Neuropsychology

The BCOS Cognitive Profile Screen: Utility and Predictive Value For Stroke

--Manuscript Draft--

Manuscript Number:	NEU-2014-1407R1
Full Title:	The BCOS Cognitive Profile Screen: Utility and Predictive Value For Stroke
Article Type:	Data-Driven Article
Abstract:	Objective: We examined the utility of the BCoS screen in discriminating cognitive profiles and recovery of function across stroke survivors. BCoS was designed for stroke-specific problems across 5 cognitive domains: controlled and spatial attention, language, memory, number processing and praxis. Methods: Based on specific inclusion criteria, this cross-section observational study analysed cognitive profiles of 657 sub-acute stroke patients, 331 of them reassessed at 9 months. Impairments on 32 measures were evaluated by comparison to 100 matched healthy controls. Measures of affect, apathy, and activities of daily living were also taken. Between-subject group comparisons of mean performance scores and impairment rates, as well as within-subject examination of impairment rates over time were conducted. Logistic regressions and general linear modelling were used for multivariate analysis of domain level effects on outcomes. Results: Individuals with repeated stroke experienced significantly less cognitive recovery at 9 months than those with a first stroke (OR=6.18) despite similar initial level of cognitive performance. Individuals with left hemisphere lesions performed more poorly than those with right hemisphere lesions but both groups showed similar extent of recovery at 9 months (OR=0.62). BCoS also revealed lesion-side specific deficits as well as common areas of persistent problems. Functional outcome at 9 months correlated with domain-level deficits in controlled attention (Lambda=0.959,p=0.036), spatial attention (Lambda=0.920,p=0.001) and praxis (Lambda=0.919,p=0.001), over and above initial dependency and concurrent levels of affect and apathy. Conclusion: The paper demonstrated how BCoS can identify differential cognitive profiles across patient groups. This can potentially help predict outcomes and inform rehabilitation.
Keywords:	stroke, cognitive screening, aphasia, neglect, attention
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Author Comments:	This is a report of a novel neuropsychology screen tailored for stroke survivors and

	stroke-specific cognitive deficits. We validate the screen and then use it to predict functional recovery. We demonstrate differences in recovery for patients with first and second stroke, even when matched for their initial deficit. We also show how the cognitive profile for a patient, across several domains, helps to predict outcome.
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Opposed Reviewers:	Ziad Nasreddine, MD Adjoint Professor, Univresity of Sherbrooke and McGill ziad.nasreddine@cedra.ca Has conflict of interest with another test.
Response to Reviewers:	Response to reviewers (comments are copied below and corresponding responses are followed by "-") Editor's comments 1) The imaging information was used as a method for inclusion and nothing else? -For the purpose of this paper, it is indeed used for inclusion of patients and categorisation of left lesion vs right lesion groups. 2) Was the AES self or informant rated? -It was self rated. We have added this to the text. 3) The use of "motivation" in the context of AES findings. -Thanks for your comment, we agree that we should adhere to the use of "apathy" to avoid confusion. We have amended the wordings accordingly. 4) Patient effort to engage. -We have not formally measured the patients' effort in the assessment and therefore have included this as a limitation of the current study. 5) Patient's ability to sustain attention for 30 mins as inclusion criteria. -This was based on clinical judgement of the treatment team in the research site whom we checked with as well as assessment by the researcher during the BCoS testing. Reviewer 1's comments Abstract 1) 2nd sentence: 5 'COGNITIVE?' domains -Added, thanks 2) Talk about 'sub-acute' stroke – what does this mean exactly? How much time has passed since the stroke? 657 analysed, 331 reassessed at 9 months – half dropped out? Why so many. Or just a subgroup tested at 9 months? -Due to the word limit of the abstract, these are addressed in the main text.

3) Repetition of the word ‘conducted’, ‘conduct’ – tighten writing
-Thanks, amended.

4) Results – ‘individuals with repeated stroke’’ – how many and how often repeated stroke x2 or more? LH lesions performed more poorly – on all cognitive domains? Or only on heavily language-based tasks? What do you mean when you say ‘similar extent of recovery’ – how assessed? What does this sentence mean ‘BCoS also revealed lesion-side specific deficits as well as common areas of persistent problems’ – can you be more specific?
-The abstract represents a summary of the key points which are explained and described in more details in the text. We have endeavoured to cover all the main points with all the allowable word counts. We have made sure that all your queries are covered in the main text.
All details are given in the section: Left vs. right unilateral lesion effects in first stroke patients. For example:
i) Individuals with LH lesions performed more poorly – main text: “Overall the LHD group had more cognitive impairments than the RHD group, completing fewer BCoS tasks ($p<0.000$) and showing a significantly worse performance in all cognitive domains with the exception of spatial attention (Table 2).”
They performed more poorly overall, not only on language-based tasks. As the BCoS tasks were designed to reduce language confounds on non-language tasks, so the profile reliably reflected the more severe deficits across domains.

ii) Similar extent of recovery – main text: “The LHD and RHD groups showed comparable extents of recovery (Table 3) (significant reduction of impairment in 4/32 measures for LHD and 6/32 measures for RHD patients).”

iii) ‘lesion-side specific deficits as well as common areas of persistent problems’ were also explained with extended text in the same section of the paper.

5) Conclusions – I find this vague – can you not be more specific?
-Thanks, the conclusion is now changed to reflect the main findings.

Introduction
1)Pg 2 middle – what do you mean by ‘supported by evidence of clustered patterns of brain activity’?
-We have re-worded the text here to make it clearer.

2) Pg 3 top – mention reliabity and validity of BCoS but then send the reader to other papers – can you please also give in this paper? And what the values were based on – patients? Controls? And what were the group sizes?
-We will stand by the editor’s guidance on this point. However this is a paper about the use of the BCoS for account for differences between patient groups and for predicting outcome; it is not a validation paper. Moreover, in the BCoS manual there are 12 large tables covering each of the 22 tasks covering:
Test-retest reliability (20 controls, 20 patients)
Inter-rater reliability (20 patients)
Construct validity (595 patients)
Convergent and divergent validity with a range of standardised assessment tasks against the BCoS tasks (upto 28 patients)
Correlations with measures of general intelligence (20 patients)

-We are not able to give reasonable summary of this volume of information without distracting from the scope of the paper. We hope this is acceptable to you.

3) Pg 3 – a summary of the BCoS would be useful here for readers who haven’t read the previous papers and also because the current study is based on this screen- a new screen for many I think…What makes it different than what is already available? Why is it a useful addition to Stroke research?
-The summary of the BCoS structure and brief descriptions of each of the tests are now listed in the Appendix and the difference BCoS made to stroke research and clinical assessment are listed in the introduction:
These include (a) making tests ‘aphasia and neglect’ friendly, when language and

spatial attention are not measured (to maximise patient inclusion); (b) including assessments for neglect, reading, apraxia and number processing which, though common after a stroke, are not measured in other screening tools; and (c) incorporating time-efficient test designs where single tests measure more than one cognitive process.

4) Pg 3 – again – what do you mean by subacute?
-Thanks, we acknowledge that there are different views about what “subacute stroke” constitutes. In the current study, we define subacute stroke being from 1 day to a month/weeks post stroke. This is reflected in our mean time post stroke in all groups.

5) Pg 3 – hypothesis 3 – independently of (I)ADL and/or depression?
-Yes, we have controlled for initial Barthel score, Anxiety and Depression scores as well as Apathy scores in our analyses.

