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Abnormal patterns of breathing during swallowing in neurological disorders

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Summary

Swallowing momentarily inhibits breathing, and normally the great majority of apnoeas which accompany a swallow are followed by expiration (xE swallows). This swallowing–breathing interaction is regarded as one of several mechanisms by which the airway is protected from aspiration during swallowing. The purpose of this study was to investigate the interaction of breathing and swallowing in two groups of neurological patients. Twenty-two patients with defined neurological disorders involving various structures or pathways (brain, spinal cord and peripheral nerves) were studied to determine whether particular lesions resulted in breakdown of the normal breathing pattern (22 normal subjects were also assessed and their breathing–swallowing pattern was compared with that of neurological patients). Subsequently, 32 patients with motor neurone disease (MND) were studied to identify factors associated with an abnormal pattern (i.e. swallow apnoeas followed by inspiration) and to clarify whether an abnormal pattern is related to chest infections, episodes of coughing and choking during meals, and prognosis. The swallow apnoea in patients with brain, spinal cord and peripheral neurological diseases was followed by inspiration more frequently than expected [20/22 (91%) patients compared with 2/22 (9%) of normal subjects, *P* < 0.001], but this was not associated with a specific site of lesion(s). However, patients with corticobulbar involvement tended to have post-apnoea inspiration more often than those without. MND patients commonly displayed an abnormal pattern during swallowing [14/32 (44%) patients] characterized by inspiration after swallow, prolonged swallow apnoea and multiple swallows per bolus. Over the period of follow-up (12–18 months) this pattern did not predict chest infections, coughing and choking episodes during meals or survival. It seems likely that post-swallowing apnoea inspiration is a non-specific concomitant of disordered swallowing and/or breathing rather than being an important mechanism of aspiration *per se* or of symptom production.

Keywords: motor neurone disease; swallow apnoea; dysphagia; respiration

Abbreviations: DRG = dorsal respiratory group; EDAT = Exeter Dysphagia Assessment Technique; FVC = forced vital capacity; MND = motor neurone disease; ND = patients with neurological disorders; NO = subjects without a history of swallowing, breathing or neurological disorders; NTS = nucleus tractus solitarius; VRG = ventral respiratory group; xE = swallow apnoea followed by expiration; xI = swallow apnoea followed by inspiration

Introduction

In humans, the pharynx serves as a common pathway for both swallowing and breathing. This anatomical configuration allows the possibility of aspiration of material into the airway. Several mechanisms minimize the risk of laryngeal penetration and/or aspiration: swallowing results in reflex closure of the glottis which acts as a protective valve against the aspiration of foreign materials into the respiratory tract (Ardran *et al.*, 1952). Strong adduction of the true vocal cords is supplemented by the closure of the false cords and approximation of the aryepiglottic folds, although adduction of the true cords alone suffices to prevent penetration into the trachea. The epiglottis contributes to deflection of the bolus away from the laryngeal aditus into the pyriform sinuses, from which it passes into the oesophagus. Swallowing must also interact with breathing so that a swallow causes minimal or no disturbance to continuous breathing. In awake human adults, studies have shown that swallow events are accompanied by an apnoeic period (the swallow apnoea) lasting between 0.6 and 2.0 s (Clark, 1920; Preiksaitis *et al.*, 1992), and this swallow apnoea is followed by expiration in 95% of swallows (Selley *et al.*, 1989*a*). This sequence of a swallow followed by expiration may be a useful mechanism for clearing the pharyngeal recesses of foreign residues before subsequent inspiration and may have a role in preventing low-grade recurrent aspiration.

The swallowing centre is a complex organization of neural elements in the cortex and brainstem of the CNS. In sheep, the neurones in the brainstem that are involved in swallowing lie mainly in the dorsal region, in and adjacent to the nucleus tractus solitarius (NTS) and the ventral region around the nucleus ambiguus with extensive involvement of the reticular formation (Jean, 1972, 1978, 1984, 1986). The two regions are represented on both sides of the brainstem and are extensively interconnected (Doty, 1968). However, whether this work on animals is also applicable to man is uncertain. Breathing is regulated from complex interactions between two functional groups of neurones in the medulla known as the dorsal (DRG) and ventral respiratory groups (VRG). The DRG is located in the dorsolateral portion of the nucleus of the solitary tract. It primarily receives inputs from the cranial nerves IX and X, and specifically from the carotid body. The DRG sends fibres to the inspiratory spinal motor neurones and to the VRG, which it modulates (Cohen *et al.*, 1974). The VRG is split into two parts: the rostral portion, primarily part of nucleus ambiguus, innervates the larynx and has both inspiratory and expiratory functions. The larger caudal part, also known as the nucleus retroambiguus, has both inspiratory and expiratory neurones innervating motor units of the diaphragm and intercostal muscles. The descending axons of neurones contained in the DRG and VRG descend in the ventrolateral columns of the spinal cord, anterior to the corticospinal tract. Both inspiratory and expiratory axons appear to descend in somewhat different parts of the ventral portion of the cord (Newsom-Davis *et al.*, 1972). The shared vagal motor innervation of pharynx and larynx via nucleus ambiguus and the close anatomical relationship between respiratory and pharyngeal afferents [to potentially overlapping regions of the nucleus of the tractus solitarius as shown in experimental animals (cat) (Kalia *et al.*, 1980)] and the medullary respiratory centres suggest the basis for the high level of coordination between breathing and swallowing, including the inhibition of breathing during swallow apnoea (Doty, 1967). Studies using magnetic brain stimulation in patients with cerebral hemisphere stroke (Hamdy *et al.*, 1996) together with previous clinical observations of swallowing in patients with cerebral hemisphere lesions (Meadows, 1973) have confirmed the importance of corticobulbar connections in facilitating swallowing in the conscious state and provide evidence for the importance of oropharyngeal afferent stimulation (Hamdy *et al.*, 1998). Magnetic stimulation techniques in patients with discrete magnetic resonance documented brainstem lesions have also clarified the lateralization and brainstem course of relevant pathways to the hypoglossal nucleus (Urban *et al.*, 1996, 1997).

