

Temporal changes to shoulder muscle mass and length following brachial plexus birth injury

Kyla B. Bosh^{1,2}, Brian M. Hua^{1,2}, Christina F. Lasdin¹, Vivian M. Mota¹, Katherine R. Saul¹, Jacqueline H. Cole^{1,2}

¹North Carolina State University, Raleigh NC, ²University of North Carolina, Chapel Hill, NC
kbosh@ncsu.edu

Disclosures: Kyla B. Bosh (N), Brian M. Hua (N), Christina F. Lasdin (N) Vivian M. Mota (N), Katherine R. Saul (N), Jacqueline H. Cole (N)

INTRODUCTION: Brachial plexus birth injury (BPBI) occurs during a difficult childbirth, causing paralysis, shoulder contracture, deformed bone growth, and lifelong arm impairments [1-3]. Nerve damage presents as nerve rupture or avulsion [2]. Rupture (*postganglionic injury*) results in muscle paralysis, limb disuse, and elbow/shoulder contracture [4], while avulsion (*preganglionic injury*) results in muscle paralysis and limb disuse without joint contracture [5]. Changes to muscle mass and length have been observed clinically [1,6] and in rodent models [4,5,7], with greater muscle mass loss for preganglionic than postganglionic injury in rotator cuff muscles at 8 weeks after injury [7]. However, the timing for when muscle changes initiate is unknown.

METHODS: Under approved IACUC protocol, four groups of Sprague Dawley rats underwent surgery on one forelimb (injured) at postnatal day 3-6: postganglionic neurectomy (n=12/endpoint) [8], preganglionic neurectomy (n=12/endpoint) [5], forelimb disarticulation (n=12/endpoint) [9], or sham neurectomy (n=8/endpoint) [9]. The contralateral limb (uninjured) served as a control. For the neurectomies, C5-C6 nerve roots were excised distal to the dorsal root ganglion modeling nerve rupture (postganglionic) [7-9] or proximal to the dorsal root ganglion modeling nerve avulsion (preganglionic) [5,7,9], or the nerve roots were left intact (sham). For forelimb disarticulation, a forelimb was amputated at the elbow to model limb disuse without nerve injury [9]. At the endpoints (2, 3, 4, 8, 16 weeks post-injury, rats were sacrificed and intact upper torsos were fixed in a neutral posture [4,9]. Muscles crossing the glenohumeral joint were dissected (pectoralis major, anterior deltoid, spinal deltoid, supraspinatus, infraspinatus, subscapularis, teres major, teres minor, biceps brachii, triceps) [9], and muscle mass and length were measured [7]. Metrics were compared between groups and across endpoints for injured-to-uninjured limb ratios using Kruskal-Wallis tests with Dunn's correction ($\alpha=0.05$, GraphPad Prism). Percent change relative to sham for the injured and uninjured limbs was also calculated.