Methods
Participants
1) Recruited between Nov 2006 and Jan 2011 from 12 different hospitals – not worried about cohort effects and/or site/context effects? (and have you compared data between sites or not and was an identical protocol/procedure/instructions used? What were they)?
-Analysis by site was not conducted. All examiners participated in a full day’s training, their first ten assessment records examined and given continuous access to the research team’s support for administration and scoring queries.

2) What do you mean by ‘medically stable’ –
-This was determined by the case medical officer whom we checked with as part of the screening process for participants.

3) Which ‘assessment by the clinical team’ – based on which criteria?
-It was based on the clinical judgement by the treatment team.

4) How did you determine if someone was ‘unable to concentrate for 35 minutes’?
-Participants were included initially based on judgement from the clinical team. Moreover, if the BCoS had to be aborted in less than 35 minutes due to individual’s fatigue or unable to hold concentration on the task, as clinically determined by the researcher, the case was also excluded.

5) How and which premorbid conditions were assessed? What about medication?
-Premorbid conditions were assessed by case notes.

6) How often were CT or MRI scans available?
-CT/MRI were available to the majority of the participants as the routine stroke care guideline in the region.

7) Why only 50% of participants followed up at 9 months? High drop-out?
-The high drop-out rate in stroke research is not unique to the current study. In a similar study by Nys et al (2005) published in Neurology, 49% participants were followed up at 6 to 10 months. We have now added Figure 1 to give details of reasons for participants not followed up in the study.

8) Plus, I’d like to know more about the participants – how were neurological/psychological problems assessed? Which medications? How many excluded? Any baseline cognitive screen done (e.g. MMSE or something else)? How do you know none had Mild Cognitive Impairment or signs of early dementia?
-Due to the resources and the focus of the study (the trialling of a new neuropsychological assessment), detailed neurological assessment was not conducted by the research team. All significant background information were obtained by the medical notes taken by the stroke team. BCoS was the cognitive screen used.

Cognitive screen measures
1) Quite hard to follow and again pointed to a website. Should this paper not ‘stand alone’
-Thanks, we have given a brief description of the assessment in the Appendix, the

	detailed descriptions of each of the 22 tasks would be outside of the scope of the current paper. 2) Norms based on 100 controls divided into 3 age groups - 30 per group? And sex/education? Ns even smaller? Or have I not understood this correctly? -The norm profile followed the 2001 census' finding of the proportion distribution of education levels of each gender group within each age group. Therefore, each participant's score was compared with their own age group (N=33 or 34 in each age group) which was representative, i.e. has similar education/gender distribution as the general population. Statistical analysis 1) Unimpaired vs impaired – how was this done? Z scores, sds? Compared to what group? -Impairment was defined as below 5th percentile cut off of the control distribution of scores for the same task (please see section under "Cognitive Screen Measures"). Results 1) Previous strokes – 2 or more? How long ago? Any attempt to cluster these 202 people? -Thanks, we have added "(two or more)" to clarify. Participants were divided only based on whether they had a previous stroke (multiple lesions from potentially different infarction/haemorrhagic origins at two or more different time points) or not. 2) Part 1 – why were patients with a first stroke tested later than those with a repeated stroke? -Thanks, we have added a sentence to clarify what it meant: that there was significant difference between the group in the measure "time post stroke" on testing. 3) What about effects of life events/changes between first and second testing – were these taken into account or not? -The presence of significant medical events occurred between the two test sessions was checked on follow up. Those who had events/medical conditions that affected the reliability of the assessment were excluded. See figure 1. Discussion: 1) Better re: organization. One question – should statistical values appear in the discussion? -Journals differ in their policy. However our judgement is that the extra statistics in the Discussion reflect points only raised at that juncture and it would be distracting to have them elsewhere. We await the editor's judgement. 2) BCoS takes an hour to complete say the authors – question: will this not put neurologists off using it? Or is it aimed at neuropsychologists? -BCoS is currently used mainly by occupational therapists or psychologists in stroke teams. 3) I miss a final 'take home message'. The paper ends with limitations…As I said in earlier comments (Introduction): Why is the BCoS a useful addition to Stroke research/practice? -Many thanks, we have added a short conclusion. Tables. 1) Table 1 – LH/RH and FU/No FU only given for first ever strokes. Not possible for repeated stroke patients? -The same analysis was conducted for the repeated stroke group with no significance in all factors at p=0.05 level. We have added a Table 2 to detail the findings Reviewer 2's comments -Many thanks. We have added the widely used but longer RBANS cognitive assessment to the introduction, as well as our comments at the discussion section of the paper highlighting potential future research and limitations in comparing the BCoS to the MMSE/MoCA.

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11.9.14

Dear Editor

The BCOS Cognitive Profile Screen: Utility and Predictive Value For Stroke

We are submitting for publication the revised version of the above paper in response to your and the reviewers' comments. The paper focuses on the utility of a new screen for cognitive deficits that has been designed specifically to detect important clinical problems after stroke whilst being uncontaminated by problems in language (aphasia) and attention (neglect). We report three new sets of results:

1. That patients with a second stroke show a less good recovery than individuals who have survived their first stroke, even when participants are matched for initial cognitive performance;

2. That there are pattern of lesion-side specific deficits, with left hemisphere lesioned patients having greater problems than patients with right hemisphere lesions; and

3. That cross-domain problems in attention and executive function can contribute significantly to outcome when combined with a deficit in a core cognitive component.

In addition to demonstrating the application of this new screening instrument, we believe the novel findings on effects of a second lesion, and on the extra contributions of cross-domain deficits, make new contributions to the field that have both theoretical and practical importance.

Yours sincerely

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The BCOS Cognitive Profile Screen: Utility and Predictive Value For Stroke

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Author note

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Nele Demeyere, M Jane Riddoch and Glyn W Humphreys are now at the Department of Psychology, University of Oxford, UK; Dawn Francis is now at Birmingham, UK; Jon Williamson and Viba Kumar are now at Mental Health Services for Older People, Birmingham and Solihull Mental Health Foundation Trust, Birmingham UK; Marietta Remoundou is now at I.C.P.S., College of Humanistic Studies, Greece; Alex Balani is now at the Department of Psychology, Edge Hill University, UK; Lara Harris is now at the Institute of Psychiatry, Kings College London, UK; Dana Samson is now at Institut de Recherché en Sciences Psychologiques, Université Catholique de Louvain, Belgium

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Bisiker, Ms Emma Clayton, Dr Louise Price, Dr John Chambers, Dr E Smith, Dr David Sandler, Dr Ruth Telfer, Dr Antony Oke, Mrs Janine Gall, and Dr Francis Vaz.

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ABSTRACT

Objective: We examined the utility of the BCoS screen in discriminating cognitive profiles and recovery of function across stroke survivors. BCoS was designed for stroke-specific problems across 5 cognitive domains: controlled and spatial attention, language, memory, number processing and praxis. *Methods:* Based on specific inclusion criteria, this cross-section observational study analysed cognitive profiles of 657 sub-acute stroke patients, 331 of them reassessed at 9 months. Impairments on 32 measures were evaluated by comparison to 100 matched healthy controls. Measures of affect, apathy, and activities of daily living were also taken. Between-subject group comparisons of mean performance scores and impairment rates, as well as within-subject examination of impairment rates over time were conducted. Logistic regressions and general linear modelling were used for multivariate analysis of domain level effects on outcomes. *Results:* Individuals with repeated stroke experienced significantly less cognitive recovery at 9 months than those with a first stroke (OR=6.18) despite similar initial level of cognitive performance. Individuals with left hemisphere lesions performed more poorly than those with right hemisphere lesions but both groups showed similar extent of recovery at 9 months (OR=0.62). BCoS also revealed lesion-side specific deficits as well as common areas of persistent problems. Functional outcome at 9 months correlated with domain-level deficits in controlled attention (Lambda=0.959, p=0.036), spatial attention (Lambda=0.920, p=0.001) and praxis (Lambda=0.919, p=0.001), over and above initial dependency and concurrent levels of affect and apathy. *Conclusion*: The paper demonstrated how BCoS can identify differential cognitive profiles across patient groups. This can potentially help predict outcomes and inform rehabilitation.