Dysphagia is a symptom that may occur for many reasons (Hughes *et al.*, 1998): there may be impaired motor control or weakness of facial, masticatory, pharyngeal or laryngo-oesophageal muscles; oropharyngeal sensation which aids triggering of the swallow reflex and protection of the airway may be abnormal; the conscious level may be diminished, thus removing in whole or part, voluntary control over deglutition; or the cerebral cortex may be damaged. A disruption of the normal coordination of swallowing and breathing has been shown previously in a small group of dysphagic neurological patients (Selley *et al.*, 1989*b*), but the extent of its clinical significance and whether specific lesions or disorders of particular pathways cause this breakdown remain unclear.

There are two main techniques for monitoring breathing during swallowing: direct airflow (oral, nasal, or both oral and nasal airflow being monitored) and measurements related to changes in inflation of the lung, focusing on movements of chest wall and abdomen (Tarrant *et al.*, 1997). The aim of our study was to investigate what factors (neurological or otherwise) determine the direction of airflow (inspiration or expiration) immediately after a swallow: this requires a sensitive technique such as that described by Selley *et al.* in the Exeter Dysphagia Assessment Technique (EDAT) based on nasal airflow (Selley *et al.,* 1989, 1990). It has been shown that EDAT is a valid (Selley *et al.*, 1994) and reliable technique (Pinnington *et al.*, 2000) in assessing breathing pattern during swallowing. We further attempted to clarify whether, in a particular disorder [motor neurone disease (MND)], postdeglutition inspiration *per se* is clearly linked to events likely to affect prognosis. First, a cross-sectional study was designed, using patients with defined neurological disorders, involving various structures or pathways, in order to determine whether lesions at particular sites resulted in the breakdown of the normal breathing pattern around a swallow. This study was not restricted to patients who complained of swallowing problems or who had clinical dysphagia. Normal subjects were also assessed and their breathing/swallowing pattern was compared with that of neurological patients. Secondly, a longitudinal study was designed to assess the interaction of breathing and swallowing in patients with MND, whose features are predominantly the result of corticobulbar/corticospinal or brainstem/spinal motor neurone pathology, and commonly associated with swallowing difficulties. We wished to identify factors associated with an abnormal pattern (i.e. swallow apnoeas followed by inspiration) and to clarify whether such a pattern is in fact related to chest infections, episodes of coughing and choking during meals, and prognosis. If this were the case, there might be specific guidance and treatment which should be considered by the speech and language therapist. Preliminary data on neurological patients (Pickersgill *et al.*, 1998) and MND patients (Hadjikoutis *et al.*, 1999) have been presented at meetings of the Association of British Neurologists.

Methods

Subjects

Patients with a variety of defined neurological disorders (ND) were recruited from the neurology ward and clinics at

Table 1 *Summary characteristics of patients studied with defined neurological disorders*

Patients	Group	Diagnosis	Sex	Age (years)	Swallowing capacity % predicted for age and sex	No. of swallow apnoeas	No. of swallows	xI swallows (%)
1	CNS	Brainstem subarachnoid haemorrhage	M	41	68.8	66	60	6.6
2	CNS	Progressive idiopathic cerebellar degeneration	M	59	66.2	45	46	8.7
3	CNS	Medullary lesion: presumed encephalitis	M	76	67.0	56	49	6.1
4	CNS	Pontine infarction	M	52	13.1*	40	42	21.4
5	CNS	Multisystem atrophy	M	63	25.8*	24	24	66.0
6	CNS	Multisystem atrophy	M	56	5.3*	25	30	10.0
7	CNS	Presumed brainstem encephalitis	F	26	22.9*	51	56	16.1
8	CNS	Amyotrophic lateral sclerosis	M	62	3.1*	81	94	27.6
9	SC	C6 incomplete tetraplegia secondary to spinal subarachnoid haemorrhage and syrinx	M	75	198.2	46	55	14.0
10	SC	Traumatic C6 complete tetraplegia	M	51	40.0*	42	42	59.5
11	SC	Traumatic C5/6 complete tetraplegia	M	31	54.0	32	35	0
12	SC	C5 incomplete tetraplegia secondary to ischaemic cervical myelopathy	F	22	60.8	30	50	10.0
13	SC	Traumatic C6/7 incomplete tetraplegia	M	69	237.2	32	32	20.6
14	SC	Traumatic C4/5 incomplete tetraplegia	M	33	61.6	32	35	5.7
15	SC	Traumatic T6 paraplegia and left brachial plexus avulsion	M	21	104.3	58	63	4.7
16	SC	Traumatic C4 complete tetraplegia	M	52	120.2	32	34	70.6
17	SC	Traumatic C6 incomplete tetraplegia	M	25	110.4	33	56	7.1
18	PNS	Progressive muscular atrophy (MND)	M	58	62.7	34	35	2.8
19	PNS	Bilateral brachial plexus neuritis with phrenic nerve palsies	M	52	121.9	42	46	43.5
20	PNS	Bell's palsy	F	42	115.8	45	41	0
21	PNS	Myasthenia gravis	F	65	59.1	66	56	5.3
22	PNS	Tethered tongue secondary to carcinoma	M	63	53.2	53	42	23.8

SC = spinal cord; M = male; F = female. *Below 95% confidence interval for predicted mean for an individual.

University Hospital of Wales, and the rehabilitation and spinal injury unit ward at Rookwood Hospital, from September 1996 to August 1998. ND patients were classified by an investigator blind to the swallowing–breathing pattern results according to the site (cerebral hemisphere, brainstem, cerebellum, spinal cord, peripheral nerves) and pathways involved in the lesions using the case notes and imaging documentation. None of the patients had a history of a primary lung disease. Table 1 summarizes the neurological diagnoses of the patients. Subjects without a history of swallowing, breathing or neurological disorders (NO) were also recruited from hospital staff and the general public. Patients with MND, diagnosed according to El Escorial criteria (El Escorial, 1998), were recruited from the neurology ward, the general neurology clinics at University Hospital of Wales and the MND clinic at Rookwood Hospital, from June 1998 to September 1999. One of the MND patients had a history of a primary lung disease (chronic obstructive airway disease). ND and NO subjects were studied on one occasion. MND patients were studied at 3 monthly intervals for 12–15 months. Figure 1 summarizes the design of the study.

