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Approaches to the management of synkinesis: a scoping review

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Abstract:
Post-paralysis facial synkinesis can develop in any facial palsy and is associated with significant functional and psychosocial consequences for affected patients. While the prevention of synkinesis especially after Bell's Palsy has been well examined, much less evidence exists regarding the management of patients with already established synkinesis. Therefore, the purpose of this review is to summarize the available literature and to provide an overview of the current therapeutic options for facial palsy patients with established synkinesis. A systematic literature review was undertaken, following the PRISMA 2020 guidelines. MEDLINE via PubMed and Cochrane Library were searched using the following strategy: ((facial palsy) OR (facial paralysis) OR (facial paresis)) AND (synkinesis) AND ((management) OR (guidelines) OR (treatment)). The initial search yielded 201 articles of which 36 original papers and 2 meta-analyses met the criteria for inclusion. Overall, the included articles provided original outcome data on 1408 patients. Articles were divided into the following treatment categories: chemodenervation (12 studies, 536 patients), facial therapy (5 studies, 206 patients), surgical (10 studies, 389 patients) and combination therapy (9 studies, 278 patients). Results are analyzed and discussed accordingly. Significant heterogeneity in study population and design, lack of control groups, differences in postoperative follow-up as well as the use of a variety of subjective and objective assessment tools to quantify synkinesis prevent direct comparison between treatment modalities. To date there is no consensus on how post-paralysis facial synkinesis is best treated. The lack of comparative studies and standardized outcome reporting hinder our understanding of this complex condition. Until higher-quality scientific evidence is available, it remains a challenge best approached in an interdisciplinary team. An individualized multimodal therapeutic concept consisting of facial therapy, chemodenervation and surgery should be tailored to meet the specific needs of the patient.

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Approaches to the management of synkinesis: a scoping review

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Conflict of Interest:

None of the authors have any conflicts of interest to disclose.

Abstract and Keywords

Post-paralysis facial synkinesis can develop in any facial palsy and is associated with significant functional and psychosocial consequences for affected patients. While the prevention of synkinesis especially after Bell's Palsy has been well examined, much less evidence exists regarding the management of patients with already established synkinesis. Therefore, the purpose of this review is to summarize the available literature and to provide an overview of the current therapeutic options for facial palsy patients with established synkinesis. A systematic literature review was undertaken, following the PRISMA 2020 guidelines. MEDLINE via PubMed and Cochrane Library were searched using the following strategy: ((facial palsy) OR (facial paralysis) OR (facial paresis)) AND (synkinesis) AND ((management) OR (guidelines) OR (treatment)). The initial search yielded 201 articles of which 36 original papers and 2 meta-analyses met the criteria for inclusion. Overall, the included articles provided original outcome data on 1408 patients. Articles were divided into the following treatment categories: chemodenervation (12 studies, 536 patients), facial therapy (5 studies, 206 patients), surgical (10 studies, 389 patients) and combination therapy (9 studies, 278 patients). Results are analyzed and discussed accordingly. Significant heterogeneity in study population and design, lack of control groups, differences in postoperative follow-up as well as the use of a variety of subjective and objective assessment tools to quantify synkinesis prevent direct comparison between treatment modalities. To date there is no consensus on how post-paralysis facial synkinesis is best treated. The lack of comparative studies and standardized outcome reporting hinder our understanding of this complex condition. Until higher-quality scientific evidence is available, it remains a challenge best approached in an interdisciplinary team. An individualized multimodal therapeutic concept consisting of facial therapy, chemodenervation and surgery should be tailored to meet the specific needs of the patient.

