and the need for a deeper understanding in regards to the often independent relationship between physical and cognitive ability. These findings suggest that it is important to assess cognition separately from functional ability and recognise the unique role that impairment in cognition can have on the rehabilitative process. The fact that men in this cohort tended to present with more cognitive impairment means that these findings may not be generalisable to other physical rehabilitation units, but it may still be necessary for such units to use other parameters such as cognitive ability to plan resources for patients.

In the stepwise logistic regression models, there was converging evidence that both ACE-R fluency and gender were significant independent predictors of additional therapy support. The finding in relation to gender in this particular sample may not be generalisable to other patients with physical disabilities who are undergoing rehabilitation, because it may be an artefact of our finding that males in our sample were significantly more impaired on the

ACE-R, and so the increased odds ratio in favour of males requiring additional support may simply reflect this. However, it seems that ACE-R fluency scores may be important and informative for clinical practice as it was possible to establish that a score of 10.5 or lower on the ACE-R fluency subtest identified patients who were likely to require additional support, and this has an implication for rehabilitation units at a clinical level. ACE-R memory and total scores did not survive the regression analyses, and it is possible that the significant bivariate analyses involving these variables represented chance findings in the context of multiple comparisons across many different variables. Alternatively, the present study may have been underpowered to detect a true effect of allthe variables entered in to the models, given the small sample available for the logistic regression analysis. A rule of thumb for logistic regression is to enter one predictor variable for every 10 people who report the outcome of interest[50] (i.e. requiring additional support), whereas the outcome frequencies in the present study did not reach a level which would allow multiple predictor variables to be entered with adequate power.

Additional analysis exploring the ability of therapy staff to accurately identify patients who would require additional support highlighted that staff tended to overestimate this. They made a significant number of false positive predictions, expecting that clients needed additional support when it transpired that they did not. This implies that clinical opinion alone is not a significantly robust predictor of additional support but the ACE-R appears to be more sensitive to this and may be better at identifying these patients.

A limitation to this study was that patients who had profound language disorders or lacked capacity to consent to research were excluded from the study. This decision was made based on the premise that patients in both these categories may have struggled to understand and in

turn provide informed consent to take part in the study. Also, there was a risk that the performance of patients with language disorders on the ACE-R would reflect their language difficulty and not other cognitive abilities in the domains of memory and executive functioning. However, in turn this inadvertently meant that patients with potentially significant cognitive impairments were under represented in the sample and may partly explain why no significant correlation was found between the ACE-R and the FIM over both time points and FIM change. This is also an important factor with regard to the relatively small proportion of the present sample who required additional support (23.3%), as it is likely that aphasic patients and those whose degree of cognitive impairment meant they lacked capacity to consent to research are the patients most likely to require additional support from therapy staff, meaning that the reported proportion of 23.3% is an underestimate of the true proportion of patients requiring additional support in the unit. Repeating the study in a way where these patients can be included is a possible direction for future research.

It could be said that another limitation is the mixed diagnostic categories of the patients included in the study, as it is difficult to comment on the particular relevance and use of the ACE-R within specific neurological populations. There were three participants in the cohort with medically unexplained symptoms and this introduces the possibility for a further confounding element e.g differential effort on cognitive testing. It is helpful to remember that many participants had a progressive neurological condition where significant regain of function is less likely. This may also help explain the low median change in FIM scores between admission and discharge, and failure for some patients to make any objective rehabilitative gains. The emergence of some borderline significant findings may indicate that the study was underpowered to detect small effects, and more significant independent

predictors for both functional outcomes and additional therapy support may have been found in a larger sample.

Conclusion

The main analysis in this study demonstrated that there was no significant relationship detected between baseline cognitive status (as measured by the ACE-R) and functional gain (as measured by the FIM), during inpatient rehabilitation in a group of adults with physical disabilities. Cognition did appear to have a role in predicting the need for additional therapy support, and it appeared that the ACE-R could better identify these patients compared to clinical opinion alone. Only ACE-R fluency and gender survived a logistic regression analysis with additional support as the dependent variable, suggesting that they are independent significant predictors of need for additional support. For clear conclusions to be drawn in regards to use of the ACE-R within this population, further research is required, e.g. incorporating the use of the FIM and the FAM together as outcome measures. The findings in this study may not be generalisable to all patients who attend inpatient rehabilitation for a physical disability because patients with more marked cognitive and language impairments were excluded from this study. Future research using the ACE-R with these patients will bean interesting area for further research. As a consequence the role of cognition in rehabilitation outcomes may be underreported. There is also the possibility that this study was underpowered and more significant and stronger relationships may have been found if the sample size was increased.

Clinical Message

- ACE-R performance at baseline did not correlate with outcome after in-patient rehabilitation, as measured by FIM change.
- ACE-R fluency score at baseline was an independent predictor of need for additional therapy support during rehabilitation.
- The present study did not include patients without capacity to consent to research, thereby leading to under-representation of patients with the most severe cognitive and communication impairments. Future studies including such patients may detect a relationship between cognitive performance at baseline and subsequent functional gain.

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Figure 1- Participant flow diagram

