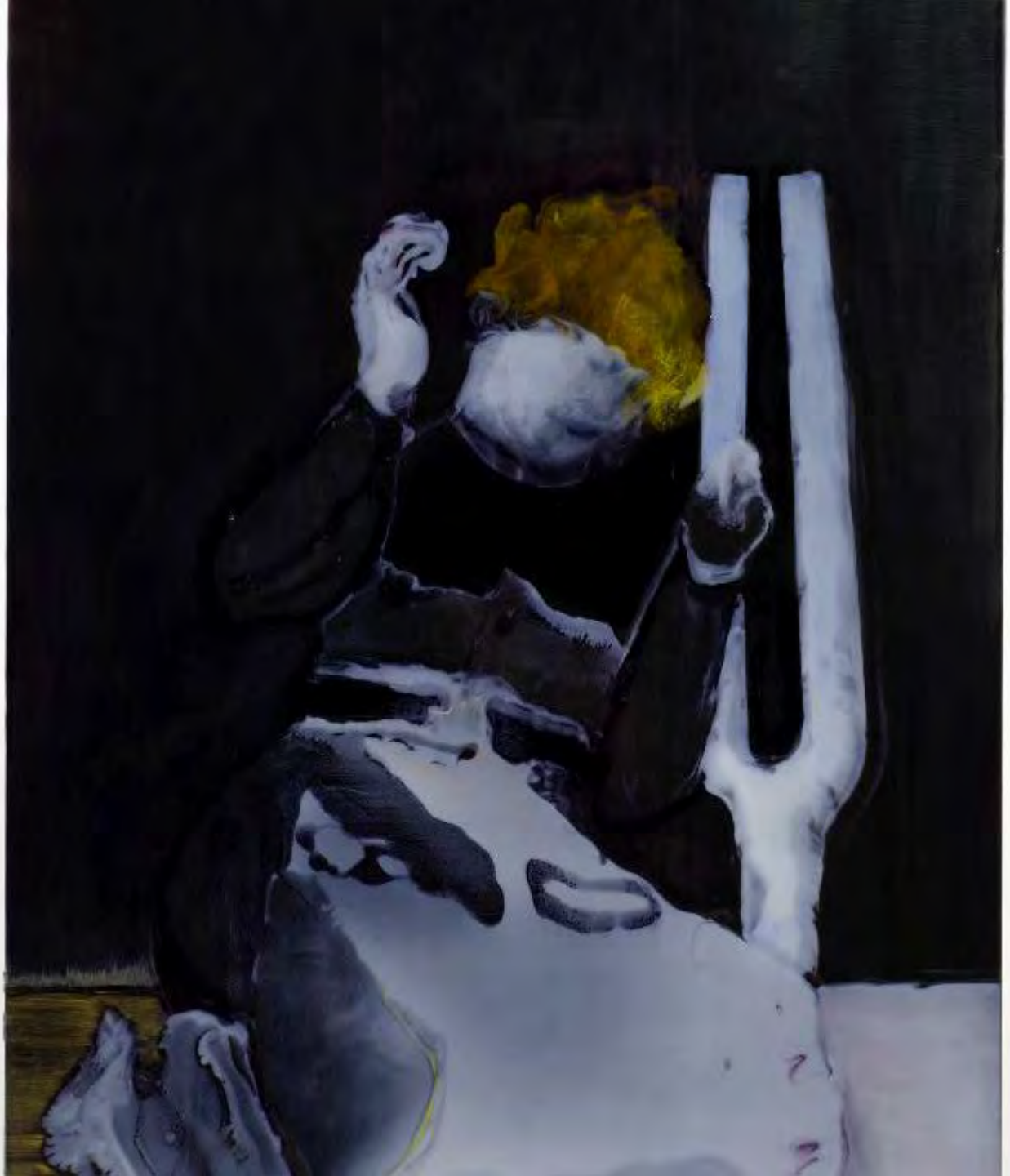
Treatment of Depression with Botulinum Toxin A: Using Facial Feedback As A Therapeutic Tool

Eric Finzi,MD,PhD

Chevy Chase Cosmetic Center



Role of Facial Expression in Emotion

- 1872 Charles Darwin – “ The free expression of an emotion intensifies it. On the other hand, the repression, as far as this is possible, of all outward signs softens our emotions”.
- Darwin proposes that human facial expressions are innate and understood by all cultures.
- 1890 William James noted “ the continuous cooperation of voluntary muscles in our emotional states. “we feel sorry because we cry, angry because we strike”. “A purely disembodied human emotion is a nonentity”.
- The facial feedback hypothesis is born but ignored until the 1960’s.

