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ACUTE ISCHAEMIC HEMISPHERIC STROKE IS ASSOCIATED WITH IMPAIRMENT OF REFLEX IN ADDITION TO VOLUNTARY COUGH

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INTRODUCTION

Stroke accounts for more than five million deaths a year worldwide. [1] Most stroke deaths are caused by complications, of which chest infections are most important. One large study showed that 30% of acute stroke patients diagnosed with pneumonia had died before hospital discharge. [2] Aspiration is common after stroke and is associated with a eleven-fold increase in risk of chest infections.[3]

Cough is important for clearing the lungs of aspirated material. This is demonstrated by studies showing a higher incidence of aspiration and chest infections in stroke patients with a weak voluntary cough [4-5] and a significant association between absent cough reflex in acute stroke patients and subsequent development of pneumonia.[6] A strong cough, whether voluntary or reflex, requires powerful, coordinated contraction of expiratory (abdominal) muscles along with adequate inspiration prior to cough, low upper airways resistance, adequate duration of glottis closure, fast and complete glottis opening and the ability to keep small airways patent during sudden rises in intra-thoracic pressure.[7] That some of these abilities are impaired after stroke is suggested by studies of stroke patients showing asymmetry of ventilation, reduced movement of the diaphragm and chest on the hemiparetic side, poor performance on volitional respiratory muscle tests and reduced voluntary cough flow rates and sound.[8-10] More recent studies suggest, as expected, cortical involvement in cough production. Cortical activation during voluntary cough has been demonstrated in healthy volunteers in functional MRI studies [11-12]. We have recently shown, using transcranial magnetic stimulation, increased latency and decreased amplitude of the motor evoked potentials from the abdominal (expiratory) muscles and reduction of the evoked rise in gastric pressure in acute stroke patients compared with controls, suggesting impaired cortical control of the abdominal muscles after stroke.[13] However, reflex cough may be more important than voluntary cough in ensuring adequate airway protection and clearance after acute stroke.[6, 14] Reflex cough is thought to be

primarily brainstem in origin but previous studies have noted cortical stroke patients with absence of reflex cough in response to food swallowing [6] or an inhaled noxious substance. [15] However these studies did not describe intensity measures (flow, pressure, sound) for any reflex cough produced.Therefore we considered further evaluation of reflex cough in hemispheric stroke to be worthwhile. The null hypotheses were that for patients with cortical hemisphere stroke, first that patients would have the same results as a group of non-stroke, age-matched controls on objective indices of both reflex cough intensity and voluntary cough intensity. As a secondary hypothesis we sought to confirm our prior observation[13] that stroke patients had no evidence of abdominal muscle weakness judged by peripheral nerve stimulation but did when assessed by voluntary tests of abdominal muscle strength It was anticipated that both our first null hypotheses would be refuted as previous studies suggest an intact cerebral cortex is required for effective voluntary and reflex cough. The primary outcome measure of cough intensity was cough flow rate for both voluntary and reflex cough.

MATERIALS AND METHODS

Study Subjects

Forty-five consecutive patients admitted to the stroke unit of King's College Hospital within two weeks of first-ever, middle cerebral artery territory ischaemic stroke were screened. Six patients were excluded as they did not wish to take part. Six patients with lacunar infarcts were excluded and fifteen were unsuitable due to diabetes, excess alcohol consumption, respiratory or neurological disease except stroke or inability to follow commands. Eighteen adults (seven women) were studied. Twenty healthy controls (five women) were recruited from a volunteer database and studied. The mean age and the proportion of female subjects were not significantly different between groups. Institutional ethical approval was obtained (LREC 02-120) and the subjects gave written informed consent.

Baseline Assessments

Smoking history, alcohol and ACE inhibitor use, height and weight were documented for all subjects. For patients, stroke diagnosis and location were confirmed by brain CT scan. Stroke severity on admission was assessed using the National Institutes of Health Stroke Scale (NIHSS) score. NIHSS score is a clinical stroke assessment tool to evaluate neurological status in acute stroke patients. The maximum score is 31, reflecting the most severe impairment.[16] Patients had a bedside swallowing assessment within 24 hours of admission, using radio-opaque contrast to detect aspiration.[17] A handheld spirometer (Jaeger SpiroPro, Erich Jaeger GmbH, Germany) was used to measure forced expiratory volume in one second (FEV_1) and forced vital capacity (FVC) which were expressed as percentage of predicted for age, sex and height.[18] Oxygen saturations were measured with subjects at rest, breathing room air. (Ohmeda Biox 3740 Pulse Oximeter, BOC Healthcare). Radiologist's reports of chest X-ray examinations (for patients only) were acquired from the hospital records.

Respiratory Muscle Strength Measurements

Measurements were made under controlled laboratory conditions with subjects on a bed, with the back rest at forty-five degrees but otherwise in accordance with the ATS/ERS Statement.[19] This ensured patients had the head end of the bed raised at an angle greater than the thirty degrees recommended to prevent aspiration and enabled inclusion of subjects unable to sit upright. Gastric and oesophageal pressures were measured using balloon catheters (CooperSurgical, USA) inserted per nasally. The catheters and a pneumotachograph were attached to individual pressure transducers (MP45, Validyne, USA). The transducer signals were amplified (CD-280 amplifier, Validyne) and acquired at 2 KHz using an analogue-to-digital converter (Powerlab, ADinstruments) and a computer running Chart 5 software. Transdiaphragmatic pressure (Pdi) was obtained by online subtraction of oesophageal pressure (Poes) from gastric pressure (Pgas).