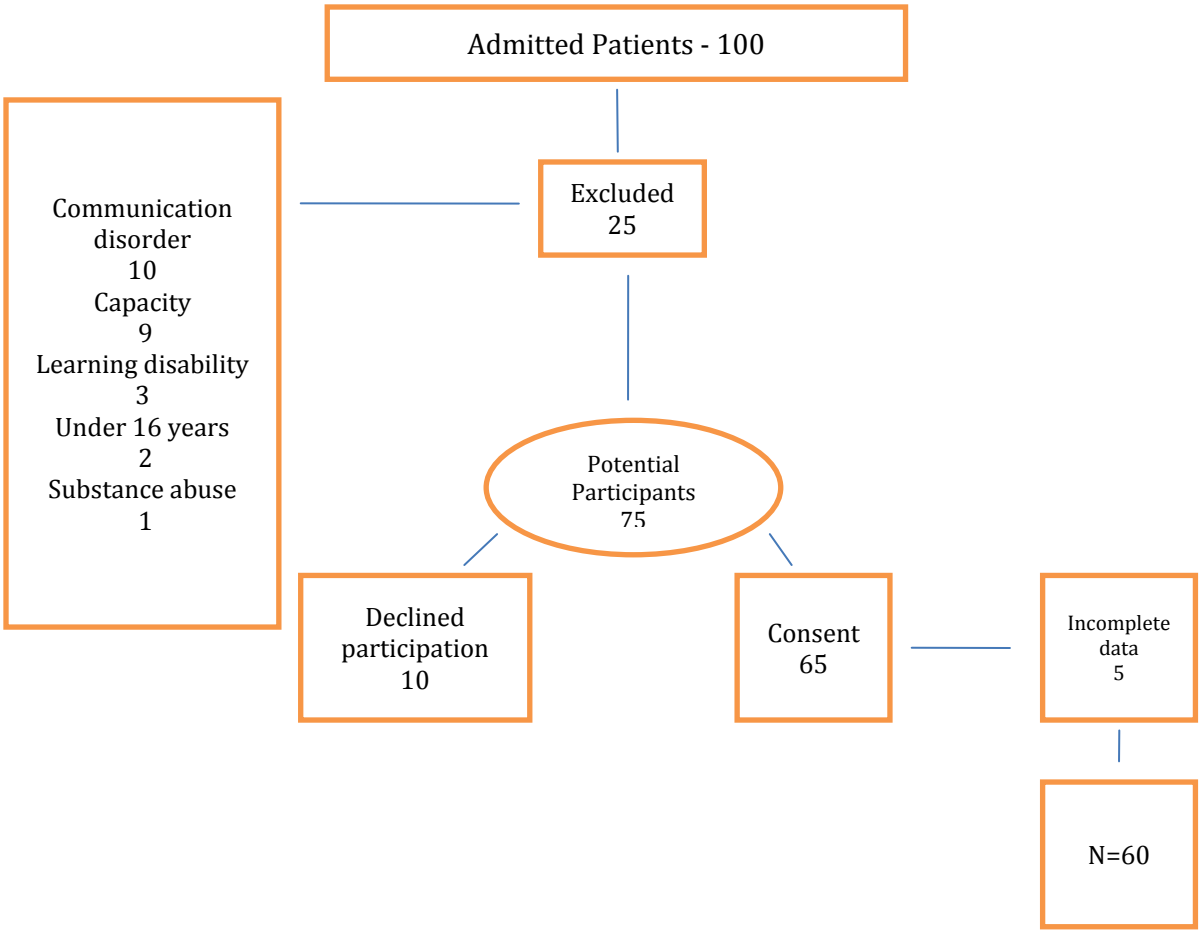

Table 1- clinical and socio-demographic data

Variables	**N (%)**	**Range**	**Median/***Mean*	**inter-quartile range (IQR))/ *SD***
Age		22-77yrs	49.84	12.01
Gender: Male Female	 23 (38.3) 37 (61.7)			
ACE-R Total (%) ACE-R Memory (raw) ACE-R Fluency (raw)	60	33-100 9-26 0-14	87 20 10	14 6 4
FIM admission FIM discharge FIM change	60	45-120 46-125 0-60	*89.08* 108 6.5	*20.34* 30 18
HADS anxiety HADS depression	60	0-18 0-18	6.5 6	6 6
SIMD quintile*	60	1-5	2.48	1.47
Diagnostic category: Multiple Sclerosis Stroke GBS Medically unexplained TBI Other	 24 (40) 9 (15) 6 (10) 3 (5) 2 (3.3) 16 (26.7)			
Bladder Continent Incontinent Catheterised Bowel Continent Incontinent Prescription of pain killers, anti epileptics, anti depressants, anti psychotics, steroids, anti spasticity agents, stimulants,	 32 (53.3) 8 (13.3) 20 (33.4) 48 (80) 12 (20)			

benzodiazepines or hypnotics Yes No Medical Co-morbidities	 51 (85) 9 (15)	 0-6	 1	
Additional support required (ARNQ) Yes No Psychology input Yes No	 14 (23.3) 46 (76.7) 27 (62.8) 16 (37.2)			

Abbreviations: GBS = Guillain Barre Syndrome, TBI = Traumatic Brain Injury, SAH = Subarachnoid Haemorrhage, ARNQ = Additional Rehabilitative Needs Questionnaire
* lower = relatively more deprived

Table 2 - Mann Whitney ACE-R and Gender

	Female		Male					
Variables	Mdn	IQR	Mdn	IQR	U	*Z*	P value	*r*
ACE-R total	88	35	81	61	258.5	-2.54	0.01	-0.32
ACE-R memory	21	16	17	16	270	-2.37	0.02	-0.31
ACE-R fluency	11	12	8	13	220.5	-3.14	0.002	-0.41

Abbrev: Mdn= median, IQR= inter quartile range

Table 3- Mann Whitney ACE-R and hypnotic medications

	Hypnotic medication		No hypnotic medication					
Variables	Mdn	IQR	Mdn	IQR	U	*Z*	P value	r
ACE-R total	57	11	87.5	67	7.00	-2.105	0.023	-0.27
ACE-R memory	11	2	20.5	17	3.5	-2.25	0.007	-0.30
ACE-R fluency	3	6	10	14	10.5	-1.97	0.04	-0.25

Abbrev: Mdn= median, IQR= inter quartile range

Table 4 –Forward Stepwise Logistic Regression

	B (SE)	95% CI lower	95% CI upper	Odds ratio	P value
Model 1*					
Gender	1.85 (0.68)	1.68	23.88	6.35	0.006
Model 2**					
Fluency	2.58(0.96)	0.64	0.93	0.77	0.007

**Model 1*,R^2=0.13(Hosmer&Lameshow), 0.13(Cox&Snell), 0.19 (Nagelkerke), $X^2(1)=8.35$, $P=0.006$*

***Model 2*, R^2=0.13 (Hosmer&Lameshow), 0.13(Cox&Snell), 0.19 (Nagelkerke), $X^2(1)=8.32$, $P=0.007$*

Chapter 3: Advanced Clinical Practice 1: Reflective Critical Account (Abstract Only)

Clinical Psychology challenged: A systems perspective

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Submitted in partial fulfilment of the requirements for the degree of Doctorate in Clinical Psychology (D.Clin.Psy)

Abstract

Introduction: This reflection focuses on my experience of working within a medically led rehabilitation inpatient unit whilst in the role of a Trainee Clinical Psychologist. It is becoming more commonly recommended in formal Government guidelines such as the National Institute of Clinical Excellence (NICE) and Scottish Intercollegiate Guidelines Network (SIGN) that Clinical Psychologist are to be present within a variety of settings and provide psychological interventions for an array of medical conditions. However, this presents certain challenges for the profession.

Reflection: I use a tripartite model to note my reflections whilst working with a specific case and detail my role at client, service and wider system levels. I discuss the personal challenges this case presented in regards to the establishment of a therapeutic alliance and then widen this to consider the role of psychology within a medical setting whilst appreciating the importance of the systems that hospital patients are surrounded by. I draw upon both the Atkins & Murphy Model of Reflection (1994) and the Rolfe et al. (2001) Framework of Reflexive Practice to structure my reflections.