Role of Facial Muscles in Emotion

- 1962 Silvan Tomkins stresses that facial expressions are innate, universal and important for emotion . The face is the prime organ for affect.

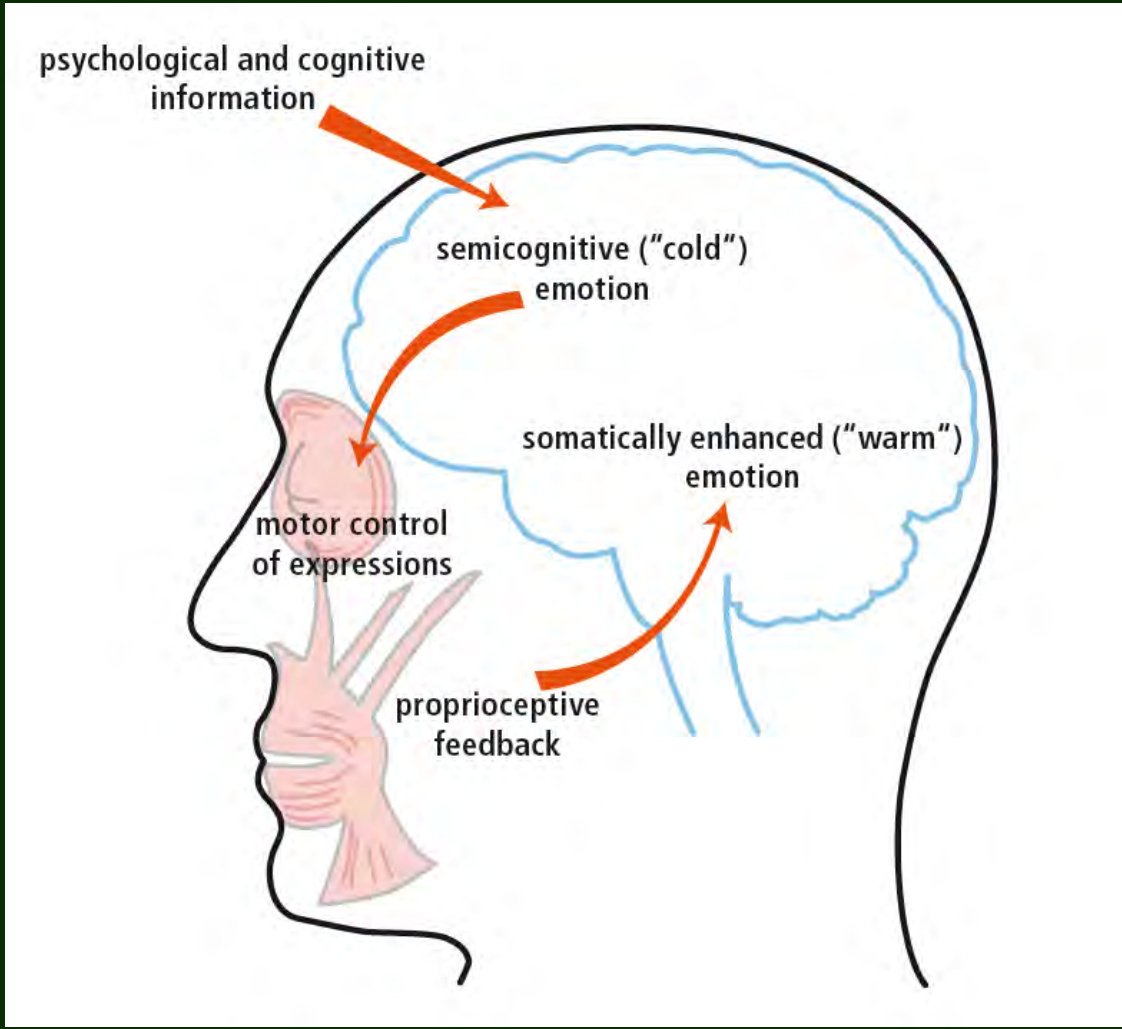
- 1969 Paul Ekman shows universality of facial expressions in literate and Stone Age cultures.