Techniques

Bulbar and respiratory assessment

A standard questionnaire on swallowing-related symptoms for which normative data is available (Hughes *et al*., 1996*a*) was administered and a detailed general neurological examination was performed where bulbar signs were documented using a semiquantitative scale (Hughes *et al.*, 1996*a*) and were divided into upper motor neurone signs [presence of a brisk jaw jerk, slow moving tongue, pseudobulbar affect (sudden loss of emotional control, i.e. laughing, crying or both occuring in response to non-specific, often inconsequential stimuli in the absence of clear association with prevailing mood state)] and lower motor neurone signs (tongue wasting, fasciculations, weakness, palatal/pharyngeal muscle weakness, absent gag reflex, uvula deviation, hoarseness of voice). However, we appreciated that in some severe cases of bulbar weakness, a definite distinction of lower and upper motor neurone weakness was difficult. A quantitative measure of swallowing capacity was obtained by a test in which the time and number of swallows required to consume a known volume of water was measured: average volume per swallow (ml), average time per swallow (s) and swallowing capacity (ml/s) were calculated (Hughes *et al.*, 1996*b*). An abnormal test of swallowing was defined as being a swallowing capacity or volume/swallow less than the lower 95% confidence interval for the individual predicted mean adjusted for age and sex. Eating habits (diet modification and feeding assistance) were documented. Respiratory function was assessed by recording forced vital capacity (FVC) using a portable spirometer (a face mask was used in patients with bulbofacial involvement).

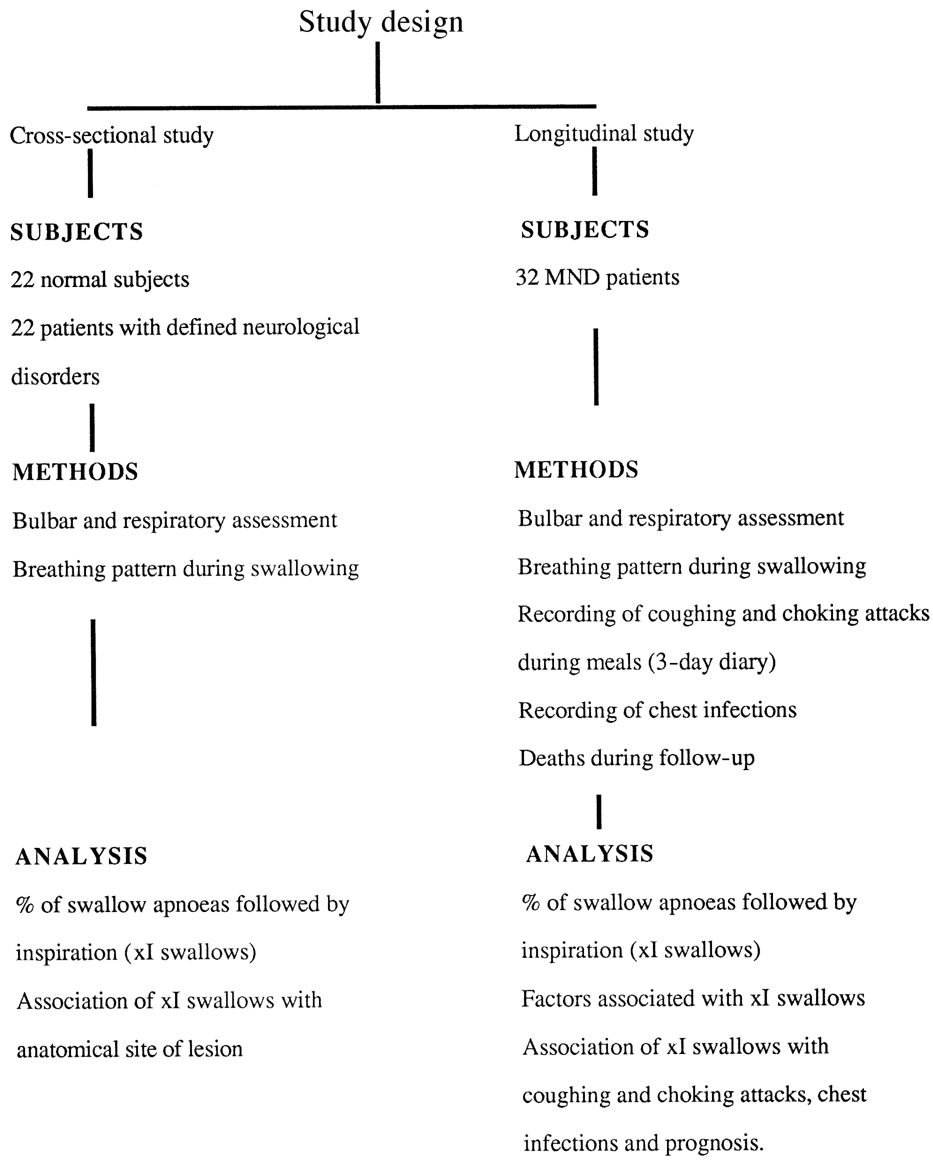

Fig. 1 Study design.

Breathing pattern during swallowing

The breathing pattern during swallowing was recorded using intranasal pressure measurement (Selley *et al.*, 1990). This method employed nasal speculae inserted into the nostrils and relied upon the reduction of pressure within the nares on inspiration and conversely, a slight increase in pressure above atmospheric on expiration due to the flowing air. By connecting the speculae to a sensitive micromanometer within the EDAT device (Bio-instrumentation Ltd, Exeter, UK) the pressure changes can be detected. Entry of a bolus into the mouth was recorded by completion of an electrical contact made with an insulated plastic cup. Swallow sounds were recorded via a throat microphone held below the angle of the mandible or lateral to the thyroid cartilage, and distinguished from artefact by using an electronic marker when elevation of the larynx was observed and swallow sounds heard via headphones. Signals from the EDAT equipment were presented in chart form using a Gould Electronics TA240 EasyGraf four channel chart recorder. The optimum chart speed for subsequent analysis of respiratory and swallow events was 10 mm/s. Subjects were asked to swallow boluses of tepid tap water presented in the plastic cup at volumes of 5, 10 and 20 ml. Eight swallows of each bolus volume were recorded for ND and NO subjects, with the exception of patients with significant dysphagia whose average volume per swallow during the timed test of swallowing dictated that boluses should be restricted to 5 or 10 ml for reasons of safety. ND and NO subjects were also asked to perform eight 'dry' swallows, i.e. no bolus being presented to them, merely to initiate a voluntary swallow. The 32 swallows were performed in random order. Between three and six boluses of each volume (5, 10 and 20 ml) were given to MND patients randomly. For each swallow, the following were recorded: (i) the number of swallows per