Reflective Summary: This process allowed me to understand the role of clinical psychology at a deeper and more meaningful level and helped to shape the practitioner that I would like to be.

Chapter 4: Advanced Clinical Practice 2: Reflective Critical Account (Abstract Only)

Clinical Neuropsychology: Its function within functional disorders.

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Submitted in partial fulfilment of the requirements for the degree of Doctorate in Clinical Psychology (D.Clin.Psy)

Abstract

Introduction: This reflection focuses on my experience of working within a Neuropsychology department whilst in the role of a Trainee Clinical Psychologist. Within Neurology services approximately, a third of patients have no organic cause for their physical illness and subsequently receive a diagnosis of 'functional disorder' (Neurological Standards, 2009). It is recognised in the Neurological Standards that psychological interventions should be offered to patients with such a diagnosis however, it is interesting to consider what skills Clinical Psychologists have to offer appropriate interventions and the challenges involved in working with this client group.

Reflection: I reflect upon the skills of a Clinical Psychologist and discuss my own experience of working with a patient with a functional diagnosis. I attempt to evaluate the role of Clinical Psychology in line with the National Occupational Standards (BPS, 2006) and highlight the personal challenges that this case presented in regards to the therapeutic alliance. I go on to develop an understanding of the systemic factors that play a pivotal role in the treatment of these cases and I draw upon both the Atkins & Murphy (1994) and the Boud et al. (1985) Models of Reflection to structure my reflections.

Reflective Summary: This process allowed me to understand the role of clinical psychology at a deeper and to use the new perspectives I have developed to guide my practice.

Appendix 1.1 - Author Guidelines

Editor: Derick Wade clinical.rehabilitation@sagepub.co.uk
Revision: Oct 6th 2010

Clinical Rehabilitation
Further Information for Authors and Reviewers

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Click the **bold** titles in the index below to go to the relevant section for further information on any of these topics (At the end of each section is a 'Return to Contents Page' link which will bring you back to this page):

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Appendix 1.2: Detailed Search Strategy

Database	Search terms used	No of papers generated
Ovid Medline	stroke*, cog*, function*, rehab*, outcome*, stroke, treatment outcome, cognitive disorders, rehabilitation, recovery of function, perceptual disorders, visual perception, limit to humans and 2000-2011	346
Embase	Cog*, outcome*, stroke*, convalescence*, cerebrovascular disorders, cognitive defect, risk factor, outcome assessment, executive function, rehabilitation centre limit to human and 2000-2011	286
Psychinfo	Cerebrovascular accidents, participation, disabilities, cognitive impairment, outcomes assessment, convalescence, sensory neglect, rehabilitation limit to humans and neglect search from 2006 +	72
CINAHL	Stroke, cognition OR cognitive disorders, functional status, perceptual disorders, unilateral neglect	88
Web of Knowledge	Stroke, cognition, rehabilitation, predictors	269

Appendix 1.3 – Methodological rating scale

STROBE Statement— Checklist for observational studies

Quality Rating Checklist Author:

Scoring
2 – informationwell presented and detailed
1 – information present but lacks adequate detail
0 – information absent

	Item No	**Recommendation**	**score**
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found (inc methods, results and conclusion)	
		Total for Title and abstract	**/4**
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	
Objectives	3	State specific objectives, including any pre-specified hypotheses	
		Total for Introduction	**/4**
Methods			
Study design	4	Present key elements of study design early in the paper	
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment.	
Participants	6	Give the eligibility criteria, and the sources and methods of selection of participants.	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders.	
Data sources/ measurement	8	*(a)* For each variable of interest, give sources of data and details of methods of assessment (measurement).	
	*	*(b)* Data provided for the reliability and validity of measurement tools used.	
	*	*(c)* Reference made to the time points that data was collected e.g on admission	

Bias	9	Describe any efforts to address potential sources of bias	
Study size	10	Explain how the study size was arrived at	
Statistical methods	11	(*a*) Describe all statistical methods, including those used to control for confounding variables.	
		(*b*) Explain how missing data were addressed	
		Total score for Methods	**/22**
Results			
Participants	12*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study and analysed	
Descriptive data	13	(a) Give characteristics of study participants (eg demographic, clinical, social)	
		(b) Indicate number of participants with missing data for each variable of interest	
Outcome data	14	Report numbers of outcome events or summary measures over time	
Main results	15*	(*a*) Give confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	
		(*b*) Report effect size/variance	
		(c) Use of tables to highlight main results.	
Other analyses	16	Report other analyses done—eg analyses of subgroups and interactions	
		Total score for Results	**/16**
Discussion			
Key results	17	Summarise key results with reference to study objectives	
Limitations	18	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	
Interpretation	19	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	
Generalisability	20	Discuss the generalisability (external validity) of the study results	
Total Score for Discussion			**/8**
		Grand Total	**/54**

Appendix 1.4 Itemised rating scale scores.

	Ones et al 2009	Ozdemir et al 2001	Man et al 2006	Zwecker et al 2002	Nas et al 2004	Leung et al 2010	Skidmore et al 2010	Fang et al 2003	Lin et al 2003	Denti et al 2008	Fong et al 2001
Title and Abstract: subtotal = 4	3	4	2	3	3	4	2	4	3	2	3
Introduction: subtotal =4	3	2	3	2	2	3	3	3	3	3	2
Methods: subtotal =22	13	12	11	12	11	19	16	13	19	17	17
Results: subtotal=16	7	6	7	6	6	14	10	10	15	16	12
Discussion: subtotal=8	6	7	3	2	2	7	8	8	7	8	6
Total =54	32	31	26	25	24	47	39	38	47	46	40

1.5- Inclusion/Exclusion Criteria

Author	Medical stability	Rehab potential	>60 yrs	Death /missing data	GCS <8	SAH	Acute co-morbidities/ Disability	Cog impairment	GCS 15	First stroke	Lng difficulty	Visual deficits/ neglect	Dementia	Trauma	Brain tumour	LOS <7 -10 days	Previous stroke	coma	Psychiatric illness	Substance abuse	TIA	Auditory deficit	Pre limb imp	CI
Denti et al 2008		y				x	x			y							x							
Fang et al 2003	Y	Y			x	x	x						X								x		x	x
Fong et al 2001							x				x	X					x					x		x
Leung et al 2010	Y			x		x	x		Y															
Lin et al 2003	Y					x							x			x	x							
Nas et al 2004	Y	Y			x						x	X				x								
Ones et al 2009	Y	y				x	x				x			X		x	x	x	x		x			
Ozdemir et al 2001	y				x		x				x	X												
Skidmore et al 2010			Y					Y			x		x											
Wai-Kwong Man et al 2006							x												x					
Zwecker et al 2002	Y	Y									x		x											