Facial Feedback hypothesis: Experimental Support

- Ekman P, Levenson RW, Friesen WV. Autonomic nervous system activity distinguishes among emotions. *Science* 1983; **221**(4616): 1208-10.
- (*Voluntarily making one of the facial expressions can generate the physiology and subjective experience of emotion)*

- Larsen RK, M; Frey, K. Facilitating the furrowed brow: an unobtrusive test of the facial feedback hypothesis applied to unpleasant affect. *Cognition Emotion* 1992; (54): 321-38.

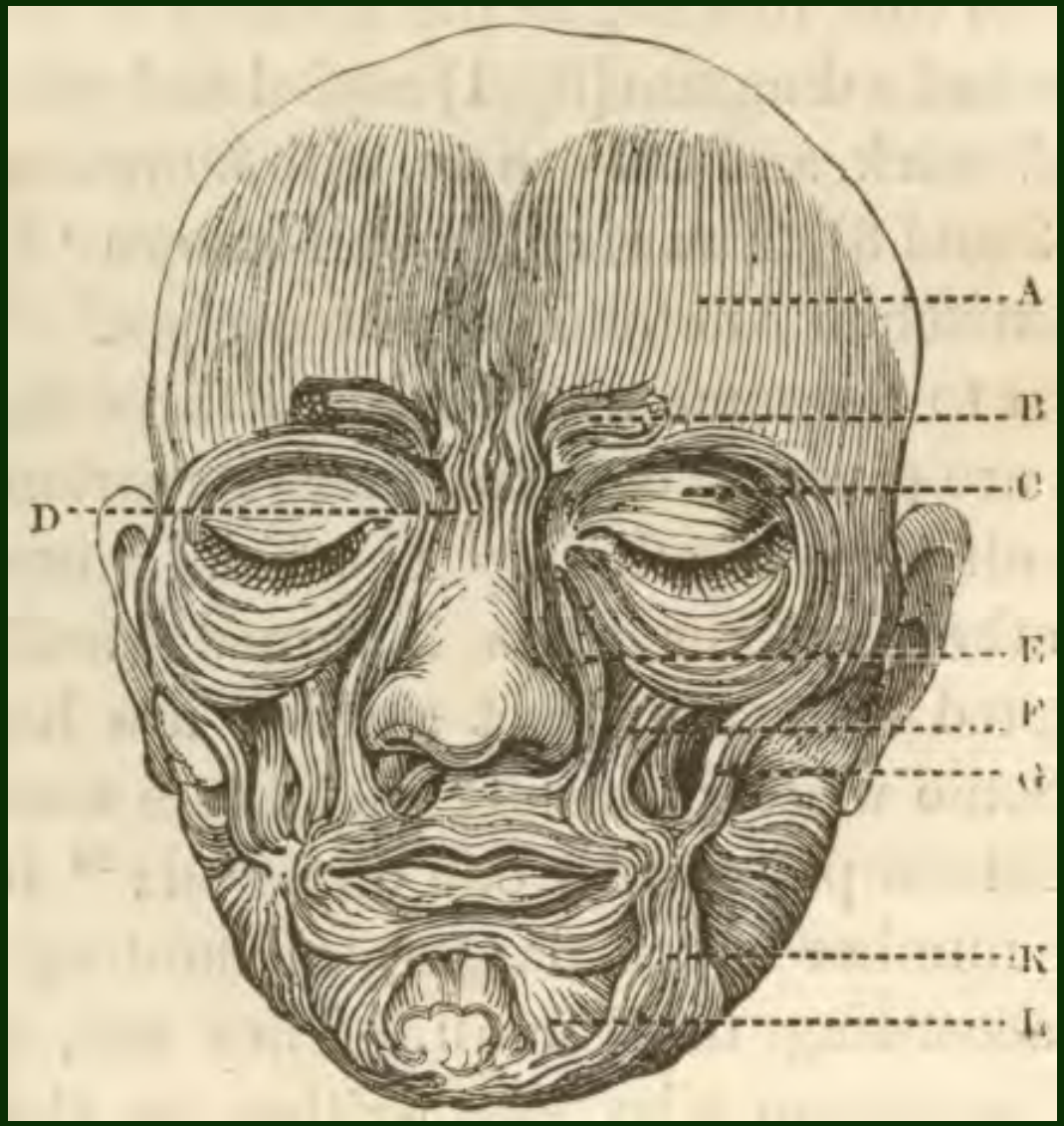
FACIAL FEEDBACK



Tillman Kruger

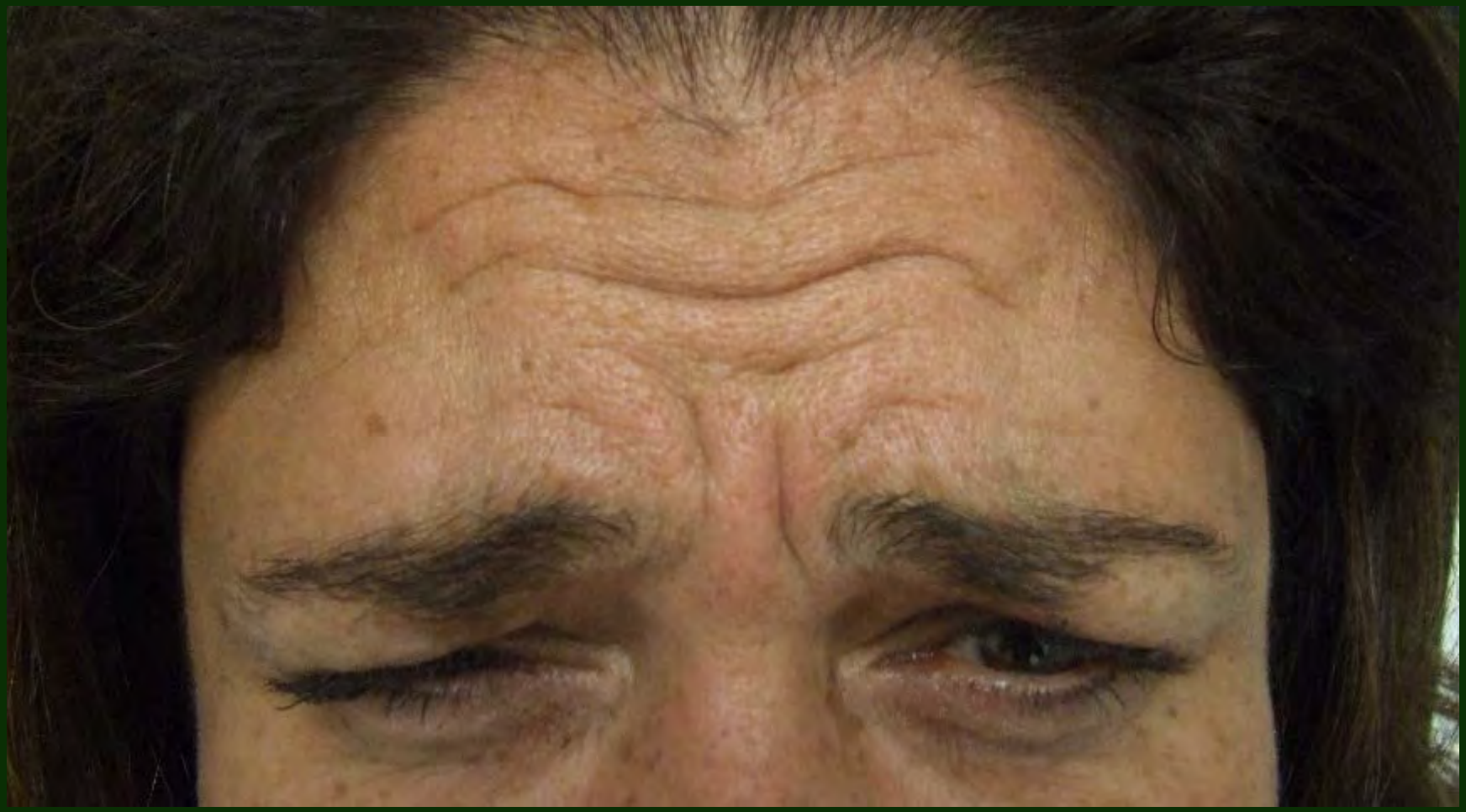
Role For Corrugator Muscle In Depression

- Darwin refers to the corrugator muscles as the “grief” muscles and describes Omega melancholium, a wrinkle (between the eyebrows) in the shape of the last letter of the Greek alphabet, (Ω) the omega.
- Ekman –shows that sadness,fear and anger all use the corrugator.



Sir Charles Bell

Omega Melancholium



Depressed subjects can be differentiated from healthy controls by their different pattern of corrugator muscle activity

- Schwartz GE, Fair PL, Salt P, Mandel MR, Klerman GL. Facial muscle patterning to affective imagery in depressed and nondepressed subjects. *Science* 1976; **192**(4238): 489-91.