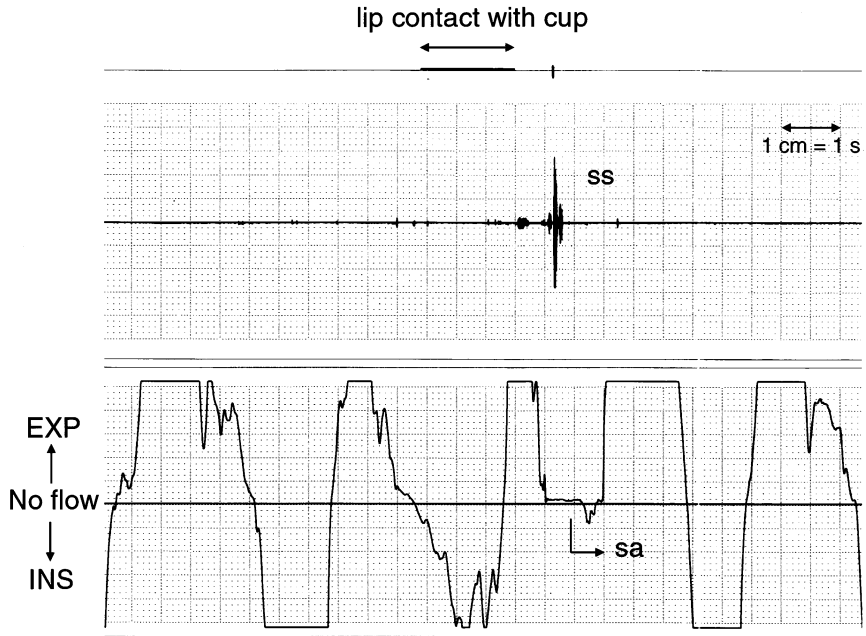

Fig. 2 Tracing of a chart (xE swallow) marked with the events described: ss = swallow sounds, sa = swallow apnoea, EXP = expiration, INS = inspiration. The small downward deflection of the trace recorded at the end of the swallow apnoea is commonly seen and it is thought to be caused by negative pressure generated by the opening of the glottis.

bolus swallow; (ii) the length of each swallow apnoea; (iii) the pattern of breathing after each swallow apnoea; (iv) respiratory rate before each swallow.

Each swallow apnoea was classified into one of two types depending on whether it was followed by expiration (xE) or inspiration (xI). Figure 2 illustrates an example of an xE swallow and measurements taken from the chart recording. The proportion of xI swallows in the individual patients with neurological disorders was compared with the grouped proportion in normal subjects. Pearson correlations and one-way analyses of variance or the Kruskal–Wallis test were used to investigate relationships between the proportion of each swallow type, and the clinical and respiratory measurements taken, both within and between the two groups.

MND patients were classified into two groups according to whether they did or did not have xI swallow apnoeas and the two groups were compared for certain prospectively defined demographic, disease related, bulbar related, respiratory related or prognostic variables. Nineteen out of 32 MND patients had a repeat assessment after an interval of 6 months (range 6–9 months). The remaining 13 patients were unable to have a second assessement: seven had died, two were unable to swallow orally, and four were unable to cooperate due to severe disability.

Coughing/choking episodes, chest infections, prognosis

MND patients used a pre-formatted sheet to maintain a detailed diary of coughing and choking events together with any association with eating and drinking over 3 days close to the day of the assessment. Patients were asked to report any chest infections during the follow-up period. The following criteria were used in defining a chest infection: fever, coughing, discoloured sputum, prescription of antibiotics for a chest infection by the general practitioner or hospital doctor. Medical notes of all patients were checked for any possible admissions in local hospitals with chest infections. Patients were assessed every 3 months for up to 15 months duration in order to record coughing and choking episodes, chest infections and prognosis. The duration of the disease from the onset of MND symptoms until the end of the study or death was recorded. Deaths were recorded via listing with the Office of Population and Census Surveys and copies of death certificates were obtained.

Ethics

The study was approved by Bro Taf Local Research Ethics Committee in Cardiff. All patients and healthy volunteers gave consent for the study.

Results

Patients with defined neurological disorders (ND) and normal subjects (NO)

Twenty-two healthy volunteers [13 female, mean age 49 (range 21–73) years] were assessed. A total of 484 swallows were analysed. Twenty out of 22 (91%) individuals always

Table 2 *Classification of patients according to the anatomical site of their neurological disease*

Clinical features	Group 1 (n = 8)	Group 2 (n = 9)	Group 3 (n = 5)	P-value*
Sex				
Male	7	8	3	
Female	1	1	2	
Age (years)	53 (13)	40 (21)	58 (9)	0.166
Percentage of swallow apnoeas followed by inspiration (xI swallows)	8.2 (7.4)	9.2 (9.5)	8.0 (10.8)	0.961
Timed test of swallowing				
Volume/time (ml/s)	11.3 (9.2)	23.4 (11.7)	9.0 (6.0)	0.023
Volume/swallow (ml)	17.6 (8.5)	34.6 (20.4)	16.2 (7.8)	0.036
FVC predicted (%)	54 (21)	48 (13)	65 (31)	0.418

The values are expressed as mean (standard deviation). Group 1 = patients with brain disease; group 2 = patients with spinal cord disease; group 3 = patients with peripheral nerve disease. *One-way analysis of variance.

displayed a swallow apnoea followed by expiration (xE) regardless of bolus size (5–20 ml); 2/22 (9%) displayed an xI swallow pattern, and this occurred only with a 20 ml bolus in 50% of swallows.

Twenty-two patients [18 male, mean age 49 (range 21–76) years] were studied, 662 water boluses were presented (5, 10, 20 ml) and 965 swallows occurred, associated with 1023 apnoeas; of these a mean of 18.9% (range in individual patients 2.8–70.6% of all swallows) in 20/22 (91%) patients were followed by inspiration (Table 1). Two patients had no xI swallows. There was a significant difference between the two groups (healthy volunteers and neurological patients) in the proportion of swallow apnoeas followed by inspiration (xI swallows) ($P < 0.001$, Kruskal–Wallis test).