Key words: stroke, cognitive screening, aphasia, neglect, attention

Cognitive deficits are prevalent at the acute stage of stroke (Jaillard, Naegele, Trabucco-Miguel, LeBas, & Hommel, 2009). They interfere with the potential benefits of rehabilitation and impact on recovery (Ballard et al., 2003; Barker-Collo & Feigin, 2006; de Haan, Nys, & van Zandvoort, 2006; Donovan et al., 2008; Edwards et al., 2006; Fure, Wyller, Engedal, & Thommessen, 2006; Narasimhalu et al., 2009; Nys et al., 2006; Pohjasvaara et al., 2000; Stephens et al., 2005; van Zandvoort, Kessels, Nys, de Haan, & Kappelle, 2005; Zinn et al., 2004). Moreover, cognitive deficits are associated with a poorer quality of life (Moon, Kim, Kim, Won, & Kim, 2004; Nichols-Larsen, Clark, Zeringue, Greenspan, & Blanton, 2005; Paul et al., 2005) and depression (Kauhanen, 1999; Nys et al., 2006).

Neuropsychological assessments have typically divided cognitive functions into several domains (e.g., attention, language, memory)(Heilman & Valenstein, 2012) and this division of cognition into different domains is supported by evidence from functional brain imaging in normal participants, where brain activity clusters into different domains for language, memory, attention and so forth (Laird et al., 2011). Prior studies show that the co-occurrence of impairments in two or more domain functions, such as impaired executive functions or sustained attention alongside language impairments/neglect, may adversely affect the rehabilitation outcome of the primary function i.e. in language (Lambon-Ralph, Snell, Fillingham, Conroy, & Sage, 2010) or visual attention (Malhotra et al., 2005; Robertson, 2001). Therefore, assessment needs to cover not only the primary symptoms but also the contributing, co-occurring impairments.

Whilst early cognitive screening for stroke is well recognised (NICE, 2008), the existing screening tools (e.g. the MMSE (Folstein, Folstein, & McHugh, 1975), the MoCA (Nasreddine et al., 2005), the ACE-III (Hsieh, Schubert, Hoon, Mioshi, &

Hodges, 2013), the RBANS (Randolph, Tierney, Mohr, & Chase, 1998) are not stroke specific. As a consequence such screens provide no evaluation of common post stroke deficits such as spatial neglect (Gottesman, 2009) and apraxia (Bickerton et al., 2012); nor do their testing procedures minimise the contaminating effects of aphasia or neglect on performance of non-language/visuospatial tasks (e.g. memory tests). The Birmingham Cognitive Screen (BCoS)(Humphreys, Bickerton, Samson, & Riddoch, 2012) aims to address these problems by providing an overarching cognitive screen (covering multiple domains of cognition) specifically designed to be sensitive to the cognitive profile of stroke patients.

The principles of the design of the BCoS and data on its validity and reliability are published elsewhere (Bickerton et al., 2012; Bickerton, Samson, Williamson, & Humphreys, 2011; Humphreys et al., 2012). The principles include (a) making tests 'aphasia and neglect' friendly, when language and spatial attention are not measured (to maximise patient inclusion); (b) including assessments for neglect, reading, apraxia and number processing which, though common after a stroke (Bickerton et al., 2012; Bickerton et al., 2011; Bowen, Lincoln, & Dewey, 2002), are not measured in screening tools derived for dementia; and (c) incorporating time-efficient test designs where single tests measure more than one cognitive process. The BCoS also has a unique reporting system in which the 'cognitive profile' of the patients across the tests is presented in a form that can be grasped 'at a glance' by clinical teams (see the Appendix).

The current paper reports data from a large-scale trial which, for the first time, assesses the utility and functional predictive value of this stroke-designed screen across a population of sub-acute stroke patients. Specifically, we investigate if the BCoS (a) reveals differential initial profiles of cognition between individuals with

first stroke and repeated stroke; as well as between individuals with left hemisphere damage (LHD) and right hemisphere damage (RHD); (b) can predict recovery patterns in patients over and above the effects of affect and initial dependency level; and (c) whether the *cognitive profile* of performance emphasized by the BCoS (taking into account variation in several domains of cognition) can help predict cognitive and functional performance at nine months follow up.

Method

Participants

Stroke survivors were recruited between Nov 2006 and Jan 2011 from 12 hospitals in the West Midlands as a part of a UK cognitive screen trial (the Birmingham University Cognitive Screen, www.bucs.bham.ac.uk). Stroke survivors were recruited if medically stable, within 3-months of their latest stroke and able to give informed consent. Diagnosis of a stroke was based on the assessment by the clinical team. Exclusion criteria were 1) insufficient understanding of English; 2) inability to concentrate for 35 minutes based on clinical judgement by the treatment team and the researcher; 3) premorbid conditions affecting cognition (e.g., dementia) as shown in case notes.

Lesion information from hospital-based CT or MRI scans (where available as part of the routine stroke care in the region) was obtained. Patients were excluded if there was no observable focal damage or if image quality was poor. About 50% of the participants took part in a 9-months follow up assessment (see figure 1 for the flow chart of the patient cohort at baseline and follow-up). Patients who completed fewer than 15/22 tasks were excluded (10%), to enable us to have relatively complete

datasets for each patient. The most common reasons given for a failure to complete all tasks were 1) fatigue, 2) a lack of time. For the analyses related to the lesion side, only patients with an identified unilateral lesion were included. Informed consent was obtained according to the approved ethics protocols of the UK National Research Ethics Committee. Data were collected by examiners (psychologists, occupational therapists or stroke researchers) who all attended a full day's training, were assessed and supported by the University team under the supervision of the chief investigator (GWH).

Cognitive Screen Measures

BCoS assesses five cognitive domains: attention and executive function, language, memory, number and praxis. Finer-grained distinctions can also be drawn within some of the domains including between (i) spatial attention (neglect, extinction) and controlled attention (executive functions, sustained attention), (ii) spoken and written language, (iii) immediate and delayed memory, and (iv) limb apraxia and constructional apraxia. Further descriptions of the tests are provided elsewhere (Humphreys et al., 2012) and at www.cognitionmatters.org.uk. There are 32 different sub-measures derived from 22 tasks (see the Appendix for brief descriptions of the 22 BCoS tasks). Age-group (50-64, 65-74, 75 or above) specific cut offs (at 5^{th} percentile) for each test were established from a hundred healthy controls stratified following the 2001 UK population census age x sex x education level distribution.

Affective and Functional/Dependency Measures

At the initial assessment, Affect was measured by the Hospital Anxiety and Depression scale (Snaith & Zigmond, 1994)(HADS) and dependency level was

measured by the Barthel index(Mahoney & Barthel, 1965). At 9 months follow-up, the above were repeated along with the Apathy Evaluation scale – self rated (Marin, Biedrzycki, & Firinciogullari, 1991)(AES) for apathy and the Nottingham Extended ADL scale (Nouri & Lincoln, 1987)(NEADL) for participation in community ADL.