RESULTS: A subset of muscle data are presented here for each endpoint (postganglionic neurectomy n=6-11; preganglionic neurectomy n=2-5; forelimb disarticulation n=2-10; sham n=1-6). **Pectoralis major:** Muscle mass increased over time for preganglionic injury (3wk < 8wk p=0.017, 4wk < 8wk p=0.047) and at 8 weeks was greater for preganglionic vs. postganglionic injury (p=0.028). No differences were observed for muscle length. **Spinal deltoid:** At 4 weeks muscle mass was greater for disarticulation vs. preganglionic injury (p=0.034) (Fig. 1) and at 4 and 8 weeks it tended to be lower (p<0.1) for preganglionic vs. postganglionic and preganglionic vs sham (-30% in injured limb). Muscle length shortened over time for preganglionic injury (4wk > 8wk p=0.021) and at 8 weeks was lower (p=0.009) relative to sham (-26.1% in injured limb). **Biceps long head:** Muscle mass increased over time for postganglionic injury (2wk < 3wk p=0.010, 2wk < 4wk p=0.005). Muscle length at 8 weeks after injury was shorter (p=0.012) for preganglionic vs. sham (-16.9% in injured limb). **Supraspinatus:** Muscle mass increased over time for postganglionic (2wk < 3wk p=0.046, 2wk < 8wk p=0.005) and at 4 weeks was lower (p=0.007) (Fig. 1) for preganglionic vs. sham (-68.3% in injured limb). Muscle length at 4 weeks was longer for postganglionic vs. preganglionic injury (p=0.021). **Infraspinatus:** Muscle mass at 3 weeks tended to be lower for preganglionic vs. disarticulation (p<0.1) and at 4 weeks tended to be lower for preganglionic vs. sham (p<0.1) and was lower for preganglionic vs. disarticulation (p=0.037) (Fig.1). Muscle length at 3 weeks was shorter for preganglionic vs. postganglionic injury (p=0.018). **Teres major:** Muscle mass at 3 weeks tended to be lower for preganglionic vs. disarticulation injury (p<0.01). No differences were observed for muscle length. **Triceps:** Muscle mass tended to be greater over time for preganglionic injury (4wk < 8wk p=0.059) and at 4 weeks was lower (p=0.013) for disarticulation vs. sham (-67.1% in injured limb) (Fig. 1). Muscle length at 3 and 4 weeks after injury tended to be shorter (p<0.1) for disarticulation vs. sham (-25% in injured limb).

DISCUSSION: Detriments in shoulder muscle mass and length were typically most severe following preganglionic BPBI. Muscle architecture changes observed in this study are similar to those reported previously for postganglionic and preganglionic groups previously at 8 weeks post-injury, when deformity is already established [7]. Our study is the first to examine these changes across earlier stages of development, and we identified onset of muscle architecture changes with preganglionic BPBI at earlier timepoints, as early as 3-4 weeks after injury. Ongoing analyses will confirm whether changes in muscle mass and length persist to 16 weeks following BPBI.

SIGNIFICANCE/CLINICAL RELEVANCE: This study provides insight into the effect of nerve injury on muscle architecture in muscles surrounding the shoulder and elbow, which contribute to upper limb movement. We present new, previously unknown information on changes to these muscles across development following different types of BPBI. Establishing a timeline for when muscle changes initiate, and examining factors that drive these muscular changes following injury, may inform better treatments to limit musculoskeletal detriments that develop following BPBI.

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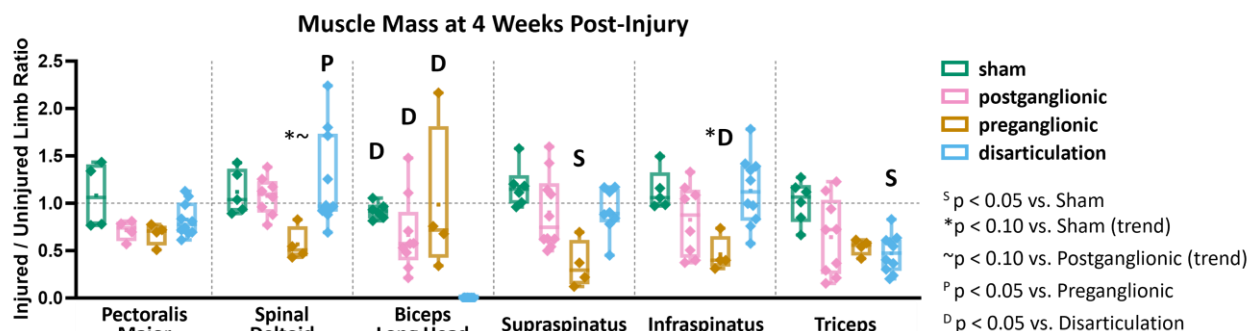


Figure 1. Detriments in muscle mass of rotator cuff muscles were more severe following preganglionic BPBI at 4 Weeks post-injury.