Respiratory muscle strength was assessed volitionally by measuring maximum static expiratory mouth pressure (PEmax), maximum static inspiratory mouth pressure (PImax) and sniff pressures. The subjects made strong expiratory efforts from total lung capacity (for PEmax) or inspiratory efforts from functional residual capacity (for PImax) against a closed shutter. The maximum (for PE max) or minimum (for PI max) mean pressure over one second was recorded. The maximum nasal (sniff Pnasal), oesophageal (sniff Poes) and transdiaphragmatic (sniff Pdi) pressure changes achieved during a sniff from functional residual capacity were also measured. Volitional respiratory muscle tests were performed at least three times until consistency was achieved. Non-volitional assessment of expiratory (abdominal) muscle strength was made using magnetic stimulation over the spine at the level of the tenth thoracic nerve roots.[19] A magnetic stimulator (MagStim 200, Magstim Co, Dyfed, Wales) set to 100% output and a 90mm diameter circular coil were used. Subjects rested for 20 minutes before stimulation to minimise twitch potentiation. A minimum of three stimulations were performed and the evoked rise in gastric pressure above baseline, (TwitchT_{10}Pgas) measured. The mean value of three reproducible twitch responses was calculated.

Voluntary and Reflex Cough Tests

Airflow rates before, during and after cough were measured with subjects wearing a face mask (Hans-Rudolf, USA) connected to a pneumotachograph (Fleisch, Switzerland). Cough inspired and expired volumes were calculated online by integration of the flow signal (Figure 1). Voluntary cough was assessed before reflex cough, to avoid any effect of tartaric acid on voluntary cough. Subjects were told to inhale maximally and produce the biggest voluntary cough possible, until five consistent readings of maximum cough gastric pressure were achieved. Reflex cough was induced by nebulising escalating doses of 5%, 10%, 15% and 20% weight in volume (w/v) L-tartaric acid solutions. L-tartaric acid is thought to act on airway C-fibres to precipitate cough.[14] The L-tartaric acid was

administered using a Porta-Neb® compressor and Sidestream® nebuliser (Philips-Respironics Ltd, Chichester, UK) attached to the pneumotachograph and face-mask via a T-piece connector. The data sheet for the nebuliser states that 80% of the particles delivered will be 0.5μm diameter or smaller. Solutions were administered for 1 minute during normal breathing. Dose escalation was undertaken until 5 or more coughs were produced; if a subject failed to respond to 20% tartaric acid, no further solutions were administered. Corresponding cough spikes on the flow and gastric pressure traces were counted as coughs; all cough spikes within a cough bout were counted.

Peak cough flow rate (PCFR) was the maximum expiratory flow achieved during cough. PCFR was recorded, and also expressed as a percentage of peak expiratory flow rate (PEFR), to correct for a difference in height between groups. Cough inspired volume and cough expired volume (Fig 1) were expressed as a percentage of predicted FVC.[20] Cough gastric pressure was the maximum rise in gastric pressure during cough.(Fig 1)

For each subject, the five coughs (voluntary and reflex) with the biggest peak cough flow rates were averaged and the following derived measures made (Fig 1); (a)Compression time: duration of zero airflow from the time cough gastric pressure started to rise to the onset of expiratory flow; this is likely to represent the glottis closure period; (b)Cough pressure acceleration: the maximum cough gastric pressure divided by the time taken to reach maximum, starting from the onset of expiratory flow; and (c)Cough volume acceleration: peak cough flow rate divided by time taken to reach maximum flow.

Sample size and Data Analysis

The primary outcome measure was cough flow rate, for both voluntary and reflex cough. In a previous study with similar methods, healthy subjects had a mean voluntary cough peak flow rate of 351 (SD 112)l/min, which was 200l/min greater than that of the stroke group.[13] Using these data and G*Power v3.0.8 software(Franz Faul, University of Kiel, Germany) it was calculated that thirteen subjects in each group were required for an 85%

chance to detect a 150 l/min difference in peak cough flow rate between groups, at a significance level of 5%. Statistical analyses were performed using Prism 5.00 (GraphPad, USA); Confidence Interval Analysis 2.2.0 [21] and SPSS 16.0.1(SPSS Inc, USA). $P<0.05$ was considered significant. Data were tested for normality using the D'Agostino and Pearson omnibus method; t-tests or Mann-Whitney u-tests for two independent groups were used for comparisons. [21]

Univariate and multiple linear regression was used to investigate possible causes for impaired voluntary and reflex cough flow rates. Patients and controls were analysed together with controls being assigned a stroke severity score (NIHSS score) of zero for the purposes of these analyses. Cough flow rate, for both voluntary and reflex cough was the dependent variable and stroke severity (NIHSS score), height and FEV_1/FVC ratio were entered as independent predictors. All models included a constant.

RESULTS

Participants

Baseline characteristics of participants are given in Table 1. Acute hemispheric infarction was present in the left hemisphere in nine and the right hemisphere in nine patients. Of the left infarcts, 3 were frontal, 1 frontoparietal, 1 temporofrontoparietal and 4 capsulostriate. Of the right infarcts, 3 were frontal, 1 frontoparietal, 4 temporofrontoparietal and 1 capsulostriate. Six of eighteen patients had been treated with thrombolysis.