Six patients had abnormal swallowing as defined by the quantitative swallowing test (Table 1) of whom four complained of swallowing symptoms. These six patients had significantly more xI swallows ($P < 0.02$, one-way analysis of variance) than those with a normal timed test of swallowing. Sex, age, forced vital capacity and respiratory rate before each swallow were not associated with the frequency of xI swallows.

Patients were divided into three groups according to the anatomical site of their neurological disorder: brain (group 1), spinal cord (group 2) and peripheral nervous system (group 3) (Table 2). Patients with brain and peripheral nervous system disease tended to have a lower swallowing capacity in terms of volume/time and volume/swallow than patients with spinal cord disease: this pertained whether absolute values were used (Table 2) or if results were expressed in relation to normal values for age and sex. Patients with spinal cord injury or disease tended to have a lower FVC than patients with brain or peripheral nervous system disease. xI swallows were not associated with any specific anatomical site of neurological disease (Table 2). Patients were also classified according to neurological pathways likely to be impaired: patients with corticobulbar involvement (four patients) had more (%) xI swallows (mean = 38.9%, SD = 22.9) than those without (mean = 15.8%, SD = 20.2), but the diference was not statistically significant (P = 0.15, Kruskal–Wallis test).

MND patients

Frequency of xI swallows

Thirty-two MND patients [22 male, mean age 67 (range 51–81) years] were studied (Table 3). Fourteen patients (44%) had at least one swallow apnoea followed by inspiration (xI patients) at the initial assessment: six patients had an xI swallow with 5 ml bolus, seven with 10 ml bolus, and 10 with 20 ml bolus (Table 4). In 18 (56%) patients, apnoea was always followed by expiration (xE patients). Figure 3 illustrates an example of a patient with an xI swallow.

Factors related to xI swallows

xI patients were more likely to have upper motor neurone bulbar signs and had a much lower swallowing capacity both in terms of volume/time and average volume/swallow than xE patients (Table 3). Age, sex, duration of the disease, respiratory rate and FVC were not associated with an abnormal respiratory pattern during swallowing (Table 3). Patients with xI swallows generally had longer swallow apnoeas (Table 4) and required more swallows to clear a bolus compared with those with xE swallows: this was significant for 20 ml (using the Kruskal–Wallis test, $P <$ 0.023 and $P < 0.002$, respectively) but not 5 and 10 ml boluses. Figure 4 illustrates an example of a patient with prolonged swallow apnoea and multiple swallows with a 20 ml bolus.

Follow-up assessments

Two out of 19 MND patients who had repeat studies of swallowing–breathing pattern developed an xI swallow at

Table 3 *Clinical characteristics of MND patients*

	All MND patients (n = 32)	MND patients with xE swallows (group 1) (n = 18)	MND patients with xI swallows (group 2) (n = 14)	P value
Sex				
Female (%)	10 (31)	4 (12)	6 (18)	0.2*
Male (%)	22 (69)	14 (88)	8 (82)	
Age (years) [mean (SD)]	67 (9)	66 (8)	68 (10)	0.694†
Duration of MND symptoms (years) [mean (SD)]	4.6 (4.8)	5.3 (5.6)	3.7 (3.4)	0.378†
Timed test of swallowing				
Volume/time (ml/s) [mean (SD)]	8.4 (8.8)	12.4 (9.4)	3.5 (4.5)	0.003†
Volume/swallow (ml) [mean (SD)]	13.6 (9.9)	18.1 (11.0)	8.0 (4.6)	0.003†
Time/swallow (s) [mean (SD)]	3.6 (3.1)	2.6 (2.5)	4.8 (3.4)	0.044†
Abnormal test of swallowing [no. (%)]	19 (60)	7 (39)	12 (86)	<0.01*
Bulbar signs				
Any UMN (%)	16 (50)	4 (25.0)	12 (75.0)	<0.001*
No UMN (%)	16 (50)	14 (87.5)	2 (12.5)	
Feeding patterns				
Altered diet				
No (%)	16 (50)	10 (55)	3 (21)	>0.05*
Yes (%)	16 (50)	8 (45)	11(79)	>0.05*
Assistance required				
No (%)	13 (40)	10 (55)	6 (43)	>0.05*
Yes (%)	19 (60)	8 (45)	8 (57)	>0.05*
PEG (number)	1	0	1	
Respiratory rate [mean (SD)]	18.6 (3.7)	18.7 (3.7)	18.5 (3.7)	0.88†
FVC predicted (%) [mean (SD)]	57.0 (19.9)	57.7 (22.8)	58.0 (16.4)	0.974†
NIPPV (number).	2	1	1	
Coughing and choking episodes during meals over 3 days [mean (SD)]	6 (9)	5 (9)	7 (8)	0.538†
Chest infections since MND symptoms + 15 months of follow-up (number)	1	1	0	>0.2*
Died during follow-up (number)	8	6	2	>0.2*
Time from EDAT to death (months) [mean (range)]	6.6 (3–14)	6.3 (3–14)	5.5 (3–8)	

PEG = percutaneous endoscopic gastrostomy; NIPPV = non-invasive positive pressure ventilation; UMN = upper motor neurone. *Chi squared test, †Kruskal–Wallis test (P refers to comparison between groups 1 and 2).

Table 4 *Effect of bolus volume on swallow type, number of swallows and duration of swallow apnoeas, in MND patients*

Bolus volume* (ml)	5	10	20
Swallow type			
xE patients	26	22	15
xI patients	6	7	10
Number of swallows			
All patients	1.5 (0.8)	2.3 (1.5)	3.3 (2.4)
xE patients	1.5 (0.7)	2.1 (1.5)	2.0 (1.4)
xI patients	1.8 (0.9)	3.0 (1.4)	5.2 (2.3)
Swallow apnoea (s)			
All patients	1.8 (1.1)	2.9 (2.5)	4.0 (2.9)
xE patients	1.8 (1.2)	2.6 (2.5)	2.8 (1.9)
xI patients	2.1 (1.2)	3.0 (2.5)	5.7 (3.3)

The values are expressed as mean (standard deviation). *Only 29 out of 32 patients were able to swallow 10 ml boluses of water and 25 out of 32 were able to swallow 20 ml boluses.

the second examination (with a 5 ml bolus), nine continued to display only xE swallows, and eight continued to display at least one xI swallow. The two patients who developed an xI swallow pattern during the follow-up (group 1) had a lower swallowing capacity and longer duration of apnoea than the patients who continued to display xE swallow (group 2) (Table 5); one required percutaneous endoscopic gastrostomy (PEG) and nocturnal assisted ventilation by nasal mask.