Statistical Analysis

For the comparison of demographic and background details between sub-groups of interest, two tailed Mann-Whitney U tests were used for continuous non-normally distributed variables, T tests were used to compare continuous data and, chi-square was used to compare categorical data. For the comparisons of cognitive profiles at the cognitive domain level, MANOVAs were performed on all the scores of the subtasks that were part of the same cognitive domain. Subsequent individual task level analyses used Mann-Whitney U tests for raw scores and chi-square for diagnosis category (unimpaired versus impaired). NcNemar tests were used to compare rates of impairment on each task individually at the initial and follow-up assessments. Bonferroni corrections were made to all multiple comparisons. Linear regressions were used to model effects on functional outcomes while controlling for other confounding factors and GLM was used to conduct multivariate analysis of domain level effects on outcomes.

Results

657 participants were included in the analyses. 90% of the patients tested at the initial sub-acute stage were able to complete >75% of the tests. 455 (69%) were survivors of first stroke and 202 (31%) had had a previous stroke (two or more). Table 1 and 2 show the demographic and health measures details of the participants, comparing across groupings of interest. We assessed whether stroke history (first or

repeated stroke) and unilateral lesion side (left hemisphere or right hemisphere) affected cognitive ability and recovery (BCoS performance) after stroke (Part 1). We then evaluated whether longer-term functional outcome for patients could be predicted from their BCoS scores (Part 2), and whether the *cognitive profile* provided by the screen can enhance predictions of cognitive and functional performance (Part 3).

Part 1: Stroke Factors Linked to Cognitive Outcomes

First vs. repeated stroke effects. There was no difference in age, gender and education across patients with their first or a repeated stroke. There was significant different in "time post stroke" on assessment. Patients who had a first stroke were tested later than those who had a repeated stroke (mean difference = 6 days, $p<0.001$). Numerically, there was a trend for higher levels of depression in repeated compared to first stroke patients but this did not reach the corrected level of significance. No other significant group difference was found.

Overall, the cognitive performance of the first and repeat stroke groups was very similar at baseline. Both groups completed an equal number of BCoS tasks (Table 3) and there were no group differences at either the cognitive domain level (all $p>0.01$, i.e. above the corrected level of significance 0.008, Table 3) or the task level (raw scores all $p>0.002$, Table 3; for the proportion of patients impaired: all $p>0.002$, Table 4).

Significant improvement (based on a reduction in the number of patients diagnosed as impaired) (Table 4) at follow-up was more frequent in the first stroke group (on average improving on 15/32 of the measures) compared to the repeated stroke group (improvements on only 4/32 measures; $\chi^2=9.06$, $p=0.003$, OR=6.18). This differential improvement did not reflect underlying contrasts in age, gender,

education and initial Barthel score, none of which differed. Patients with multiple strokes tended to be more depressed, which may have reduced their motivation to engage in rehabilitation. However we found no differences in the extent of task recovery between depressed and non-depressed patients with multiple strokes ($t(86)=-0.92$, $p=0.362$). The data also revealed instances of persistent deficits across both groups for spatial neglect (cancellation task accuracy and asymmetry) and verbal memory (immediate and delayed verbal recall and recognition measures). Within the praxis domain, gesture production and recognition deficits were more persistent than other impairments (though note the relatively lower initial impairment rates for gesture production and recognition).

Left vs. right unilateral lesion effects in first stroke patients. Grouping by unilateral brain lesion side revealed no differences in the demographic details, the initial functional performance and level of affect (anxiety, depression) across the groups (Table 1).

Overall the LHD group had more cognitive impairments than the RHD group, completing fewer BCoS tasks ($p<0.000$) and showing a significantly worse performance in all cognitive domains with the exception of spatial attention (Table 3). In the spatial attention domain, the RHD patients performed more poorly than the LHD individuals on the cancellation task (overall scores and lateralized error scores) as well as on the left visual and tactile extinction tasks (all $p<=0.001$); individuals with LHD were more impaired in the right tactile extinction task ($p<0.001$).

The LHD and RHD groups showed comparable extents of recovery (Table 4) (significant reduction of impairment in 4/32 measures for LHD and 6/32 measures for RHD patients). However, the LHD and RHD groups did differ in which specific tasks/domains improved (Table 4). Some of these differential patterns of recovery

can be explained by the higher initial rates of impairment in some tasks leading to a higher probability of performance improvement (e.g. left visual extinction for RHD vs. LHD patients). However, this was not the case for the sentence construction task, the rule finding and switching task and the MOT task, where in each instance both groups started with similar rates of impairment but only the RHD group showed significant recovery; also the RHD group was less impaired initially at imitation but showed greater improvement.

Part 2: Cognitive Predictors of Functional Recovery in First Stroke Patients

There was a trend for follow-up patients to have more years in education (mean difference 0.6, p=0.022) and to be more depressed than those not followed up (p=0.017)(not significant corrected)(Table 2). No other significant differences were found on the demographic, initial functional and affective characteristics of the groups. Concerning the initial cognitive profile, no significant difference was found between the follow-up and non-follow-up groups.

Using as predictors the overall cognitive impairment at initial assessment (here the proportion of tasks impaired), and controlling for the initial Barthel score, follow-up HADS scores and follow-up apathy scores, the proportion of BCoS tasks impaired was a significant predicting factor for the NEADL score (B(SE)=-3.47(1.22), beta=-0.173, p=0.005) (Table 5).

We then used as a predictor a domain level diagnosis: “impaired” when performance on any one task was impaired, or not completed within a domain, versus “not impaired” when performance was unimpaired on all tasks within a domain (Table 6). Three domains were significant predictors of the NEADL score: spatial attention (Lambda=0.920, p=0.001), controlled attention (Lambda=0.959, p=0.036)

and praxis (Lambda=0.919, p=0.001). No predictors were found for the follow up Barthel scores.

Part 3: The Importance of Co-occurring Deficits

Long-term performance in the important domains of language and spatial attention could be better predicted when tests sensitive to cross-domain processes (sustained attention, executive function) were taken into consideration. For example, picture naming and sentence construction at 9 months were better predicted by taking the initial auditory attention score (including verbal working memory and sustained attention) into account along with initial picture naming (β=0.023, 95% CI 0.006, 0.04, p=0.01) and sentence construction (β=0.013, 95% CI 0.004, 0.022, p=0.005) respectively. As an index of spatial attention, cancellation accuracy at 9 months was better predicted when taking into account the initial executive function score (β=0.214, 95% CI 0.049, 0.378, p=0.011) along with the initial cancellation task; while reductions in cancellation asymmetry (neglect) were better explained by including the initial auditory attention score (β=0.039, 95% CI 0.007, 0.07, p=0.018) alongside the first measure of cancellation asymmetry. The measures of working memory, sustained attention, and response inhibition (assessed in the auditory attention task) and executive function (assessed in the rule finding and switching test from BCoS), led to better prediction of longer-term language and spatial attention problems. There was also better prediction for in the NEADL. For example, the praxis domain was linked to NEADL (see section 2) but the variance accounted for increased when the attention domains were considered (R^2 increased reliably by 7.5%, p<0.001 to 55.5%). These data are consistent with the argument that cognitive profiling, taking measures of attention and executive function into account, can add to predictions from single deficits alone.

