

Investigations on the nervous mechanisms underlying the somatosensory cervical response in man

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SUMMARY The main features (amplitude, latency and shape) of the cervical activity evoked by stimulation of the median nerve, recorded throughout the cervical spine, have been concurrently investigated by monopolar, bipolar longitudinal and bipolar transverse recordings. In some subjects the derivation C₇–Sn (suprasternal notch) has been employed as well. A comparative evaluation of the refractory period of each component of the cervical responses under investigation has been performed to differentiate presynaptic from postsynaptic events. Additional information has been obtained by cervical activity recorded by longitudinal and transverse bipolar derivations upon stimulation of the lower limb. It was thus demonstrated that both presynaptic and postsynaptic events were responsible for the cervical sensory evoked potential, as appearing when recorded against a cranial reference (that is the upper midfrontal region). The structures involved were the brachial plexus (N₉), the cervical roots (P₁₀ and a minor part of N_{11a}), the dorsal columns both at caudal (N_{11a}) and rostral (N_{11b}) cervical levels, and the dorsal column nuclei (N₁₃). However a contribution of the spinal segmental activity to the postsynaptic portion of the cervical response, more specifically to N₁₃, should be considered as well, though direct evidence is still inadequate.

The waveform of the cervical response evoked by stimulation of the median nerve at the wrist, as appearing when recorded against a cranial reference (either the ear¹ or the upper midfrontal region^{2–4}) is now well established, but the functional significance of its components is not completely understood. In particular, it is not clear whether such components are generated from fixed sites, either spinal or supraspinal, or from a travelling wave in the system of the dorsal columns.⁵

Intracranial components of the cervical response may be distinguished from extracranial ones by concurrent recordings over the scalp. In fact, every extracranial event recorded from the scalp, either spinal or supraspinal in origin, should change in polarity when the reference electrode is shifted from the ear to the forehead.¹ This is the case with the N₉, N₁₁ and N₁₃ waves, the opposite being true for N₁₄,

which thus represents the first sensory evoked potential component of intracranial origin.⁶ It is likely, also, that the segment of the cervical response following N₁₄ will be entangled with both spinal and supraspinal events.⁷ The present views on the nervous structures involved in the origin of the cervical response (apart from the N₉ component, which appears to be generated in the region of the brachial plexus³) are still controversial. Evidence on the respective contribution of radicular, spinal (either segmental or conducted) and supraspinal events to the cervical response so far available is inadequate or contradictory or both.

To clarify these issues, the main features (amplitude, latency and shape) of the activity evoked by stimulation of the median nerve (at the wrist) were concurrently recorded, both monopolarly and bipolarly, throughout the cervical spine. Additional information was obtained by recording the cervical activity evoked by stimulation of the lower limb. A comparative evaluation of the refractory period of each component and/or response under investigation was also performed, in order to differentiate presynaptic from postsynaptic events.

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Material and methods

The observations were made on 13 volunteers ranging in age from 26 to 40 years. The subjects were kept relaxed on a couch in a quiet room. The median and the tibial nerves were stimulated at the wrist and at the popliteal fossa respectively, using surface electrodes (Disa 13K62) with the cathode proximal to the anode. The limbs were gently warmed by infrared lamp throughout the experiment to ensure a skin temperature of 36–38°C. Square pulses were delivered by a Disa 14E01 Ministim stimulator (pulse duration 0.2 ms) at a rate of 1 Hz. The stimulus intensity, both at the wrist and at the popliteal fossa, was three to four times the motor threshold of the innervated muscles. Recordings were performed by means of fine subcutaneous needles with electrode impedance of 1000–2000 ohms. Simultaneous recordings of the cervical activity evoked by stimulation of the median nerve were obtained from each subject at low (C₇), mid (C₅) and high (C₃) cervical levels by monopolar (fig 1), bipolar longitudinal (fig 2) and bipolar transversal (fig 3) derivations. In four subjects the deri-

vation C₇-Sn (suprasternal notch) was employed as well (fig 5). The cervical activity evoked by stimulation of the lower limb was led off through longitudinal and transverse bipolar derivations at low cervical level (fig 4) in three subjects, the same interelectrode distance being used. The input from the recording electrodes was fed into differential amplifiers (Evoked potentials amplifiers Ote 2305) and simultaneously recorded on magnetic tape (Philips PM 8125). The frequency response of the recording apparatus was 16–10 000 Hz (3 db). Analysis times of 20 or 50 ms were used and usually 512 or 1024 responses were summated. Number, shape and polarity of the recorded potentials were analysed visually. Peak latencies were measured on the plot or with a cursor on the computer oscilloscope.