- When subjects imagine happy, sad, and angry situations, different patterns of facial muscle activity are produced which can be measured by electromyography. These subtle, typically covert, facial expression patterns differentiate depressed from nondepressed subjects. Facial electromyography can provide a sensitive, objective index of normal and clinical mood states.

Jonathan Cole - 1988

- Studies Mobius syndrome- partial facial paralysis from birth
- His patient states ‘ ‘I
- think happy or I think sad, not
- actually feeling happy or feeling
- sad.’ ’
- Cole goes on to conclude
- that ‘ ‘losing facial
- animation meant not only losing
- expression and communication
- with others but led to a reduced
- intensity and delineation of feeling
- within oneself.

Implicating the corrugator muscle in depression

- Voluntary contraction of facial muscles into a smile or a frown can induce feelings of happiness or sadness.
- ⇧ corrugator activity in depression(Schwartz et al,1976)
- Facial EMG is a predictor of treatment outcome in depression
- (Carney et al, 1981, Greden et al, 1985)
- Normal subjects who view depressive imagery have ⇧ corrugator activity

Specific impairment of smiling increases the severity of depressive symptoms in patients with facial neuromuscular disorders.

- .
- Aesthetic Plast Surg. 1999 Nov-Dec;23(6):416-23

VanSwearingen JM, Cohn JF, Bajaj-Luthra A.

Department of Physical Therapy, University of Pittsburgh, Pennsylvania 15260 USA. jessievs+@pitt.edu

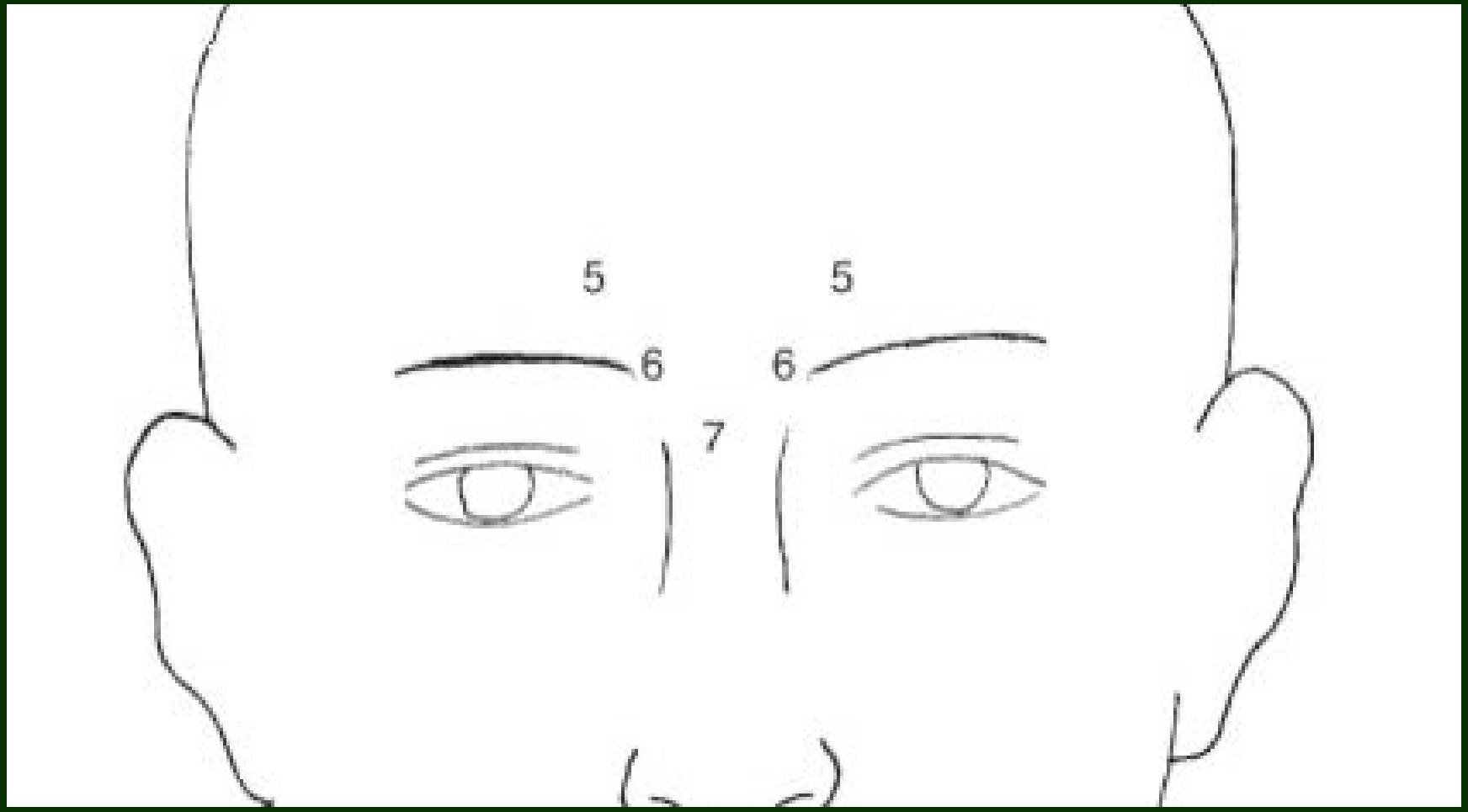
Depressive symptoms and related emotional distress are prevalent among patients with facial neuromuscular disorders, and the psychological distress impacts the functional disabilities associated with the facial impairment. A specific impairment in the ability to smile may elevate the risk for depression, with patients experiencing a reduced physiological feedback associated with smiling as well as the social consequences of the inability to communicate positive emotion. We tested the hypothesis that specific impairments in the ability to smile increase the severity of depressive symptoms in patients with facial neuromuscular disorders. Twenty-nine consecutive patients (mean age, 50.2 years; SD, 17.0 years; range, 18-81 years) with a facial neuromuscular disorder, who volunteered and completed all of the assessment measures participated. Facial neuromuscular impairments were assessed using multiple measures of facial motility and dysfunction, and emotional functioning was assessed using self-report measures of depression, anxiety, and positive and negative affect. Severity of global facial impairment was statistically controlled in evaluating the association between specific impairment in smiling and the degree of depressive symptoms. Separate hierarchical linear regression analyses indicated the specific impairment of smiling contributed to the prediction of depression ($R(2) = .41$, $df = 3,25$, $p = .00$) and anxiety ($R(2) = .35$, $df = 3,25$, $p = .00$), controlling first for the contribution of global impairment and facial physical disability. The specific impairment of smiling did not contribute to the prediction of positive emotional experience. Specific impairment of smiling and physical disability, but not global impairment of facial motion, were key predictors of depression in patients with facial neuromuscular disorders. The results emphasize the need to assess and treat depression and anxiety in patients with a facial neuromuscular disorder.