Table 1 Baseline Characteristics

		Stroke patients	Controls	Difference in means, medians or proportions	95% CI	P-value
		n=18	n=20			
Age (years)	Mean	62	56	6	-3 to 17	0.183
	SD	15	16			
Sex	Males	11	15			
	Females	7	5			
	Proportion male	0.61	0.75	-0.14	-0.40 to 0.15	0.489*
Height (cm)	Mean	166	176	-10	-4 to -14	0.001
	SD	7	9			
BMI (kg/m^2)	Median	24	24	-1	-4 to 2	0.538
	IQR	21-27	23-28			
Smoking (pack years)	Median	35	0	30	10 to 45	0.003
	IQR	14-53	0-5			
Days from stroke onset to test	Mean	6	-			
	SD	3	-			
Stroke severity (NIHSS score)	Mean	14	-			
31= most severe stroke	SD	8	-			
Dysphagic	Number	4	-			
	Proportion	0.22	-			
Taking ACE inhibitor	Number	9	0			
	Proportion	0.50	0			

Key for Table 1

*P-value for difference in proportions calculated using Fisher's exact test.

Pulmonary Function and Respiratory Muscle Tests

Results are given in Table 2. Patients showed significant impairments on spirometry and volitional respiratory muscle tests. There was no difference between patient and control groups on the non-volitional expiratory muscle strength test, $TwT_{10}Pgas$. The patients' group's mean $TwT_{10}Pgas$ of 26.4cmH_20 (SD 6.6) was well above the published normal minimum value of 16cmH_20, indicating that the expiratory muscles themselves were not weak but that the stroke patients could not fully recruit them volitionally.

Patients' oxygen saturations were lower than those of controls and their respiratory rate was higher. (Table 2) Nurses measured patients' oxygen saturations hourly for the first 48 hours after stroke and then every four hours subsequently. No patient had an oxygen saturation recording below 92% at any time.

Reports of chest radiographs taken during the admission for stroke were available for fourteen out of eighteen patients. For ten patients, the radiologist reported the lung fields and pleura to be clear. For two patients, chest radiographs were reported as showing signs of chronic obstructive pulmonary disease (COPD) although these patients had not had a diagnosis of COPD made previously. One radiograph showed interstitial pulmonary oedema but as the relevant patient was unable to perform spirometry or cough, this did not affect group results for these tests. One radiograph showed a small left pleural effusion.

Table 2 Lung function and Respiratory Muscle Tests

		Stroke patients n=18†	Controls n=20	Mean or Median difference (95% CI)	P-value
	Normal value for male [22]	Mean (Standard Deviation) or Median (IQ range)*			
Respiratory rate (breaths per minute, resting)		19 (5)	13 (2)	6 (3 to 8)	<0.001
FEV_1% predicted		60 (22)	102 (23)	-42 (-59 to 24)	<0.001
FVC% predicted		73 (22)	108 (23)	-35 (-52 to 17)	<0.001
FEV_1/VC ratio % *		71 (55-76)	77 (73-80)	-7 (-17 to 1)	0.019
O_2 saturations % *		96 (92-98)	98 (97-100)	-2 (-4 to 1)	0.014
PEmax (cmH_2O) *†	>80	50.5 (39.5-69.5)	106.0 (82.9-140.0)	-55.7 (-74.3 to 31.7)	<0.001
$TwT_{10}Pgas$ (cmH_2O)	>16	26.4 (6.6)	32.0 (14.1)	-5.6 (-15.0 to 4.0)	0.258
PImax (cmH_2O) †	>45	38.9 (25.1)	95.1 (33.0)	-56.2 (-77.7 to -34.7)	<0.001
Sniff nasal pressure(cmH_2O) †	>50	40.7 (25.8)	92.7 (25.9)	-52.0 (-70.2 to -33.8)	<0.001
Sniff Poes (cmH_2O) †	>55	57.7 (36.7)	109.3 (28.7)	-51.7 (-76.1 to -27.3)	<0.001
Sniff Pdi (cmH_2O) †	>100	63.2 (40.6)	121.1 (38.7)	-58.0 (-88.4 to -27.4)	0.001

Key for Table 2

* PEmax, FEV_1/FVC ratio and O_2 saturations data are skewed; values given are medians (IQ range) and median difference (95% CI). P-value is calculated using the Mann-Whitney u-test.

† 3 patients were unable to perform spirometry, PEmax, PImax and sniff tests so n=15 for these tests in the stroke group.