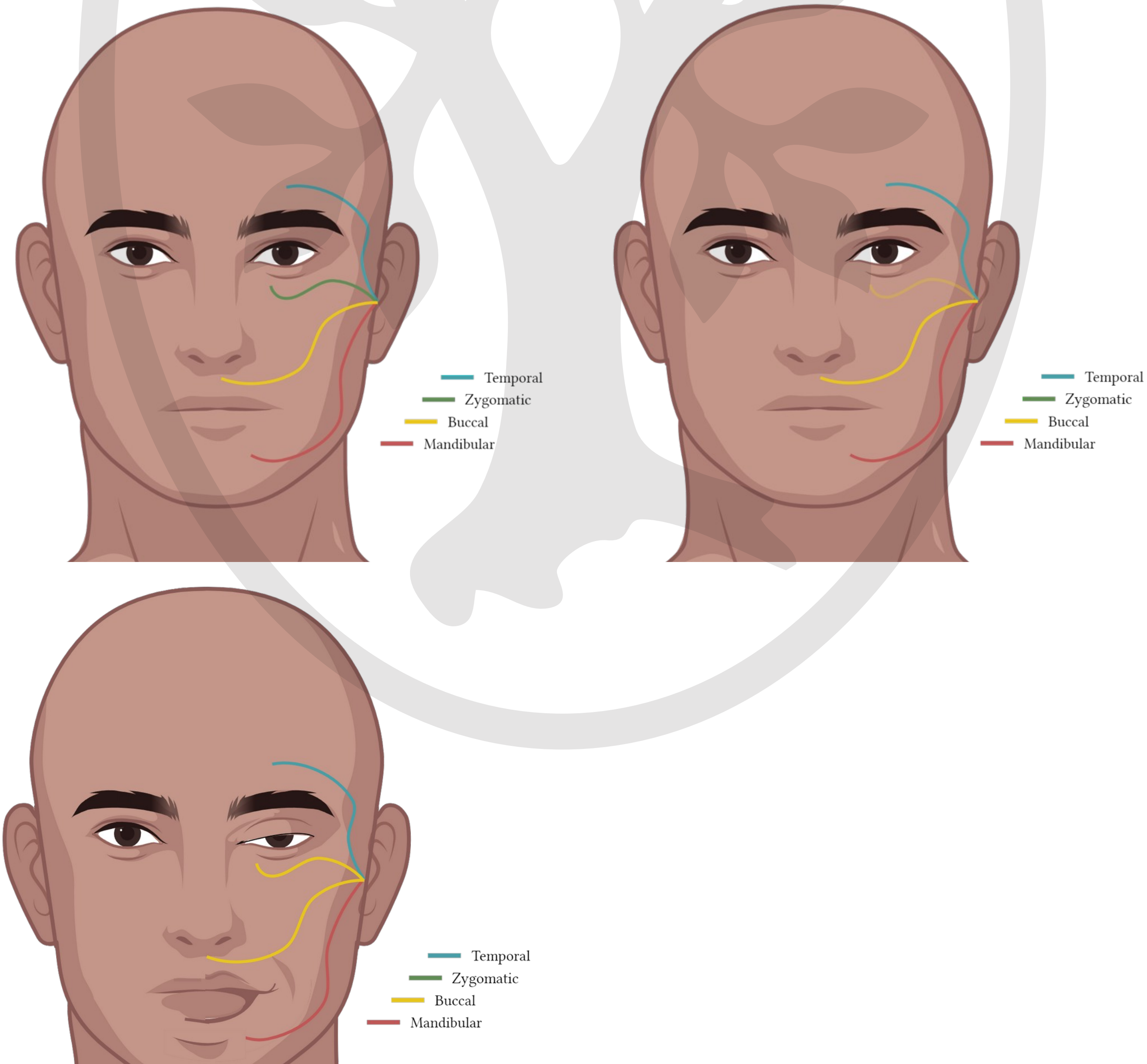
Keywords: facial palsy, synkinesis, systematic review, Bell's Palsy

Introduction

Facial synkinesis, defined as the presence of unintentional muscle motion produced during intentional movement in another area, is often described as one of the most frustrating sequelae of facial palsy.[1] Post-paralysis facial synkinesis (PPFS) can develop after any type of physical trauma or condition associated with damage to or partial recovery of the facial nerve. The proposed mechanism behind synkinesis is the aberrant regeneration of the facial nerve when, for example, fascicles from the buccal branch erroneously regenerate along the zygomatic branch, and the patient develops involuntary closure of their eye when they smile[2] (Figure 1). Alternative explanations focus on peripheral ephaptic transmissions between neighboring regenerating axons or synaptic reorganization and hyperexcitability of the facial nerve nucleus.[3] However, newer findings such as reduced intrinsic connectivity in sub-networks of the central nervous system highlight that the full extent of the pathophysiology may not yet be completely understood.[4] Synkinetic movements have an undeniable aesthetic impact and can, in severe cases, be quite painful. Overall, PPFS can be socially debilitating, limit interpersonal interactions and has a significant impact on the quality of life of affected patients.[5,6]

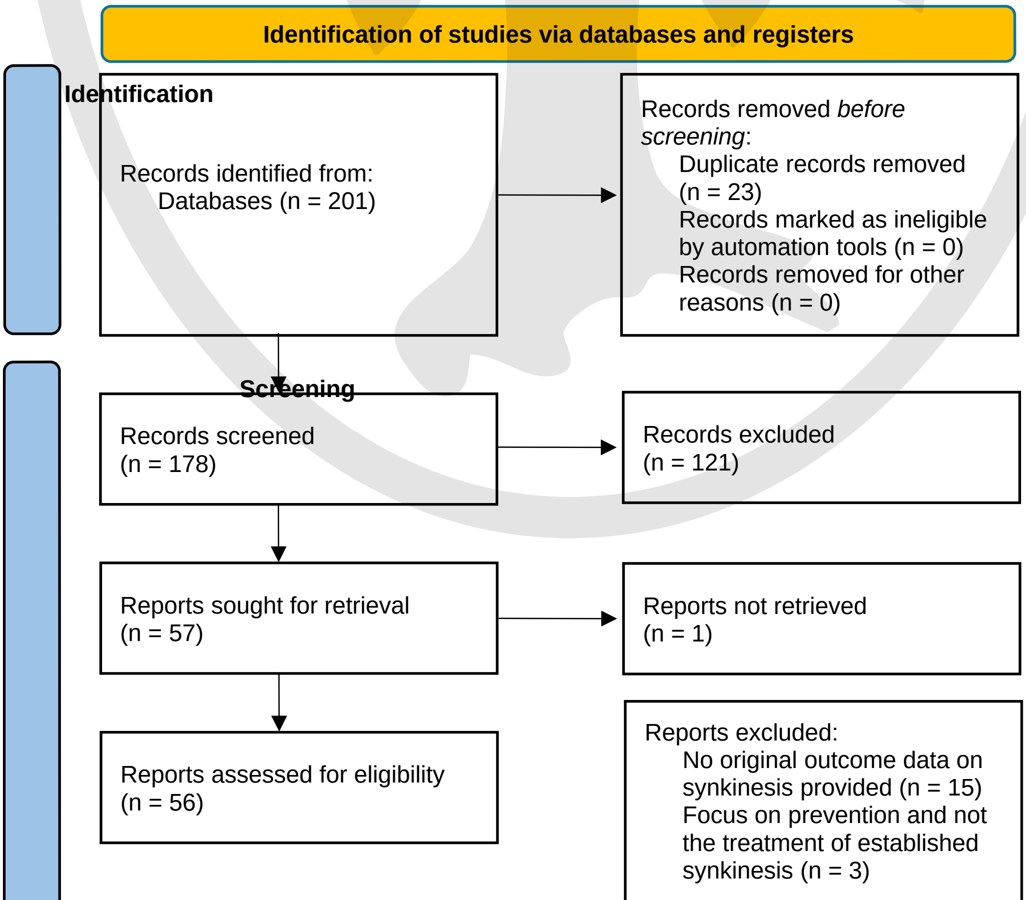
Bell's Palsy is an idiopathic, acute-onset (typically less than 72 hours), unilateral facial nerve weakness. It is the most common cause of peripheral facial weakness, and accounts for 60-75% of all cases of unilateral facial paralysis. Clinically, it presents as a patient who is unable to properly close an eye, retract the angle of the mouth, and/or raise an eyebrow/wrinkle the forehead.[7] It can also have accompanying retro-/auricular pain, changes in tearing, hyperacusis, changes in sensation and taste, and/or other pain.[7–10] The etiology of Bell's Palsy remains unclear, but the belief is that most cases are secondary to reactivation of latent herpes simplex virus (HSV) infection.[7,11] Although the return to normal facial nerve function can range from 71-86%,[8,10] it is heavily dependent upon the initial severity of the paralysis (94% recovery in partial; 61% in complete) and interval between onset and the beginning of remission.[10] Combined with an incidence of 20-43 cases per 100,000 person-years in the United States, Bell's Palsy causes a great deal of morbidity.[8,9,11–13]