Hypothesis

If muscles of facial expression help generate emotional states, and the corrugator muscles are intimately involved with negative emotions, can we affect mood by inhibiting the corrugator?

Can we treat depression through botulinum toxin inhibition of the frown?

Standard OBA Injection Sites for Treating the Frown



Botulinum Toxin A(OBA)

- Neurotoxin protein
- Inhibits acetylcholine release at neuromuscular junction
- 2002 FDA approved for treatment of frown lines
- Causes temporary deenervation of muscles injected

FDA Approved Medical Uses of Botulinum Toxin A

- Cervical Dystonia
- Blepharospasm
- Strabismus
- Hyperhidrosis
- Muscle Stiffness (elbow,wrist and finger)
- Chronic Migraine
- Overactive Bladder with or without Urinary Incontinence

Botulinum Toxin A

- Although well known for its uses in cosmetic medicine ,greater than 50% of all botulinum toxin is now used for medical conditions
- In addition to FDA approved uses, off-label use has been reported for-
- Anal fissure
- Pyriformis syndrome
- Spastic disorders associated with injury or disease of the
- central nervous system including trauma, stroke, multiple sclerosis,
- Parkinson's disease, or cerebral palsy
- Focal dystonias affecting the limbs, face, jaw, or vocal cords
- TMJ pain disorders
- diabetic neuropathy
- Premature ejaculation

Botulinum Toxin A

- If a muscle is part of a disease process, whether a proximal cause, or part of a neuronal circuit integral to the disease, and the muscle can be injected, then Botulinum Toxin A may be of therapeutic value.

Treatment of Depression with Botulinum Toxin A: A Case Series

Eric Finzi, MD, PhD,*† and Erika Wasserman, PhD‡

BACKGROUND Major depression is a common and serious disease that may be resistant to routine pharmacologic and psychotherapeutic treatment approaches.

OBJECTIVE To evaluate the efficacy of botulinum toxin A treatment of glabellar frown lines in treating patients with major depression, using a small open pilot trial.