Table 2 Abbreviations: FEV_1=Forced Expiratory Volume in 1 Second; FVC=Forced Vital Capacity; PEmax=Maximum Static Expiratory Mouth Pressure; $TwT_{10}Pgas$=rise in gastric pressure after magnetic stimulation over the spine, at the level of T_{10}; PImax=Maximum Static Inspiratory Mouth Pressure; Sniff Poes= Sniff Oesophageal pressure; Sniff Pdi= Sniff Transdiaphragmatic Pressure

Voluntary Cough

Voluntary cough was significantly impaired in patients (Table 3, Fig 2). Two patients were unable to produce any voluntary coughs and so were excluded from the cough intensity analysis. Patients' mean cough gastric pressure of 98.5cmH_20 is well below the cutoff value of 130cmH_20 used to aid diagnosis of expiratory muscle weakness.[22]

Table 3 Maximum Voluntary Cough

	Stroke (n=16)	Controls (n=20)	Mean difference (95% CI)	P-value for difference
	Mean (standard deviation)			
Peak Cough Flow Rate (l/min)	287 (171)	497 (122)	-210 (-314 to -106)	<0.001
Peak Cough Flow Rate as % predicted PEFR	70 (43)	102 (19)	-32 (-55 to -10)	0.005
Cough Expired Volume(ml)	1170 (755)	2100 (864)	-930 (-1541 to -319)	0.004
Cough Expired Volume as % predicted FVC	33 (21)	47 (16)	-14 (-28 to -1)	0.041
Peak Inspiratory Flow Rate (l/min)*	112 (80 to 164)	213 (157 to 256)	-88 (-136 to -42)	<0.001
Cough Inspired Volume (ml)	1519 (546)	2710 (818)	-1191 (-1773 to -609)	0.003
Cough Inspired Volume as % predicted FVC	43 (21)	62 (18)	-19 (-34 to -3)	0.020
Cough Gastric Pressure(cmH_2O)	98.5 (61.6)	208.5 (61.3)	-110.0 (-152.4 to -67.6)	<0.001
Cough Pressure Acceleration(cmH_2O/s)	583 (512)	927 (303)	-344 (-644 to -45)	0.026
Compression Time (ms)	212 (105)	261 (127)	-49 (-138 to 40)	0.265
Cough Vol Acceleration (l/s^2)	83 (57)	200 (70)	118 (-165 to 70)	<0.001

Table 3 Abbreviations: PEFR=peak expiratory flow rate; FVC=forced vital capacity.
* Peak inspiratory flow rate data are skewed: values given are medians (IQ range) and median difference (95% CI). P-value is calculated using the Mann-Whitney u-test.

Reflex cough

Results for reflex cough are given in Table 4. The median concentration of tartaric acid solution required to produce 5 coughs was 10% for both patients and controls. One patient and two controls found tartaric acid inhalation intolerable so the reflex cough test was not performed. Three of the remaining 17 patients (17.6%) had no reflex cough response to 20% tartaric acid; all 18 normal subjects produced a cough response (0% non-responders).

The subjects who did not cough were not included in the cough intensity analysis. Patients' mean reflex cough gastric pressure of 179.0cmH_20 was well above the normal cutoff value of 130cmH_20 for voluntary cough gastric pressure.[22]

Table 4 Maximum Reflex Cough Response to L-Tartaric Acid

	Stroke (n=14) Mean(standard deviation)	Control (n=18)	Mean difference (95% CI)	P-value for difference*
Tartaric Acid Concentration Required to Produce Five (Or More) Coughs in One Minute*	10 (5-10)	10 (10-20)	0 (-5 to 0)	0.610
Number of Coughs Elicited in One Minute by Suprathreshold Tartaric Acid Stimulus	11.4 (5.0)	12.3 (7.6)	0.9 (-3.9 to 5.7)	0.705
Peak Cough Flow Rate (l/min)	204 (111)	379 (110)	-175 (-253 to -96)	<0.001
Peak Cough Flow Rate as % predicted PEFR	43 (34)	77 (20)	34 (-54 to -15)	<0.001
Cough Expired Volume (ml)	478 (203)	1269 (1119)	791 (-1412 to-169)	0.015
Cough Expired Volume as %predicted FVC	13 (5)	27 (25)	-14 (-29 to -0.3)	0.046
Cough Inspired Volume (ml)	763 (406)	1172 (699)	-410 (-893 to -74)	0.093
Cough Inspired Volume as % predicted FVC	22 (13)	26 (15)	-4 (-15 to 7)	0.479
Cough Gastric Pressure (cmH_2O)	179.0 (78.0)	208.2 (77.4)	-29.3 (-81.9 to 23.4)	0.266
Cough Pressure Acceleration (cmH_2O/s)	788 (297)	947 (216)	-159 (-393 to 75)	0.171
Compression Time (ms)*	280 (236 to 383)	270 (197 to 325)	23 (-52 to 99)	0.661
Cough Volume Acceleration (l/s^2)	99 (58)	179 (64)	-80 (-129 to 31)	0.003

Key for Table 4: *Tartaric acid strength data are ordinal and compression time data are skewed. Values given are medians (IQ range) and median difference and P-value calculated using Mann-Whitney u-tests.

Table 4 Abbreviations: PEFR=peak expiratory flow rate; FVC=forced vital capacity

Predictors of Voluntary and Reflex Cough Flow Rate

The results of univariate linear regression with peak cough flow rate as the dependent variable and stroke severity as the predictor are shown in Figure 4, for both voluntary and reflex cough. Voluntary cough flow rate was predicted by a model including NIHSS score, height and FEV_1/FVC ratio. Adjusted R^2 for the model = 0.653, P<0.001. Stroke severity (NIHSS score) had the greatest and most significant effect. [Regression coefficient -12.6 l/min per point on NIHSS score, 95% CI -19.2 to -6.1, P<0.001]. Further details of the linear regression model are given in an online data supplement, Table S1. The only significant predictor of reflex cough flow rate was NIHSS score; details are given in Figure 4. ACE inhibitor use (or not) was tried as a predictor for both voluntary and reflex cough but did not exert a statistically significant effect.

