Subcomponents of the cervical evoked response in patients with intracerebral circulatory arrest

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SUMMARY The subcomponents of the cervical evoked response, N11, N13, N14, and the following positivity, were studied in 13 patients with full arrest of the intracerebral circulation, isoelectric EEGs and abolished cortical somatosensory evoked responses. The peak negativity (N13) and the following positive wave were present in all patients. Also N11 and N14 could be identified in most patients either at standard stimulation frequency (2 Hz) or by increasing the stimulation rate. The results point to a spinal origin of these sub-components in the human cervical evoked response.

The human cervical evoked responses, recorded from the neck, typically consists of an initial small positive deflection, a following large negative wave and a final relatively wide positive potential. The peak of the negativity, N13, generally is preceded by a small notch, N11, on the ascending negativity and is followed by another small inflection, N14, on the descending negative slope.¹⁻⁵ Various mechanisms have been proposed for each of these sub-components.¹⁻¹⁹

The cervical evoked response is used extensively in clinical diagnostic neurology either alone or with the plexus and cortical evoked responses to determine the central afferent conduction times.²⁰⁻³⁰ A full knowledge of the mechanisms and site of origin of the different components in this response therefore evidently is of value.

In the present investigation the various components of the cervical evoked response were examined in a sample of 13 carefully selected patients with maintained cervical evoked responses but extinguished cortical responses, isoelectric EEGs and complete arrest of intracerebral circulation. The purpose of the study was to determine which subcomponents of the human cervical evoked response were of spinal and which of intra-cerebral origin with particular emphasis on the N14 and the following positivity.

Materials and methods

Materials

The patients comprised 13 subjects out of a larger group of comatose patients examined with somatosensory evoked potential (SEP) and EEG. The criteria for the present sample were that the cortical evoked responses should be bilaterally abolished while the plexus and cervical responses be well preserved. The EEG taken simultaneously should be isoelectric and four vessel selective high pressure cerebral angiography showing complete arrest of intracerebral circulation should have been performed before or within a maximum of three hours after the EEG and SEP tests. Age and the main diagnostic groups of the patients are shown in table 1. The four patients under the diagnostic column "other" comprise two with complete cerebral infarction after an intracerebral haemorrhage, one with a postoperative cerebral herniation and one with cerebral herniation of unknown aetiology.

Stimulation

The median nerve was stimulated percutaneously either in the wrist or in the elbow. A bipolar commercially available "saddle" electrode (Medelec) was used for stimulation and the stimuli were delivered by a Medelec IS/V stimulator. Stimulus strength were 150-200 V, duration 0.2 ms. Generally 300-1000 stimuli were delivered to each nerve at standard frequency of 2 Hz. High frequency stimulation (10-50 Hz) were performed in 10 patients to enhance N11 and N14.¹

Recording

The responses were simultaneously recorded and averaged from the brachial plexus (N9), the neck 6-8 cm proximal to the 7th cervical spina and from the contralateral hand projection area on the skull (approximately corresponding to P₃ or P₄ in the 10-20 international EEG system). The

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Table 1 Age, sex and the main diagnostic groups of the patients

No	Sex		Age		Main diagnostic group		
	Male	Female	Median	Range	Subarachnoid haemorrhage	Head trauma	Other
13	8	5	25	9-69	3	6	4

common reference electrode was placed on the forehead. This reference location was used since the subcomponent N14 is most conspicuous with the reference electrode on the skull¹⁰ and the following positivity is also relatively prominent with a skull reference. Furthermore, our normative data were based on this reference location.^{1 22}

Commercially available Ag/AgCl electrodes were used for recording, in the skull bentonite was added to keep the electrodes in situ. The signals were recorded and averaged on a modified Medelec MS6 electrophysiological system. High and low pass filters were set to 16 Hz and 3.2 KHz respectively. Most of the SEP records were taped on a multichannel FM tape recorded for later detailed analysis.

