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Kinematic measures provide useful information after intracranial aneurysm treatment

Rachael K Raw[1], Richard M Wilkie[1], Mark Mon-Williams[1], Stuart A Ross[2], Kenan Deniz[2], Tony Goddard[2] and Tufail Patankar[2]

Abstract

Introduction: Current methods of assessing the outcomes of intracranial aneurysm treatment for aneurysmal subarachnoid haemorrhage are relatively insensitive, and thus unlikely to detect subtle deficits. Failures to identify cognitive and motor outcomes of intracranial aneurysm treatment might prevent delivery of optimal post-operative care. There are also concerns over risks associated with using intracranial aneurysm treatment as a preventative measure.

Methods: We explored whether our kinematic tool would yield useful information regarding motor/cognitive function in patients who underwent intracranial aneurysm treatment for aneurysmal subarachnoid haemorrhage or unruptured aneurysm. Computerised kinematic motor and learning tasks were administered alongside standardised clinical outcome measures of cognition and functional ability, in 10 patients, as a pilot trial. Tests at post-intracranial aneurysm treatment discharge and six-week follow-up were compared to see which measures detected changes.

Results: Kinematic tests captured significant improvements from discharge to six-week follow-up, indexed by reduced motor errors and improved learning. Increased Addenbrooke's Cognitive Examination-Revised scores reflected some recovery of memory function for most individuals, but other standardised cognitive measures, functional outcome scores and a psychological questionnaire showed no changes.

Conclusions: Kinematic measures can identify variation in performance in individuals with only slightly improved abilities post-intracranial aneurysm treatment. These measures may provide a sensitive way to explore post-operative outcomes following intracranial aneurysm treatment, or other similar surgical procedures.

Keywords

Stroke, intracranial aneurysm, subarachnoid haemorrhage, kinematic analysis, stroke rehabilitation

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Introduction

Previously we have shown that our Kinematic Assessment Tool (KAT) can reliably distinguish between poor and proficient performance in adults and children, with and without neurological impairment.[1–7] Utilising kinematic analysis technology, KAT allows many of the properties of a given movement to be independently and objectively assessed. This way, we can empirically describe the qualities of a movement beyond making a judgement at a functional level, on whether it has been successful or unsuccessful. Specifically, KAT captures the horizontal and vertical movements of the hand (X and Y coordinates) as participants carry out visual-spatial tasks, and independently records various kinematic outcomes (e.g. reaction time, movement speed, accuracy, pressure, etc.) through its integration with any commercially available tablet PC.[1] When installed on a tablet laptop, the screen can be rotated and folded backwards to allow participants to interact in a manner reminiscent of using a pen and paper, which is practical for use

[1]Faculty of Medicine and Health, School of Psychology, University of Leeds, Leeds, UK
[2]Department of Neurosciences, Leeds General Infirmary, Leeds, UK

Corresponding author:
Rachael K Raw, University of Leeds, Leeds LS29JT, UK.
Email: pscrkr@leeds.ac.uk

with a diverse range of populations. The portability of the system makes it particularly suitable for working in clinical settings, where assessment often takes place at bedside and/or in outpatient clinics. Most importantly, analysing motor control (and indeed cognitive performance) at this level of detail provides a basis for developing specific hypotheses about the characteristics that determine functional success versus failure with a given task, and in turn, provides information about the parameters that must be targeted by rehabilitative interventions.

In school settings, KAT has proven particularly successful,[5] and is demonstrably far superior to non-computerised (e.g. pen-and-paper) tests. Furthermore, in healthy older adult groups, KAT can identify age-related decline in motor ability,[3,4,6] as well as changes in cognitive function.[7] What is uncertain, however, is the extent to which this method can be used in clinical populations. It has been established that KAT is useful in establishing the motor ability of young children and even predicting the relationship between a child's motor skill and well-being,[8] but few studies have examined the efficacy of this form of kinematic analysis in the context of stroke, and we are unsure of whether kinematics measures can be used to inform rehabilitation. In the present small-scale pilot study, we therefore aimed to test the value of KAT in a group of patients that underwent intracranial aneurysm treatment (IAT) – the outcomes of which are relatively uncertain.[9]

Aneurysmal subarachnoid haemorrhage (aSAH) is a type of stroke that occurs when an intracranial aneurysm (IA) bursts, causing blood to leak into the subarachnoid space (i.e. the area between the arachnoid membrane and pia layers of the protective meninges). The overall incidence of aSAH in the western world is 6–8 per 100,000 per year,[10] with approximately 50% overall mortality.[9] Survival is associated with long-term deficits in cognitive function (particularly language and memory).[9,11] Treatment options include endovascular techniques, where aneurysms are filled with coils under X-ray control; and neurosurgical clipping, which involves opening the skull, dissecting through the brain spaces and placing a clip across the aneurysm neck.[12] Both options aim to prevent re-bleeding and are used to treat aSAH. These techniques are also used to treat 'asymptomatic' patients who electively undergo IAT as a preventative measure.