Clinical significance of xI swallows

Four patients had had chest infections since the diagnosis of MND; two of those always had xE swallows, whereas two sometimes had xI swallows (25–33% of swallows for 20 ml bolus). Fifteen out of 32 patients recorded episodes of coughing and choking during meals during the 3 days close to the day of the assessment. The number of coughing and choking episodes was not associated with an abnormal breathing pattern during swallowing (Table 3). Seven out of

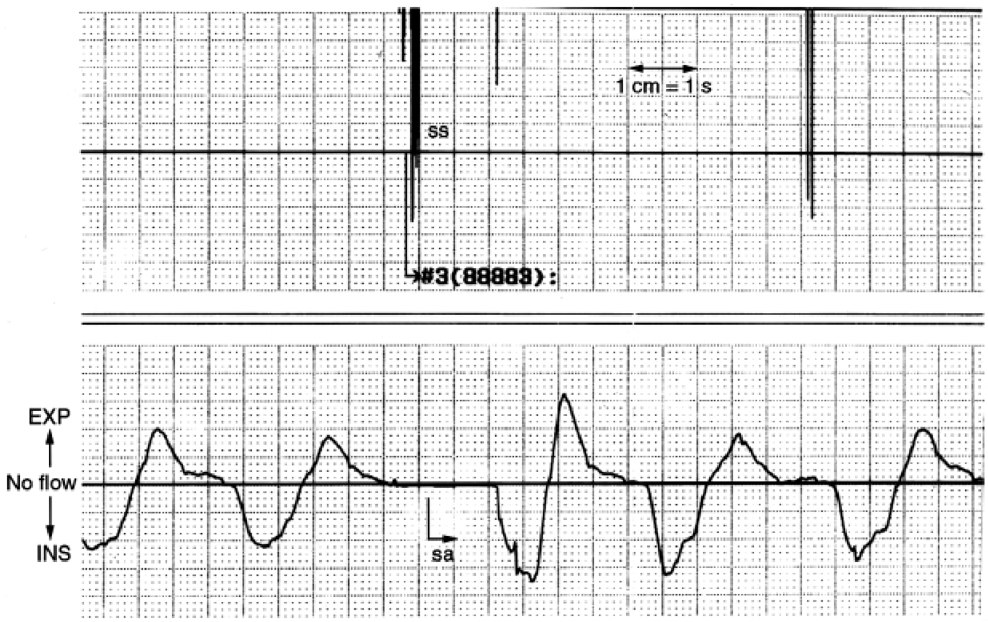

Fig. 3 An xI swallow pattern in an MND patient. ss = swallow sounds, sa = swallow apnoea, EXP = expiration, INS = inspiration.

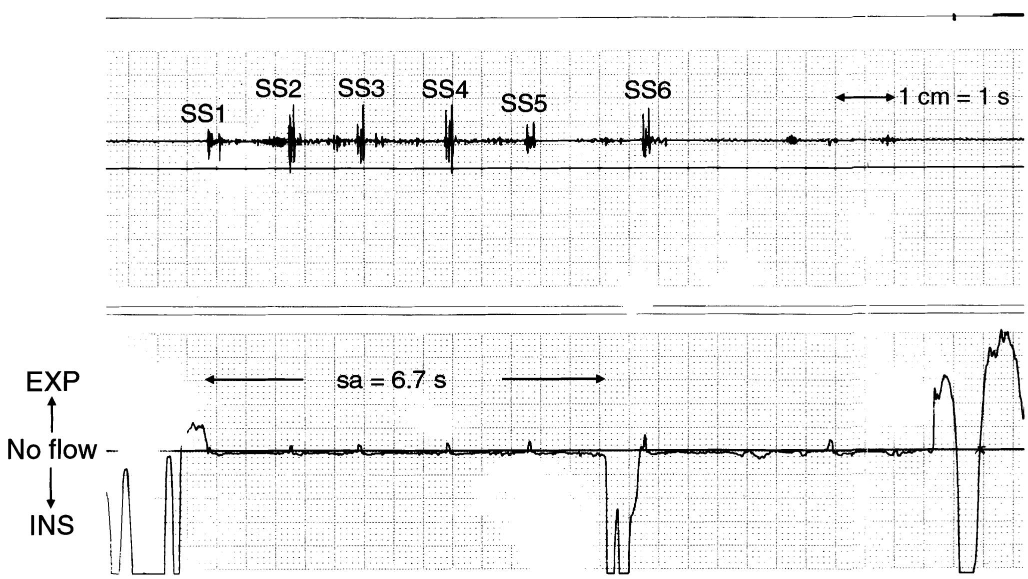

Fig. 4 An xI pattern in an MND patient characterized by a prolonged swallow apnoea (sa) and multiple swallows (SS) during a 20 ml bolus. EXP = expiration, INS = inspiration.

32 patients died during the 18 months follow-up of whom two had had an abnormal respiratory pattern during swallowing (Table 3).

Discussion

The coordination of respiration and swallowing in healthy volunteers and patients with defined neurological disorders has been studied. The study confirmed that the great majority of swallow apnoeas in normal awake adults are followed by expiration (Nishino *et al.*, 1985; Selley *et al.*, 1989*a*). However, in a variety of neurological disorders and lesion sites, the swallow apnoea is followed by inspiration more frequently than expected. This might increase the risk of aspiration or laryngeal penetration. It might be expected that the motor neurone activity in the nucleus ambiguus innervating pharyngeal and laryngeal muscles is functionally linked to activation of respiratory motor neurones. Lesions in the region of the nucleus of the tractus solitarius, or more generally in the medulla oblongata might be anticipated to cause more disruption of this link than simple respiratory or pharyngeal/laryngeal muscle weakness due to spinal or peripheral neuromuscular diseases. However, the study indicates that an abnormal respiratory pattern during

