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Objective evaluation of iatrogenic lingual nerve injuries using the jaw-opening reflex

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Summary The extent of reflex inhibition of masseteric electromyographic activity, after an electrical stimulus applied to lingual mucosa, was used as a test of the ability of the lingual nerve to conduct nerve impulses and this was compared with the results of standard clinical tests. Two groups of subjects were assessed: healthy subjects ($n = 10$) and patients with lingual nerve injuries ($n = 17$). The patients were tested 8—9 weeks after their injury and retested 6 months later when they were retrospectively allocated to either a temporary injury or a permanent injury group. The group measure of reflex inhibition after stimulation of the tongue on the opposite side to the injury was no different from the same measure in controls, whereas two-point discrimination did differ. Group measures of inhibition and of subjective function after stimulation on the side of the injury were significantly different from controls whereas light touch and two-point discrimination were not. There was good agreement between quantified masseteric inhibition and subjective function, but it was not possible at 8—9 weeks after the injury to differentiate between those that would recover and those that would be permanent.

Introduction

Tests of sensory function usually rely on a subjective report from the patient (two-point discrimination, light touch, discrimination between sharp and blunt), but these yield variable results. There is also poor correlation between these tests and the outlook for recovery of nerve function,[1] possibly because they are sensitive to differences in the examiner's expertise[2] and are wholly reliant on accurate responses from the patient.[3] There are totally objective tests of neurosensory function, such as detection of somatosensory evoked potentials and

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reflex responses, or of conduction in nerves, which involve no interpretation by the patient and are better tests of injury to the inferior alveolar nerve.[4]

The present study follows the suggestion by Donoff[5] that 'The long term goal of electrophysiologic studies should be to predict the outcome of injury'. However, he also suggested that such studies should 'provide substantiation of current clinical methods of testing as guides to decision making'. It is probably more appropriate to establish which of the subjective tests correlates best with the electrophysiological tests.

The effect of injury of the lingual nerve on the linguodigastric (jaw-opening) reflex has been investigated in rats. Reduction or loss of the reflex occurred immediately after injury to the lingual nerve by freezing, stretching, crushing, or division, with complex longer term changes.[6] We have studied the equivalent human reflex, which produces masseteric inhibition after stimulation of the tongue. Our working hypothesis was that, after injuries to the lingual nerve that were classified as neurapraxia and were going to recover, there would be only moderate interference with conduction in the lingual nerve and comparable effects on reflex inhibition. Conversely, our expectation was that injuries that were going to have permanent effects would comprise severe neurapraxia, axonotmesis, or even neurotmesis, and would result in severe loss or complete absence of nerve conduction and suppression of the reflex. In such cases it has been common practice to assess any sensory loss with reference to the response on the uninjured side but the validity of this practice is being increasingly questioned.[7]

We tested two hypotheses, namely that reflexes elicited from sites on the tongue on the side opposite to an injury did not differ from responses in control subjects; and that an objective test, the linguo-masseteric inhibitory reflex,[8] done within 10 weeks of the injury can predict the subsequent extent of recovery of the nerve.

Patients and methods

Control subjects were recruited from the staff of the department and from patients with no symptoms referable to the lingual nerve. The experimental groups were recruited from patients referred to us with iatrogenic injury to the lingual nerve. In both cases recruitment was purely on the basis of availability during the period of the study.

All patients and subjects consented in accordance with the regulations of the local ethics committee. Exclusion criteria included a history of craniomandibular disorders, medical conditions that might impede neural function (diabetes, collagen disease, neuromuscular disorders, and taking psychotropic drugs), and previous experience of the research method. The control group consisted of 10 subjects. All the patients who presented with lingual nerve injury were assessed prospectively and allocated to an injury group only after 6 months. Those in whom the nerve recovered before 6 months were allocated retrospectively to the temporary injury group ($n = 8$) and those patients in whom the effects persisted at 6 months were retrospectively allocated to the long-term or permanently injury group ($n = 9$). In all patients routine mechanosensory and objective reflex tests were done at the initial visit and again at a review appointment. The control group was tested in the same way but only once.