While IAT for aSAH is associated with improved survival, especially when applied one-to-three days after a haemorrhage,[13,14] the long-term outcomes (and their neurological correlates) associated with IAT are poorly understood.[1] Patients with aSAH rarely resume their previous lifestyle due to residual functional problems,[15] – with 50% of survivors failing to return to the same level of employment.[16,17] Crucially, current methods of assessing the outcomes of aSAH are crude, meaning patients can slip 'under the radar' because the long-term difficulties they face are not detected in the short post-operative period. For example, patients may be classified as having 'zero disability' by immediate post-treatment tests, whilst still experiencing deficits in cognition, language and memory, the extent of which can predict quality of life (QoL) and functional ability.[17,18]

The Glasgow Outcome Scale (GOS),[19] which scores patients 1–5 (1 = Dead, 5 = Good Recovery) for 'level of disability', is often used as a global marker of recovery, where a patient scoring '5' should be able to resume 'normal' daily life, albeit with the possibility of minor neurological deficits. Though this provides an overall prediction of recovery, subjective scales like GOS are not sensitive enough to capture any subtle motor or cognitive changes, nor are they able to detect and/or describe psychological symptoms.[20,21] Patients who have 'recovered' (based on GOS scores) may therefore have problems that emerge years after IAT when the patient is outside specialist services, making treatment more difficult. This is concerning given that a delay in treatment can cause a deterioration in physical and mental health,[18] and greater recovery is usually achieved when rehabilitation programmes start early.[22]

The patient group most vulnerable to the insensitivities of current post-treatment tests is likely to be comprised of individuals with unruptured aneurysms (UA). These aneurysms can lie dormant for many years, and typically go un-detected until a patient has a brain scan, usually for an un-related diagnostic reason. Patients are then faced with the decision to have their aneurysm treated to avoid rupture, or they can 'watch and wait'. The likelihood of a UA bursting is predominantly related to aneurysm-specific characteristics (namely size and location) and to the patients' prior history of aSAH (i.e. whether a different UA has ruptured previously[23]). The risk of aSAH in untreated UA also increases with each year of life.[24] These points must be carefully considered when making a choice about treatment, especially considering the recent 'A Randomized trial of Unruptured Brain Arteriovenous malformations' trial ('ARUBA'), which suggests that medical management of UA (as opposed to interventional methods) might be less likely to cause critical side effects, such as neurological deficits and post-operative stroke.[25]

Unsurprisingly, one of the most common questions that patients ask when diagnosed with UA regards the extent to which IAT might affect their QoL. Some research implies IAT for UA is safe (e.g. an observational study reported low mortality, no risk of neurological deficit and successful obliteration of the UA in just under 90% of cases[26]); though to the authors'

knowledge, no trial has yet included a set of neuropsychological tests to examine subtle outcomes of IAT in an UA group. Furthermore, anecdotal reports from the clinic suggest that IAT for UAs can yield post-operative side effects, with patients citing changes of a mild psychological and cognitive nature (e.g. forgetfulness, anxiety and 'not feeling quite the same'). Indeed, the importance of developing sensitive post-treatment measures is particularly pertinent in this elective UA group because (i) a patients' decision to go ahead with IAT must be based on the correct information about recovery; and (ii) clinicians need to be informed about the nature of changes induced by IAT for UA if effective rehabilitation of patients is to be undertaken.

It is clearly essential that sensitive outcome measures are developed for use in aSAH and UA populations alike, which is why we selected this group to examine the efficacy of KAT for assessing post-operative outcomes. The present study involved two types of kinematic task – firstly a collection of motor tests that can identify poor and proficient motor performance in older and younger adults,[5] and secondly a Sequence Learning Task designed to measure complex sequence learning as a marker of cognitive ability.[7] The tests were administered to UA and aSAH patients on the day of discharge from hospital ('Discharge') and again at six weeks post-IAT ('6/52'). A sensitive measure should be able to detect changes in performance, as well as identify individuals that fail to improve. We predicted that most patients would initially experience impaired motor and cognitive performance (caused by factors associated with IAT) but then show improvements after a period of recuperation. Standardised clinical measures of cognition, functional ability and psychological symptoms were administered alongside the kinematic measures of motor performance and learning. A standardised self-report questionnaire on psychological symptoms was also completed by participants, to measure the anxiety and depression symptoms that aSAH and UA patients often mention.

Methods

The study was approved in the UK by The Leeds Teaching Hospitals NHS Trust Research and Development Ethics Committee (LTHT R&D Number: PY13/11002; REC reference: 14/YH/0009) confirmed on 12 March 2014. Participants (including patients and healthy controls) provided written informed consent in accordance with the Declaration of Helsinki.