X=excluded

Appendix 2.1 - Ethics Written Approval

WoSRES
West of Scotland Research Ethics Service

West of Scotland REC 3
Ground Floor – The Tennent Institute
Western Infirmary
38 Church Street
Glasgow G11 6NT
www.nhsggc.org.uk

Dr Breda Cullen
Clinical Psychologist
NHS Greater Glasgow & Clyde
Physical Disability Rehabilitation Unit
Southern General Hospital
Glasgow G51 4TF

Date 11th August 2011
Your Ref
Our Ref
Direct line 0141 211 2123
Fax 0141 211 1847
E-mail Liz.Jamieson@ggc.scot.nhs.uk

Dear Dr Cullen

Study title: **An investigation in to the use of Addenbrooke's Cognitive Examination – revised (ACE-R) as a means of predicting rehab outcomes in adults aged 16 or over.**

REC reference: **11/WS/0018**

The Research Ethics Committee reviewed the above application at the meeting held on 04 August 2011. Thank you for attending to discuss the study.

Ethical opinion

The members of the Committee present gave a favourable ethical opinion of the above research on the basis described in the application form, protocol and supporting documentation, subject to the conditions specified below.

Discussion

1) The Committee agreed that the recruitment process was inappropriate, i.e. you already work in the area and would be approaching people for research when you are already involved in their clinical care. In discussion you agreed that this recruitment process was inappropriate and suggested that other colleagues within the Unit who are not clinically involved or part of the research could make the first approach on behalf of the Research Team. Alternatively the administration staff within the Unit could distribute the study documentation to the patients when they come to the clinic. After the you left the meeting the Committee agreed that the recruitment process should be altered in line with the discussion i.e.

   - Colleagues within the Unit not involved either clinically or are part of the research team should make the first approach, or
   - The administrative staff hand out details of the study to the patients when they come to the clinic for their appointment.

Ethical review of research sites

NHS Sites

The favourable opinion applies to all NHS sites taking part in the study, subject to management permission being obtained from the NHS/HSC R&D office prior to the start of the study (see "Conditions of the favourable opinion" below).

Conditions of the favourable opinion

The favourable opinion is subject to the following conditions being met prior to the start of the study.

Management permission or approval must be obtained from each host organisation prior to the start of the study at the site concerned.

Management permission ("R&D approval") should be sought from all NHS organisations involved in the study in accordance with NHS research governance arrangements.

Guidance on applying for NHS permission for research is available in the Integrated Research Application System or at http://www.rdforum.nhs.uk.

Where a NHS organisation's role in the study is limited to identifying and referring potential participants to research sites ("participant identification centre"), guidance should be sought from the R&D office on the information it requires to give permission for this activity.

For non-NHS sites, site management permission should be obtained in accordance with the procedures of the relevant host organisation.

Sponsors are not required to notify the Committee of approvals from host organisations

OTHER CONDITIONS SPECIFIED BY THE REC

a) Please confirm in writing that the recruitment process will be amended in line with the discussion at the meeting.

b) There are some editorial issues in the study documentation which require to be clarified or amended as follows:

Application Form

- At A14-1 it states that patients, service users, and/or either carers, or members of the public have been involved in the design of the study. Please confirm in writing that this box should not have been ticked.

- At A21 it states that participants will only be in the study in total for 30 minutes. Please confirm in writing that participants will be involved for the duration of the study.

- At A49 it states that participants' GPs will not be informed of their participation in the study. However the Consent Form asks participants to consent to their GP being informed. Please confirm in writing that the GP will be informed.

Participant Information Sheet

- A sentence should be added 'Will my GP be informed of my participation in the study' - Yes with your permission.

Consent Form

- There should be contact details at the beginning.
- The words 'Please Initial' should be inserted above the boxes.

It is responsibility of the sponsor to ensure that all the conditions are complied with before the start of the study or its initiation at a particular site (as applicable).

You should notify the REC in writing once all conditions have been met (except for site approvals from host organisations) and provide copies of any revised documentation with updated version numbers. Confirmation should also be provided to host organisations together with relevant documentation

Approved documents

The documents reviewed and approved at the meeting were:

Document	*Version*	*Date*
Investigator CV		13 July 2011
Other: CV - Susan Lennie - Student		11 July 2011
Other: CV - Professor J Evans		
Participant Consent Form	1	30 May 2011
Participant Information Sheet	2	11 July 2011
Protocol	2	11 July 2011
REC application		11 July 2011

Membership of the Committee

The members of the Ethics Committee who were present at the meeting are listed on the attached sheet.

Statement of compliance

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees (July 2001) and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

After ethical review

Reporting requirements

The attached document "After ethical review – guidance for researchers" gives detailed guidance on reporting requirements for studies with a favourable opinion, including:

- Notifying substantial amendments
- Adding new sites and investigators

- Notification of serious breaches of the protocol
- Progress and safety reports
- Notifying the end of the study

The NRES website also provides guidance on these topics, which is updated in the light of changes in reporting requirements or procedures.

Feedback

You are invited to give your view of the service that you have received from the National Research Ethics Service and the application procedure. If you wish to make your views known please use the feedback form available on the website.

Further information is available at National Research Ethics Service website > After Review

11/WS/0018	**Please quote this number on all correspondence**

With the Committee's best wishes for the success of this project

Yours sincerely

Liz Jamieson
Committee Co-ordinator
On behalf of Dr Adam Burnel, Alternate Vice Chair

Coordinator/Administrator: Dr Erica Packard/Mrs Elaine O'Neill
Telephone Number: 0141 211 6208
E-Mail: erica.packard@ggc.scot.nhs.uk
Website: www.nhsggc.org.uk/r&d

R&D Management Office
Western Infirmary
Tennent Institute
1st Floor 38 Church Street
Glasgow, G11 6NT,

1 September 2011

Dr Breda Cullen
Clinical Neuropsychologist
Physical Disability Rehabilitation Unit
Southern General Hospital
1345 Govan Road
Glasgow G51 4TF

NHS GG&C Board Approval

Dear Dr Cullen,

Study Title:	**An investigation in to the use of Addenbrooke's Cognitive Examination - revised (ACE- R) as a means of predicting rehab outcomes in adults ages 16 years or older.**
Principal Investigator:	**Dr Breda Cullen**
GG&C HB site	**Southern General Hospital**
Sponsor	**NHS Greater Glasgow and Clyde**
R&D reference:	**GN11CP204**
REC reference:	**11/WS/0018**
Protocol no: (including version and date)	**V2.1; 31/08/11**

I am pleased to confirm that Greater Glasgow & Clyde Health Board is now able to grant **Approval** for the above study.

