Unravelling cossed wires : dysfunction in obstetric brachial plexus lesions in the light of intertwined effects of the peripheral and central nervous system

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Chapter 5

Cocontraction in adults with obstetric brachial plexus lesion

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Abstract

Introduction Cocontraction due to axonal misrouting may contribute to the functional deficit in obstetric brachial plexus lesion (OBPL); we aimed to quantify its presence.

Method We obtained supramaximal CMAPs of the biceps muscles in 19 healthy adults (median age 23y; nine men) and 17 conservatively treated OBPL adults (median age 38y; five men) after electrical stimulation at Erb's point. We simultaneously measured CMAPs over the deltoid and triceps muscles, reflecting volume conduction as well as misrouting, with two stimulating and two recording methods. Misrouting should result in more activity measured over the deltoid and triceps muscles during biceps activation in patients than in controls.

Results A branched recording electrode resulted in the least amount of coregistration. No stimulation method was superior to the other. The cocontraction amount did not differ between patients and controls.

Interpretation The branched electrodes improved recording selectivity. None of the methods statistically proved the presence of contraction in OBPL patients.

Introduction

Obstetric Brachial Plexus Lesion (OBPL) concerns a closed traction injury of the brachial plexus during birth, with an incidence of 0.5 to 2.6 per 1000 live births.[1] A systematic literature search showed residual deficit in 20 to 30% of cases.[2] Severe OBPL can result in permanent impairment of arm function, skeletal malformations, cosmetic deformities, behavioural problems and socio-economic limitations.[3, 4] Functional recovery following OBPL depends on the number of outgrowing motor axons that reinnervate muscle fibres, but also on the extent of axonal misrouting.[5-8] The misrouted axons may innervate an agonist (e.g. an axon meant for the biceps ends up in the brachialis muscle), an antagonist (e.g. reinnervation of the triceps instead of the biceps muscle), or a muscle with another function (e.g. deltoid instead of biceps).[8] If a sizable number of axons is misrouted, two muscles will contract together, known as cocontraction. Cocontraction may cause more problems in OBPL than primary muscle weakness.[6, 9, 10] However, triceps and deltoid muscle cocontraction during biceps activation has not been quantified yet. To quantify misrouting, the effects of costimulation, e.g. stimulating unintended nerves, and coregistration, e.g. recording unwanted activity due to volume conduction, must first be minimized.

As for costimulation, electrical stimulation of the brachial plexus at Erb's point is commonly used for the evaluation of proximal nerve disorders.[11-13] The conventional stimulating method involves moving the stimulator over the skin at Erb's point, located in a triangle formed by the clavicle and the sternocleidomastoid and trapezius muscles. Compound muscle action potentials (CMAPs) of a proximal arm muscle are recorded until a stimulation site is found where the largest amplitude is obtained with the lowest current intensity. This paper focuses on the biceps muscle and its innervation through the C6 root, the superior trunk, lateral cord and musculocutaneous nerve. Stimulation in Erb's point is likely to stimulate several plexus elements simultaneously, so we designed an additional stimulation method based on stimulation of the lateral cutaneous antebrachial nerve (LCAN) as the sensory branch of the musculocutaneous nerve. Stimulating the LCAN while recording nerve action potentials (NAPs) at various sites over the plexus should reveal the precise location of axons running to the musculocutaneous nerve (Figure 1).

As for coregistration, CMAPs are conventionally recorded with one electrode over the muscle belly and one over the tendon[12], but this method also records activity of adjacent muscles through volume conduction.[14] A 'branched electrode'[15] has been shown to improve the selectivity of CMAP recordings appreciably.[16]

We first aimed to minimize the effects of costimulation and coregistration comparing two stimulation and two recording methods in healthy subjects. Secondly, the results were used to quantify triceps and deltoid muscle cocontraction during biceps activation in conservatively treated OBPL adults. We previously showed in the same patient group that misrouting was qualitatively present in over half of cases for the biceps muscle and nearly half for the deltoid muscle.[8]

Methods

Participants

Seventeen adults with OBPL and nineteen adult healthy subjects participated. Exclusion criteria were the presence of any relevant disorder affecting movement or sensation. The protocol was approved by the Medical Ethics Committee of the LUMC. All participants provided informed consent.

Stimulation methods

The conventional stimulation method to optimize biceps stimulation involved varying the stimulation site near Erb's point, with the best site defined as the one resulting in a supramaximal biceps CMAP at the lowest current intensity. For the new method, the LCAN was located in the forearm by sliding a stimulator using 8 mA stimuli along a line perpendicular to the direction of the nerve.[17] Once found, stimulating electrodes were attached and 500 stimuli of 8 mA were given, while averaging responses from four recording sites over Erb's point (Figure 1). The site with the highest nerve action amplitude (NAP) was used to identify nerve fibers running to the musculocutaneous nerve. When amplitudes were equally high at two recording sites, a site in between was chosen.