Participants

Ten patients (7 females; 3 males) aged 24–72 years (mean = 52.80, SD = 16.29) formed an opportunistic sample. The sample size ($N = 10$) was based on our previous work using kinematic measures of motor ability in older and younger healthy adults that has demonstrated reliable group differences.[3] Nine patients were right-handed, indicated by the Edinburgh Handedness Inventory (EHI; mean score excluding left-handed patient = 89.9 of 100, SD = 12.76; scores $\geq$40 indicate right-handedness[27]). Six patients underwent IAT for aSAH (one neurosurgical; five endovascular) and four underwent IAT for UA (one neurosurgical; three endovascular). Patients were recruited prior to IAT, or when recovering on the ward, and met the following inclusion criteria: (i) $\geq$16 years old; (ii) diagnosed with UA or aSAH identified by computerized tomographic angiography; (iii) underwent IAT with standardised method under general anaesthesia; (iv) no neurological disability from previous strokes/haemorrhage; (v) no intracranial tumour; (vi) no previous craniotomy; (vii) no cognitive deficit (indicated by scores $\leq$27/30 on Mini Mental State Evaluation (MMSE);[28] (viii) no ophthalmological problems; (ix) capable of personally consenting; (x) able to work unsupported with a stylus/mouse for 20 min. Further to the inclusion criteria, a Clinical Recovery Score (CRS[29,30]) was administered to determine patients' 'readiness for discharge', and recovery from general anaesthesia – all patients included in the study had to meet the CRS cut-off score of 11/12 to ensure equal suitability for participation across individuals. One patient asked to withdraw from the study, as when it was time for their procedure, they did not feel well enough physically or emotionally to be involved. The Addenbrooke's Cognitive Examination-Revised (ACE-R), Self-Report Barthel Index (SRBI) and Hospital Anxiety and Depression Scale (HADs) (see 'Standardised clinical outcome measures' section) were not administered to two patients because of logistical issues. To identify whether patients were capable of responding with 'normal' levels of cognitive and motor performance on the kinematic tests, a second opportunistic sample formed a 'control group', consisting of healthy people recruited from the local community in Leeds ($N = 35$, with the same average age as the patients (mean = 53.48 years, SD = 21.6).

Measures and data collection

Consent was obtained from everyone at the point of testing. Healthy controls were tested in an office environment, seated at a table and chair. For patients, tests were administered for the first time (i.e. 'Discharge') at bedside or in bed, with the computerised tasks appearing on a laptop, and pen-and-paper questionnaires placed on the pull-across table (standardised clinical outcome measures were delivered first, immediately followed by the kinematic motor tests (KAT)). Tasks were

then administered again six weeks later ('6/52'), with patients this time seated at a table in a private clinic room. The same researcher, who had prior experience of delivering the tool to healthy younger and older adults,[3,4,6,7] was present to lead the sessions and answer any questions upon request.

Kinematic motor tests

The KAT computerised tasks were presented on a tablet PC (screen = 260 × 163 mm). For the motor tests, the screen was folded down horizontally to mimic a writing position (see Figure 1), and patients used a digitising stylus in their preferred hand. A battery of four tasks ran back-to-back with integrated onscreen instructions, each taking 3–5 min to complete.[1,2,5–7]

Figure 1. An example of a participant (NB: not a patient from the present study) using the stylus to complete the KAT tracking task (guided) on the tablet PC with the screen in the horizontal position.
KAT: Kinematic Assessment Tool.

(i) Tracking: participants kept the stylus on a dot as it moved around the screen in a figure-of-eight (Figure 2(a)). Dot speed increased from slow (4 s per figure-of-eight), to medium (8 s) to fast (16 s), with three repetitions at each speed (i.e. nine trials total). The task was performed once with ('Guided') and once without ('Unguided') a spatial guide (i.e. a figure-of-eight shape; Figure 2(b)). Root mean square error (RMSE) was calculated as the average distance (mm) of the stylus from the closest reference point on the centre of the figure-of-eight. Higher RMSE values = reduced accuracy.
(ii) Aiming: participants made discrete movements between dots that appeared in a recurring shape of a pentagram. The five movements comprising the pentagram shape repeated 10 times (i.e. 50 movements; Figure 2(c)). Mean movement time (MT; time taken to complete all movements) was calculated, where lower MTs = reduced speed.
(iii) Steering: participants traced a path, keeping the stylus within a moving box that progressed every 5 s (Figure 2(d)). Across six trials, the path shape became a mirror-image of itself on every other trial. The moving box constrained speed, allowing