Discussion

The BCoS provides a cognitive screen for stroke that is relatively time efficient (completed in around 1 hour) and inclusive (90% of patients tested at a sub-acute stage were able to complete >75% of the tests). The high inclusion rate is facilitated by the tests being designed to be 'aphasia and neglect friendly'. BCoS alsoprovides a novel 'cognitive profile' for patients covering language, memory, number processing, praxis and spatial and controlled attention, easily reported to clinicians (see the Appendix).

Our results indicate that (i) there were differential effects of whether patients have suffered their first stroke or had a repeat stroke, (ii) and whether the stroke affected the left or right hemisphere, while (iii) overall cognitive performance predicted outcome at 9 months, taking into account the initial functional performance score (the Barthel index) and affective characteristics (depression, anxiety and apathy measures). In addition, predictions of the cognitive and functional abilities of patients improved when performance on domain-general processes (attention and executive functions) were taken into account in addition to performance in single domains. We consider each point in turn.

First vs. Repeat Stroke

There were no reliable differences in overall cognitive performance in patients who suffered their first stroke relative to those who had a prior history of stroke, and for all patients the spatial attention and verbal memory problems were most persistent (showing fewest gains in terms of the patients who were impaired at follow-up compared with the initial test). There were interesting differences however in the numbers of patients who did and did not show recovery. In particular, more first-

stroke patients went from an impaired to a non-impaired category relative to patients with repeat strokes. This was not due to initial differences in task performance, overall physical function (Barthel index) or age (the groups did not differ on any of these variables). There was also no difference in the initial time of testing between patients who did and those who did not show recovery ($t(329)=0.485$, $p=0.612$) and nor did the recovering and the non-recovering patients differ in their initial affect (Anxiety, $t(311)=-0.967$, Depression, $t(311)=-0.293$). This last result means that the lack of recovery after repeat stroke is unlikely to reflect purely motivational factors. One alternative account is that neural plasticity decreases after there has been an earlier neurological insult. This speculative proposal requires further verification in experimental models, however it does fit with the relatively high incidence of dementia that can arise after stroke (Narasimhalu et al., 2009).

Left vs. Right Hemisphere Damage.

Patients with unilateral left hemisphere damage overall fared worse than patients with a unilateral right hemisphere lesion. At a domain level, the LHD patients were worse on the language, memory, number and praxis tests, with the opposite pattern present only for spatial attention. It can be argued that many of these tests required language and/or communication abilities (language, praxis and number tests), and this was also the case for memory given that the BCoS features a verbal LTM task (though forced-choice tests are used to assess recognition memory). Indeed many of the tests not showing a reliable contrast between LHD and RHD patients (rule finding and switching task, multiple object use and figure copy) were putatively less language demanding. The RHD patients were impaired across a range of spatial attention tasks testing neglect and extinction, consistent with the right hemisphere playing a dominant role in controlling human attention (Corbetta & Shulman, 2002).

Interestingly, though the LHD and RHD patients were both impaired on the rule finding and shifting task and the multiple object use task, only the RHD patients showed significant recovery of function. The recovery of the patients on the rule finding and shifting task correlated with recovery in neglect ($\chi^2(1)=7.297$, $p=0.007$) but this was not the case for the multiple object use task ($\chi^2(1)=0.195$, $p=0.659$). If recovery based on reductions in neglect is implausible for the multiple object use task, then an alternative possibility for is that, for this task, the presence of relatively spared language abilities in the RHD group enabled them to improve by using a verbal record of the actions carried out (Bickerton, Humphreys, & Riddoch, 2006). One result consistent with this is that the patients who improved on the rule and multiple object tasks tended to have better language functions than those who did not improve ($t(71)=3.320$, $p=0.002$ and $t(63)=2.516$, $p=0017$, for picture naming and sentence construction).

Predicting Functional Outcome

Previous studies have indicated that functional outcomes can be accounted for by measures of cognitive deficits (Nys et al., 2006). Similar to these studies, we demonstrated that an easy-to-derive index from BCoS, the number of sub-tests where an impairment was detected, predicted our primary outcome measure of function at 9 months – scores on the NEADL. The lack of significant findings relating to the follow up Barthel index was due to a lack of variance in the follow-up Barthel scores as a large proportion of patients achieved maximum Barthel score at 9 months. Predictions from the BCoS occurred over and above effects due to neuropsychiatric symptoms (depression, anxiety and apathy) and both initial and longer-term motor impairment (Barthel index). The domains that were most effective for capturing the NEADL were spatial attention, controlled attention and praxis (Table 6). It is

interesting that few other general screens for cognitive problems (e.g., the MOCA; the ACE-III, the RBANS) provide specific measures of spatial attention and praxis and none (to our knowledge) capture the conjoint effects of working memory, selective and sustained attention as does the auditory attention task here. Indeed, measures of important cognitive functions such as picture naming, sentence comprehension and spatial neglect improved when cross-domain assessments of sustained attention, working memory and executive functions ('controlled attention') were taken into account. The finding that deficits in controlled attention predict functional outcome is also of interest because models of cognition suppose that aspects of the controlled attention tests interact with other processes to support different cognitive abilities. For example, working memory and sustained attention are important to support processes ranging from scanning the environment through to sentence comprehension and production (Francis, Clark, & Humphreys, 2003; Malhotra et al., 2005), while attentional suppression (e.g., affecting the ability to ignore irrelevant stimuli) may facilitate multiple tasks where distractors are present (Morady & Humphreys, 2011). The data here point to the utility of using a battery such as the BCoS, which derives a cognitive profile including measures of working memory, sustained attention and executive function. This, when coupled with the inclusivity of the battery (e.g., for aphasic and neglect patients), the sensitivity to important clinical impairments after stroke (e.g., apraxia (Koski, Iacoboni, & Mazziotta, 2002) and neglect (Bowen, McKenna, & Tallis, 1999) affirms BCoS's potential benefit to stroke care. We also note the utility of the easy clinical reporting scheme for the BCoS, as illustrated by Bisiker and Bickerton's (2013) clinical example (see too the Appendix).

Limitations of the Study

We note several limitations to the study.

One is that we did not include vascular risk factors in our analysis as such factors have shown to impact on cognitive abilities in stroke-free cohort (Unverzagt et al., 2011). We also excluded individuals who could not complete the majority of the tasks to improve the validity of our analysis. While this last step could potentially induce a selection bias, only 10% of the participants were excluded and so the effect of this exclusion should be small. This also demonstrates that BCoS is indeed highly accessible for individuals at a sub-acute stage of recovery.

The second is that patients with a second stroke were tested earlier on the initial screen than the patients with a first stroke. One possibility is that the tendency for the second stroke patients to be more depressed led to the clinical teams alerting testers to the patients earlier. However, the earlier testing appears to have had little impact on the results as the initial levels of cognitive deficits did not differ.

A third limitation concerns drop-out. As common to stroke research, the loss to follow up was substantial. However, we have shown that (Table 2) there were no major demographic or cognitive differences across the group that was followed up and the group that was not. Hence it is unlikely to be the case that the study has missed out the more severe cases at follow up. Nevertheless, further research should include more thorough assessment of additional clinical factors and patients' effort to engage which might have an impact on cognitive assessment and recovery. As the most wide used cognitive screen measures e.g. MMSE/MoCA are shorter and less informative than BCoS, it would also be interesting to formally compare the clinical utility of BCoS with a non-stroke specific cognitive screen of similar length e.g. the RBANS.

Conclusion

Early identification of specific and interacting post-stroke cognitive deficits would help predict outcomes and inform timely interventions. This paper demonstrates how BCoS can contribute by being an aphasic and neglect "friendly", domain specific and efficient assessment for differential cognitive profiles across patient groups.