Following Bell's Palsy, synkinesis can develop in up to 21.3% of patients, with 6.6% being moderate-to-severe cases.[14] However, in patients that develop long-term paralysis, some degree of synkinesis is expected in almost all patients.[15] Interestingly, data suggests that PPFS affects significantly more females than male patients and appears significantly more often in older patients.[15] While the roles of corticosteroids[16], antivirals[17], early surgical intervention[18] and physical therapy[19] in the prevention of synkinesis after developing Bell's Palsy have been comparably well examined, much less high-level evidence exists regarding the management of patients with already established PPFS.[20] Therefore, the purpose of this review was to summarize the available literature and to provide an overview of the current therapeutic options and level of evidence in the treatment of facial palsy patients with established synkinesis.



Methods

A systematic literature review was undertaken, following the Preferred Reporting Items of Systematic Reviews and Meta-analyses (PRISMA 2020) guidelines.[21] MEDLINE via PubMed (National Library of Medicine, Bethesda, Maryland) and Cochrane Library were searched on November 13, 2023. The following search strategy was used: ((facial palsy) OR (facial paralysis) OR (facial paresis)) AND (synkinesis) AND ((management) OR (guidelines) OR (treatment)). Only publications written in English and with full text availability were considered. No limitations for inclusion were set regarding the time period. After discarding duplicates, all titles and abstracts of studies located by the search were screened for relevance by two study members, where there was a conflict, a senior author decided. Studies of potential importance were then reviewed in full text. Only studies providing original outcome data on the treatment of established PPFS were included. Reviews, case reports, animal studies and cadaveric studies were excluded. Due to the nature of this study, formal ethics application and approval by the institutional review board were not required.



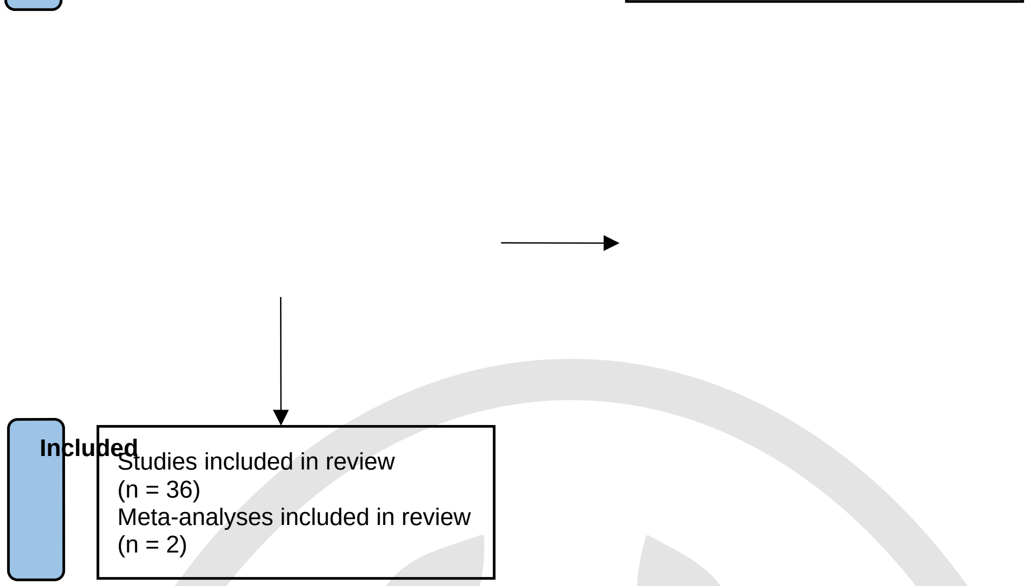


Figure 2: flow diagram of eligible studies. After screening and applying exclusion criteria, 38 studies from the initial 201 items were included in this systematic review.