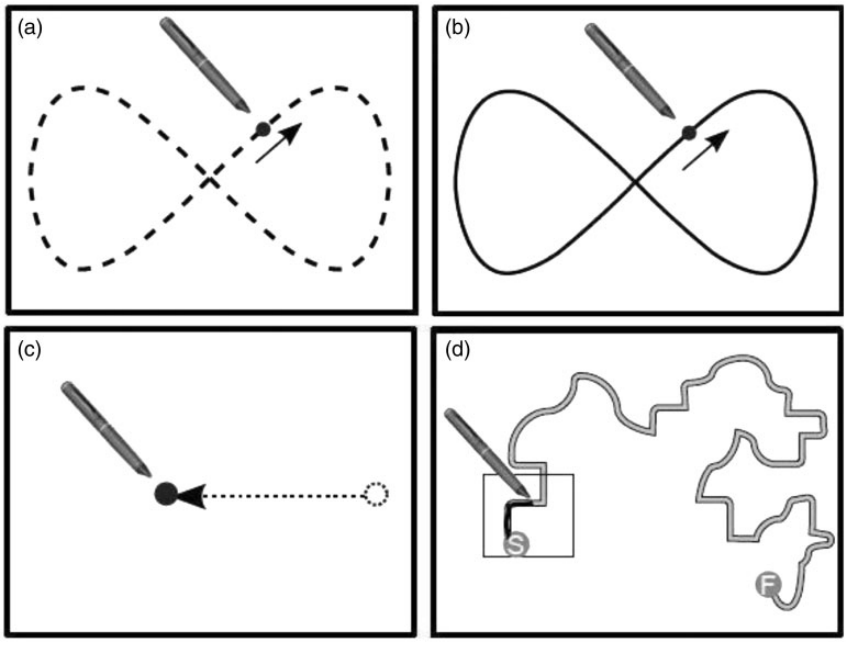

Figure 2. KAT tasks comprising the kinematic motor test battery, completed by participants with a handheld stylus pen (Nb: not to scale). (a) Tracking (unguided). (b) Tracking (guided). (c) Aiming. (d) Steering.
KAT: Kinematic Assessment Tool.

accuracy to be compared across participants (since this limited speed-accuracy trade-offs). Shape error (SE) was calculated by taking each traced path and analysing the difference in comparison to an 'ideal' reference that fell in the exact centre of path. Higher SE = reduced accuracy.

Sequence Learning Task

A Sequence Learning Task was delivered on the same tablet PC with the screen in the standard vertical position, to allow patients a better view of the stimuli. Participants used a PC mouse and learned a sequence of movements made to eight targets on the screen. 'Training' and 'Test' trials alternated, providing 10 opportunities for participants to practice and recall a sequence (Training × 10 + Test × 10 = 20 trials). In the Training trials (Figure 3(a)), a central box was encircled by eight identical 'target' boxes (Figure 3(a),(b)). An arrow appeared in the central box to indicate where to move the mouse (e.g. top left in Figure 3(a)) before returning to the centre. There were 16 moves that followed the same irregular pattern for every Training trial and, in between Training trials, patients recalled the sequence by moving the cursor back-and-forth between the centre and targets as quickly and as accurately as possible without any arrow cues (Figure 3(b),(d)). Two practices were given of a Training and Test trial (featuring a different 16-move sequence) before starting the experimental session. The full task took around 20–30 min to complete, and a new 16-move sequence was used at the 6/52 session to avoid learning effects.

Standardised clinical outcome measures

Two measures of cognitive and psychomotor ability were administered, along with a disability scale, and two questionnaires to act as self-report measures of functional ability and psychological symptoms. The following tests were selected as they commonly appear in relevant literature.[1]

(i) Digit symbol substitution test (DSST): a cognitive and psychomotor test involving matching symbols to their corresponding numbers in 90 s (max score = 93).[31] This test was included as it has been used previously to determine changes in cognition following sedation and general anaesthesia.[32,33] Note that the DSST does not emphasise motor accuracy, because if symbols are copied in a legible manner, a point is always awarded – participants can hence score higher by not paying attention to detail.

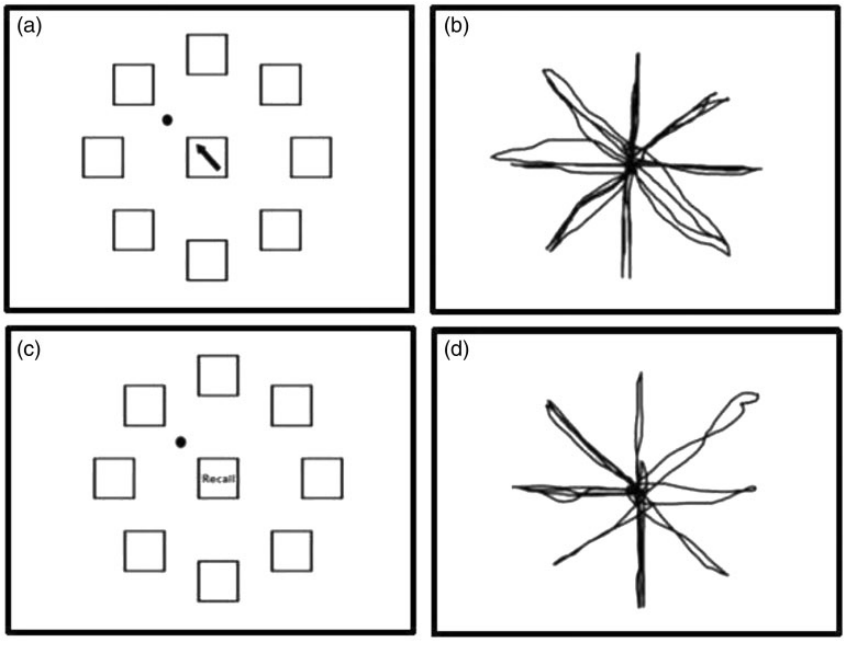

Figure 3. KAT Sequence Learning Task, completed by participants with a standard PC mouse (Nb: not to scale). (a) Training trial, requiring participants to move the dot into the box corresponding to the direction indicated by an arrow that appeared in the central box (e.g. top left in this example). (b) Example trajectories produced during a Training trial. (c) Test trial whereby participants recalled the pattern of movements previously learned in the Training trial; and (d) example trajectories produced during a Test trial.
KAT: Kinematic Assessment Tool.