Conditions of Approval

1. **For Clinical Trials** as defined by the Medicines for Human Use Clinical Trial Regulations, 2004
   a. During the life span of the study GGHB requires the following information relating to this site
      i. Notification of any potential serious breaches.
      ii. Notification of any regulatory inspections.

It is your responsibility to ensure that all staff involved in the study at this site have the appropriate GCP training according to the GGHB GCP policy (www.nhsggc.org.uk/content/default.asp?page=s1411), evidence of such training to be filed in the site file.

NHS
Greater Glasgow and Clyde

2. **For all studies** the following information is required during their lifespan.
   a. Recruitment Numbers on a quarterly basis
   b. Any change of staff named on the original SSI form
   c. Any amendments – Substantial or Non Substantial
   d. Notification of Trial/study end including final recruitment figures
   e. Final Report & Copies of Publications/Abstracts

Please add this approval to your study file as this letter may be subject to audit and monitoring.

Your personal information will be held on a secure national web-based NHS database.

I wish you every success with this research study

Yours sincerely,

EPackard

Dr Erica Packard
Research Co-ordinator

Appendix 2.2 – Additional Rehabilitation Needs Questionnaire

<u>To be completed by the Keyworker on behalf of the team at the first goal planning meeting</u>

In the team's opinion, will this client require support above and beyond what would be normally expected with someone who has a similar physical disability?

Yes No

If so, is this the result of a cognitive impairment?

Yes No

If you answered yes then do you think the client will need:

One to one sessions

A quiet, non-distracting environment

More prompting from staff

More time

Goals re-evaluated and adapted

More than one discipline working towards joint goals (e.g. psychology and physiotherapy working with client to achieve goals in the gym)

Other (please specify)

_____

_____

_____

****

To be completed at the pre-discharge meeting

Now the client is due to be discharged, did it turn out that the client's cognitive impairment required them to have additional support?

Yes No

What were these additional supports?

One to one sessions

A quiet, non-distracting environment

More prompting from staff

More time

Goals re-evaluated and adapted

More than one discipline working towards joint goals (e.g. psychology and physiotherapy working with client to achieve goals in the gym)

Other (please specify)

_____

_____

_____

Did the person receive psychological intervention?

Yes No

Appendix 2.3 – Patient Information Sheet

Patient information sheet

Title: An investigation in to the use of Addenbrooke's Cognitive Examination – revised (ACE-R) as a means of predicting rehab outcomes in adults aged 16 or over.

Contact details: Susan Lennie
University of Glasgow,
Section of Psychological Medicine,
1055 Great Western Road,
Glasgow, G12 0XH
Email: s.lennie.1@research.gla.ac.uk

We would like to invite you to take part in our research study. Before you decide, we would like you to understand why the research is being done and what it will involve. Someone involved in the research will go through the information sheet with you and answer any questions you have. This should take about 10 minutes and it gives you an opportunity to ask us anything that is not clear. You do not have to make an immediate decision.

Who is conducting the research?
This study is being carried out by Susan Lennie and is being supervised by Dr Breda Cullen and Professor Jon Evans from the University of Glasgow.

What is the purpose of this study?
The present study aims to examine how well the ACE-R (a cognitive screening tool) predicts rehabilitation resource needs and outcomes in a sample of adults with physically disabling conditions. This study will also be submitted as part of the main researcher's (Susan Lennie) portfolio for examination by the University of Glasgow as part of the Doctorate in Clinical Psychology.

Why have I been invited?
We are looking for people who are aged 16 or over, who have some form of physical disability and are currently engaged in a rehabilitation programme. We believe that you might fit this criteria and this is why we have invited you to take part.

Do I have to take part?
It is up to you to decide if you want to join the study, participation is voluntary. We will describe the study and go through this information sheet, which we will then give to you. If you agree to take part, we will then ask you to sign a consent form. You are free to withdraw at any time, without giving any reason. This would not affect the standard of care you receive.

What will happen to me if I take part?
If you agree to take part in the study then we will ask you to meet with one of the researchers. This would be a one off meeting and would last for no more than **30 minutes**. During this meeting the researcher will ask you to complete an assessment called the Addenbrooke's Cognitive Examination-Revised (ACE-R). This involves different tasks that allow us to measure things such as memory and language skills. This is all that would be asked of you that is over and above the normal procedures within the physical disability rehabilitation unit (PDRU) that you are currently staying in.

With your consent, we would like to access your file so we can obtain some information about your background and medical condition.

What are the possible disadvantages and risks of taking part?
This is a very low risk study however as you will have been asked to concentrate on a task for 30 minutes some people may experience some tiredness afterwards.

What are the possible benefits of taking part?
You may not see a direct benefit from taking part in the study but we hope that information gained from this study will allow us to develop a more reliable way of identifying individuals who may benefit from additional support during their rehabilitation.

Will you contact my GP?
With your permission, we will send your GP a short letter to let them know that you are taking part in the study, and we will also let them know of any test results that might be helpful to include in your medical records.

Who has reviewed the study?
This study has been reviewed by the West of Scotland Research Ethics Committee.

If you have any further questions?
We will give you a copy of the information sheet and signed consent form to keep. If you would like more information about the study and wish to speak to someone **not** closely linked to the study, please contact **Dr Sue Turnbull, Research Tutor, University of Glasgow, Section of Psychological Medicine, email: s.turnbull@clinmed.gla.ac.uk, Tel no: 0141 211 3927.**

If you have a complaint about any aspect of the study?
If you are unhappy about any aspect of the study and wish to make a complaint, please contact the researcher in the first instance but the normal NHS complaint mechanism is also available to you.

Contact Details:

Susan Lennie
Trainee Clinical Psychologist
University of Glasgow
Section of Psychological Medicine
1055 Great Western Road
Glasgow, G12 0XH
Email: s.lennie.1@research.gla.ac.uk

Tel: 0141 211 0694

Professor Jon Evans
University of Glasgow
Section of Psychological Medicine
1055 Great Western Road
Glasgow, G12 0XH
Email: jonathan.evans@glasgow.ac.uk

Thank you for taking the time to read this information sheet.