Results

The initial search yielded 201 articles of which 38 fulfilled the study's inclusion criteria (Figure 2). Table 1 shows the details of the studies included, as well as their characteristics.

Overall, the 36 original articles reported data on 1408 patients. Articles were divided into the following treatment categories: 1) chemodenervation (12 studies, 536 patients, 45 patients/study), 2) facial therapy (5 studies, 206 patients, 41 patients/study), 3) surgical (10 studies, 389 patients, 39 patients/study) and 4) combination therapy (9 studies, 278 patients, 31 patients/study). Only one of these studies was specifically concerned with PPFS in the pediatric population.

Of the two meta-analyses, one examined the effect of chemodenervation (106 patients) and one the success of facial therapy (179 patients).

The Sunnybrook Facial Grading System (FGS) was the most commonly used clinical assessment tool to quantify the severity of synkinesis, reported in 20/38 (53%) of studies. Patient Reported Outcome Measures (PROMs) were assessed in 11/38 (29%) of studies, most often using the Synkinesis Assessment Questionnaire (SAQ). Other modalities, including expert review or clinical judgement (3/38, 8%), were utilized in 14/38 (37%) of papers (Table 1).

Discussion:

To date there is no consensus on how PPFS is best treated. Although certain concepts are common, the exact management varies greatly between centers and often relies on expert opinion.[20] While there is ample literature on the treatment of facial palsy, most studies focus on facial reanimation. Synkinesis is mostly mentioned as an adverse secondary outcome and its prevention investigated. Comparably few articles examine the treatment of patients with already established synkinesis and hence generate outcome data specific to this population. Furthermore, no clinical tool for synkinesis assessment and therefore outcome reporting is universally accepted. Most frequently, the Sunnybrook Facial Grading System is used as the objective measurement because it allows for a separate quantification of the degree of synkinesis. However, it was found that this assessment of synkinesis is not consistent between examiners.[22] Subjective outcome measures in the form of PROMs are evaluated increasingly more often. Yet, the most common tool, the Synkinesis Assessment Questionnaire (SAQ)[23] was still only used in 21% of studies.

Another key challenge is the clinical heterogeneity of patients suffering from PPFS. There is a high level of variation in the number and extent of involved muscles as well as the strength of synkinesis. Furthermore, in most cases synkinesis does not exist as a standalone symptom but as part of a more complex affliction involving varying degrees of paresis, hyperkinesia, stiffness and spasms of the facial musculature, which also have to be addressed. Therefore, attempts have been made to classify synkinesis based on the preservation of smile and degree of synkinesis and to target the therapy accordingly.[24]

However, no such classification has been widely adapted. For the purpose of this review, we have separated articles based on intervention as described below.

<u>Management Strategies – Chemodenervation:</u>

Most of the included studies (58%) were focused on treating synkinesis with botulinum toxin A (BTX-A) injections. 13 articles examined BTX-A alone and 9 in combination with surgery or facial therapy. BTX-A injections have been used to treat facial synkinesis for over 30 years.[25] BTX-A, the most potent of the neurotoxins, produces paralysis by blocking presynaptic release of the neurotransmitter (acetylcholine) at the neuromuscular junction, with reversible chemical denervation of the muscle fiber, thereby inducing partial paralysis and atrophy. Through targeting the synkinetic muscles on the affected side, as well as hyperactive ones on the healthy side, the goal is to control synkinesis and restore facial symmetry.

Although there are many reports examining the effect of BTX-A treatment on PPFS, the studies are typically single cohorts comparing synkinetic complaints pre- and post-injection, with no separate matched control group, making it difficult to draw any definitive conclusions. Based on improved objective synkinesis measurements, these articles report that BTX-A treatment is effective in reducing facial synkinesis and improving facial symmetry both at rest and during voluntary movements.[26,27] Furthermore, improvement in subjective symptomatic burden and quality of life[28,29] have been documented, an effect that persists with repeated injections.[30]

Lately, focus has pivoted to further improving treatment success by not only targeting the classic mimetic muscles, but also others that are innervated by the facial nerve. Muscle tightness in the neck and banding may be addressed by targeting the platsyma[31], residual facial tightness with buccinator[32,33] injections and jaw discomfort by infiltrating the posterior belly of the digastric muscle[34]. In properly selected cases, these individualized adaptations to the standard regimen provided improved synkinesis scores and subjective symptom control.

While BTX-A is the most widely used neurotoxin to treat PPFS, other derivatives are available, and usage appears to depend mainly on personal preference and regional supply. Limited data exists on their respective efficacies: one randomized controlled trial in 28 patients compared three types of BTX-A. Abobotulinumtoxin A (Dysport®), onabotulinumtoxin A (Botox®) and incobotulinumtoxin A (Xeomin®) all showed similar effects during the first four weeks after injection. After that, incobotulinumtoxin A (Xeomin®) had significantly less effect on the SAQ compared with onabotulinumtoxin A (Botox®), due to a suspected shorter duration of action. The authors conclude that shorter intervals between treatments or larger doses may be required when using incobotulinumtoxin A (Xeomin®) for facial synkinesis.[35]

Whilst rare, adverse events associated with BTX-A treatment mainly depend on location and dosage as well as technique of infiltration. They include, but are not limited to, hematomas, headache, stiff face, difficulty speaking, ptosis of both lip and eyes, dry eyes, diplopia and epiphora.[25,36] Unfortunately, studies seldomly report and elaborate on these adverse events and those that do present heterogeneous data that is incomplete, making it impossible to reliably estimate their incidence in PPFS patients treated with BTX-A in comparison to the general population.[36]

A recent meta-analysis tried to objectify the benefit of BTX-A in patients with synkinesis. Of the 4299 articles screened only 3 studies (covering 106 patients) met the criteria for inclusion in the quantitative analysis. The evaluation showed a significant effect of BTX-A treatment on the SAQ scores, and therefore patient reported outcomes, two weeks after injection. Due to inconsistencies in reporting, follow-up and outcome measurements, no other analysis was possible.[36]

Management Strategies – Facial therapy:

Thirteen included studies evaluated the efficacy of physical therapy, six as their main focus and seven in combinations with other treatment options.