DISCUSSION

This study shows that voluntary and reflex cough are both impaired after acute hemispheric infarction. Impairments of respiratory muscle function when measured by volitional tests and reductions in voluntary cough flows and gastric pressure in stroke patients have been described previously,[4-5, 13, 23] but reflex cough may be considered more important for airway protection and clearance.[24] The novel and important finding of this study is that despite patients achieving normal reflex cough gastric pressures, flow rates and expired volumes for reflex cough are both decreased.

Critique of the Method

The differences in reflex cough flow rate, reflex cough expired air volume and reflex cough volume acceleration between patients and controls could not be attributed to differences in air volume inspired prior to cough, concentration of tartaric acid solution required to produce five or more coughs, duration of glottis closure, peripheral nerve conduction or expiratory muscle strength. Higher stroke severity score predicted impairment of both voluntary and reflex cough flow rates, suggesting a physiological basis for impaired cough in acute stroke.

Spirometry, respiratory muscle strength and voluntary cough are measured by volitional tests in the sense that they require a patient to make a maximal effort and their interpretation depends on the vigour of that effort being maximal. Stroke patients may theoretically perform badly because the tests depend upon subject understanding and effort [19], although strokes more obvious manifestations concern motor skills. Even so these factors would not affect reflex cough where any impairment observed is likely to be due to non-volitional factors. Gastric pressures and glottis closure times in patients were no different to controls. Reflex cough inspired air volume tended to be smaller for patients but this did not reach statistical significance.

It is possible that reduced functional residual capacity (FRC) in patients may have contributed to reduced cough flow rates as a lower starting lung volume will result in higher airways resistance and reduced flow rates. Little is known of FRC in stroke patients at rest (and none at all during cough) but one small study showed normal FRC in moderately severe patients at 2-4 weeks post-onset.[9] Patients had more airways obstruction than controls (significantly reduced FEV_1 and FEV_1/FVC ratio). Airways obstruction would be expected to lead to reduced voluntary cough flow rate although from the regression models, the influence of FEV_1/FVC ratio on voluntary cough flow rates was smaller and less significant than the effect of stroke severity. Neither FEV_1 nor FEV1/FVC ratio were significant predictors of reflex cough flow rate.

Previous studies have separately described intra-abdominal pressure changes during reflex and voluntary cough in normals [24] but this is the first study to describe peak cough flow rates, volumes and pressures during reflex and voluntary cough in an homogeneous sample of stroke patients and controls. A merit of our study is that subjects with diabetes or previous heavy alcohol use were excluded because these may affect cough.[25-26] Similarly application of lidocaine to the pharynx, (to pass pressure catheters) can alter cough [27] so cough tests were performed at least 90 minutes after administration. Lastly, although ACE inhibitor use was recorded because of the previously described effect on cough[28], it was not found to be a significant independent predictor of cough flow rate in our study.

Significance of the findings

The rapid rise of gastric pressure but not expiratory flow during reflex cough suggests that the sensory pathways are intact since abdominal muscles must be recruited to generate a positive Pgas. However the slower rise of expiratory flow suggests an additional flow limitation as a manifestation of ischaemic cortical injury. We suspect that this injury may

affect the coordinated activation of the upper airway muscles with the abdominal and thoracic muscles used for cough production.[7] Cortical involvement in reflex and voluntary cough is supported by studies showing voluntary suppression of capsaicin-induced reflex cough in healthy volunteers, [29] absent or delayed conduction in cortico-respiratory tracts on stimulating the affected hemisphere of stroke patients [13] and cortical modulation of pharyngeal coordination in stroke.[30]

This study is of modest size but the sample appears representative and shows baseline characteristics similar to those in other studies. The patients' mean voluntary cough peak cough flow rate found here is similar to that found 6 days post stroke onset in a recent study of 96 patients (261±188 l/min).[23] As the definition of effective cough remains elusive, [14] it is impossible to know whether the reduction in patients' cough flows are clinically meaningful. One method would be to correlate cough impairments with incidence of chest infections but the number of events in this study (n=2) precludes such analysis. Reflex cough produced in the laboratory does not accurately replicate the response to aspirated fluid or food, which cannot easily be studied for safety reasons. Although desirable, measurements and imaging of the upper airways during cough could not be performed because of logistic and patient discomfort considerations.

This study shows that acute stroke patients have impaired voluntary and reflex cough; this may result in impaired lung clearance. The data suggests that impairment may be in part due to ineffective coordination of different muscle groups following cerebral injury. Further studies are required of the mechanisms that may underlie reflex and voluntary cough impairment and to test interventions that may improve cough function, in order to try and reduce the incidence and consequences of aspiration after stroke.

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ETHICS

The study was approved by the Ethics Committee of King's College Hospital, LREC 02-120.