Appendix 2.4 – Consent Form

Study Number:
Participant Identification Number for this study:

Consent Form

Contact Details:
Susan Lennie
Trainee Clinical Psychologist
University of Glasgow
Section of Psychological Medicine
1055 Great Western Road
Glasgow, G12 0XH
Email: s.lennie.1@research.gla.ac.uk

Professor Jon Evans
University of Glasgow
Section of Psychological Medicine
1055 Great Western Road
Glasgow, G12 0XH
Email: jonathan.evans@glasgow.ac.uk
Tel: 0141 211 0694

Title of project: An investigation in to the use of Addenbrooke's Cognitive Examination – revised (ACE-R) as a means of predicting rehab outcomes in adults aged 16 or over.

	Please initial
1. I confirm that I have read and understand the information sheet dated 18/08/11 (version 3) for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily.	☐
2. I understand that my participation is voluntary and that I am free to withdraw at any time without giving any reason, without my medical care or legal rights being affected.	☐
3. I understand that relevant sections of my medical notes and data collected during the study, may be looked at by individuals from the University of Glasgow and NHS Greater Glasgow & Clyde where it is relevant to my taking part in this research. I give permission for these individuals to have access to my records.	☐
4. I agree to my GP being informed of my participation in the study.	☐
5. I agree to take part in the above study.	☐

_____	_____	_____
Name of participant	Date	Signature
_____	_____	_____
Name of person	Date	Signature

taking consent

If the person is unable to provide written consent then a witness must sign on behalf of the participant confirming that verbal consent has been given.

_____	_____	_____
Witness (where appropriate)	Date	Signature

Appendix 2.5 – Major Research Proposal

Title: An investigation in to the use of Addenbrooke's Cognitive Examination – revised (ACE-R) as a means of predicting rehab outcomes in adults ages 16 years or older.

Summary

Cognitive impairment, whether mild or more significant, is a common feature of many physically disabling neurological conditions. The presence of cognitive impairment may be a source of concern for patients and may adversely affect their day-to-day functioning, including how well they progress in their physical rehabilitation. The ACE-R is a widely used cognitive screen in the context of dementia but its suitability of use in a rehabilitation setting has not been investigated. The present study aims to examine how well the ACE-R predicts rehabilitation resource needs and outcomes in a sample of adults aged 16 or over with physically disabling conditions.

Introduction

Why cognition has a role in predicting rehabilitation outcomes

Successful inpatient rehabilitation is critical in determining long-term functional outcomes and accounts for 60-75% of overall long-term functional gain after a disabling medical event (Fiedler et al, 2000). However, there seems to be a degree of variance in actual rehabilitation outcomes. This has been the focus of research as professionals try to understand the variables involved which could predict rehab outcomes and explain the variance witnessed in clinical settings. In some neurological conditions such as stroke, research suggests that medical co-morbidities (Gray et al 1989), demographics (Kolita et al 1986, Glaski et al 1993) and psychological factors (Lenze et al 2004) are all relevant to predict functional outcomes.

Another important factor that has received attention in this field is cognition. In rehabilitative settings, there are certain demands placed upon a person's cognitive capacity as they need to be able to attend to, process and learn new information. If an individual has attention difficulties and subsequently struggles to concentrate in the busy setting of a rehab unit or has memory problems where they are unable to learn new techniques, then it would be reasonable to assume that they may face more difficulties in achieving their rehab goals compared to those without cognitive impairment. There are studies supporting the idea that cognitive impairment is a valuable predictor for rehabilitative outcomes. Studies looking at prosthetics use and frequency of power wheel chair use reported negative correlations between cognitive impairment and functional outcomes (Barnfield 1996, Larner et al 2003 and Cullen et al 2008). Many of these studies report that cognitive impairment, specifically memory, account for a large portion of variance in rehab outcomes. However, O'Neill and Evans (2009) suspected that looking at cognitive function by domain, specifically executive functioning measured by verbal fluency, would add to the variance explained by memory alone and this hypothesis was supported. They found that prosthesis use at 6 months follow up was predicted by verbal fluency and mobility by memory. This adds to the evidence from Robertson et al (1997) who found that sustained attention deficits, a frontal lobe function, 2 months post stroke predicted motor recovery at a 2 year follow up. However, there may be some inconsistency in findings relating to this as Hyndman et al (2008) found only an indirect relationship between attention and function.

Why cognitive screening is important to investigate in this setting

A full, comprehensive neuropsychological assessment is one method by which a person's cognitive ability can be assessed. An individuals cognitive strengths and weaknesses are highlighted in detail and it allows for a more accurate inference to be made about the severity of cognitive impairment (Tsaousides & Gordon, 2009). Whilst it is acknowledged that this method allows for a more thorough and reliable measure of ability, there are various factors which would make this less practical. Batteries of assessment are often lengthy and taxing upon the client. Furthermore, many services have no access to specialist staff for a full assessment making it important to have some method of briefly and quickly screening for cognitive deficits (Gaber 2008). Access to cognitive screening tools allow staff to identify the patients who may require additional needs, or trigger a referral to another professional. Screening tools would then help to ensure that the referrals being made to services such as Psychology, a valuable and often limited resource, are appropriate and help direct input

towards clients who would benefit from it most. Not only would this aid the efficiency of rehab units, but would also benefit the client as more time/resources (e.g. one to one session, a longer stay etc) could be allocated to facilitate better, targeted rehabilitative efforts (Cullen et al 2008). There is still some debate about the suitability of screening tools as often their use has not been validated for the clinical population for which they are used (Cullen et al 2007). However, some literature validating the use of certain screening tools in a population of younger clients with neurological conditions has been positive (Benedict & Zivandinov 2006, Adunsky et al 2002, Barak et al 2002). More importantly, there is evidence stemming from research in older adult populations that suggest cognitive screening tools (e.g. MMSE) to be a reliable method of predicting functional outcomes in post stroke and hip fracture rehabilitation settings (Feng et al 2010, Ones et al 2009, Galski et al 1993).

The ACE-R as a screening tool

Within dementia related research the use of the ACE-R as a brief cognitive screening tool is widely acknowledged and its appropriateness of use has been recognised in Government Guidelines (National Institute of Clinical Excellence (NICE) 2006, Scottish Intercollegiate Guidelines Network (SIGN), 2006). The ACE-R was developed by Mioshi et al (2006) following on from the already existing ACE (Mathuranath et al., 2000). It incorporates the Mini Mental Sate Examination (MMSE) (Folstein et al 1975) and allows for the assessment of the following cognitive domains; attention and orientation, verbal fluency, language, visuospatial and memory. The ACE-R is somewhat superior to the MMSE as it gives more attention to memory and executive functioning. The ACE-R is an attractive tool as it is quick and easy to administer and clinicians are readily familiar with it. Amongst clinicians, the MMSE is frequently and widely used in practice (Cullen et al 2007) but the ACE-R is quickly growing in popularity in part due to the increased emphasis given to memory and executive functioning, both of which are recognised as barriers to rehabilitation (Barnfield 1996, Larner et al 2003 and Cullen et al 2008, Gaber 2008).