Historically, various techniques have been used for facial palsy rehabilitation. Early efforts focused on global activation and animation of the paralyzed face were later adapted to minimize synkinetic motion.[37] One of these techniques, neuromuscular retraining therapy (NMRT), provides patients with an individualized training program incorporating patient education, facial exercises, massages and typically some sort of feedback (surface electromyography (EMG), biofeedback, mirroring). A proof-of-concept study analyzing electromyographic feedback pre and post mirror therapy with a computerized treatment system (Specular Face biofeedback) showed that visual mirror feedback therapy changes the pattern of synkinesis and the facial muscle function as well as improves involuntary discriminatory capacity of the muscle activity in patients with PPFS.[38]

Clinical findings suggest that neuromuscular retraining not only leads to significant improvements in facial symmetry but also allows patients to overcome synkinesis.[39] Although great differences in the exact regimen exist between centers, adaptations of NMRT are nowadays in use worldwide, often in combination with BTX-A injections. This combination has been shown to improve facial movements and synkinesis control in patients with chronic PPFS regardless of the degrees of facial synkinesis and asymmetry before treatment[40], an effect that seems to last even long after the effect of BTX-A has faded.[41,42] Long-term facial therapy, supported by repeated BTX-A injections have therefore become standard. However, evidence suggests that a certain plateau of improvement is reached after 4 sessions of this combined therapy.[43]

Yet, the question as to what extent BTX-A contributes to the success of combination therapy remains controversial. One study separated 34 participants into two groups: one group (treatment) received a single BTX-A dose followed by four months of rehabilitation with muscle stretching and EMG-biofeedback sessions three times weekly as well as mirror biofeedback at home, the second group (placebo) received a single saline injection followed by the same rehab protocol. While both groups showed significant improvements in facial symmetry, voluntary movements as well as synkinesis, multiple analysis modalities failed to demonstrate any significant difference between the two groups.[44] Conversely, Monini et al. demonstrated that BTX-A pretreatment resulted in significantly better outcomes.[45] Collagen 'filler' injections have also been used to augment the effect of physical therapy, however no significant improvement was demonstrated.[46]

Mime therapy has also gained increased popularity in recent years. This approach combines elements of auto-massage, relaxation exercises, inhibition of synkinesis, coordination exercises and emotional expression exercises. One retrospective study of 155 patients undergoing between 3 and 5 months of mime therapy demonstrated significant improvement in facial impairment, disability, and quality of life. Interestingly, after therapy the number of patients with synkinesis increased, however, the overall average of synkinesis-severity decreased significantly.[47] This was followed up with a randomized controlled trial involving 48 patients which compared mime therapy with patient without any treatment. The results confirmed that patients undergoing three months of mime therapy not only increased their facial symmetry at rest and with voluntary movement, but also significantly decreased their synkinesis score.[48]

Despite these findings, high-quality evidence regarding the overall efficacy of facial therapy in patients with established PPFS remains sparse. In 2023, a meta-analysis of randomized controlled trials showed that that physical therapy reduces non-recovery in patients with acute peripheral facial palsy. However, it also concluded that the efficacy of facial therapy in reducing sequelae such as synkinesis remains uncertain.[49] Fujiwara et al. noted that while physical rehabilitation, including mirror biofeedback and massage, prevented worsening of synkinesis in female and younger patients, synkinesis scores still deteriorated in older patients and especially in males.[50]

Management Strategies – Surgery:

Largely due to the success of facial therapy and chemodenervation, surgery has traditionally only played a secondary role in treatment of synkinesis, with some questioning its role at all.[37] Although a multitude of procedures have been described, two main surgical approaches exist: selective neurectomy and myectomy. Our search yielded 10 studies reporting surgery as the main treatment for synkinesis and two reporting surgical outcomes as part of a multimodal approach in combination with BTX-A and biofeedback. All included surgical papers described retrospective cohorts and often presented a new technique pioneered at a particular center or even by a single surgeon.

