Supplementary Online Content

Shinn JR, Nwabueze NN, Du L, et al. Treatment patterns and outcomes in botulinum therapy for patients with facial synkinesis. *JAMA Facial Plast Surg*. Published online January 31, 2019. doi:10.1001/jamafacial.2018.1962

This supplementary material has been provided by the authors to give readers additional information about their work.

eAppendix. Muscle-Specific Considerations

Orbicularis oculi: This muscle complex is commonly affected resulting in visual field impairment and aesthetic disfigurement, whether by hyperkinesis at rest or dynamic synkinesis. Initial therapy begins in the superioris and inferioris laterally, with injections placed just above and below the canthus. Injections are placed in two separate depots at the level of the orbital rim just under the skin in order to avoid unintended deep diffusion. Initial average dose at each injection site is 1.25 U and increases with subsequent treatment as needed. Additional injection sites on the upper and lower eyelids located more medially targeting the palpebral portion of the orbicularis oculi are added over time in refractory cases. In the upper lid, medial injection sites are typically very low doses (i.e. 0.75 U). Care must be taken to inject superficially to avoid blepharoptosis from diffusion to the levator palpebrae muscle and to use small does to avoid overtreatment and resultant lagophthalmos. In the lower eyelid, there is less risk in causing lagophthalmos from over-treatment, and we generally increase dosing up to 1.25 U and add medial injections at this site first with reasonable safety.

Frontalis: The primary goal of ipsilateral frontalis treatment is to soften the hypertonic, adynamic, and excessively high arched brow. Two injection sites in the mid-forehead region can reshape the brow appearance and restore symmetry to the opposite side. Normal side frontalis treatment can also be helpful in a patient with very expressive brows to limit the degree of elevation and notable asymmetry with the adynamic synkinetic side.

Corrugator: Patients can have a conspicuous bulge from a hyperkinetic corrugator that can also ache from constant contraction. This muscle is one of the core group of muscles in the initial treatment paradigm as it has high patient satisfaction with very little risk.

Levator Labii/Nasalis: Treatment at this site can be very helpful to reduce the "snarl" appearance on the affected side, restore symmetry to the nasolabial fold, and alleviate achiness or tenderness within the nasolabial fold from constant contraction. Previously, the injection site was primarily within the levator labii superioris (junction of the horizontal level of the alar groove and vertical level of the medial limbus). However, even our smallest dose of 0.75 U resulted in an unacceptably high rate of patient-reported lip droop. In recent years, including all patients in this study, the injection site is at the junction between the nasalis and levator labii superioris alaeque nasi – directly at the nasofacial junction – with no reported complications of lip droop and excellent resolution of the undesired "snarl" appearance.

Zygomaticus: This muscle is uncommonly treated at our center as maximizing superior commissure and lip excursion is a goal of most patients. Normal side zygomaticus treatment can be quite helpful to minimize the asymmetry in patients with particularly wide smiles, though this option is considered after several treatment sessions.

Buccinator: The buccinators muscle is a previously under-recognized, though important contributor to the frozen oral commissure seen in many patients with synkinesis. It is the only muscle accessed through a transoral injection. Two sites along the dental line are used, one anterior at the modiolus and a second more posterior near the 2nd and 3rd molars. The muscle is located quite superficial, immediately under the mucosa anteriorly, though EMG guidance can be helpful for the slightly deeper posterior placement. On initial treatment, EMG also provides diagnostic guidance to determine if there is significant hyperkinetic or synkinetic activity relative to the unaffected muscle. We favor a larger does in the posterior site (or beginning only with the posterior site) in order to avoid mild oral incompetence that can occur from an anterior site injection. A typical initial therapy for applicable patients is 2.5 U posteriorly and 1.25 U anteriorly, then adjusted with time to steady state.

Risorius: Similar to the buccinator muscle, though much smaller in mass, the risorius can contribute to a frozen adynamic oral commissure in the setting of hyperkinesis. The injection site is just lateral to the nasolabial fold at the horizontal level of the commissure.