Table 5 *Follow-up assessment of swallowing–breathing pattern in MND patients*

	Group 1 (n = 2)				Group 2 (n = 9)		Group 3 (n = 8)	
	Patient 1		Patient 2					
	Assessment 1	Assessment 2	Assessment 1	Assessment 2	Assessment 1*	Assessment 2*	Assessment 1*	Assessment 2*
Average volume/swallow (ml)	8.3	10.0	3.7	2.2	18.5 (13.8)	14.1 (12.2)	8.5 (5.0)	5.5 (2.9)
Average time/swallow(s)	2.7	5.6	8.2	10.2	3.2 (3.0)	3.0 (1.9)	5.4 (4.1)	6.0 (4.4)
Swallowing capacity (ml/s)	3.1	1.8	0.4	0.2	12.4 (10.5)	9.1 (10.1)	3.9 (5.1)	1.8 (1.9
Swallow apnoea (5 ml) (s)	1.8	3.1	3.0	1.5	1.7 (0.8)	1.5 (0.8)	2.0 (1.5)	2.9 (1.4)

Group 1 = MND patients with xE swallows at first assessment and xI swallows at second assessment; group 2 = MND patients with xE swallows at both assessments; group 3 = MND patients with xI swallows at both assessments. The interval between the first and second assessments was 6–9 months. Patients from groups 1 and 3 were unable to swallow >5 ml boluses of water during the second assessment. *Values given are mean (standard deviation).

swallowing (xI swallows) can occur in a purely spinal disorder or in a purely peripheral neuromuscular disorder affecting breathing or swallowing: indeed CNS (including brainstem) pathology was no more likely to cause disruption than peripheral pathology. In particular, a patient with selective peripheral involvement of inspiratory muscles (patient 19) due to phrenic nerve palsies had a marked tendency to postdeglutition inspiration. One patient (11) with intact inspiratory function but severe impairment of expiratory muscle function had no xI swallows whilst others with lower cervical cord lesions and thus impairment of expiratory muscle function had an increased incidence of such xI swallows. Respiratory muscle dysfunction with normal swallowing may thus be associated with disruption of the normal pattern in the absence of any clinical suggestion of brainstem impairment. A patient with no neurological lesion but mechanical tethering of the tongue (22) and a modest reduction in swallowing capacity had xI swallows on almost 25% of attempts. Such findings suggest that direct neural involvement of swallowing related pathways is not necessary for xI swallows to occur and, conversely, that intact swallowing and brainstem function does not necessarily prevent postdeglutition inspiration, whatever its cause. This suggests that breakdown of the normal pattern may be the result of disorded swallowing or breathing in some individuals rather than the two problems having common cause. Possible explanations for this may include a respiratory override if the swallow apnoea is long or multiple swallows are required to clear a bolus (e.g. Fig. 4).

A significant proportion (44%) of MND patients displayed post-apnoea inspiration after a swallow: there may be several reasons for this. Reduced swallowing capacity (caused by reduced volume/swallow and/or increased time/swallow), prolonged swallow apnoeas and increased number of swallows to clear large boluses (20 ml) are significantly associated with xI swallows. The two patients who initially had a normal respiratory pattern during swallowing but developed an xI swallow pattern during follow-up had also developed a significant decline in their swallowing capacity. It seems possible that the automatic respiratory control system prevails over the swallowing reflexes when the maintenance of ventilation is particularly important in conditions of loaded breathing, since the time available for breathing could be significantly reduced by repeated swallows and prolonged swallow apnoeas. Furthermore, many patients with MND probably develop type II respiratory failure due to denervation of the respiratory muscles. Hypercapnia influences the co-ordination of breathing and reflex swallowing by increasing the frequency of inspiration immediately after the swallow apnoea (Nishino *et al.*, 1998). One may suppose that, even though a reduced FVC was not associated with xI swallows in this study, at a critical point during the development of respiratory failure, very prolonged swallow apnoeas and raised $PaCO_2$ contribute to make an xI swallow more likely. A serial study with measurement of oxygen saturation and $PaCO_2$ might be required to investigate this further. One of the limitations of this study is that we have not used non-volitional respiratory tests. Volitional control of respiration can be impaired by corticospinal tract lesions (Howard *et al.*, 1992), as may occur in MND, and therefore FVC measurements give an incomplete picture of respiratory function in these patients.

The cross-sectional study has shown that the specific nature and location of the neurological lesion does not seem to be closely associated with changes in the respiratory pattern during swallowing. However, patients with corticobulbar involvement tended to display greater percentage xI swallow than those without. The longitudinal study in patients with MND has clearly shown that patients with upper motor neurone bulbar signs had significantly more xI swallows than those without. Loss of corticobulbar fibres may weaken descending inhibition of inspiration during swallow apnoea and increase the likelihood of an inspiration event triggered by the automatic respiratory system following a swallow.

It has been suggested that the coupling of swallows with expiration may be one of several mechanisms by which the airway is protected from aspiration during swallowing (Smith, 1989). Therefore it could be anticipated that post deglutition inspiration might contribute to the risk of aspiration or laryngeal penetration so that more episodes of coughing and choking might be expected. However, abnormal respiratory pattern during swallowing was unrelated to chest infections, episodes of coughing and choking during meals and prognosis. Although we have not systematically used videofluoroscopy to assess silent aspiration in these patients, the low frequency of clinical respiratory events makes it unlikely that any aspiration was major or clinically significant. Recent studies support the view that other factors apart from mechanical aspiration should be considered in the pathogenesis of aspiration pneumonia: these include oral/dental status, host resistance, pulmonary clearance and smoking (Langmore, 1998). Furthermore, it is also important to emphasize that the pattern of breathing after a swallow as assessed by a water bolus may not necessarily be the same as that associated with other types of bolus (e.g. solid or semisolid food, or thickened fluids) (Preiksaitis *et al.*, 1996). It is evident from Table 3 that some MND patients were already on a modified diet at the time of the assessment so that the respiratory pattern recorded during the test procedure might not be fully representative of that during normal life at home (e.g. some patients avoided water).

In conclusion, the swallow apnoea in patients with brain, spinal cord and peripheral neurological lesions is followed by inspiration more frequently than expected. This seems to occur irrespective of the site of the lesion(s). MND patients commonly display an abnormal respiratory pattern during swallowing characterized by: inspiration after swallow, prolonged swallow apnoea and multiple swallows per bolus, but this was unrelated to chest infections, coughing and choking episodes during meals and prognosis. It seems likely that postdeglutition apnoea inspiration is more important as an indicator of disordered swallowing or breathing rather than being an important mechanism of aspiration *per se* or of symptom production.