METHODS Patients who met DSM-IV criteria for ongoing major depression in spite of pharmacologic or psychotherapeutic treatment were evaluated with the Beck Depression Inventory II (BDI-II) before receiving botulinum toxin A to their glabellar frown lines. Two months later, all patients were re-evaluated clinically and with the BDI-II.

RESULTS Ten depressed patients were treated with botulinum toxin A, and 9 of 10 patients were no longer depressed 2 months after treatment. The tenth patient had an improvement in mood.

CONCLUSION To our knowledge, these are the first reported cases of depression treated with botulinum toxin A.

Dr. Finzi has applied for a patent using botulinum toxin A to treat depression.

Dermatol Surg. 2006 May;32(5):645-9; discussion 649-50.

RESULTS: 9 out of the 10 patients were no longer depressed. The 10th patient had improvement of mood.

TABLE 1. Summary of Patient Characteristics and Response of Depression to Treatment with Botulinum Toxin A

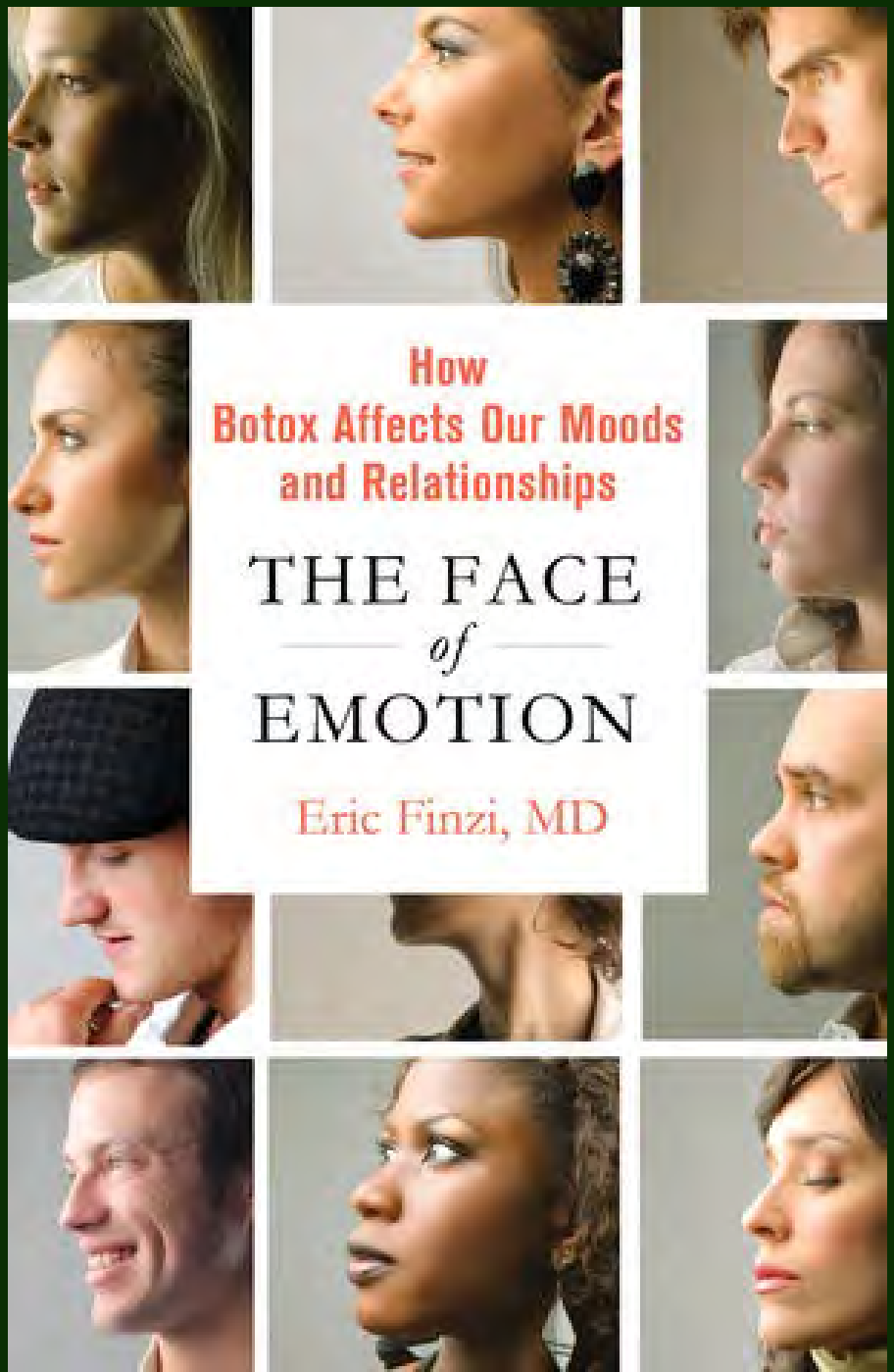
Patient No.	*Age (Years)/ Sex*	*Previous Treatments*	*Current Treatment*	*Duration of Depression (Years)*	*Pretreatment BDI-II score*	*Post-treatment BDI-II score*
1	62/f	B, P, Psy	B	11	27	5
2	62/f	F, P, R, Psy	P, R, Psy	7	30	7
3	37/f	B, P	—	5	30	2
4	36/f	B, F, V, Psy	F	2	41	6
5	47/f	B, D, G	B, D, G	17	46	33
6	63/f	E	—	2	22	8
7	38/f	—	—	1	27	0
8	63/f	B, Psy	B	10	21	4
9	38/f	—	—	2	31	2
10	38/f	—	—	1	32	14