Within dementia literature, there are a number of studies that report the ACE-R to be both sensitive and specific in identifying those with and without cognitive impairment (Mioshi et al 2006, Dudas et al 2005, Galton et al 2005). Despite this, studies examining the use of the ACE-R in non-dementia client groups are scarce. There is one study to date that has examined the sensitivity of the ACE-R in post acute brain injury, with encouraging results (Gaber 2008). However, there is no published research on the use of the ACE-R in other

neurological conditions such as multiple sclerosis. Therefore, there would appear to be a need to examine the predictive power of the ACE-R in relation to rehab outcomes in adults aged 16 or over with neurological conditions.

Aim

To investigate the utility of the Addenbrookes Cognitive Examination – Revised (ACE-R) in predicting rehabilitation resource needs and outcomes in a sample of adults aged 16 or over with physically disabling conditions admitted to an in-patient rehabilitation unit.

Hypothesis

3) Clients with lower ACE-R scores on admission will show less change on the Functional Independence Measure between admission and discharge, compared with clients who have higher ACE-R scores. More specifically, poorer rehabilitative outcomes will be predicted by low memory and verbal fluency sub scores.
4) Clients who were reported by staff to require additional input to achieve rehab goals will have lower ACE-R total, verbal fluency and memory scores.

Plan of Investigation

Participants

Patients in the Physically Disabled Rehabilitation Unit (PDRU) at the Southern General Hospital in Glasgow will be invited to participate in this study and they will be aged 16 or over. Looking at data retrospectively for this time period, it seems that a conservative estimate would suggest that at least 80 new patients would be admitted over the proposed time scale of six months. Further exploration of existing data suggests that these clients would fall equally in to one of three categories: no cognitive impairment, cognitive impairment which does not affect daily functioning, and cognitive impairment which does affect daily functioning. This means that the sample involved in the study should be representative of the clients normally admitted to such a unit. As little will be asked of the patients that is over and above the normal standard of care it is expected that there will be a high recruitment rate and of the 80 clients admitted, an estimated 60 participants will consent to take part. It is also expected that there would be a high retention rate.

Inclusion and exclusion criteria

All PDRU patients will be asked to partake in this study unless the degree of cognitive impairment means they are unable to fully give consent. If there are any queries in regards to a persons capacity to consent it is possible to seek advice and assessment from the Rehabilitative Consultants based in the unit. In the instance where medical staff identify clients who are using substances in the unit or where they believe a client may be under the influence of substances upon their return from a weekend pass from the unit then their data will be removed from the study. In addition, any known substance users identified through case notes will be excluded. Speech and Language colleagues will be asked to identify any clients with profound language disorders or those who are not fluent in English and they too will be excluded from the study on the basis that the ACE-R can place a certain level of demands on verbal skills. Case note reviews will also allow any clients with a formal learning disability to be identified and they will also be excluded.

Recruitment procedure

Researchers will be based at the PDRU and every consecutively admitted patient over a 6 month period will be approached by one of the researchers to participate in the study. The researchers will be working as part of the clinical team and as such will have access to patient information as part of routine clinical practice for the unit. Whichever researcher approaches, consents and assesses the patient for the project will not be the person who sees them clinically during their stay. This serves as dual purpose; to maintain blinding for the study and to minimise any role blurring for the patient between research and clinical input from the team. If the participants meet the inclusion criteria, then they will be presented with a patient information sheet that details the piece of research they are being asked to take part in. If they agree then they will be asked to give their consent and the client will be assessed using the ACE-R before their first goal planning meeting, which usually takes place 1-2 weeks after admission date.

Recruitment will begin in October 2010. The median and mean length of stay is 36 and 48.1 days respectively. With the necessary outliers removed, the 25^{th} to 75^{th} percentile range is 22 – 59 days. Given this data recruitment will stop in April to allow 60 days to collect any follow up data and allow for a full data set to be gathered for analysis in June.

Measures

Participants will be assessed using the following measures:

Cognitive Functioning:	Addenbrooke's Cognitive Examination – Revised (ACE-R; Mioshi et al 2006)
Mood State:	Hospital Anxiety and Depression Questionnaire (HADS; Zigmond & Snaith (1983)
Overall functioning:	Functional Independence Measure (FIM; Turner Stokes et al (1999)
Rehabilitation needs:	Additional Rehabilitation Needs Questionnaire (see attached). The multi-disciplinary team will be asked to identify patients for whom standard clinical practice needed to be modified in some way, because of cognitive impairment. There are two versions, one to be completed at the beginning and the other at the end of rehab.

Data regarding other factors which may influence outcome will also be collected e.g. age, diagnosis, co-morbid conditions, continence, current medications, substance use, education, occupation and social deprivation (as indicated by postcode using national statistics (http://www.scotland.gov.uk/Topics/Statistics/SIMD/SIMDPostocedLookup).

Design

This is a prospective correlational study of the relationship between baseline measures and rehabilitation outcome. The primary baseline measures will comprise the ACE-R, initial FIM score and a brief questionnaire eliciting the multi-disciplinary team's perception of the client's cognition and prediction of additional input. The outcome measures will include a record of any additional input and FIM score at discharge. Staff members have been consulted to establish what steps would be taken by clinical staff if they felt clients required

additional input (see appendix 1). Rehabilitation Medicine Consultants suggested non-psychological factors that might affect outcome, as listed in the Measures section above

In order to minimise bias, both Susan Lennie and Dr Breda Cullen will be involved in data collection with each one blind to either the ACE-R scores or the teams predictions and actual outcomes. This is necessary so there is no possibility that researchers can influence clinical staff members predictions on the Additional Rehabilitation Needs Questionnaire.

Procedure

The first researcher will complete the ACE-R and the HADS within 2 weeks of admission with each client who agrees to participate in the study. Alongside this, the second researcher, who will be blind to the ACE-R score, will ask clinical staff members at the first goal planning meeting (approx 10 days in to the clients stay at the PDRU) to complete the first part of the Additional Rehabilitation Needs Questionnaire. At this point clinical staff will be asked whether the client will require support above and beyond what would be normally expected with someone who has a similar physical disability and if so, is this due to a cognitive impairment. They will also be asked to specify what adaptations or additional needs they think the client will require.

The second researcher will then ask staff members at the clients discharge meeting (approx 6 weeks post admission) to complete the second part of the Additional Rehabilitation Needs Questionnaire and state whether their predictions with regard to additional needs were accurate, and if so, were they due to the client's cognitive impairment or other factors. Clinical staff at point of admission and again at discharge routinely administers the FIM. These scores will be available to the researchers. In line with normal clinical practice, each clients MMSE score and HADS score will be reported in their case notes. Background data will be obtained from the medical case notes.