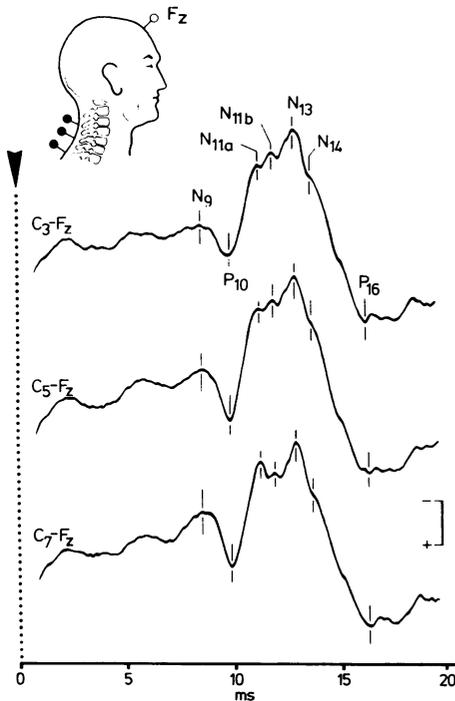


Fig 1 Cervical responses evoked by stimulation of the median nerve at the wrist simultaneously recorded at low (C₇), mid (C₅) and high (C₃) cervical levels against a cranial reference (F_z). Note that (a) none of the sensory evoked potential components shifts in latency from the lower to the upper cervical level; (b) N₁₁ is split into two fixed latency subcomponents; (c) N_{11a} is higher than N_{11b} at C₇, the opposite occurring at C₃. Calibration: 0.3 μV; 512 responses were summated.

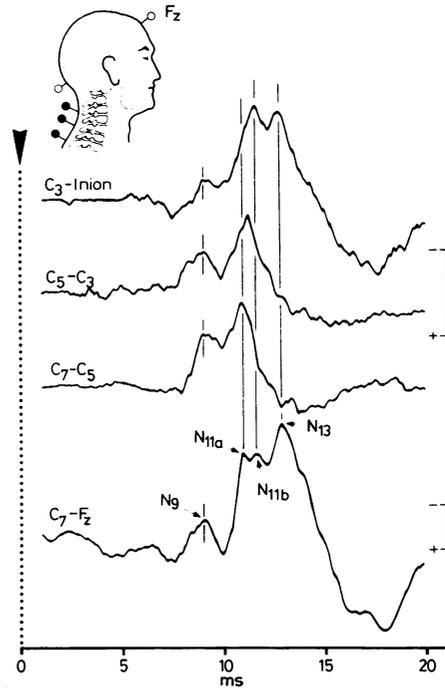


Fig 2 Cervical responses evoked by stimulation of the median nerve at the wrist, simultaneously recorded from monopolar (lower trace) and bipolar longitudinal derivations. The longitudinal recordings show: (a) a small fixed latency negative peak chronologically coincident with N₉; (b) a negative peak with a variable latency shifting from lower (C₇-C₃) to upper (C₃-inion) cervical derivations with proportionally intermediate latency over the mid neck (C₅-C₃); this peak is chronologically coincident with N_{11a} and N_{11b} at lower and upper cervical levels respectively; (c) a peak with a fixed latency chronologically coincident with N₁₃, showing a reversal in polarity from C₇-C₅ (positive) to C₃-inion (negative). Calibration: 0.3 μV; 1024 responses were summated.

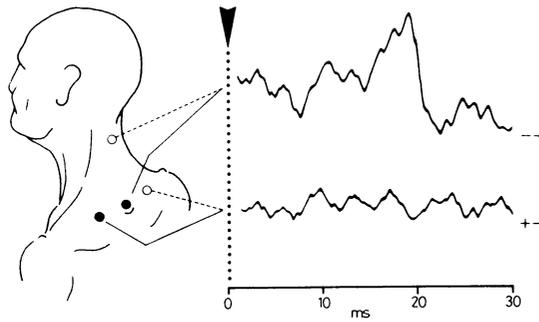


Fig 3 Concurrent neck recordings following tibial nerve stimulation at the popliteal fossa. The longitudinal derivation (upper trace) picks up a clear-cut response, while the bipolar transverse derivation (lower trace) fails to demonstrate any definite evoked activity. Calibration: $0.3 \mu\text{V}$; 1024 responses were summated.