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Table 1 Demographic and health measures of patients compared by stroke history, and lesion side

						first stroke only				
	First stroke		**Repeated stroke**			**LHD**		**RHD**		
		SD		**SD**	**p[a]**		**SD**		**SD**	**p[a]**
N	455		202			152		181		
Age	69.31	14.34	71.38	12.60	NS	69.34	13.93	69.42	14.51	NS
Gender (% female)	44.80		39.6		NS	46.70		42.00		NS
Year of education	11.52	2.76	11.19	2.76	NS	11.55	2.79	11.66	2.83	NS
Time post current stroke	26.65	22.36	20.44	17.29	0.000**	28.52	23.96	25.89	21.72	NS
Initial Barthel	13.01	5.76	13.34	5.43	NS	12.72	5.92	12.63	5.96	NS
Initial HADS anxiety	6.22	4.50	6.70	4.98	NS	6.11	4.44	6.08	4.62	NS
Initial HADS depression	5.71	4.05	6.66	4.29	0.009	5.64	4.24	5.64	4.02	NS
For followed up subgroup										
Proportion followed up %	52.70		45.00		NS	50.00		59.70		NS
Followed up Barthel	17.00	4.11	17.19	3.84	NS	17.39	3.58	16.19	4.78	NS
NEADL	12.79	6.48	12.90	6.56	NS	12.36	7.01	12.29	6.51	NS
FU HADS anxiety	5.58	4.38	6.21	4.85	NS	4.86	3.55	6.08	4.56	0.050
FU HADS depression	5.43	3.71	6.69	4.39	0.018	4.96	3.78	5.75	3.72	NS
Apathy evaluation score	31.91	9.99	34.36	10.10	NS	31.46	8.64	33.00	10.89	NS

[a]T-test significance NS at= 0.05 level; **statistical significance with Bonferroni correction, p at 0.05/7=0.007;
SD=standard deviation; LHD=left hemisphere damage; RHD=right hemisphere damage; HADS=Hospital Anxiety and Depression Scale;
NEADL= Nottingham Extended Activity of Daily Living Scale

Table 2 Demographic and health measures of patients with first and repeated stroke compared by followed-up status

	First stroke group					**Repeated stroke group**				
	FU		**no FU**			**FU**		**no FU**		
		SD		**SD**	**p[a]**		**SD**		**SD**	**p[a]**
N	240		215			91		111		
Age	70.00	13.26	68.53	15.44	NS	69.49	11.80	72.92	13.06	NS
Gender (% female)	45.00		44.70		NS	39.60		39.60		NS
Year of education	11.80	2.91	11.20	2.55	0.022	11.57	2.97	10.87	2.53	NS
Time post current stroke	26.83	20.95	26.46	23.88	NS	20.71	18.66	20.21	16.17	NS
Initial Barthel	12.60	5.70	13.47	5.80	NS	13.89	5.38	12.88	5.45	NS
Initial HADS anxiety	6.61	4.59	5.77	4.36	NS	6.26	5.15	7.10	4.81	NS
Initial HADS depression	6.15	4.13	5.20	3.90	0.017	6.32	3.96	6.97	4.57	NS

[a]T-test significance NS at= 0.05 level; **statistical significance with Bonferroni correction, p at 0.05/7=0.007;
SD=standard deviation; FU=follow up; HADS=Hospital Anxiety and Depression Scale;
NEADL= Nottingham Extended Activity of Daily Living Scale

Table 3 Baseline cognitive profile of patients grouped by stroke history and lesion side

			Comparing first and repeated stroke					Comparing LHD vs RHD (first stroke only)				
Domain	**Measure**	**Max.**	**first**		**repeated**			**LHD**		**RHD**		
		score	**Mean**	**SD**	**Mean**	**SD**	**p[a]**	**Mean**	**SD**	**Mean**	**SD**	**p[a]**
No. tasks completed (out of 22)			21.03	1.76	20.96	1.71	NS	20.58	2.23	**21.35**	1.29	0.000**
Attention							**NS**					**0.000****
Attention	cancellation accuracy	50	39.94	13.14	39.55	13.45	NS	**43.27[b]**	9.83	36.20	14.94	0.000**
- Spatial	*page based asymmetry (abs)[c,]*	20	2.69	3.92	2.99	4.89	NS	**1.45**	1.89	3.89	4.82	0.000**
	object based asymmetry (abs)[c,]	20	1.47	3.48	2.02	5.31	NS	**0.81**	2.68	2.38	4.46	0.001**
	left visual bilateral	8	6.95	2.45	6.95	2.49	NS	**7.85**	0.65	5.97	3.16	0.000**
	left tactile bilateral	8	6.95	2.39	7.08	2.18	NS	**7.78**	1.00	6.01	3.11	0.000**
	right visual bilateral	8	7.62	1.49	7.47	1.73	NS	7.28	2.12	7.83	0.94	0.005
	right tactile bilateral	8	7.63	1.36	7.49	1.57	NS	7.09	2.16	**7.92**	0.43	0.000**
Attention	rule finding and switching	18	7.15	5.86	6.47	5.29	NS	7.23	5.79	7.30	5.75	NS
- Controlled	auditory attention accuracy	54	43.64	13.90	43.64	12.42	NS	37.89	16.24	**46.91**	11.20	0.000**
	practice required	3	1.44	0.75	1.52	0.77	NS	1.63	0.84	1.35	0.70	0.004
	word recalled	3	2.62	0.67	2.55	0.75	NS	2.48	0.75	2.70	0.59	0.011
Language							**NS**					**0.000****
	picture naming	14	11.32	2.67	11.30	2.46	NS	10.71	3.14	11.69	2.21	0.003
	sentence construction	8	7.06	1.73	7.10	1.60	NS	6.95	1.96	7.18	1.41	NS
	sentence reading (accuracy)	42	38.88	7.33	37.67	8.31	NS	38.07	8.56	39.04	7.08	NS
	nonword reading (accuracy)	6	4.58	1.83	4.59	1.91	NS	3.86	2.15	**4.92**	1.53	0.000**
	word writing	5	3.24	1.63	3.19	1.73	NS	2.80	1.77	**3.48**	1.53	0.001**
	Comprehension	3	2.91	0.30	2.88	0.35	NS	2.87	0.36	2.93	0.26	NS

Memory							**NS**					**0.000****
	personal info	8	7.66	0.99	7.59	1.00	NS	7.35	1.42	**7.83**	0.52	0.000**
	time and space	6	5.62	0.79	5.55	0.84	NS	5.61	0.94	5.62	0.69	NS
	immed free recall	15	6.52	3.23	6.16	3.13	NS	5.72	3.17	**7.18**	3.15	0.000**
	immed recognition	15	12.26	2.85	11.92	3.04	NS	11.73	3.27	12.71	2.35	0.004
	delayed free recall	15	7.32	4.16	6.45	4.03	0.021	6.18	4.37	**7.99**	3.80	0.000**
	delayed recognition	15	12.96	2.84	12.53	2.92	NS	12.27	3.47	**13.34**	2.34	0.001**
	task recognition	10	8.64	1.89	8.33	1.99	NS	8.31	1.97	8.83	1.60	0.016
Number							**NS**					**0.000****
	number reading	9	7.60	2.51	7.35	2.76	NS	6.70	3.29	**8.09**	1.83	0.000**
	number writing	5	3.89	1.63	3.68	1.74	NS	3.39	1.93	**4.25**	1.20	0.000**
	Calculation	4	2.54	1.39	2.37	1.45	NS	2.25	1.50	2.71	1.27	0.004
Praxis							**0.017**					**0.000****
	multiple object use	12	10.20	3.28	10.15	3.42	NS	9.82	3.78	10.15	3.08	NS
	gesture production	12	10.43	2.57	10.55	2.44	NS	9.26	3.44	**11.09**	1.43	0.000**
	gesture recognition	6	5.02	1.19	4.90	1.21	NS	4.65	1.44	**5.22**	0.98	0.000**
	gesture imitation	12	9.44	2.74	9.05	3.09	NS	8.86	3.11	9.74	2.47	0.005
	figure copy	47	34.86	11.19	32.06	12.79	0.007	35.22	11.23	33.79	11.54	NS