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Figure 1 Voluntary Cough Trace for a Stroke Patient with Guide to Measurements Made

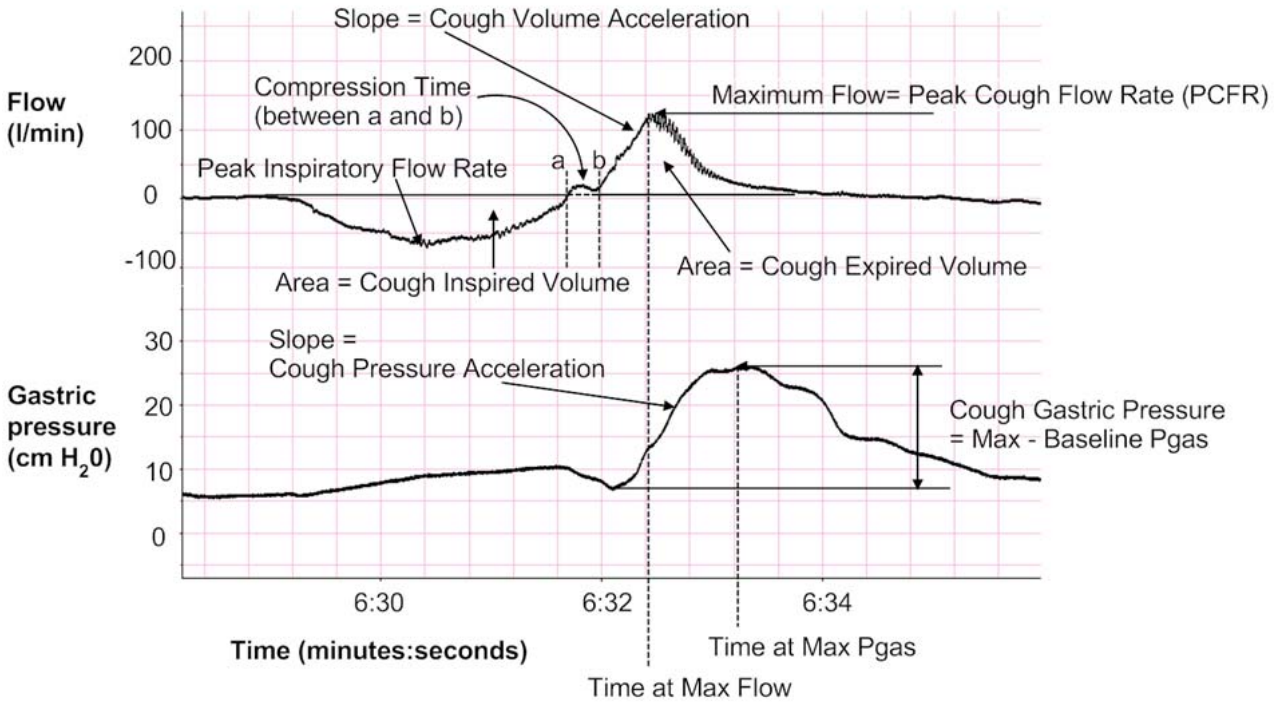


Figure 2: Voluntary Cough in Normal Subject Compared to Stroke Patient

A five second sweep of flow and gastric pressure traces during maximum voluntary cough. The traces for a moderately impaired stroke patient (in black) are superimposed on those of control subject (in grey). Note the patient's cough flow does not appear so severely impaired as the gastric pressure.

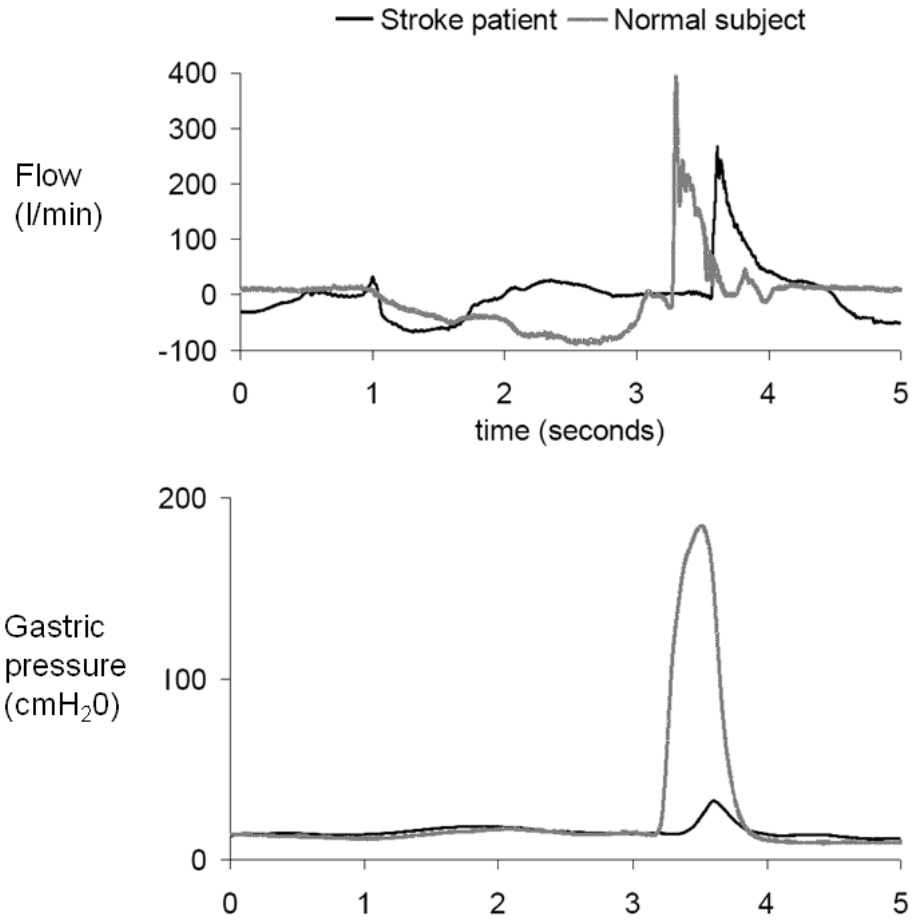

Stroke patient
Normal subject
Flow
(l/min)
400
300
200
100
0
-100
0
1
2
3
4
5
time (seconds)
Gastric
pressure
(cmH20)
200
100
0
0
1
2
3
4
5