Conventional clinical tests

Standard tests of two-point discrimination and light touch were used to assess the extent of sensory function. Subjective function was assessed by blunt probing the lingual mucosa on the opposite side and the same side as the injury and asking the subject to score the second sensation relative to the first, 10/10 being equal sensation on the two sides and 0/10 being a complete absence of sensation on the injured side.

Electromyography

The electromyographic (EMG) methods are fully described in another paper[8] and only a brief account is given here. The threshold stimulus for eliciting reflex inhibition of EMG activity in the masseter was first measured (using an electrode applied to normally inervated lingual mucosa); the stimulus had a duration of 0.1 ms and was generated by a constant current stimulator. The test stimulus subsequently used was 30% greater than the threshold stimulus and was usually in the range 3—5 mA. EMG activity was recorded bilaterally from surface electrodes over the masseter muscles. These signals were differentially amplified (Bioamp with MacLab/8e system; AD Instruments, Hastings, UK), band-pass filtered (10 Hz to 1 KHz), digitised at 10 kHz and saved on the Maclab 8e system together with the stimulus. Scope 3.5 software was used to full wave rectify the EMG signals, which were subjected to constant time reset integration (5 ms blocks) after which a mean of 16 records of the response to a stimulus was calculated. The visual display of the EMG activity lasted for 256 ms and this was

divided into two sections, which were processed separately:

The 80 ms before the stimulus and the 176 ms after the stimulus. The mean of the data before the stimulus was established and the area enclosed between that mean and the sequence of values falling below the mean was obtained. The data for the period after the stimulus, which showed any inhibitory reflex response (values falling below the mean before the stimulus to a greater extent than in that period), was processed in the same way and scaled to correct for its longer duration. These values will be referred to as 'areas below mean'. The critical value was the ratio of the area below the mean after the stimulus to the area before the stimulus, expressed as a percentage which will be referred to as "scaled inhibition". If no reflex was present, there would be no difference between the signals before and after the stimulus and the test value would approximate to 100%. In normal subjects with intact reflexes, the test values were usually about 400%.

The processed data for each subject were allocated to the appropriate group retrospectively at 6 months. The 'below mean areas' in the periods both before and after stimulation were separately analysed for differences between the three groups and also for differences between right and left sides.

Statistical tests were done with the Statistical Package for the Social Sciences (SPSS Version 10.0 for Windows). The significance of differences between the control, temporary injury, and permanent injury groups was assessed using one-way ANOVA followed by a *t*-test with Bonferroni correction. Nominal data were tested with the chi square test to establish the significance of differences between groups. Correlations between test results were assessed by Pearson's coefficient of linear correlation.

Results

Group characteristics

The subjects in the control group had a mean (S.E.) age of 29 (6.8) years, patients in the temporary injury group of 26 (3.1) years, and those in the permanent injury group of 31 (4.3) years. There was no significant difference between the groups in the sex composition, the overall M:F ratio being 1:2.4. The mean (S.E.) delays from the time of nerve injury to first assessment were similar for the injury groups (temporary injury group, 8.4 (1.2) weeks; permanent injury group, 8.9 (2) weeks).

Measurements of sensation using mechanical stimuli

There were differences between the injured (temporary and permanent) groups and the control group with respect to light touch threshold, two-point discrimination, and subjective function tests. The injured groups had significantly higher two-point discrimination and light touch thresholds on the injured side than the control group (Table 1). The subjective sensory function in subjects in the control group was the expected 10 out of 10, which was significantly different from both injured groups (Table 1). No significant differences were found with sensory function when comparing the temporarily and permanently injured groups.

Table 1 Results of clinical tests of lingual sensation in normal subjects and patients with lingual nerve injury.