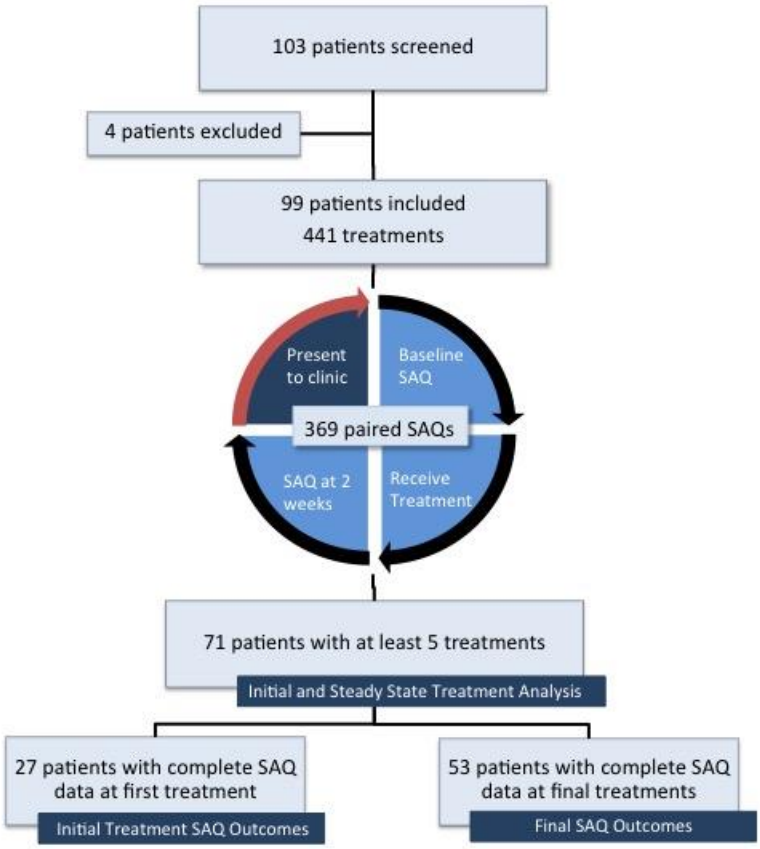
Mentalis: Part of the core group of muscles commonly treated at initial therapy, symptoms associated with mentalis synkinesis are the unfavorable dimpling of the chin and an annoying spasm or twitching sensation. Treatment of this muscle has essentially no risk for functional impairment or disfigurement. A more medial placement of a single injection site allows for less asymmetry across the chin.

Depressor Anguli Oris (DAO): One of the primary depressors of the commissure, treatment of this muscle can be quite effective in counteracting the downward pull that prevents superior commissure excursion with a voluntary smile. The best candidates are those with a sigmoid shaped lip contour at rest, indicative of hyperkinetic DOA activity pulling the affected side commissure down at baseline. To avoid oral competence or speech articulation difficulties, we inject at the lower portion of the DAO just medial to the marionette line and 5-10 mm above the inferior border of the mandible. This area where the DOA and platysma overlap is often one of the most prominent sites of hyperkinesis on EMG testing.

Depressor Labii Inferioris (DLI): Treatment of this smaller lip depressor muscle is relatively new at our center with current on-going investigation for "smile sculpting". We have mixed success with treatment on the affected side with most patients reporting undesirable speech and lip control issues even with small BT doses. However, there are promising signs that treatment of the normal side lower lip can be quite helpful in balancing the appearance of the lower lip during smiling. Those patients who demonstrate a high riding lower lip with lip biting on the affected side and a notable downward swoop on the normal side are the ideal candidates for this treatment. The combination of DAO treatment on the affected side and DLI on the normal side can be quite helpful in this subset of patients with synkinesis/hyperkinesis.

Platysma: One of the core group of muscles commonly treated at initial therapy, the platysma is one of the depressors of the lip and commissure. Comprehensive treatment using four separate injection sites is effective at softening the downward pull of the mouth, thus allowing any diminished but desired superior commissure and lip excursion to be unmasked. Undesirable hyperkinetic bands and neck tightness can also be addressed with platysmal injection. There is minimal risk to comprehensive treatment of this muscle with several valuable benefits, so treatment at initial therapy is quite common.