Recording methods

Two types of recording electrodes were used: a standard bipolar recording and the 'branched electrode'.[15] The latter was chosen due to its superiority and simplicity in reducing crosstalk in surface EMG recordings.[15, 16] Disposable surface electrodes of 2.2 by 3.2 cm were used for the standard recording with a distance of 0.5 cm between their edges, placed with the shorter sides of the electrodes adjacent to each other. The branched electrode consisted of three circular electroencephalography (EEG) electrodes of 5 mm diameter with distances of 0.5 cm between their rims. The two outer electrodes were connected to one another, recording a difference between the potential of the middle electrode and the mean potential at the outer electrodes. CMAPs measured with a branched electrode are half the size of those measured with a bipolar electrode.[16] Both types of recording electrodes were fastened on the muscle belly, next to one another and separated by 0.5 cm.[18] The electrode that was placed medially was varied randomly.

Quantifying misrouting

The right arm of the healthy subjects and the affected arm of the OBPL patients were fixed to the examination table to prevent movement artifacts. Supramaximal shocks were given at the standard and LCAN-derived sites to obtain biceps CMAPs. Deltoid and triceps CMAPs were simultaneously measured; these reflect effects of costimulation, coregistration and misrouting. All CMAPs were measured with both bipolar and branched electrodes. Activity was recorded over 30 ms with a band pass-filter of 20 Hz – 2 kHz using a Medelec Synergy EMG apparatus. Twelve CMAPs (2 stimulation methods x 2 recording methods x 3 muscles) were acquired per subject, and peak-to-peak amplitudes were noted.

To assess cocontraction we reasoned as follows: if the CMAP amplitude of the biceps muscle is large, mere volume conduction will cause the simultaneously measured activity over the deltoid and triceps muscles to be large as well. Over a group of subjects, a relation between these amplitudes is therefore to be expected. Misrouting should cause an additional increase of amplitude measured over the deltoid and triceps muscles. As a result, the nature of the relation of deltoid/triceps activity to biceps activity should differ between the groups: the relation in the control groups reflects costimulation and coregistration only, while that in the patient group also reflects misrouting.

Statistical analysis

IBM SPSS Statistics 20.0 (Armonk, NY: IBM Corp.) was used for statistical analysis. Demographic characteristics were compared with a Mann-Whitney *U* test. We used the natural logarithm of CMAPs for further analysis because the data were not normally distributed. A multivariate linear regression was used for three statistical analyses: 1) comparing the recording electrodes, 2) comparing the stimulation methods, and 3) comparing OBPL patients with healthy subjects.

In the first analysis the natural logarithm of triceps CMAPs was the outcome and recording electrode (bipolar or branched) the predictor with the natural logarithm of biceps CMAPs as a confounder. The analysis was performed for each stimulation method (conventional or LCAN) separately. In the second analysis the natural logarithm of triceps CMAPs was the outcome and stimulation method the predictor with the natural logarithm of biceps CMAPs as a confounder. This was performed for each recording method separately. Both analyses were performed only in healthy individuals and were repeated using the natural logarithm of deltoid CMAPs instead of triceps CMAPs as the outcome. A Bonferroni corrected significance threshold of 0.006 (0.05/8) was used considering the eight comparisons (2 muscles x 2 recording electrodes x 2 stimulation methods). In the third analysis the natural logarithm of triceps CMAPs was the outcome and patient and control group the predictor with the natural logarithm of biceps CMAPs as a confounder. This analysis was performed separately for each of the four combinations of recording and stimulation method. This analysis was repeated using the natural logarithm of deltoid CMAPs instead of triceps CMAPs as the outcome. A Bonferroni corrected significance threshold of 0.006 (0.05/8) was used. This analysis was repeated for the triceps comparing healthy subjects with a subgroup of nine patients with qualitatively present misrouting in the triceps, as determined in a previous study[8], and also for the deltoid muscle with a corresponding subgroup of seven patients with qualitatively present misrouting in the deltoid.

The natural exponential of the coefficients from the regression analyses were reported. These numbers represent how many times the triceps or deltoid CMAP would increase when changing the stimulating or recording method, or patients relative to controls. For example, when comparing patients and

controls, a natural exponential of a regression coefficient of 1.5 indicates that CMAP amplitudes are 1.5 times higher in patients than in healthy subjects.