In 1991, Guerrissi presented his experience resecting the zygomaticus major for treatment of oculo-oral synkinesis.[51] The study proposed that selective myectomy yields superior outcomes over neurectomy due to the complex and variable anastomoses between terminal nerve branches of the facial nerve. Additionally, the study concluded that the upper part of the buccinator and zygomaticus minor are sufficient to compensate for the loss of zygomaticus major, hence the ability to elevate the corner of the mouth was unaffected following myectomy.[51]

Similarly, Yoshioka suggested partial orbicularis neuromyectomy.[52] The study describes resecting a peripheral 1cm wide strip of the lower orbicularis oculi muscle to address synkinetic eye closure. The multitude of terminal facial nerve branches in this region are resected together with the muscle, resulting in a definitive neurectomy of the branches of the facial nerve that innervate the lower orbicularis oculi muscle. However, the disadvantage of this procedure is that it results in complete paralysis of the lower orbicularis muscle for several months. Furthermore, slight recurrence of synkinesis has been observed 6 months after the operation.[52] Alternative procedures, such as endoscopic brow lifting, have also been explored as a treatment option for periocular synkinesis and are reported to control synkinesis symptoms more effectively than BTX-A.[53]

For patients with moderate-to-severe synkinesis, especially when combined with an unacceptable smile, a more radical approach with combined myectomy and neurectomy followed by free functioning muscle transplantation has been proposed.[54] Following extensive neuromyectomies of the synkinetic muscles and triggering facial nerve branches in the cheek, nose, and neck regions, a free functioning gracilis flap is used for hemifacial reanimation. Although reporting good outcomes for synkinesis control and smile reanimation, revision surgery for secondary deformity was necessary in 53%.[54]

In similar cases, other studies implement a single-stage masseteric-zygomatic nerve transfer. The procedure aims to separate the innervation of the eyelids from that of the zygomatic muscular complex which in turn becomes reinnervated by the masseteric nerve. This technique corrects the synkinesis and simultaneously enhances muscle tone at rest and smile excursion.[55] A cross-facial nerve graft (CFNG) can be added end-to-side to the zygomatic nerve to enhance synchrony between the healthy and pathological side of the face and to restore spontaneity.[56]

Alternatively, a two-stage procedure with CFNGs has also been used to directly innervate the synkinetic muscle groups via their corresponding nerves from the healthy contralateral side.[57,58]

Recently, the most common surgical approach to PPFS patients with some degree of remaining active zygomatic muscle function has been selective neurectomy. Although various techniques have been described, a standard rhytidectomy approach is usually chosen to access the distal branches of the facial nerve. Once identified, the individual branches are isolated and selectively transected to separate smile and eye closure (Figure 3). It also aims at reducing the activity of antagonistic muscles while preserving the neural input to key muscles, therefore effectively strengthening the smile mechanism.[59] Larger cohorts undergoing such procedures are now starting to appear. In 2023, Park et al. published their experience with selective neurectomy based on a retrospective analysis of 122 cases. The findings demonstrate that selective neurectomy provides satisfactory outcome regarding facial tightness as well as narrowing of the eyelid aperture and improves the vertical inclination of the corner of the mouth, however, the improvement of the horizontal angles remain suboptimal.[60]

Currently, there is only limited reporting regarding the longevity of these surgical interventions. Van Veen et al. demonstrated that, although patients undergoing selective neurectomy for periocular synkinesis usually experience a symptom free interval after the surgery, most required renewed BTX-A treatment later on; At 3.5 years post-surgery follow-up, nine out of 10 patients required treatment with BTX-A. Additionally, the study noted that patients maintained a larger palpebral fissure width long-term, and that previously refractory patients now demonstrated good response to BTX-A.[61]