(ii) ACE-R and MMSE: screening tools for Mild Cognitive Impairment and Dementia. Sub-tests include Attention and Orientation, Memory, Fluency, Language and Visuospatial Ability (max score = 100).[34] MMSE sub-items (max score = 30), and total ACE-R scores were calculated. ACE-R scores <88 give an 89% specificity for dementia, scores <82 give 100% specificity for dementia. The National Institute of Clinical Excellence (NICE) recommends a cut-off score of 27 for classifying absence of cognitive impairment. Our choice of the ACE-R and MMSE as cognitive measures is supported by their frequent use in populations where cognitive disturbance is expected. While these tests are designed ideally as a dementia screening tool, they have been used before to assess cognitive performance after stroke, albeit with some reported ceiling effects and questionable specificity.[34–39]

(iii) GOS: Five-point global outcome scale, used to assess disability following brain injury and stroke.[40] Categories include Dead [1], Vegetative State [2], Severe Disability [3], Moderate Disability [4] and Good Recovery [5].

(iv) SRBI: a questionnaire (max score = 20) for establishing independence in daily tasks.[41–43] The SRBI has often been cited in prior studies as a tool for documenting functional ability in stroke groups, though it notably has a ceiling effect and cannot detect minor motor impairments.[44–46]

(v) HADs: a self-report scale to detect symptoms of anxiety and depression.[47,48] Separate scores for depression and anxiety can be normal (1–7), borderline abnormal (8–10) or abnormal (11–21). The decision to also record psychological symptoms stemmed from our experience of patients in outpatient clinics often reporting feelings of anxiety in relation to their diagnosis and/or recovery.

Data analysis

For the KAT, mean RMSE, MT and SE across all trials were calculated for each participant and separate repeated-measures ANOVAs applied to compare performance between Discharge and 6/52 (NB. IBM SPSS Statistics for Windows, Version 21.0, was used for statistical analyses). One additional ANOVA was calculated for the tracking tasks to analyse the effect of speed on RMSE. To determine whether motor performance was within a normal range, data were compared with scores in the healthy control group. For this, the mean and % confidence interval (CI) of the control group's performance was used as the criterion for identifying 'normal' performance by the patients. Z-scores on each task were calculated (using the mean and SD of healthy controls) and an average taken for each patient. A z-score of −.35 or less indicates performance outside of mean +95% CI.

In the Sequence Learning Test, the accuracy of recall during the Test trials was indicated by the maximum number of moves performed in the correct sequential order (correctly recalled (CR): max score = 16; points not deducted for incorrect moves) across all trials, and these scores were compared between Discharge and 6/52 follow-up. Performance was compared to a control group of healthy adults ($N = 32$) with the same average age as the patients (mean = 52.36, SD = 25.1). Average group performance minus 95% CI (CR = 9 − 2) was the cut-off criteria for identifying 'normal' performance the patients.

Statistical analysis was not completed on the standardised clinical outcome measures, rather, scores at each testing session were merely calculated and recorded to compare for changes across time. The inclusion of these tests was to test the hypothesis that standardised tests fail to detect changes that can otherwise be registered by more objective sensitive measures, like the kinematic tests used in the present research.

Results

Standardised clinical outcome measures

Most standard measures did not differ markedly between sessions. Because of the categorical/ordinal nature of these scores, the limited change in scores and the small numbers of participants, it is not useful to examine these data using grouped statistical methods. Instead, we examined measures for each individual and compared individual scores with ceiling performance on the tests. There was no change in GOS between sessions, as nine patients received the highest classification (i.e. 'Good Recovery') at Discharge and 6/52. One patient was scored as having 'Moderate Disability' (score = 4) at Discharge and 6/52. The pattern was similar for SRBI – six patients were 'functionally independent' (score = 20) at both sessions, one patient scored 19 at both sessions, and one patient scored 18 at Discharge and 17 at 6/52. There were also no systematic changes in the HADs measure. At Discharge, four of eight patients had 'borderline abnormal' or 'abnormal' Anxiety scores (scores = 8, 8, 8, 12), and at 6/52, two scores remained unchanged as 'borderline abnormal', with one patient going from 'normal' to 'abnormal' (6 to 16) and another from 'abnormal' to 'normal' (12 to 6). On the Depression scale, two scores were 'abnormal' or 'borderline abnormal' at Discharge and at 6/52. Raw data for the SRBI and the HADs subscales are given in Table 1.