Results

Group description

The median age (10^{th}-90^{th} percentile) was 38 (20-58) years in the OBPL group and 23 (10^{th}-90^{th} percentile: 20–55) years in the healthy subject group (p=0.24). There were five men in the OBPL group and nine in the control group (p=0.32). The right hand was affected in nine of 17 OBPL patients. There were six left-handed subjects in the OBPL group and two among 19 healthy subjects (p=0.074). There were seven OBPL subjects with a lesion level C5-C6, seven with lesion level C5-C7 and three with either C5-C8 or C5-Th1.

Costimulation and coregistration

Table 1 shows biceps, deltoid and triceps CMAP amplitudes. The branched electrode resulted in significantly smaller CMAP amplitudes compared to the bipolar one for both stimulation methods (two left columns of Table 2) and there were no significant differences in CMAP amplitude between the stimulation methods in control subjects. (two right columns of Table 2) Figure 2 shows an example of NAP measurement following LCAN stimulation in a healthy subject. In two healthy subjects NAPs revealed multiple peaks. These data were excluded from the analysis. An example CMAP recording is shown in Figure 3.

Quantifying misrouting

Triceps and deltoid cocontraction did not differ significantly between patients and healthy subjects, (Table 3) and this also held for the patients with qualitatively present misrouting.

Discussion

Costimulation and coregistration

The branched electrode proved superior to the bipolar electrode in minimizing coregistration, but the two stimulation methods did not differ in their ability to limit costimulation. As expected, CMAPs measured with the branched electrode were half the size of those measured with the bipolar electrode.[16] This lower amplitude will only present problems when absolute amplitudes are very small, but this was not the case for the 3.5-5 mV range in the present study. We advise the use of the branched electrode in similar studies to improve recording selectivity. The two stimulation methods did not differ in their ability to find the optimal stimulation site; the resulting two stimulation points were very close together.

Quantifying misrouting

There were no differences in the degree of cocontraction between OBPL patients and healthy subjects for either the triceps or deltoid muscles.

We found no significant proportion of cocontraction in the triceps or the deltoid to be due to misrouting in OBPL patients, not even in a subgroup of patients in whom in a previous study the qualitative presence of misrouting was established.[8] The apparent discrepancy with the current findings can be explained in several ways.

The first is that the number of misrouted axons causing cocontraction in our population was in fact low. Apart from misrouting, problems with the formation of central motor commands have been implied in cocontraction.[6, 9, 10, 19] In view of the present results this explanation becomes more attractive. This may mean that the present population concerned only moderately severe lesions with little misrouting. The second explanation is that we failed to suppress the effects of costimulation and coregistration sufficiently to allow cocontraction to be quantified, despite the use of a combination of conventional and novel ways to do so.

Limitations and implications

The design could not disentangle effects of costimulation and coregistration completely: activity measured over the deltoid and triceps muscles could be due to volume-conducted biceps activity as well as to activation of axons running to these muscles. The use of supramaximal electrical stimulation has the advantage of excluding the effects of voluntary activation which may be mistaken for misrouting. However, the proportion of activated misrouted axons to the triceps compared to the activated biceps axons may be higher during voluntary flexion than during supramaximal stimulation and thus may be functionally impairing. Future research should elucidate the contribution of misrouting to impairment at more functional activation levels.

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Table 1: Compound muscle action potential (CMAP) amplitudes of the biceps, triceps and deltoid muscles (median milliVolt (10^{th}-90^{th} percentile)) for the healthy subjects (n=19) and obstetric brachial plexus lesion (OBPL) patients (n=17). LCAN - lateral cutaneous antebrachial nerve

		Bipolar recording electrode		Branched recording electrode	
		Conventional stimulation	LCAN stimulation	Conventional stimulation	LCAN stimulation
Healthy subjects	CMAP biceps	7.2 (3.3-11.4)	7.4 (2.7–12.4)	5.0 (1.7–9.4)	3.5 (1.3–9.2)
	CMAP triceps	1.8 (1.0–4.8)	2.9 (0.6–8.2)	0.5 (0.2–1.6)	0.4 (0.1–3.0)
	CMAP deltoid	3.0 (0.4–7.8)	3.8 (0.8–9.4)	0.6 (0.2–2.5)	0.8 (0.2–2.1)
OBPL patients	CMAP biceps	5.6 (1.8-11.2)	5.3 (1.4-10.9)	1.2 (0.3-3.6)	1.2 (0.3-3.4)
	CMAP triceps	1.7 (0.4-4.9)	1.5 (0.2-5.5)	0.3 (0.04-1.2)	0.3 (0.05-1.2)
	CMAP deltoid	3.1 (1.4-8.8)	2.9 (1.5-10.8)	0.7 (0.09-1.8)	0.7 (0.1-2.2)