Settings and Equipment

The study will be based within a Physical Disability Rehabilitation Unit at the Southern General Hospital in Glasgow. This is a regional, neuro-rehabilitation service receiving a large number of admissions from Greater Glasgow and Clyde, Lanarkshire and the Isles. A multidisciplinary team including Medical staff, Occupational Therapy, Physiotherapy, Speech & Language and Psychology staff are employed within the unit and adopt a person

centred, goal orientated approach. It is a 30-bedded unit where patients stay for an average of 6 weeks. All clients will have some form of physical disability, most commonly as a result of a neurological condition e.g. stroke, MS, ABI.

Copies of the ACE-R are readily accessible to the researchers and questionnaires will be provided to the staff (see appendix 2). Confidential material (such as the ACE-R) will be locked in a filing cabinet on NHS Greater Glasgow & Clyde grounds.

Power Calculation

Available literature which looks at the use of cognitive screening tools, cognition as a predictor of rehabilitation and those who employ a similar design (O'Neill et al 2009, Cullen et al 2008, Lenze et al 2004, Larner et al 2003, Barak et al 2002) report medium to large effect sizes (f^2= 0.27-4.26) and provide evidence to suggest that a large portion of variance is explained by cognitive variables (24% - 81%). Preliminary studies looking at the ACE-R in different clinical populations (Gaber, 2008) suggest that it is highly sensitive in distinguishing those with and without cognitive impairment. We would therefore predict at least a medium effect size in our study and this would be required for the ACE-R to have real clinical utility.

Each factor being measured will yield individual scores (e.g. HADS score, ACE-R Score). Overall, there will be 9 primary predictor variables, as follows: ACE-R total score, ACE-R sub-scores x 5, HADS anxiety score, HADS depression score, and baseline FIM score. Other baseline factors will be considered as potential co-variates (e.g. social deprivation index). It is expected that due to inter correlations and non significance of certain variables, it will be possible to use correlation matrices and comparisons of means to reduce the number of variables to be included in the regression analyses.

G*Power, a general power analysis program, was used to conduct a power calculation for regression modelling, with power set at 0.80 and alpha set at 0.05. Aside from the effect size based method used by G*Power, there are other traditional rules of thumb (e.g. Green, 1981) which have been used to obtain more conservative power estimates for regression modelling. In recognition of this, the present study will use the more conservative estimate produced by

G*Power. It is therefore expected that in a sample size of 60 and using an f^2 value of 0.27, 8 predictor variables can be included in the regression models to achieve a power of 0.80.

Data Analysis

Descriptive statistics will be provided and based on the normality of the data an array of parametric or non parametric statistics will be conducted. Frequency counts will allow the ratio of male and females to be established and mean ages of the participants will be calculated. For baseline data, correlations will be carried out between ACE-R scores and baseline FIM score. To test the hypotheses, the following statistics will be carried out:

Hypothesis 1

For outcome data, correlations will be carried out between baseline ACE-R scores and FIM change scores (FIM change score will be calculated by subtracting the FIM discharge score with the FIM admission score). If more than one variable is thought to be predictive of outcome (e.g. ACE-R score plus mood), then multivariate statistics (e.g. regression or ANOVA) can be carried out.

Hypothesis 2

The sample will be grouped into those with who needed additional input and those who did not, so that a comparison of mean ACE-R scores can be calculated between these groups (e.g. via T-tests). It may also be of interest to investigate the accuracy of the staff member's prediction by carrying out a Chi Square analyses between baseline and outcome data. If more than one variable is thought to influence the need for extra support then multivariate statistics (e.g. logistic regression or ANOVA) can be carried out.

A ROC analysis will make it possible to establish what the suggested cut off score on the ACE-R should be in order to identify clients who may require additional support to achieve rehab goals. The Predictive Analytics Software 18 (PASW – 18) package will used for all analysis.

Health and Safety Issues

There are no foreseeable safety issues in regards to either researcher or participants. The PDRU has procedures in place to ensure staff safety. Every assessment will be carried within normal working hours (8am – 5pm) on week days only. This ensures that the ward is fully staffed and the researcher will not be on the ward on their own. Appropriate rooms equipped with panic and nurses buttons within the unit will be used for all assessments. If, prior to assessment, a client is known to be aggressive then it is possible to have a second staff member sit in on the assessment. This is also helpful for client safety as in the event they do become distressed or aggressive medical professionals can ensure that they do not unsafely try and remove themselves from their wheel chair for example.

Ethical Issues and data protection

By taking part in the study, clients will not be denied any aspect of their normal care. As two researchers are involved in the study, clients may also undergo a more comprehensive assessment of cognition by the team psychologist (blind to ACE-R score) as part of routine assessment procedures. This also allows for psychological input to continue at the team planning and discharge meetings without biasing the study. Use of the ACE-R ensures that clients are not engaging in extensive neuropsychological testing, which some may find taxing and administration of the HADS and FIM is normal clinical practice. It may be that the HADS identifies individuals with possible depression or researchers may identify clients who appear distressed or depressed. In such an instance, it is possible to refer the client to the team psychologist for assessment and intervention. Information sheets will be provided and written consent obtained from all participants. If clients are unable to give written consent, verbal consent will be obtained instead with a witness present who will sign to confirm that this protocol was followed. If any participants wish to withdraw their consent then any existing data obtained regarding them will be safely discarded and not included in the analysis. There are also means to establish a person's ability to consent to the study should there be a query regarding capacity.

The scores from the measures used will be stored on a database with all identifiers removed and a coding system employed. In the interest of maintaining the blinding of the study each researchers findings will not be made available to the other until the end of data collection. All data will be stored on an NHS Greater Glasgow & Clyde computer or an encrypted laptop.

Financial Implications

Costs for this study should be minimal. Copies of the ACE-R are readily available meaning that the only additional cost would be that of the paper needed for this and for the staff questionnaires.

Timescale

September 2011 or before	Application to NHS Greater Glasgow & Clyde ethics committee
October 2011 – May 2012	Data collection
June 2012 – July 2012	Data Analysis and write up.

Practical application

Findings from this study will be used to inform service development and increase the evidence base that practitioners can draw upon to support their practice. If the ACE-R is found to be a useful cognitive screening tool for this client group then it will help identify those who could benefit from additional input whilst making efficient use of the limited psychological resources. It is also hoped that the findings can be generalised to similar rehabilitation units who operate with an MDT approach and employ a goal setting system.

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