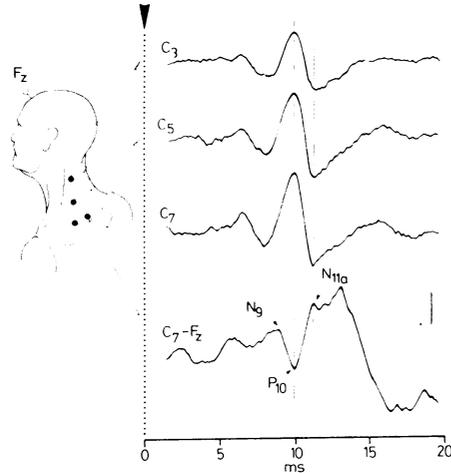


Fig 4 Cervical responses evoked by stimulation of the median nerve at the wrist, simultaneously recorded from monopolar (lower trace) and bipolar transverse derivations. The transverse recordings show: (a) a small fixed latency negative peak occurring 2–3 ms earlier than N_9 ; (b) a chronological coincidence of the main negative peak and the subsequent positive one respectively with P_{10} and N_{11a} ; (c) a progressive decrease in amplitude of the response from the lower (C_7) to the upper (C_3) cervical level. Calibration: $0.3 \mu\text{V}$; 512 responses were summated.

Results

(A) The general waveform of the sensory evoked potential recorded over C_7 , with a midfrontal reference was essentially similar to previous descriptions, being characterised by four negative components (N_9 , N_{11} , N_{13} and N_{14}) followed by a slow positive deflection (P_{16}). Apart from a clearcut reduction in

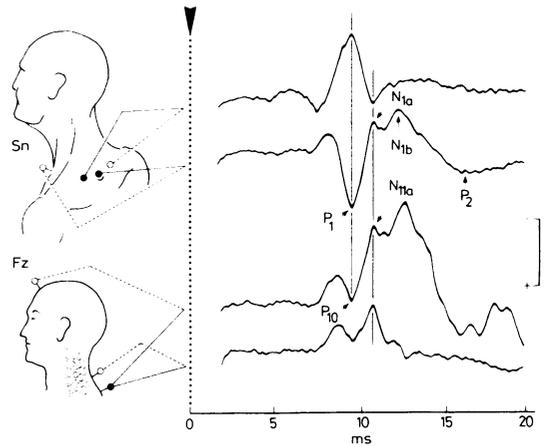


Fig 5 Concurrent recordings obtained at lower cervical level (C_7) by four different derivations. Note that: (a) both P_1 and P_{10} components are chronologically coincident with the main negative peak of the transverse recording (upper trace); (b) both N_{11a} and N_{11a} subcomponents occur simultaneously with the main negative peak of the longitudinal recording (lower trace) as well as with the second positive peak of the transverse recording (upper trace). Calibration: $0.3 \mu\text{V}$; 1024 responses were summated.

amplitude of N_9 at the upper cervical level, equivalent components were recorded both at C_5 and C_3 . In addition, a small positive peak occurring between N_9 and N_{11} could be observed, particularly when the recordings were made at C_7 . Currently, this peak, referred to as P_{10} , is not thought to be a distinct component owing to its small amplitude. None of these components shifted usually in latency from the lower to the upper cervical level. This was only partially true for N_{11} ; in the majority of cases (9 out of 13), N_{11} clearly resolved into two subcomponents with a fixed latency (N_{11a} and N_{11b}) and with different amplitudes (fig 1). In particular, N_{11a} was higher than N_{11b} in the lower neck, the opposite occurring in the upper neck. In the other cases (4 out of 13) N_{11} showed a single peak the latency of which could be either unvaried (2 out of 13) or definitely longer at C_3 than at C_7 (2 out of 13). In a few subjects the peak of N_{13} was bifid, but, at variance with N_{11} , no consistent amplitude distribution of the subcomponents could be observed.