**significant at 0.002 level. Abbreviations: LHD = left brain damaged; RHD = right hemisphere damaged; SD = standard deviation. [a]Statistical significance at domain level (in bold) refers to the multivariate statistics; at task level, it refers to between subject effects, NS at 0.05 level. [b]Figure in bold and underlined are the scores showing significant better performance (i.e. higher scores, except for the cancellation asymmetry scores and the auditory attention number of practice required (task names in italic, these are error based scores, the lower the scores, the better the performance)). [c]Page based asymmetry score for the cancellation task indicates extent of egocentric neglect, object based asymmetry score indicates allocentric neglect[30].

Table 4 Comparing percentage impairments across assessments in each measure between groups of different stroke history and different lesion sides

-		**First Stroke**			**Repeated Stroke**			**LHD**			**RHD**		
N		240			91			76			108		
Domain	**Measure**	**initial**	**FU**	**p[a]**	**initial**	**FU**	**p[a]**	**initial**	**FU**	**p[a]**	**initial**	**FU**	**p[a]**
Attention	cancellation accuracy	32.80	27.50	NS	31.6	20.3	0.035	19.70	21.20	NS	44.10	36.60	NS
- Spatial	page based asymmetry (abs)	26.50	18.60	0.029	27.8	21.5	NS	13.60	15.20	NS	38.70	25.80	0.043
	object based asymmetry (abs)	24.90	15.60	0.004	17.7	12.7	NS	15.20	6.10	NS	35.10	24.50	NS
	left visual bilateral	20.20	14.20	0.016	18.2	10.2	NS	5.50	2.70	NS	33.60	21.50	0.001**
	left tactile bilateral	19.50	13.00	0.003	15.6	12.2	NS	4.20	2.80	NS	32.10	22.60	0.013
	right visual bilateral	13.70	8.20	0.024	10.2	12.5	NS	19.20	9.60	0.039	7.50	4.70	NS
	right tactile bilateral	13.00	5.20	0.001**	12.2	6.7	NS	26.80	9.90	0.004	5.70	1.90	NS
Attention	rule finding and switching	41.00	24.80	0.000**	41.7	32.1	NS	37.70	26.10	NS	38.20	21.60	0.002**
- Controlled	auditory attention accuracy	41.50	28.60	0.000**	51.2	32.6	0.005	57.40	32.40	0.000**	32.40	24.80	NS
	practice required	25.90	21.40	NS	37.2	16.3	0.001**	35.30	32.40	NS	20.00	16.20	NS
	word recalled	22.00	8.10	0.000**	22.4	15.3	NS	30.90	11.80	0.004	19.00	6.70	0.002**
Language	picture naming	25.70	16.50	0.000**	23.1	14.3	NS	41.90	24.30	0.001**	13.90	12.00	NS
	sentence construction	27.80	9.70	0.000**	25	15.9	NS	26.20	12.30	0.022	28.70	6.50	0.000**
	sentence reading (accuracy)	43.90	35.90	0.008	50	34.9	0.004	52.90	48.50	NS	38.30	26.20	0.011
	nonword reading (accuracy)	29.70	22.70	0.011	22.6	7.1	0.001**	48.50	35.50	0.022	19.60	15.00	NS
	word writing	28.50	19.90	0.001**	26.7	23.3	NS	43.50	31.90	0.039	20.00	13.00	NS
	Comprehension	11.80	4.60	0.002**	7.7	2.2	NS	14.70	9.30	NS	9.30	0.90	0.004

Memory	personal info	20.80	14.80	0.034	17.8	11.1	NS	35.60	19.20	0.002**	11.20	12.10	NS
	time and space	24.70	13.40	0.000**	20.9	16.5	NS	25.30	13.30	0.049	20.40	11.10	0.041
	immed free recall	25.60	17.20	0.011	28.2	18.8	NS	30.50	22.00	NS	17.50	8.70	0.035
	immed recognition	32.40	26.10	NS	30	31.1	NS	48.70	32.90	0.012	20.60	19.60	NS
	delayed free recall	26.40	24.00	NS	30.6	28.2	NS	36.70	31.70	NS	16.00	17.00	NS
	delayed recognition	27.00	22.60	NS	27.8	24.4	NS	42.30	32.40	NS	14.30	12.40	NS
	task recognition	24.60	13.00	0.000**	25.6	14.6	0.022	30.20	20.60	NS	15.30	5.10	0.021
Number	number reading	23.60	12.30	0.000**	20.9	7	0.000**	33.30	16.70	0.007	15.50	8.70	NS
	number writing	28.40	18.00	0.000**	30.7	19.3	0.041	42.90	24.30	0.000**	18.60	14.70	NS
	Calculation	23.30	13.50	0.001**	22.2	13	NS	34.90	18.60	0.016	18.30	10.00	NS
Praxis	multiple object use	22.80	10.50	0.000**	15.7	5.6	0.022	26.00	12.30	0.006	24.50	7.80	0.000**
	gesture production	15.40	11.10	NS	10	5.6	NS	29.30	18.70	NS	2.90	3.80	NS
	gesture recognition	14.70	10.30	NS	12.2	15.6	NS	25.70	17.60	NS	7.70	4.80	NS
	gesture imitation	30.20	16.80	0.000**	29.2	13.5	0.003	38.40	24.70	0.031	25.70	9.50	0.002**
	figure copy	53.00	42.00	0.004	51.8	31.8	0.000**	52.90	41.40	NS	59.00	45.00	0.029

**significant at 0.002 level. [a]McNemar test. Abbreviations: LHD = left brain damaged; RHD = right hemisphere damaged; FU = follow up

Table 5 Multivariate linear regression models for effects of physical, affective and cognitive performance on functional outcomes

-		B	SE	95% CI	p
Model 1					
Outcome = Barthel FU	Barthel	0.36	0.05	0.264 to 0.456	0.000
	Anxiety FU	-0.02	0.07	-0.155 to 0.121	0.806
	Depression FU	-0.17	0.10	-0.364 to 0.022	0.081
	Apathy	-0.05	0.03	-0.108 to 0.017	0.149
	Proportion of tasks impaired	-0.71	0.86	-2.403 to 0.989	0.411
Model 2					
Outcome = NEADL	Barthel	0.50	0.07	0.361 to 0.633	0.000
	Anxiety FU	0.13	0.10	-0.063 to 0.327	0.184
	Depression FU	-0.40	0.14	-0.672 to -0.127	0.004
	Apathy	-0.16	0.05	-0.248 to -0.072	0.000
	Proportion of tasks impaired	-3.47	1.22	-5.866 to -1.067	0.005

Abbreviations: CI = confidence interval; SE = standard error; FU = follow up

Table 6 GLM modelling of domain effects on long term everyday functions, controlling for initial Barthel scores, follow up affect and apathy level