Table 1. Individual patient scores on standardised outcome measures and kinematic tests at Discharge (D) and 6/52 weeks post-operation (6/52).[a]

P	Age	SRBI Discharge	_6/52	HADS (A) Discharge	_6/52	HADS (D) Discharge	_6/52	CR Discharge	6/52	Motor Discharge	6/52	ACE-R Discharge	6/52	DSST Discharge	6/52
#1	52	20	20	6	2	2	2	7	5	−1.35	−0.16	84	85	51	**51**
#2	74	20	20	8	8	4	2	4	6	−2.49	−0.91	#N/A	#N/A	27	27
#3	54	20	20	12	6	8	0	7	6	−0.87	−0.35	92	**98**	38	**48**
#4	72	20	20	0	0	0	0	2	6	−3.38	0.14	82	82	17	30
#5	68	20	20	8	8	3	1	5	6	−1.12	0.59	94	**99**	56	62
#6	31	20	20	3	2	1	1	2	9	0.99	1.34	92	**95**	43	75
#7	55	19	19	6	16	5	8	10	13	−1	−0.38	100	99	64	**79**
#8	49	18	17	8	7	10	9	10	16	−2.32	**0.23**	89	97	35	25
#9	49	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A	16	16	0.79	1.12	#N/A	#N/A	55	55
#10	24	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A	16	16	0.75	1.44	93	99	52	65

[a]The age of each participant is given, along with the following individual patient scores on (i) SRBI (max = 20); (ii) Anxiety (A) and Depression (D) subscales of HADs (max = 21 per subscale); (iii) maximum number of items correctly recalled (CR) out of the full 16 movement sequence comprising the Sequence Learning Task; (iv) a composite measure of motor performance (z-scores) on the motor task battery, including tracking, steering and aiming tests (i.e. a motor measure); (v) ACE-R (max = 100) and (vi) DSST (max = 93). Impaired performance measures are highlighted in red text. Dark grey shaded cells highlight patients with impaired CR at 6/52, and light grey shaded cells highlight those with motor difficulties at 6/52. For clarity values of ACE-R and DSST that are inconsistent with CR and motor impairments have been emboldened and marked with a box.

The only standardised measures that showed systematic changes were the ACE-R and DSST. The ACE-R scores for six of eight patients improved from Discharge to 6/52 (mean = 93 increasing to 98) to scores that are near to maximum. This increase seemed to be driven mainly by improved Memory scores on the ACE-R (measuring recall, anterograde memory and retrograde memory), with an average increase from 21 to 25 out of 26 for the memory component. The remaining two individuals who did not improve on the memory element (scores at Discharge = 12 and 14; 6/52 = 21 and 19, respectively) also performed poorly (i.e. scores <88, which is the cut-off with 94% sensitivity and 89% specificity for dementia) across the whole ACE-R at both testing sessions. Interestingly, neither of these patients fell below the MMSE cut-off for cognitive impairment (both patients scored 27 on the MMSE, which if one point less, would have indicated cognitive impairment). In fact, there were no reliable changes in the MMSE sub-test of the ACE-R across the whole group, with most participants scoring the same at both sessions. The other remaining ACE-R sub-tests also failed to display any impairment (e.g. all except one patient scored 15–16 for Visuospatial Ability at both sessions). Finally, DSST scores improved for six of 10 patients, as scores improved from 45 points at Discharge to 60 points (out of 93) by 6/52. Scores for the other four individuals either remained the same at both sessions (i.e. DSST score = 45 at both sessions for three patients) or declined between sessions (DSST reduced from 35 to 25 for one patient).

Kinematic motor tests

Analyses of the tracking task showed patients improved performance accuracy from Discharge to 6/52 (F (1, 9) = 14.20, $p < .001$, $\eta 2p = .61$; mean RMSE at Discharge = 17.10 mm; 6/52 = 12.27 mm). Accuracy also increased as dot-tracking speed reduced (i.e. 'Slow' tracking; $F(2, 18) = 60.23$, $p < .001$, $\eta 2p = .87$, $\varepsilon = .53$). There were no session × speed interactions suggesting performance improved between sessions similarly for all speeds. A single measure across speeds was taken to simplify further analysis. This 'combined' measure showed seven out of 10 patients exhibited 'abnormal' tracking performance at Discharge (i.e. worse than mean healthy controls' performance + 95% CI; $t(18) = 1.93$, $p < .05$). Furthermore, despite all patients showing some degree of improvement, two patients still exhibited 'abnormal' tracking at 6/52 (Figure 4).

A similar pattern was seen in the other motor tests (Figure 5). The steering task detected impaired accuracy compared to controls at Discharge ($t(18) = 2.02$, $p < .05$) and accuracy improved from Discharge to 6/52 (F (1, 9) = 9.90, $p < .01$, $\eta 2p = .52$) – all patients improved to some degree; but three of 10 were still abnormal at 6/52. Aiming performance was only marginally worse compared to controls at Discharge ($t(18) = 1.58$, $p = .074$) but this group performance still improved between Discharge (mean MT = 1.67 s) and 6/52 (mean MT = 1.37 s) with shorter duration movements for seven of 10 patients ($t(9) = 2.12$, $p < .05$), though movement duration was still 'abnormal' for two patients at 6/52. These findings suggest that our KAT motor tests were

sufficiently sensitive to detect improvements in performance between sessions, and identify individuals that had not yet fully recovered (through comparing performance with healthy controls).