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References

Ardra GM, Kemp FH. The protection of laryngeal airway during swallowing. Br J Radiol 1952; 25: 406–16.

Clark GA. Deglutition apnoea. J Physiol (Lond) 1920; 54: 59.

Cohen MI, Piercey MF, Gootman PM, Wolotsky P. Synaptic connections between medullary inspiratory neurons and phrenic motoneurons as revealed by cross-correlation. Brain Res 1974; 81: 319–24.

Doty R. Influence of stimulus pattern on reflex deglutition. Am J Physiol 1967; 166: 142–58.

Doty R. Neural organisation of deglutition. In: Code CF, editor. Handbook of physiology, Sect. 6: alimentary canal. Washington (DC): American Physiological Society; 1968. p. 1861–902.

El Escorial revisited: Revisited criteria for the diagnosis of amyotrophic lateral sclerosis. A concensus conference held at Airlie House, Warrenton, Virginia, April 2–4, 1998. In print (website: www.wfnals.org/Articles/elescorial1998.htm).

Hadjikoutis S, Eccles R, Wiles CM. Coughing and choking in motor neurone disease [abstract]. J Neurol Neurosurg Psychiatry 1999; 67: 843.

Hamdy S, Aziz Q, Rothwell JC, Singh KD, Barlow J, Hughes DG, et al. The cortical topography of human swallowing musculature in health and disease. Nat Med 1996; 2: 1217–24.

Hamdy S, Rothwell JC, Aziz Q, Singh KD, Thompson DG. Long-term reorganization of human motor cortex driven by short-term sensory stimulation. Nat Neurosci 1998; 1: 64–8.

Howard RS, Newsom-Davis J. Neural control of respiration. In: Crockard A, Hayward R, Hoff JT, editors. Neurosurgery: the scientific basis of clinical practice. 2nd ed. Oxford: Blackwell; 1992. p. 318–33.

Hughes TA, Wiles CM. Palatal and pharyngeal reflexes in health and in motor neuron disease. J Neurol Neurosurg Psychiatry 1996a; 61: 96–8.

Hughes TA, Wiles CM. Clinical measurement of swallowing in health and in neurogenic dysphagia. Q J M 1996b; 89: 109–16.

Hughes TA, Wiles CM. Neurogenic dysphagia: the role of the neurologist [editorial]. [Review]. J Neurol Neurosurg Psychiatry 1998; 64: 569–72.

Jean A. Localisation et activite des deglutiteurs bulbaires. J Physiol (Paris) 1972; 64: 227–68.

Jean A. Localisation et activite des motoneurones oesophagiens chez le mouton. Etude par microelectrodes. J Physiol (Paris) 1978; 74: 737–42.

Jean A. Brainstem organization of the swallowing network. Brain Behav Evol 1984a; 25: 109–16.

Jean A. Control of the central swallowing program by inputs from the peripheral receptors: review. [Review]. J Auton Nerv Sys 1984b; 10: 225–33.

Kalia M, Mesulam MM. Brain stem projections of sensory and motor components of the vagus complex in the cat. II. Laryngeal, tracheobronchial, pulmonary, cardiac, and gastrointestinal branches. J Comp Neurol 1980; 193: 467–508.

Langmore SE, Terpenning MS, Schork A, Chen Y, Murray JT, Lopatin D, et al. Predictors of aspiration pneumonia: how important is dysphagia? Dysphagia 1998; 13: 69–81.

Meadows JC. Dysphagia in unilateral cerebral lesions. J Neurol Neurosurg Psychiatry 1973; 36: 853–60.

Miller AJ. Deglutition. [Review] Physiol Rev 1982; 62: 129–84.

Newsom-Davis J, Plum F. Separation of descending spinal pathways to respiratory motoneurons. Exp Neurol 1972; 34: 78–94.

Nishino T, Yonezawa T, Honda Y. Effects of swallowing on the pattern of continuous respiration in human adults. Am Rev Respir Dis 1985; 132: 1219–22.

Nishino T, Hasegawa R, Ide T, Isono S. Hypercapnia enhances the development of coughing during continuous infusion of water into the pharynx. Am J Resp Crit Care Med 1998; 157: 815–21.

Pickersgill TP, Dawson K, Wiles CM. Abnormal breathing patterns before and after swallowing in neurological disorders [abstract]. J Neurol Neurosurg Psychiatry 1998; 64: 702.

Pinnington LL, Muhuddin KA, Lobeck M, Pearce VR. Interrater and intrarater reliability of the Exeter Dysphagia Assessment Technique applied to healthy elderly adults. Dysphagia 2000; 15: 6–9.

Preiksatis HG, Mills CA. Coordination of breathing and swallowing: effects of bolus consistency and presentation in normal adults. J Appl Physiol 1996; 81: 1707–14.

Preiksatis HG, Mayrand S, Robins K, Diamant NE. Coordination of respiration and swallowing: effect of bolus volume in normal adults. Am J Physiol 1992; 263: R-624–30.

Selley WG, Flack FC, Ellis RE, Brooks WA. Respiratory patterns associated with swallowing: Part 1. The normal adult pattern and changes with age. Age Ageing 1989a; 18: 168–72.

Selley WG, Flack FC, Ellis RE, Brooks WA. Respiratory patterns associated with swallowing: Part 2. Neurologically impaired dysphagic patients. Age Ageing 1989b; 18: 173–6.

Selley WG, Flack FC, Ellis RE, Brooks WA. The Exeter Dysphagia Assessment Technique. Dysphagia 1994; 9: 162–7.

Tarrant SC, Ellis RE, Flack FC, Selley WG. Comparative review of techniques for recording respiratory events at rest and during deglutition. Dysphagia 1997; 12: 24–38.

Urban PP, Hopf HC, Connemann B, Hundemer HP, Koehler J. The course of cortico-hypoglossal projections in the human brainstem: functional testing using transcranial magnetic stimulation. Brain 1996; 119: 1031–38.

Urban PP, Hopf HC, Fleisher S, Zorowka PG, Muller-Forell W. Impaired cortico-bulbar tract function in dysarthria due to hemispheric stroke. Functional testing using transcranial magnetic stimulation. Brain 1997; 120: 1077–84.

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