	Control ($n = 10$)	Temporary injury ($n = 8$)	Permanent injury ($n = 9$)	*P* value[a]
Two-point discrimination on side of lesion	3.1 (0.31)	14.5 (1.99)	10.67 (1.97)	0.002
Two-point discrimination on opposite side	3.1 (0.31)	4.25 (0.31)	4.89 (0.7)	0.03
Light touch on side of lesion	3 (0)	12.38 (2.93)	10 (2.67)	0.02
Light touch on opposite side	3 (0)	3.13 (0.1)	3.44 (0.34)	0.31
Subjective function	10 (0)	3.43 (0.83)	2.28 (0.5)	<0.001

Mean (S.E.). No significant difference was seen between temporary and permanent groups.
[a] Between both types of paralysis and control.

Measurements of asymmetry in masseteric EMG activity

There were no significant differences in the summed deviations of the EMG signal below the prestimulus mean between the control group and the temporary and permanent injury groups at rest or during clenching on the electrode housing (bite block) with no stimulus applied. There were also no significant differences in EMG activity between the right and left masseter, before or after stimulation in control subjects or after stimulation of the injured or uninjured side in the patient groups.

Measurements of EMG activity after electrical stimulation

The reflex threshold was established by simple inspection of the displayed EMG (background masseteric muscle activity held at 20% of that during maximum voluntary contraction) as stimulus strength was increased. The reflex threshold in control subjects (first sign of inhibition), and after stimulation of the uninjured side in the injury groups, was usually between 2 and 4 mA (duration 0.1 ms). In the subsequent tests, the stimulus strength used was 30% higher than the individual threshold.

In injured subjects who reported a major loss of sensation there was little or no evidence of a change in EMG activity after the application of the stimulus (normalised inhibition was close to 100%). Conversely, in those with only moderately reduced sensation, there was evidence of a reduced inhibitory responses (normalised inhibition >100% but <300%).

In the injured groups, the 'scaled inhibition' elicited from the affected side was always reduced compared with control subjects (Table 2). In both right and left masseters the control group showed a scaled inhibition similar to that in the temporary injury group and in the permanent injury group when the uninjured side was stimulated. The control group showed significantly greater scaled inhibition in both right and left masseters than either the temporary injury group ($p < 0.05$) or the permanent injury group ($p < 0.01$) on stimulation of the injured side. The scaled inhibition elicited by stimulation of the side opposite to the injury was not significantly different from the reflex activity seen in the control groups (Table 2).

Table 2 Scaled inhibition in the masseter, elicited by stimulation of the lateral border of the tongue in normal subjects and in patients with lingual nerve injury.

	Mean	S.E.
Control subjects ($n = 10$)	409.2	32.9
Temporary lesions ($n = 8$)		
Stimulus contralateral to lesion	229.5	94.5
Stimulus ipsilateral to lesion	206.9	53.3
Permanent lesions ($n = 9$)		
Stimulus contralateral to lesion	326	64.7
Stimulus ipsilateral to lesion	116.7	18.3

The correlation between the results of the three different mechanosensory tests and 'scaled inhibition' was examined using Pearson's correlation coefficient. The strongest correlation found was that between subjective function and scaled inhibition (right masseter $R = 0.646$; left masseter $R = 0.517$). There was also a correlation between scaled inhibition and both two-point discrimination test (right $R = -0.522$; left $R = -0.452$) and light touch test (right $R = -0.502$; left $R = -0.374$).