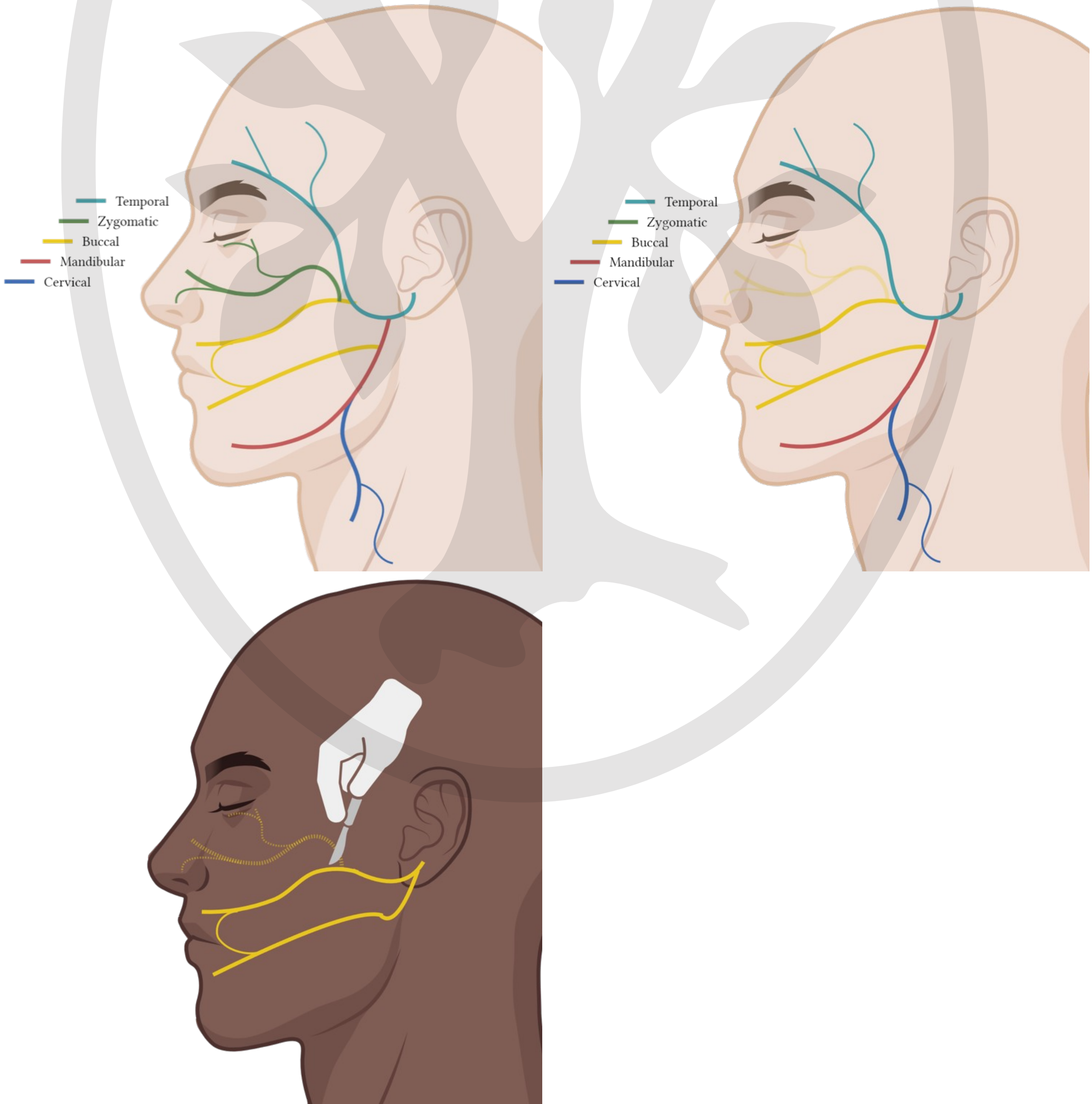


Figure 3: A) normal anatomy. B) aberrant regeneration of fascicles from the buccal branch along the zygomatic branch after facial nerve injury resulting in oculo-oral synkinesis. C) selective neurectomy: individual branches are isolated and selectively transected to separate smile and eye closure.

Limitations, Challenges and Prospects

As discussed initially, there are many limitations encountered in this study. The majority of included studies were either observational cohorts (79%) or of a retrospective design (45%). Most of these studies were rated to be of poor quality according to the Newcastle-Ottawa Scale for Cohort Studies.[62] Only six papers (16%) represented prospective, randomized controlled trials, yet with an average number of 32.7 participants (range 20-48) they were small, leaving on average only 16.3 participants per intervention group and associated with a significant risk of bias.

In general, most studies only involved a very limited number of patients, 47% less than 30. While cohorts with more significant numbers of participants have been published in recent years, the issue remains that many of these publications report on a centers daily practice rather than investigate a specific scientific question. The significant heterogeneity in study population and design, lack of control groups, differences in postoperative follow-up as well as the use of a variety of subjective and objective assessment tools to quantify synkinesis make comparison between studies difficult and render quantitative meta-analysis almost impossible. The fact that 54% of all in included studies were published in the last 5 years (46% in the last 3 years) illustrates that these issues are still very much ongoing.

The available clinical cohorts show that most patients with PPFS are treated in a multimodal approach. While highlighting the success of such a combination of facial therapy, chemodenervation and surgery, this also makes it almost impossible to determine to what extent each modality contributed to the final outcome.[57,58] Comparing modalities based on the available single-therapy cohorts is prone to bias as is obvious from the example of BTX-A versus selective neurectomy: Firstly, patients referred for and willing to undergo selective neurectomy tend to represent more severe cases. Secondly, these are usually patients that have exhausted or failed conservative treatments such as BTX-A or facial rehabilitation.[60]

Selective chemodenervation with botulinum toxin and facial therapy remain the cornerstones in the treatment of PPFS. BTX-A offers patients a quick symptomatic improvement, reduction of synkinesis, and overall symmetrization of the face. There are few contraindications and although adverse events occasionally occur, the effect is reversible within 3-4 months.[26] BTX-A has been used since 1984[63], has an established safety profile and is a relatively cost-effective intervention.[64] Specialized facial therapy using forms of neuromuscular retraining or mime therapy paired with a direct feedback-mechanism not only enhance these effects but also achieve stable long-term improvements for the patient. The combination of these two modalities seems to be particularly successful and has led to many theories being postulated. Perhaps the best explanation is that BTX-A injections allow patients to overcome aberrant facial movements and concentrate on neuromuscular relearning of untargeted muscles during the temporary chemodenervation, therefore basically creating a window of opportunity for facial therapy.[41]

Surgical options are being refined and have shown promising results. Nevertheless, a certain unpredictability, significant revision rate and steep learning curve remain.[59] Furthermore, surgical techniques and expertise vary greatly between centers. For now, the use of these techniques primarily seems suitable for patients with severe synkinesis or those who did not adequately respond to conservative measures.

In general, patients with established PPFS should be managed by an interdisciplinary team able to offer all available options, tailored to the specific needs of the individual patient. Such a multimodal approach not only reduces objective synkinesis scores but also patient reported outcome measures. Although even helpful in those with chronically neglected synkinesis, it should be established as soon as possible to achieve the best possible outcome.[65]

Conclusions:

PPFS is associated with significant functional and psychosocial consequences for affected patients. The lack of comparative studies, standardized evaluation tools as well as inconsistencies in outcome reporting hinder our understanding of this complex condition. Until higher-quality scientific evidence is available, it remains a challenge best approached in an interdisciplinary team. An individualized multimodal therapeutic concept consisting of facial therapy, chemodenervation and surgery should be tailored to meet the specific needs of the patient.