Table 2: Natural exponential of the regression coefficients comparing compound muscle action potentials between the two recording and two stimulation methods in the healthy subjects (n=19), with corresponding p-values. A significance threshold of 0.006 was used. LCAN - lateral cutaneous antebrachial nerve

	Bipolar vs. branched recording electrode		Conventional vs. LCAN stimulation method	
	Conventional	LCAN	Bipolar	Branched
Triceps (p)	0.34 (0.004)	0.25 (0.001)	0.19 (0.2)	1 (1.0)
Deltoid (p)	0.28 (0.001)	0.23 (<0.001)	1.15 (0.4)	1 (1.0)

Table 3: Natural exponential of the regression coefficients comparing compound muscle action potentials between obstetric brachial plexus lesion patients (n=17) and healthy subjects (n=19), with corresponding p-values. A significance threshold of 0.006 was used. LCAN - lateral cutaneous antebrachial nerve

	Bipolar recording electrode		Branched recording electrode	
	Conventional stimulation	LCAN stimulation	Conventional stimulation	LCAN stimulation
Triceps (p)	0.87 (0.602)	0.73 (0.286)	1.02 (0.970)	1.12 (0.779)
Deltoid (p)	1.73 (0.071)	1.25 (0.430)	1.64 (0.202)	1.12 (0.745)

Figure 1: Stimulation sites.

Left panel: The conventional way of finding Erb's point is to vary the site of a stimulation electrode in the triangle formed by the clavicle and the sternocleidomastoid and the trapezius muscles. *Right panel:* Determination of the four recording electrodes for the LCAN method, relative to the clavicle and brachial plexus. A line was drawn on the skin from the insertion of the sternocleidomastoid muscle to the clavicle to the intersection of the clavicle with an imagery line extended down the boundary of the trapezius muscle. A second line was drawn parallel to the first one, 1.5 cm in the cranial direction. Four silver-silver-chloride round electroencephalography (EEG) electrodes with a diameter of 5 mm were placed at 1 cm distances on this line with the third electrode on the middle of the line.

Figure 2: Typical measurement over the four supraclavicular electrodes after LCAN stimulation of a healthy subject with NAPs from top to bottom: 1.7, 1.9, 2.2, 2.1 μV.

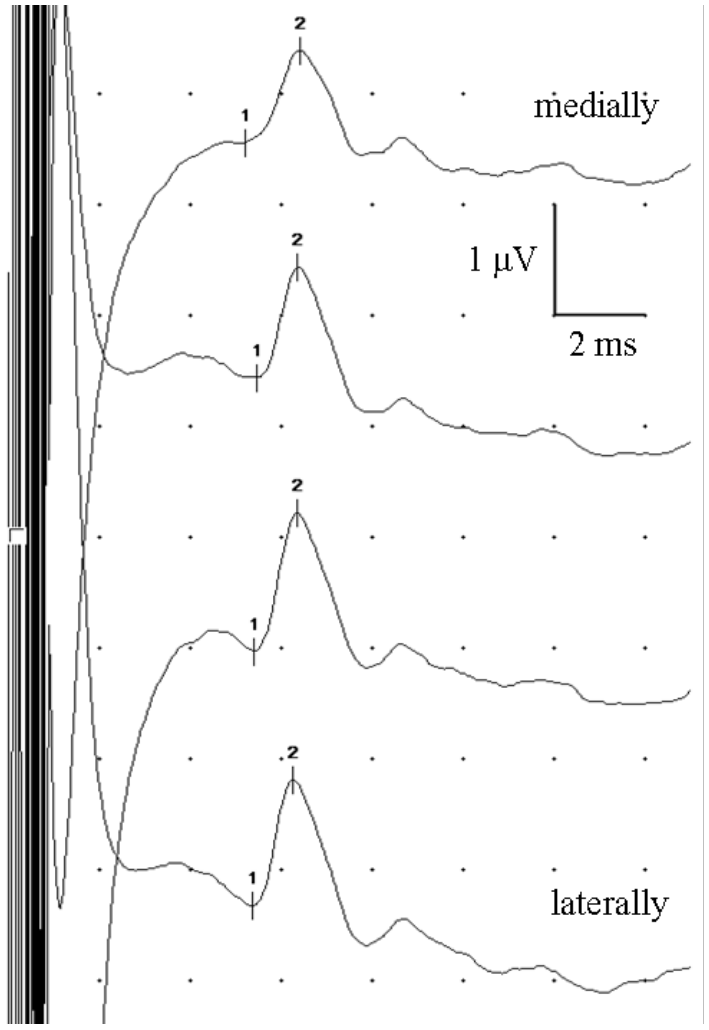

Figure 3: Typical compound muscle action potential measurement of a healthy subject with A. the bipolar and B. the branched electrode over biceps, triceps and deltoid muscles during Erb's point stimulation.