

咬肌及顳肌注射肉毒桿菌神經毒素之後對大屬顱顏生長發育之影響

Evaluation of Craniofacial Growth and Development Following Injections of Botulinum Neurotoxin into Masseter and Temporalis Muscles of Rats

中文摘要

本研究目的是藉由將肉毒桿菌神經毒素 A 型 (Botox®, Allergan Pharmaceuticals, Irvine, CA, USA) 注入大鼠咬肌及顳肌，使咬肌和顳肌麻痺、萎縮，來探討咬肌和顳肌對顱顏生長發育之影響。研究方法是選取 60 隻 28 天大的 Long-Evans 雄性之大鼠，隨機分為四組，每組 15 隻，依部位將 25U/mL 的 A 型肉毒桿菌神經毒素 (BoNT/A) 注射於大鼠：Group I 之雙側咬肌(雙側顳肌則施打等量之 0.9%生理食鹽水)；Group II 之雙側顳肌(雙側咬肌則施打等量之 0.9%生理食鹽水)；Group III 之雙側咬肌和顳肌；Group IV 為對照組，雙側咬肌及顳肌只施打 0.9%生理食鹽水。每星期一次，連續七週，測量老鼠之體重。而後將 77 天大的大鼠犧牲，取下咬肌和顳肌，測量其重量及量測乾燥頭顱骨大小(共 40 項測量項目)。

最後完成研究總計有 53 隻大鼠。結果發現四組的平均體重在七個星期中並無明顯之統計上的差異。顳肌平均重量 Group I 和 Group IV($\mu=0.64\pm0.03g$ 和 $0.061\pm0.09g$)較 Group II 及 Group III(分別為 $\mu=0.43\pm0.03g$ 和 $0.33\pm0.02g$)大；咬肌平均重量 Group II 和 Group IV(分別為 $\mu=1.41\pm0.07g$ 和 $1.38\pm0.04g$)較 Group I 及 Group III(分別為 $\mu=1.26\pm0.07g$ 和 $1.04\pm0.04g$)大。肌肉之平均重量具統計上的差異($p<0.001$)。乾燥頭顱骨的 40 項測量中，16 項具有統計意義($p<0.05$)，分別為：(1)頭顱向實驗組之 maximum skull height 及 upper anterior facial height 比對照組小、lower anterior facial height 和 total anterior facial height 比對照組大。(2)上顎向之 U8 bimaxillary distance 在 Group III 是最大的，而對照組是最小的。(3)下顎向測量項目中之 total mandibular length I~III 及 corpus length 實驗組較對照組大，而 Group III 是最大的；在 ramus height I~IV 方面，實驗組較對照組大，而 Group I 是最大的；在 mandibular plane angle 方面實驗組比對照組平坦，且 Group III 的角度是最小的；在 bicoronoid width 和 bigonial width 中，實驗組左右寬度較對照組小，而 Group III 是最小的。

本研究結果顯示咀嚼肌麻痺、萎縮且功能降低後會造成生長發育偏向垂直方向生長形成長臉型之顱面外觀。上臉部顯得矮短而下臉部變長，下顎骨體長度及下顎枝後緣高度也比正常大，下顎冠狀突及下顎骨角左右之間的距離也呈現狹窄之現象。研究證實了咀嚼肌萎縮後確實會影響顱顏骨型態及生長發育。

英文摘要

This study seeks to evaluate the craniofacial growth and development of growing rats following injections of botulinum neurotoxin type A (Botox®, Allergan Pharmaceuticals, Irvine, CA, USA) into masseter and temporalis muscles of rats. It aims to achieve masseter and temporalis muscle paralysis, inducing a decreased masticatory function, and to investigate the influences of masticatory hypofunction on cranial, maxillary, and mandibular bone growth and development.

The study was comprised of 60 Long-Evans rats which were 28 days old and randomly divided into four groups. A 25U/mL of botulinum neurotoxin type A (BoNT/A) was injected according to the following groups: Group I injection of bilateral masseter muscles (bilateral temporalis muscles received equal amounts of 0.9% sterile, non-preserved saline); Group II injection of bilateral temporalis muscles (bilateral masseter muscles received equal amounts of 0.9% sterile, non-preserved saline); Group III injection of bilateral masseter and temporalis muscles; Group IV is the control, both bilateral masseter and temporalis muscles received 0.9% sterile, non-preserved saline. The animals were weighed every week for a period of 7 consecutive weeks. After 49 days, the mature rats were perfused and sacrificed. The masseter and temporalis muscles were carefully dissected and harvested and the mean muscle mass were recorded. With the preparation of the dried skulls, direct anthropometric cranial, maxillary, and mandibular measurements (a total of 40 parameters) were carried out on the dried skulls.

At the end of the experiment, 53 animals completed the study. The mean changes in animal weights over the 7 weeks did not show any statistical significance. Following injections of BoNT-A, the mean temporalis mass in Group I and Group IV ($\mu=0.64\pm0.03\text{g}$ and $0.61\pm0.09\text{g}$ respectively) were more than Group II and Group III ($\mu=0.43\pm0.03\text{g}$ and $0.33\pm0.02\text{g}$ respectively); the mean masseter muscle mass in Group II and Group IV ($\mu=1.41\pm0.07\text{g}$ and $1.38\pm0.04\text{g}$) were more than Group I and Group III ($\mu=1.26\pm0.22\text{g}$ and $1.04\pm0.04\text{g}$ respectively). The differences in mean muscle wet mass were statistically significant ($p<0.001$). Out of the 40 parameters measured, 16 direct anthropometric measurements were statistically significant ($p<0.05$) and were as follows: (1) The cranial measurements in the experimental groups were smaller in the maximum skull height and upper anterior facial height and longer in the lower anterior facial height and the total anterior facial height. (2) The maxillary measurements of U8 bimolar distance were the widest in Group III and the narrowest in the control. (3) The mandibular measurements of total mandibular length I~III and the corpus length were longer in the experimental groups with the longest in Group III; in ramus height I~IV, the experimental groups were shorter than the control and Group I had the longest ramus height of all; the

mandibular plane angles were flatter in the experimental groups and Group III had the smallest angle of all; in the bicoronoidal width and the bigonial width, the narrowest was in Group III.

The results shown that, following paralysis and atrophy of the masticatory muscles, a short upper anterior facial height with a lengthy lower anterior facial height would be observed. The mandibular length and the ramus height would be longer than normal and the distance between the right and left coronoid processes and the gonial angles would be shorter in width. This is typical of a facial profile that favors a vertical growth rotation and a formulation of dolichofacial pattern. It is demonstrated that atrophy of masticatory muscles would alter craniofacial growth and development.