(B) Sequential bipolar recordings obtained from electrode pairs (the interelectrode distance varying from 4 to 6 cm) suitably positioned over the cervical spine, along the midline, were characterised by a triphasic (positive-negative-positive) potential preceded by a small fixed latency negative peak chronologically coincident with N_9 (fig 2). The negative phase of the triphasic potential, which was generally more clearly defined than the positive ones,

showed a significant increase in latency from the lower (11.04 ± 0.31 ms) to the upper (11.72 ± 0.41 ms) cervical level ($\Delta = 0.68 \pm 0.14$ ms; $F = 67.36$, $p < 0.001$, one way analysis of variance for repeated measures), with proportionally intermediate values over the mid neck (11.37 ± 0.30 ms). Concurrent bipolar longitudinal and monopolar recordings (fig 2) revealed a clear coincidence of the negative phase of the cervical bipolar response, recorded at lower and upper cervical levels, with N_{11a} and N_{11b} respectively (11.04 ± 0.31 ms vs 11.06 ± 0.32 ms; 11.72 ± 0.41 ms vs 11.69 ± 0.31 ms). It was also found that the cervical bipolar response was constantly characterised by a small fixed latency peak, chronologically coincident with N_{13} , which showed a clearcut polarity reversal from lower (positive) to upper (negative) neck records (fig 2).

The latency shift of the main negative phase of the cervical bipolar response could be related to the rostral propagation of afferent activity in the dorsal column, or to the sequential activation of low, mid and high cervical segments. In our subjects the mean distance between C_7 and C_3 spinous processes was 85 ± 5 mm, and the corresponding shift in latency was 0.68 ± 0.14 ms. Provided that the distance between the presumed zones of actual recording is approximately 45–50 mm (cf. Desmedt and Cheron⁸) the values of conduction velocity can be tentatively placed at about 65–70 m/s, that is, exceedingly high for the sequential activation of cervical segments. Therefore, the latency shift most probably reflects an advancing wavefront of depolarisation in the cervical dorsal column.

(C) The possible radicular contribution to the cervical sensory evoked response was evaluated by transverse bipolar derivations performed at low, mid and high cervical levels. Such derivations are better suited to detect radicular events, which are presumably related to horizontally oriented dipoles, at least at the cervical level. Such an assumption was indirectly verified through the stimulation of the lower limb, which at the cervical level evokes exclusively cord-conducted events. It was found that, following stimulation of the tibial nerve, a clearcut response could be obtained from the longitudinal derivation (C_7-C_2) while, as expected, no definite evoked activity could be detected from the transverse derivation at the low cervical level, although the same interelectrode distance was being used (fig 3).

The cervical response obtained from the transverse derivation upon stimulation of the median nerve was characterised by a fixed latency triphasic (positive-negative-positive) potential of progressively decreasing amplitude from the lower to the upper cervical level (fig 4). This potential was often preceded by a small, fixed latency, negative peak,

apparently generated in the proximal portion of the median nerve,⁹ being at least 2.5 ms earlier than N_9 . Concurrent bipolar transverse and monopolar derivations showed that the main negative peak and the subsequent positive one of the transverse recordings were coincident with P_{10} and N_{11a} respectively (figs 4 and 5) (9.91 ± 0.27 ms vs 9.97 ± 0.25 ms; 11.12 ± 0.32 ms vs 11.06 ± 0.32 ms). Similar results have been obtained by concurrent "sagittal" (C_7-Sn) and monopolar recordings (fig 5). In fact, the positive (P_1) and negative (N_{1a}) peaks of the early positive-negative deflection of the "sagittal" response, which are held to represent the incoming volleys conducted through the cervical roots,¹⁰ were coincident with P_{10} and N_{11a} respectively. As expected, P_1 and N_{1a} components coincided also with the main negative peak and the subsequent positive one of the transverse recordings (fig 5).