Sequence Learning Task

Analyses of the maximum number of moves that patients could recall across the Sequence Learning Task (i.e. CR) showed that only two patients correctly recalled all 16 moves in both sessions (i.e. showing no impairment and thus no room for improvement). Four patients improved by 2–6 correct responses from Discharge to 6/52 (some data were not recorded for two patients at Discharge due to disruptions on the ward, hence initial performance could not be assessed), but at 6/52 there were still five patients who could only recall 5–6 items correctly (out of 16). Two of these patients also struggled with the ACE-R Memory subtests (patients 1 and 4 in Table 1), but the other three scored normally on the ACE-R (i.e. no clear cognitive impairment identified by the ACE-R).

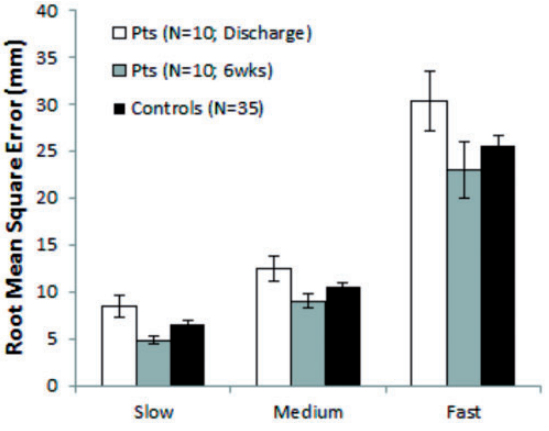

Figure 4. Mean root mean square error (RMSE; mm) in the Tracking Tasks of the Motor Control Battery (KAT; Nb. data from unguided and guided versions has been combined) in the slow, medium and fast speed tracking conditions, recorded at Discharge (white bars) and at 6/52 (dark grey bars) for patients ('Pts'), as compared with a healthy control group (black bars; 'Controls'). Larger RMSE values indicate reduced accuracy. The bars represent the standard error of the mean (SEM). KAT: Kinematic Assessment Tool.

Discussion

In the present pilot study, we examined the efficacy of KAT (a system previously shown to detect discrepancies in performance in young and older healthy groups[1–8]) for detecting post-operative changes in movement and cognition in patients with UA and aSAH. Aneurysmal subarachnoid hemorrhage (aSAH) is associated with motor and cognitive deficits, which can lead to reduced quality of life.[10,11,16,17] Less is known about the outcomes of preventative IAT for UA, though anecdotal reports suggest elective IAT is not entirely free of side effects either.

There is no doubt that IAT improves a patient's chance of survival, but current methods for assessing long-term outcomes lack the sensitivity necessary for identifying subtle neurological problems. The physician might consider the patient as having made a 'good recovery' (e.g. based on global disability scales, such as GOS[18]) yet patients often complain of anxiety (e.g. fear of stroke), memory problems and an inability

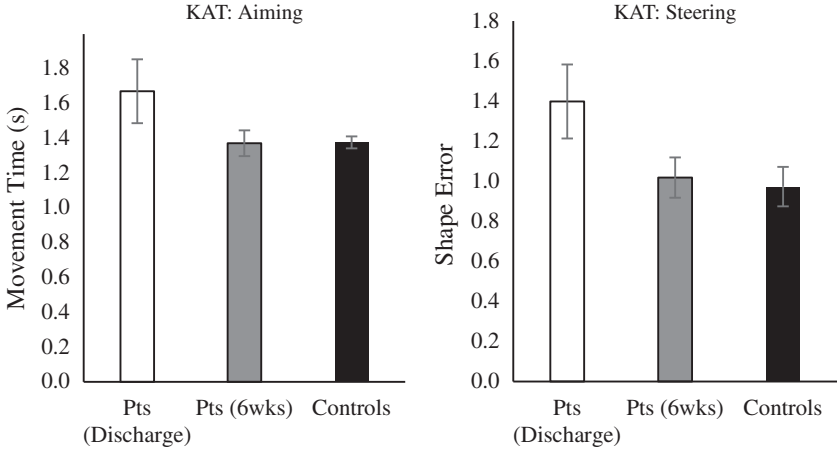

Figure 5. Aiming and Steering Tasks from the Motor Control Battery (KAT), recorded at Discharge (white bars) and at 6/52 (dark grey bars) for patients ('Pts'), as compared with a healthy control group (black bars; 'Controls'). Larger values indicate worse performance (slower time or greater shape error). The bars represent the standard error of the mean (SEM). KAT: Kinematic Assessment Tool.

to resume the same level of employment prior to IAT.[16,17] The lack of sensitive measures makes it difficult to properly evaluate the relative costs and benefits of intervention. The potential costs of treatment may be drastically underestimated if the measures lack the sensitivity to identify subtle yet important impairments. This issue may be of less consequence when the choice is between IAT and severe disability (i.e. following an aSAH); however, it could be critical when deciding upon a treatment regime for an individual with UA (particularly a small aneurysm), when IAT is a choice, not an emergency.