Results

The main negative component of the cervical evoked response (as defined by the selection criteria) was present in all patients, while the cortical evoked responses invariably were extinguished bilaterally. The notch on the ascending negativity (N11) was easily identified in most patients at standard stimulation frequency of 2 Hz.

The notch (N14) on the descending negativity was present in eight out of the 13 patients and generally seen as a very small inflection at standard stimulation frequency. The latencies between the peak of N9 and N11, N13 and N14 respectively are given in table 2. The results were based on 10 tests in eight patients. Since N14 frequently was inconspicuous exact determination of the N9-N14 time often was difficult. The normative data were taken from a previous investigation of the human cervical evoked response.¹

When the stimulation rate was increased (10-50 Hz), the amplitude of the main negative wave (N13) typically was reduced while N11 and N14 were relatively enhanced often being visible as small separate potentials. The identification rate of each subcomponent at standard and high frequency stimulation is given in table 3. A distinct positive wave following the main negative wave was present in all patients tested (table 3). Two examples of the responses obtained are shown in figs 1 and 2.

The data in fig 1 were from a 24-year-old male patient with severe head injuries after a traffic accident. When SEP and EEG were recorded he had clinical signs of cerebral herniation: no respiration, dilated nonreactive pupils, no vestibulo-ocular reflexes. His EEG (fig 1A) was isoelectric and the SEP test (fig 1B) showed no cortical responses. The

Table 2 Peak to peak latencies between the plexus evoked responses (N9) and the different subcomponents of the cervical evoked responses at 2 Hz stimulation rate. The normative data were taken from a previous study.¹

	Latencies (ms)			
	Normative data		Patient data	
	$\bar{x}$	$\pm SD$	$\bar{x}$	$\pm SD$
N9-N11	2.05	0.3	1.98	0.47
N9-N13	3.3	0.28	3.41	0.4
N9-N14	4.38	0.29	4.73	0.58

cervical responses were, however, present and all subcomponents: N11, N13, N14 and the ensuing positivity, could be identified at standard stimulation frequency. When the stimulation rate was increased (fig 1C) N11 and N14 were enhanced relatively to the N13. Four vessel selective high pressure cerebral angiography (fig 1D) was performed 2½ hours after the SEP and EEG and showed full arrest of all intracranial circulation.

The second example (fig 2) was taken from a 15-year-old boy with severe head injuries after a traffic accident. His EEG (not displayed in the figure) was isoelectric and the SEP test (fig 2B) showed bilaterally extinguished cortical responses. The cervical evoked response was present and of normal amplitude (>1 µV). The subcomponents N11 and N14 were, however, difficult to identify being visible as minor inflections on the rising and falling negativity at standard 2 Hz stimulation. Increasing the stimulation rate produced a typical reduction of N13 while N11 and N14 were enhanced being visible as separate small potentials (fig 2C). Four vessel selective cerebral angiography was performed 30 minutes after the SEP and EEG test and verified a full intracerebral circulatory arrest (fig 2A).

Discussion

The human cervical evoked response recorded from the surface of the neck comprise several subcomponents, the generation site and mechanisms of which are still debated. Previous experimental studies in humans have emphasised the similarity between the cervical evoked response and the spinal cord potentials obtained in experimental animals.^{1 4-6}

Most human data^{1-2 +6 10-19} point to N11 and N13

Table 3 Identification ratio of the different subcomponents at standard 2 Hz stimulation and at higher stimulation frequencies

Stim mode	No.	Subcomponents of cervical evoked SEP			
		N11	N13	N14	Pos wave
2 Hz	13	10	13	8	13
10-50 Hz	10	10	—	9	—

as potentials of spinal origin. Thus, N11 probably reflects activity in the primary afferent fibres either in the dorsal root entry zone or in the dorsal columns, while N13 evidently has a post-synaptic origin¹ and probably corresponds to the N1 wave of the dorsal cord potential of animals which is produced by synaptic activity in the middle layers of the dorsal horn.³¹⁻³⁷ The present data, showing that N11 and N13 were present in most patients with full arrest of the intracerebral circulation further confirmed the spinal origin of these subcomponents. Few investiga-

tions have explicitly studied N14 and the following positive wave. N14 generally is very small and may even in healthy cooperative subjects be inconspicuous or absent at standard stimulation frequency (2 Hz).¹