(D) The possible contribution of spinal potentials generated in the dorsal horn neurons, near the spinal entry of the volley, was investigated by the cervical "sagittal" derivation (C_7-Sn). The negative-positive wave ($N_{1b}-P_2$) following the early positive-negative deflection (P_1-N_{1a}) is believed to reflect the interneuronal activity and the primary afferent depolarisation in the spinal cord.¹⁰ Concurrent "sagittal" (C_7-Sn) and monopolar (C_7-F_2) recordings showed that components N_{1b} and P_2 are chronologically close, but not coincident, with N_{13} and P_{16} respectively (fig 5), thus confirming our previous findings.⁷

(E) The results of double pulse experiments can be summarised as follows: (a) N_9 , P_{10} , and N_{11} had a very short refractory period. When equal paired stimuli were delivered to the median nerve at different intervals, a complete recovery could be observed within 2 ms. Therefore, we conclude that all these components are presynaptic in origin; (b) on the contrary, N_{13} seemed to be postsynaptic in nature, its complete recovery never requiring less than 5 ms; (c) no definite conclusions could be reached on the subsequent segment of the cervical monopolar response, but it seemed very likely to be postsynaptic in origin; (d) cervical responses obtained both from longitudinal (except for the peak chronologically coincident with N_{13}) and transverse bipolar derivations must be considered presynaptic, since they recovered completely within 2 ms; (e) the effect of equal paired stimuli with different interstimulus intervals on the various components of the "sagittal" response had been reported elsewhere.⁷

Discussion

Monopolar recordings of the cervical response evoked by stimulation of the median nerve failed to

show consistent shifts in latency from the lower to the upper cervical spine, at least in the majority of cases, thus apparently supporting the original concept of Matthews *et al.*,² that is, that all the components of the cervical sensory evoked potential are generated at fixed sites. According to these authors, a possible contribution of the spinal cord pathways should be excluded, provided that in this case "both the onset and the peak latencies should be expected to be greater at more rostral recording sites". However, the peak of N_{11} , at variance with the other components, was frequently split into two fixed latency subcomponents³ (N_{11a} and N_{11b}) which might be related to the rostral propagation of the afferent activity in the dorsal column, between C_7 and C_3 . Indeed, sequential bipolar longitudinal recordings obtained by electrode pairs suitably positioned over the cervical spine, along the midline, demonstrated a progressive increase in latency of the cervical response to the stimulation of the upper limb. In particular, the negative peak of the triphasic potential (positive-negative-positive) picked up by bipolar longitudinal derivations shifted significantly from the lower to the upper cervical level, with proportionally intermediate values over the mid neck. This latency shift is most probably related to an advancing wavefront of depolarisation in a vertically oriented trunk situated between C_7 and C_3 vertebrae, rather than to a sequential activation of low, mid and high cervical segments. We were able to show that the rostral propagation of the afferent activity in the dorsal column system between C_7 and C_3 , upon stimulation of the median nerve, can be easily demonstrated, provided that cervical longitudinal derivations are used (see also Cracco¹¹). In addition, cervical monopolar recordings timed with cervical bipolar longitudinal recordings showed a clear coincidence of N_{11a} and N_{11b} with the major negative peak of the cervical bipolar response picked up at lower and upper cervical levels respectively. Therefore, both N_{11a} and N_{11b} could be ascribed to the volley in primary afferent fibres at caudal (N_{11a}) and rostral (N_{11b}) levels of the cervical dorsal column, as recently suggested by Allison and Hume.¹² This interpretation is supported also by the different amplitude distribution usually shown by the two subcomponents of N_{11} . In fact, N_{11a} was higher than N_{11b} in the lower neck, while the opposite pattern occurred in the upper neck (see also Jones,³ fig 1, subject SJ), possibly due to the far field conduction of the related signals from the lower to the upper cervical electrode and *vice-versa*. As to the unsplit cases, it is conceivable that when volume conduction is very high, N_{11a} and N_{11b} tend to fuse into a single fixed latency peak throughout the cervical spine. On the other hand, when volume conduction is particu-

larly low, the spatial and temporal separation of N_{11a} and N_{11b} may be extremely clear (see also Allison and Hume,¹² fig 3), so that a shift in latency of N_{11} from the lower to the upper cervical lead can be observed. It follows that, although exceptionally, referential recordings can be suitable to detect a travelling wave, even in spite of the relatively short distance between the active electrode (i.e. C_7 and C_3) and the position of the reference (i.e. the mid-frontal region).