To determine whether more sensitive tests could be composed, we administered standardised clinical outcome measures and novel kinematic tests at Discharge and 6/52 post-IAT. Two tests of functional ability (GOS and SRBI) were used as a marker of how independent patients were in daily activities after IAT. The GOS provides a global measure of disability, and while quick and easy to administer, there are concerns in the literature over its lack of specificity between categories, mostly when distinguishing between 'Moderate' and 'Severe' disability.[40] In our study, GOS scores did not change between Discharge and 6/52, and nine of 10 patients were classed as having made a 'good recovery' with only a single patient rated as 'moderately disabled' at both time-points. The SRBI is a more comprehensive test of functional outcome, but this also showed no difference in scores between Discharge and 6/52; with seven of eight patients classified as 'fully independent' in activities of daily living at both sessions (see Table 1).

There were only two clinical measures that appeared to detect improvements in the patients between sessions, which were the ACE-R and DSST. Whilst most ACE-R subcomponents remained stable, the memory sub-test improved in six of eight patients, with performance essentially reaching ceiling for these individuals at 6/52, to suggest a full recovery (see Table 1). With the DSST there were only improvements in six of 10 patients. Even though the DSST has been shown to correlate strongly with age (due to age-related declines in psychomotor ability[49]) it is unclear whether this test was sufficiently sensitive to detect the subtle changes experienced by the patient population studied here. This finding is discussed later when comparing the DSST to the kinematic motor measures.

One issue that did materialise via standardised testing was the frequency of patients experiencing psychological symptoms, which was indexed by the HADs. During the testing period, patients regularly expressed significant concern about being diagnosed with UA, and felt unrest when trying to make their decision about treatment (e.g. surgical versus endovascular methods). Anxiety often plays a role in decisions to treat.[50] Some patients can harbour feelings of worry and anxiety when an UA is left untreated,[50] yet 50% of patients in our study scored as $\geq$ 'borderline abnormal' on the HADs Anxiety scale at Discharge, even though their aneurysms had been successfully treated. Verbal reports during testing did indeed reveal that the most common concerns were recurrence of an UA, or another aSAH happening in the future.

In contrast with the 'pen-and-paper' standardised tests, our novel kinematic motor and sequence learning tests reliably detected changes in performance at the Discharge testing session post-IAT, as well as functional recovery across the patient group at 6/52. The motor tests could identify four individuals that were experiencing movement difficulties at 6/52 (see light grey shaded cells in Table 1; patients 1–3, 7). The Sequence Learning Test also identified six patients (see dark grey shaded cells in Table 1; patients 1–6) exhibiting cognitive difficulties at 6/52. Whilst there was some overlap between the Motor and Sequence Learning Tests scores (i.e. patients 1–3 struggled on both tasks), the ACE-R failed to detect performance difficulties for patient 3, and the DSST did not detect marked performance difficulties relative to healthy age-matched individuals for patients 1 and 3 (see bold text in rightmost columns of Table 1). There was one patient that exhibited motor problems without memory problems (patient 7) which was not identified by the DSST, and another two patients that exhibited memory problems without motor problems (patients 5–6) which equally was not identified by the ACE-R. There was a single patient (patient 8) identified with problems via the DSST that was not highlighted as being outside of the normal range using the composite tracking motor test measure, but the aiming sub-test did identify performance outside the normal range for this individual. This result suggests that future research may show that specific types of task provide greater specificity (i.e. that tracing relies upon feed-forward control mechanisms that can be affected in isolation after IAT treatment).

The present findings have multiple implications, not only for improving the methods used to assess patients' post-IAT, but also for informing patients' decision to undergo IAT electively. In elective cases, the surgeon and patient must weigh up the evidence to decide whether to treat the UA (usually based on location and size) and, if so, which method to use (i.e. endovascular or neurosurgical). It is vital that the relatively insensitive measures used at present are improved, since more informative measures could determine whether IAT for UA can cause disturbances in motor and cognitive function (even in the absence of a haemorrhage). This evidence would provide further information for the surgeon and patient to consider when calculating the potential risks of undergoing IAT as a preventative measure.[51] Furthermore, in the future we aim to use KAT in larger and more diverse clinical

groups, to establish markers of recovery that would be a useful adjunct to the current standardised outcomes measures used when assessing rehabilitative efforts. The present work is the first step towards achieving this, as is highlights the feasibility of administrating KAT in clinical contexts (i.e. at bedside and in clinic settings), and its capacity to detect minor changes in movement and cognition.

In summary, KAT provides a useful method for measuring the outcomes associated with IAT, and thus has the potential for use as an assessment tool in other similar clinical populations. Future studies employing kinematic analysis will allow: (i) improved understanding of the nature and longevity of subtle deficits associated with IAT; and (ii) exploration of the differences in outcomes of IAT between treatment methods (i.e. endovascular vs. neurosurgical). More generally, KAT tasks can be developed to examine the neural underpinnings of post-operative deficits, by comparing kinematic data with structural changes in the brain. It may also help gather information to inform screening methods that support post-operative care, and subsequent rehabilitation programmes.

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Guarantor

RR

Contributorship

RR researched the literature and conceived the study along with MMW, RW and TP. RR applied for and gained ethical approval. TP, TG, SR, KD all assisted in the recruitment of patients from neurovascular clinics. Data was analysed by RR and RW - figures by RW. RR wrote the first draft of the manuscript. All authors reviewed and edited the manuscript and approved the final version of the manuscript.

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