Both N14 and the following positivity have been related to far field potentials of intracerebral origin,^{6-7 10-11 16 17 19} an assumption based either on clinical neurological data or from variations in the cervical evoked response obtained in healthy subjects with different electrode positions. Inferring the generator site of a local intracerebral or spinal potential from variations in the surface recorded "far field" potentials is however at best an uncertain method since it is often virtually impossible to predict the geometrical surface "far field" distribution of a given local intracerebral potential.

On the other hand, the fact that N14 and the following positivity in humans also are present in the well known spinal cord potential in experimental

Fig 1 Records from a patient with cerebral herniation. A: EEG B: SEP recorded simultaneously from Erb's, neck and skull at standard stimulation frequency of 2 Hz. C: The cervical evoked responses at standard and 10 Hz stimulation. Lower record represent the plexus response. Note that the lower calibration line in B & C (2.5 μV) is for the plexus responses only. Calibration for the cortical and cervical responses (2.5 μV) is given by the uppermost line in B. D: Selective four vessel cerebral angiography in the same patients 2½ hours after the EEG and SEP records.

Fig 2 Enhancement of N_{11} and N_{14} by high frequency stimulation. A: Selective four vessel cerebral angiography. B: SEP recorded from Erb's point, neck and skull at standard 2 Hz stimulation. Note the inconspicuous N_{11} on both sides and the non-visible N_{14} on the right side. C: Effect of high frequency stimulation on the cervical evoked response. Note the relative enhancement of N_{11} and N_{14} and the reduction of N_{13} . The SEP records in B and C were taken 30 minutes before the cerebral angiography in A. Calibration lines represents 2.5 μ V.

animals, does not automatically imply a common mechanism.

Recent experimental data from humans,¹ using conventional neurophysiological test techniques such as resistance to high frequency stimulation, effect of paired stimuli and graded stimulus strength have however confirmed that N_{14} and the following positive wave in humans have many properties in common with the N_{2} notch and following positivity in experimental animals.

Based on these data it has been proposed that N_{14} represented a potential generated in the spinal cord by (presynaptic) activity in a group of relatively slow conducting high threshold afferent fibres.¹

The present data gave more direct support for a spinal origin of N_{14} , showing that this notch was present in eight out of the 13 patients examined when

standard 2 Hz stimulation rate was used. Furthermore, N_{14} was typically enhanced¹ and readily seen as a small separate potential in almost all patients (nine of 10) when the stimulus frequency was increased.

Experiments on the human cervical evoked response have indicated that the positive wave following after the main negative wave, represents an inhibitory mechanism¹⁸ with many parallels to the dorsal root potential (DRP) studied in experimental animals.³³⁻³⁶⁻⁴⁰ The present investigation also provided arguments for the positive wave being a spinal cord potential since it was invariably present in all patients examined although their intracerebral circulation was arrested, their EEGs isoelectric and the cortical somatosensory evoked responses extinguished. This does not exclude, however, that far

field potentials of intracerebral origin normally may contribute to this positivity of the cervical evoked potential. In fact the amplitude of the positive wave generally was larger in normal subjects compared to the present group of patients.

The possibility that some of the patients at the time of the SEP and EEG tests should have had a small intracranial residual-perfusion and thus functioning intracerebral structures giving rise to N14 or the positive wave seems unlikely. All patients had clinical signs of cerebral herniation at the SEP and EEG examination time, and the fact that their EEGs invariably were isoelectric and the cortical evoked responses extinguished probably are incompatible with residual intracerebral function. The N14 and the positive wave also were present in patients where the final four vessel angiography was performed before or immediately after the SEP and EEG records (fig 2).

Based on the present data we therefore propose that the main subcomponents N11, N13, N14 and the following positive wave in the human cervical evoked response are all integral parts of this response, generated in the spinal cord.

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