Figure 3: Ten second trace of flow and gastric pressure traces in a healthy control subject and a severely affected patient.

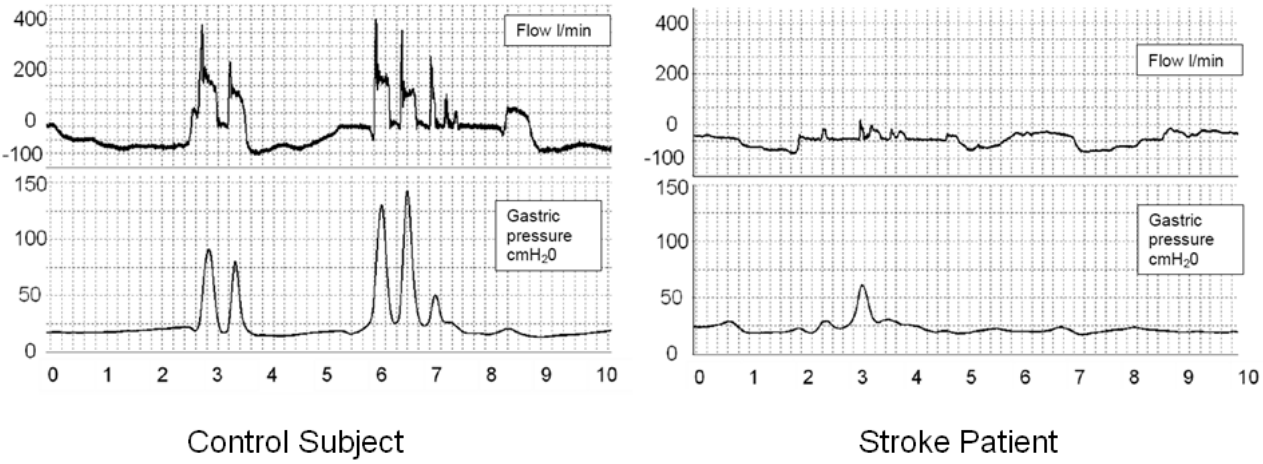


Figure 4: Univariate Linear Regression

Figure 4A
Regression line (with 95% mean prediction interval) drawn on a scatter diagram relating voluntary cough flow rate and stroke severity in 36 subjects able to produce a voluntary cough. Regression slope is -15 l/min per one point of NIHSS score, 95% CI -20 to -9l/min, $P<0.001$. Adjusted $R^2 = 0.465$. A maximum NIHSS score of 31 reflects the most severe stroke.