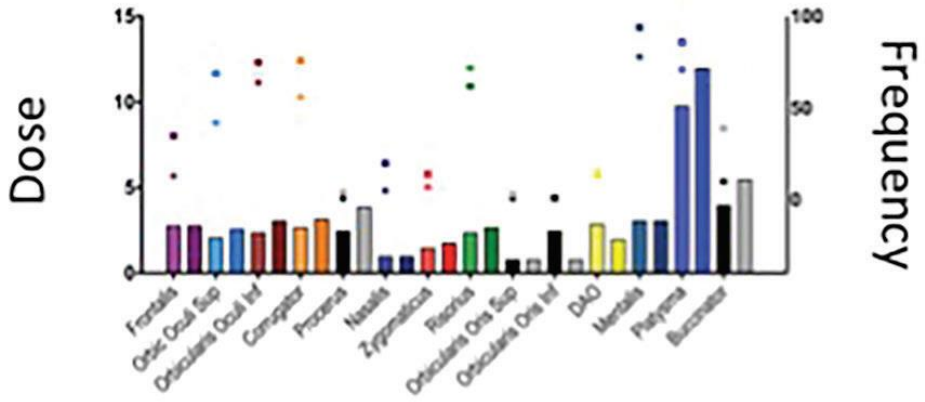
eFigure 1. Study Design



Ninety-nine patients treated with onabotulinum toxinA for facial synkinesis (441 treatment sessions) were included in analysis. Three hundred and sixty nine paired SAQs (pre- and post-botulinum treatment) were available for review. Patients with at least five therapy sessions (n=71) were included in steady state analysis with initial and final dosing and muscle targeting data. Of these, 53 patients completed pre- and post-treatment SAQ surveys. Due to the relatively new (January 2016) incorporation of SAQ data, only 27 patients began their treatment after this time. Analysis of initial SAQ outcomes was limited to these patients.

eFigure 2. Treatment Patterns and Dose and Frequency of Treatment

Treatment Patterns				
	Initial Injection		Steady State	
	Percent	Dose	Percent	Dose
Frontalis	13	2.8	35	2.8
Orbic Oculi Sup	42	2.1	69	2.6
Orbic Oculi Infer	64	2.4	75	3.1
Corrugator	56	2.7	76	3.2
Procerus	1	2.5	4	3.9
Nasalis	5	1.0	20	1.0
Zygomaticus	7	1.5	14	1.8
Risorius	72	2.4	62	2.7
Orbic Oris Sup	1	0.8	3	0.8
Orbic Oris Inf	1	2.5	1	0.8
DAO	14	2.9	14	2.0
Mentalis	78	3.2	94	3.1
Platysma	71	9.8	86	12.0
Buccinator	10	4.0	39	5.5
Total Dose				
Upper Face Dose		5.2		8.1
Midface Dose		2.8		4.5
Lower Face Dose		3.3		3.3
Neck/Platysma Dose		9.8		12.0
Average Total Dose		16.6		23.0



Mean dose for initial injection and steady-state injection. In the graph, the left y-axis (bars) represents mean dose of initial and steady-state treatments; right y-axis

(filled circles), the percentage a muscle is treated for each therapy session. Each muscle is represented by a specific color. Sup represents superioris; inf or infer, inferioris; DAO, depressor anguli oris.

eTable 1. Wilcoxon Signed Rank Test Results for Individual Survey Responses

Question	Wilcoxon Signed Rank				
	<0, %	0, %	>0, %	Median Difference (95% CI)[a]	*P* Value
1: When I smile, my eye closes	48.2	39.1	12.7	−1.0 (−1.0 to −1.0)	<.001
2: When I speak, my eye closes	37	51.4	11.6	−1.0 (−1.0 to −0.5)	<.001
3: When I whistle or pucker my lips, my eye closes	41.7	40.9	17.4	−1.0 (−1.0 to −0.5)	<.001
4: When I smile, my neck tightens	48.9	40.2	10.9	−1.5 (−1.5 to −1.0)	<.001
5: When I close my eyes, my face gets tight	51.8	35.9	12.3	−1.0 (−1.5 to −1.0)	<.001
6: When I close my eyes, the corner of my mouth moves	46	40.6	13.4	−1.0 (−1.5 to −1.0)	<.001
7: When I close my eyes, my neck tightens	47.5	41.3	11.2	−1.0 (−1.5 to −1.0)	<.001
8: When I eat, my eye waters	31.5	59.4	9.1	−1.0 (−1.0 to −1.0)	<.001
9: When I move my face, my chin develops a dimple	52.9	39.5	7.6	−1.5 (−2.0 to −1.5)	<.001

[a]Median of difference from original score (postscore minus prescore).

eTable 2. Linear Regression of Synkinesis Assessment Questionnaire Outcomes

Question	Linear Regression	
	Mean Difference (95% CI)[a]	*P* Value
1: When I smile, my eye closes	−0.6 (−0.7 to −0.4)	<.001
2: When I speak, my eye closes	−0.4 (−0.5 to −0.2)	<.001
3: When I whistle or pucker my lips, my eye closes	−0.4 (−0.6 to −0.2)	<.001
4: When I smile, my neck tightens	−0.7 (−0.9 to −0.5)	<.001
5: When I close my eyes, my face gets tight	−0.6 (−0.8 to −0.5)	<.001
6: When I close my eyes, the corner of my mouth moves	−0.6 (−0.8 to −0.4)	<.001
7: When I close my eyes, my neck tightens	−0.6 (−0.8 to −0.4)	<.001
8: When I eat, my eye waters	−0.3 (−0.4 to −0.2)	<.001
9: When I move my face, my chin develops a dimple	−0.9 (−1.1 to −0.7)	<.001

[a]Estimated mean difference (postscore minus prescore) of original score.