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Conflict of interest

none declared

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Author	Year	Treatment	Study design	Prospective / Retros	Number of	Age Focus	Principal Synkinesis Outcome measurement

				pective	**Patie nts**		
Mountain[25]	1992	Chemode nervation	cohort study	Retrosp ective	4	Adults	Expert review of photographs + custom patient reported outcome
Toffola[26]	2010	Chemode nervation	cohort study	Prospect ive	30	Adults	Sunnybrook Facial Grading System
Filipo[29]	2012	Chemode nervation	cohort study	Retrosp ective	41	Adults	Sunnybrook Facial Grading System + Synkinesis Assessment Questionnaire
Dall'Angel o[31]	2014	Chemode nervation	cohort study	Retrosp ective	45	Adults	Sunnybrook Facial Grading System + custom platysma-specific evaluation of presence and severity of synkinesis
Maria[27]	2017	Chemode nervation	cohort study	Retrosp ective	142	Adults	Sunnybrook Facial Grading System
Neville[30]	2017	Chemode nervation	cohort study	Prospect ive	51	Adults	Synkinesis Assessment Questionnaire
Patel[32]	2018	Chemode nervation	cohort study	Prospect ive	23	Adults	Synkinesis Assessment Questionnaire
Andrew[35]	2018	Chemode nervation	randomized control trial	Prospect ive	28	Adults	Synkinesis Assessment Questionnaire
Kanerva[33]	2021	Chemode nervation	cohort study	Retrosp ective	83	Adults	Patient-reported symptoms (custom)
Pescarini[34]	2021	Chemode nervation	cohort study	Prospect ive	33	Adults	Synkinesis Assessment Questionnaire
Krag[66]	2021	Chemode nervation	cohort study	Prospect ive	36	Adults	Emotrics and FaceGram photographic analyses
Díaz-Aristizabal[28]	2023	Chemode nervation	cohort study	Prospect ive	20	Adults	Sunnybrook Facial Grading System + Synkinesis Assessment Questionnaire
Beurskens[48]	2006	Facial therapy	randomized control trial	Prospect ive	48	Adults	Sunnybrook Facial Grading System
Fujiwara[50]	2018	Facial therapy	cohort study	Retrosp ective	37	Adults	Sunnybrook Facial Grading System
Micarelli[46]	2021	Facial therapy	randomized control trial	Prospect ive	40	Adults	Sunnybrook Facial Grading System

Gil-Martínez[38]	2021	Facial therapy	cohort study	Prospective	5	Adults	Electromyographic feedback
Neville[65]	2022	Facial therapy	cohort study	Retrospective	75	Adults	Sunnybrook Facial Grading System
Guerrissi[51]	1991	Surgery	cohort study	Retrospective	6	Adults	Expert judgement
Bran[53]	2014	Surgery	cohort study	Retrospective	9	Adults	Custom adaptation of the Hemifacial spasm questionnaire (HFS-30)
Chuang[24]	2015	Surgery	cohort study	Retrospective	48	Adults	Sunnybrook Facial Grading System
Yoshioka[52]	2015	Surgery	cohort study	Retrospective	11	Adults	Sunnybrook Facial Grading System
Biglioli[56]	2017	Surgery	cohort study	Retrospective	18	Adults	Dichotomous clinical judgement (synkinesis present / not present)
van Veen[61]	2018	Surgery	cohort study	Retrospective	10	Adults	Palpebral fissure width + Mean units of botulinum toxin necessary pre- and postoperatively
Azizzadeh[59]	2019	Surgery	cohort study	Retrospective	63	Adults	eFACE
Gray[55]	2020	Surgery	cohort study	Retrospective	8	Adults	Emotrics software
Chuang[54]	2022	Surgery	cohort study	Retrospective	94	Adults	Sunnybrook Facial Grading System
Park[60]	2023	Surgery	cohort study	Retrospective	122	Adults	Synkinesis Assessment Questionnaire + palpebral fissure width
Monini[45]	2011	Chemodenervation + facial therapy vs. facial therapy alone	randomized control trial	Prospective	20	Adults	Sunnybrook Facial Grading System
Azuma[41]	2012	Chemodenervation + facial	cohort study	Prospective	13	Adults	Palpebral fissure width

		therapy					
Pourmomeny[44]	2015	Chemodenervation + facial therapy vs. facial therapy alone	randomized control trial	Prospective	34	Adults	Sunnybrook Facial Grading System + custom measurements on photographs
Lee[42]	2015	Chemodenervation + facial therapy	cohort study	Prospective	17	Adults	Sunnybrook Facial Grading System
Mandrini[43]	2016	Chemodenervation + facial therapy	cohort study	Retrospective	27	Adults	Sunnybrook Facial Grading System
Pourmomeny[39]	2021	Chemodenervation vs. facial therapy	randomized control trial	Prospective	26	Adults	Sunnybrook Facial Grading System
Jeong[40]	2023	Chemodenervation + facial therapy	cohort study	Prospective	99	Adults	Computer-based numerical scoring system
Terzis[58]	2012	Surgery +/- Chemodenervation and facial therapy	cohort study	Retrospective	11	Children	Sunnybrook Facial Grading System
Terzis[57]	2012	Surgery +/- Chemodenervation and facial therapy	cohort study	Retrospective	31	Adults	Sunnybrook Facial Grading System
de Jongh[36]	2023	Chemode	Meta-	Retrosp	106	Adults	Synkinesis Assessment Questionnaire

		nervation	analysis	ective			
Nakano[49]	2023	Facial therapy	Meta- analysis	Retrosp ective	179	Adults	Sunnybrook Facial Grading System

Table 1: characteristics of the included studies