Although both N_{11a} and N_{11b} are very likely to reflect dorsal column activity, a radicular contribution to N_{11a} should be considered as well. In fact, the reduction in amplitude of N_{11a} (and, to some extent, of P_{10}) in the upper neck seems to parallel the progressive decrease of the cervical transverse recordings from the lower to the upper cervical level. In this connection, it may be pointed out that: (a) transverse derivations are particularly suited to picking up horizontal dipoles, ignoring vertical ones, as demonstrated by the absence of evoked activity in the cervical transverse derivation upon stimulation of the lower limb; (b) the afferent volley to stimulation of the median nerve reaches spinal cord segments C_7 - C_6 (cf Desmedt and Cheron⁸), the corresponding spinal roots being horizontally oriented; (c) such a volley could be simultaneously recorded by volume conduction even at more rostral levels, its amplitude being progressively reduced. The chronological coincidence between the cervical transverse response and the early positive-negative deflection (P_1 - N_{1a}) of the "sagittal" response obtained from C_7 -Sn derivation should be considered. This deflection is believed to represent the incoming volleys conducted through the cervical roots.⁷ Moreover, the simultaneous occurrence of both the transverse response and the P_1 - N_{1a} deflection with the P_{10} - N_{11a} complex suggests that all of them, which are presynaptic in origin, reflect horizontally oriented dipoles, probably located at the level of the cervical roots. This conclusion does not conflict with the previous attribution of N_{11a} to dorsal column activity, since this component is likely to be simply contaminated by a radicular contribution. Accordingly, the equivalence $N_{11} = N_{1a}$ proposed by Sedgwick (personal communication) should be restated as follows: the first component of N_{11} (N_{11a}) is partially equivalent to N_{1a} . The postsynaptic properties of N_{11} previously reported by El Negamy and Sedgwick⁴ could not be confirmed by double pulse experiments. In brief we believe that the activation of the spinal roots is reflected by P_{10} and, at least in part, by N_{11a} which incorporates both radicular and spinal conducted events, while N_{11b} should be entirely related to the dorsal column activity.

The origin of N_{13} cannot be established on the basis of its latency. In fact, the latter could suggest an origin of N_{13} either in the spinal cord, adjacent to the spinal entry, provided that one or possibly two synapses are involved, or even more rostrally, for example in the brainstem, through one synapse at the most. In patients with well localised lesions in the lemniscal pathway N_{13} can be preserved following thalamic¹³ as well as brainstem¹⁴ haemorrhage, while this component disappears after a complete spinal cord lesion at C_5 .⁴ Therefore, although the exact source of N_{13} is still disputed,⁸ it seems reasonable to conclude that N_{13} arises caudal to the brainstem but immediately rostral to the spinal cord. In our opinion there is little doubt that N_{13} is extracranial in origin since the corresponding peak recorded over the scalp changes in polarity when the reference electrode is shifted from the ear to the forehead.¹ The polarity reversal of N_{13} near the occipito-cervical junction observed in bipolar longitudinal recordings suggests that the generator of N_{13} could be located at this level. The clear reduction in amplitude of N_{13} during double pulse experiments indicates that this event is postsynaptic in origin. Finally, the unvaried latency of N_{13} in bipolar longitudinal recordings points to the existence of a fixed dipole probably located at the level of dorsal column nuclei, as previously suggested.^{3 13-16}

The latter hypothesis has been recently challenged by Mauguère and Courjon,¹⁷ who feel that N_{13} could originate in the dorsal horns close to the spinal entry of the volley. In fact, in one of their patients the cervical response evoked by stimulation of the right median nerve showed a negative peak at 14 ms though the right dorsal funiculus and related nucleus had been destroyed by a tumour down to the C_5 level. Indeed, this discrepancy with previous findings could be due to a partial contamination of N_{13} with spinal segmental events, as demonstrated by concurrent "sagittal" (C_7 -Sn) and monopolar recordings. It was found that the negative positive wave (N_{1b} - P_2), which is held to reflect the inter-neuronal activity and the related primary afferent depolarisation in the spinal cord,¹⁰ is chronologically very close, although not coincident, with N_{13} and P_{16} respectively.⁷

In conclusion, both presynaptic and postsynaptic events contribute to the cervical sensory evoked potential. The structures involved are the brachial plexus (N_9), the cervical roots (P_{10} and a minor part of N_{11a}), the dorsal columns both at caudal (N_{11a}) and rostral (N_{11b}) cervical levels and the dorsal column nuclei (N_{13}). However a possible contribution of the spinal segmental activity to the postsynaptic portion of the cervical response, more specifically to N_{13} , should be considered as well, though direct evidence is still inadequate.

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