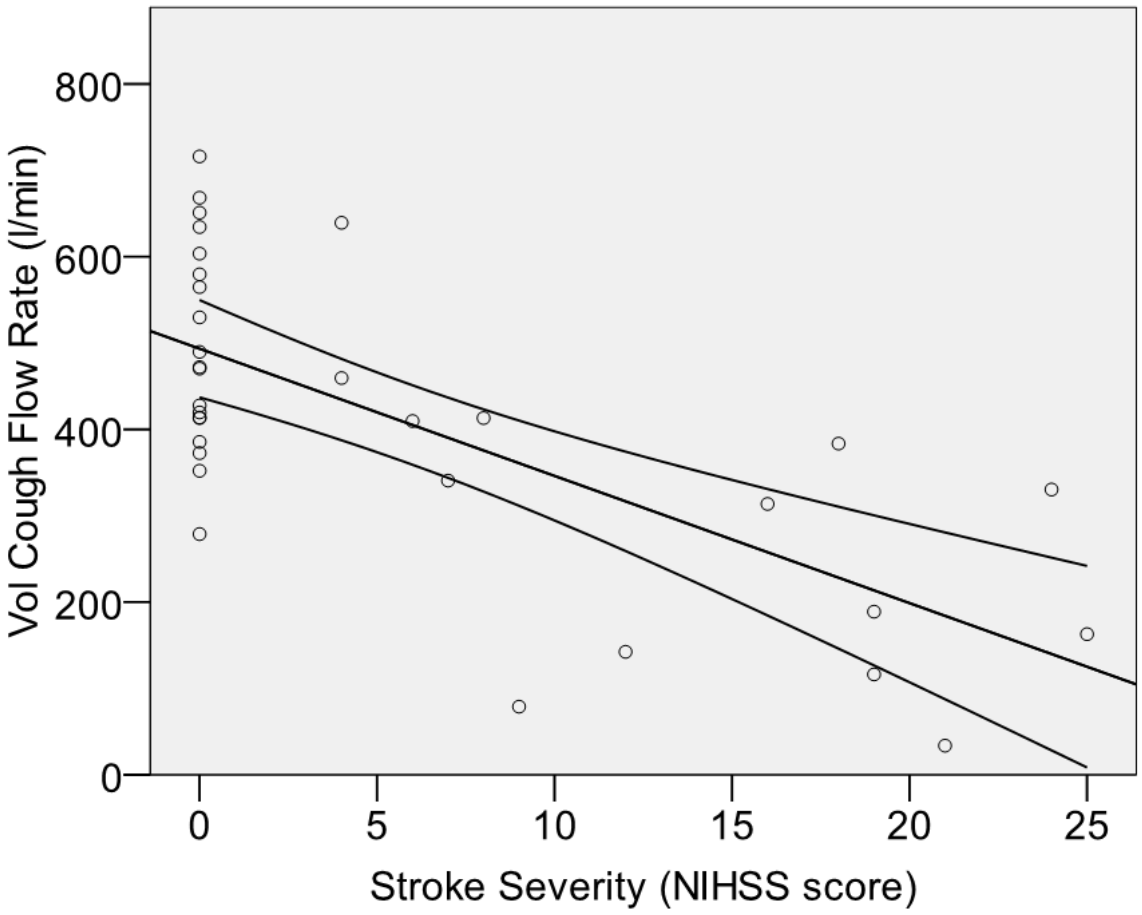
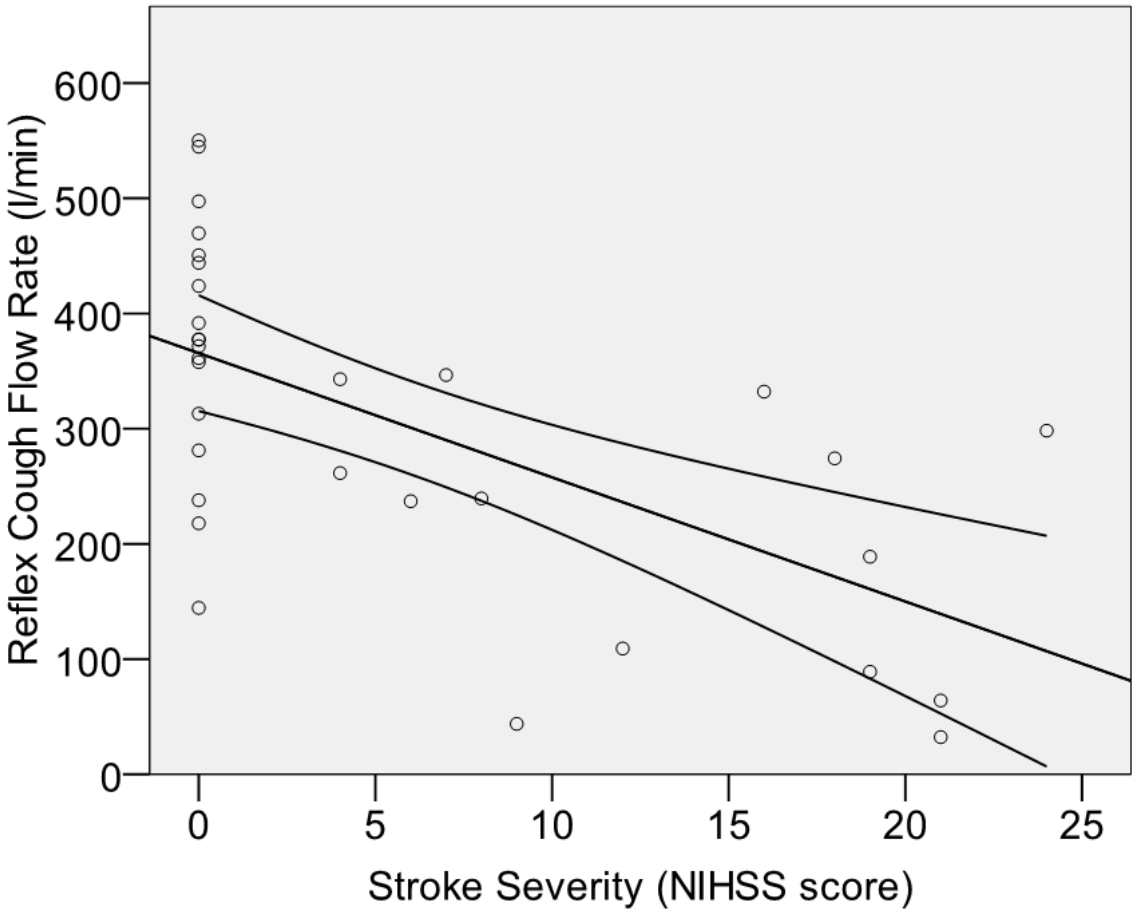


Figure 4B
Regression line (with 95% mean prediction interval) drawn on a scatter diagram relating reflex cough flow rate and stroke severity in 32 subjects able to produce a reflex cough. Regression slope is -11 l/min per one point of NIHSS score, 95% CI -16 to -6l/min, P<0.001. Adjusted $R^2 = 0.367$.


Reflex Cough Flow Rate (l/min)
600
500
400
300
200
100
0
0
5
10
15
20
25
Stroke Severity (NIHSS score)