-	Domain		W. Lambda	p	Eta	Power
Multivariate	Spatial Attention		0.920	0.001	0.080	0.917
between subject effects		Barthel FU		NS		
between subject effects		NEADL		0.003	0.072	0.930
Multivariate	Controlled attention		0.959	0.036	0.041	0.631
between subject effects		Barthel FU		NS		
Between subject effects		NEADL		0.035	0.028	0.560
Multivariate	Language		0.978	NS	0.022	0.370
between subject effects		Barthel FU		NS		
between subject effects		NEADL		NS		
Multivariate	Memory		0.984	NS	0.016	0.279
between subject effects		Barthel FU		NS		
between subject effects		NEADL		NS		
Multivariate	Number		0.971	NS	0.029	0.471
between subject effects		Barthel FU		NS		
between subject effects		NEADL		NS		
Multivariate	Praxis		0.919	0.001	0.081	0.922
between subject effects		Barthel FU		NS		
between subject effects		NEADL		0.001	0.063	0.898

Abbreviations: FU = follow up; NEADL = Nottingham Extended ADL scale

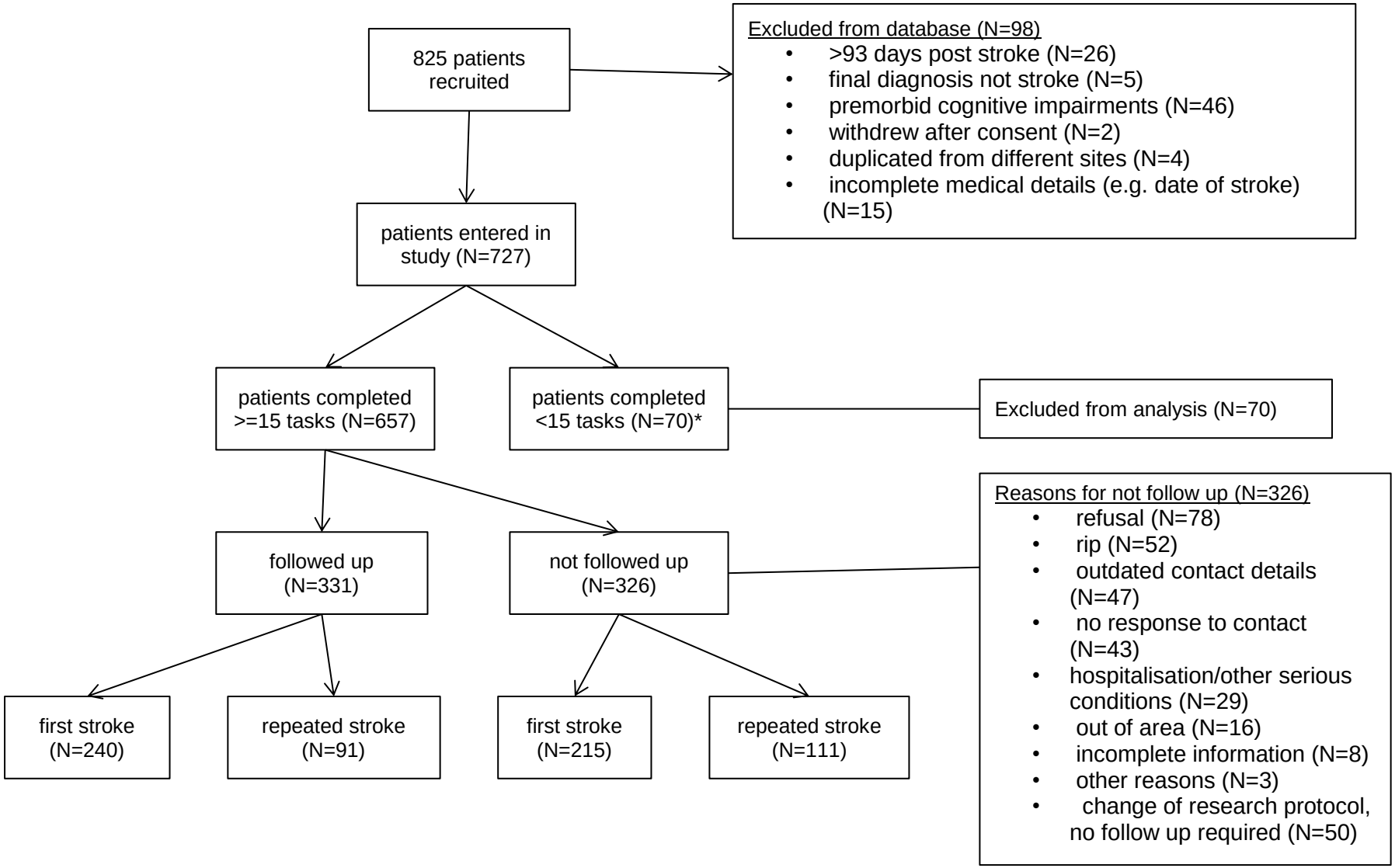

Figure 1: Flow chart of patient cohort at baseline and follow-up

Appendix

The structure and descriptions of the BCoS tasks

Test Domain	Test	Description	Measures
Attention and executive function	Auditory attention	Remember and respond to occurrences of 3 word targets while ignoring 3 related distractor words across 3 blocks of trials	Working memory, response inhibition, sustained attention
	Rule finding and switching	Find a rule in a visual pattern across trials and switch the rule when itn changes	Rule finding and set shifting
	Apple cancellation	Cancel full apples and ignore broken apple distractors	Egocentric and allocentric neglect
	Visual extinction	Detection of one or two visual targets (finger movements by tester)	Neglect (unilateral trials) and extinction (bilateral trials)
	Tactile extinction	Detection of one or two tactile targets (finger touch by testers)	Neglect (unilateral trials) and extinction (bilateral trials)
Language	Picture naming	Name low drawings with low frequency names	Object recognition and naming
	Sentence construction	Generate a sentence to a describe a picture	Syntactic and semantic aspects of speech production
	Instruction comprehension	Clinical judgement of the ability to understand task instructions	Qualitative measures of verbal comprehension
	Sentence reading	Reading sentences aloud, including exception words, regular words and function words	Different forms of dyslexia
	Read nonwords	Reading nonwords	Phonological dyslexia
	Write words and nonwords	Writing irregular words and nonwords	Different forms of dysgraphia
Memory	Orientation	Understanding time and place	Memory for current circumstances
	Story recall and	Recall and recognition of a	Immediate and delayed recall and

	recognition	story immediately and after a delay	recognition (verbal)
	Task recall and recognition	Recall and recognition of stimuli from tasks performed	Immediate and delayed recall and recognition (non-verbal)
Number processing	Number/price/time reading	Read numbers, prices, clock times	Correct parsing and verbal production of numbers
	Number/price writing	Write numbers, prices	Correct parsing and written production of numbers
	Calculation	Calculate additions, subtractions, multiplication, division	Basic maths abilities
Praxis	Complex figure copy	Copy a complex figure	Constructional apraxia
	Multi-step object use	Carry-out a multi-step task with objects whilst ignoring distractor objects	Everyday action object selection, step production, perseveration
	Gesture production	Produce familiar gestures to names	Gesture production for transitive and intransitive actions
	Gesture recognition	Identify familiar gestures produced by the tester	Gesture recognition for transitive and intransitive actions
	Imitation	Copy meaningless gestures produced by the tester	Gesture imitation