Discussion

After an injury, the uninjured side of the body is commonly used as a reference against which to judge sensory loss. The normal assumption is that sensory and reflex functions are bilaterally symmetrical and that significant asymmetry of those functions indicates disease. However, normally occurring asymmetry of the jaw-opening reflex and of other motor functions has been reported in animals,[9,10] and asymmetry of the number of nerve fibres entering the lingual nerves and of other sensory pathways has been reported both in humans and animals.[11–14] Although there is a general assumption that a unilateral nerve injury produces only unilateral effects, there is accumulating evidence to the contrary.[7,15–18] These findings bring into question the uncritical use of the opposite side to an injury as a reference or control side. We therefore considered it to be important to establish that neither asymmetry nor contralateral effects of injury alone could account for the differences in masseteric inhibition that we measured in this study. Two-point discrimination tests on the side opposite to the injury showed raised thresholds in patients with both temporary and permanent injuries compared with control subjects, which suggests the likelihood of a contralateral effect of the injury. However, this was not the case for masseteric inhibition where there were no significant differences between controls and either of the injury groups. The fact that there was a difference between the responses to two different methods of testing can, however, be explained by the fact that different nerve fibres

were being stimulated in different ways in the two methods; natural stimulation of mechanoreceptors produces asynchronous action potentials in single nerve fibres, whereas electrical stimulation produces synchronous action potentials in a number of submucosal nerve fibres. The two modes of stimulation differ with respect to both their central[19] and reflex[20] effects. The apparent immunity of the linguo-masseteric inhibitory reflex to the effects of nerve injury on the opposite side may be fortuitous but is a clear advantage for clinical purposes.

We found no significant differences in the extent of masseteric activity between right and left sides, whether at rest or after stimulation of the normal or of the injured side of the tongue, which is consistent with other reports of bilateral responses elicited from sites served by the trigeminal nerve.[21,22] Although the bilaterally symmetrical extent of activity found in this study suggest that the procedure might be simplified by recording masseteric EMG activity unilaterally, the report of an occasional considerable asymmetry of the reflex[22] indicates that this would be unwise in the present state of knowledge.

The primary hypothesis was that injuries destined to be temporary were likely to be milder than injuries destined to be permanent. The assumption was that the milder injuries would be associated with less interference with nerve conduction and that this in turn would be reflected in less disturbance of sensory function and of the jaw-opening (linguo-masseteric inhibitory) reflex. This view was not, however, supported by the responses to two-point discrimination, light touch, or subjective function tests applied on the side of the injury, where there were no significant differences between the temporary and permanent injury groups. Moreover, in two cases, the mean values for temporary and permanent injury were ranked quite contrary to the hypothesis. Similarly, when using reflex inhibition as a measure, there was no clear difference between the temporary and permanent injury groups. However, whether using scaled inhibition, two-point discrimination, or subjective function tests as measures, it was clear that the permanent injury group differed substantially from the control group; this was, however, not true for light touch. The results of the reflex assessments did correlate with the patients' perceived subjective functions. Although the coefficients of linear correlation of the pooled data ($r = 0.646$ and 0.517) were unremarkable in this study, in a previous study[9] we made successive assessments during graded sensory loss and found a substantially higher coefficient of linear correlation ($r = 0.93$). This suggests that, given repeated testing, the correlation is sufficiently sensitive to follow the early stages of recovery from nerve injury.

The data relating to patients in the two injury groups were those obtained on only a single occasion, 8—9 weeks after injury. Consequently, individual recoveries were not followed over time, the clinical and reflex test results being used solely to spot differences in the grouped responses of the patients allocated to the temporary and permanent injury groups. Variations in inter-individual factors that cause changes in reflex thresholds (such as mental concentration,[23] hyperventilation[24]) occur even when the extent of background EMG activity and the stimulus strength are controlled.[25] Variation in normalised inhibition would, consequently, still be expected to occur within each group and it seems from the reflex data that the two groups of patients were far less homogenous than we had anticipated. The variation within each group together with the relatively small numbers of patients in each group meant that a significant difference between the groups would not be shown unless the difference was quite large, as it was between controls and both injury groups. However, there were no significant differences between the temporary and permanent injury groups with respect to any of the clinical subjective or objective reflex measures. This indicates that, pending a study with a larger number of patients with iatrogenic nerve injuries, not only should the original hypothesis (that single reflex tests would be predictive of the subsequent extent of recovery of the nerve) be rejected, but that the same judgement should be applied to spot clinical tests.

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