B, Bupropion, D, divalproex sodium, E, escitalopram oxalate, F, fluoxetine, G, gabapentin, P, paroxetine, Psy, psychotherapy, R, remeron, V, venlafaxine.

Patient 1: “My life did a 360 turn around after botox treatment.” She applied for a new job and “rekindled a 47 year-old romance.”

Patient 4: “When the Botox wore off, I became depressed again.” A second round, once again, led to resolution of my depressive symptoms.

Patient 5: Remained depressed but felt better. The only bipolar patient in the study.


How
Botox Affects Our Moods
and Relationships
THE FACE
of
EMOTION
Eric Finzi, MD

Facial Expressions

- Communicative function to others in social relationships.
- Embodiment of our emotions.
- Communication of our emotional state to ourselves

Can we replicate initial results in a larger trial?

Does a depressed patient need an observable frown at rest to be helped by OBA?

Treatment of depression with onabotulinumtoxinA: A randomized, double-blind, placebo controlled trial

Eric Finzi [a,*], Norman E. Rosenthal [b,c]

[a] *Chevy Chase Cosmetic Center, Chevy Chase, MD 20815, USA*
[b] *Capital Clinical Research Associates, Rockville, MD 20852, USA*
[c] *Georgetown Medical School, Washington, DC 20057, USA*

ARTICLE INFO

Article history:
Received 27 August 2013
Received in revised form
13 November 2013
Accepted 20 November 2013

Keywords:
OnabotulinumtoxinA
Depression
Double blind
Clinical trial
Antidepressant
Corrugator

ABSTRACT

Converging lines of evidence suggest a role for facial expressions in the pathophysiology and treatment of mood disorders.

To determine the antidepressant effect of onabotulinumtoxinA (OBA) treatment of corrugator and procerus muscles in people with major depressive disorder, we conducted a double blind, randomized, placebo-controlled trial. In an outpatient clinical research center, eighty-five subjects with DSM-IV major depression were randomized to receive either OBA (29 units for females and 40 units for males) or saline injections into corrugator and procerus frown muscles (74 subjects were entered into the analysis). Subjects were rated at screening, and 3 and 6 weeks after OBA treatment. The primary outcome measure was the response rate, as defined by $\geq$ 50% decrease in score on the Montgomery–Asberg Depression Rating Scale (MADRS). Response rates at 6 weeks from the date of injection were 52% and 15% in the OBA and placebo groups, respectively (Chi-Square (1) = 11.2, $p < 0.001$, Fisher $p < 0.001$). The secondary outcome measure of remission rate (MADRS score of 10 or less) was 27% with OBA and 7% with placebo (Chi-square (1) = 5.1, $p < 0.02$, Fisher $p < 0.03$). Six weeks after a single treatment, MADRS scores of subjects were reduced on average by 47% in those given OBA, and by 21% in those given placebo (Mann–Whitney *U*, $p < 0.0005$).

In conclusion, a single treatment with OBA to the corrugator and procerus muscles appears to induce a significant and sustained antidepressant effect in patients with major depression.

Trial Registration: clinicaltrials.gov Identifier: NCT01556971.

J Psychiatric Res. 52 (2014) 1-6.

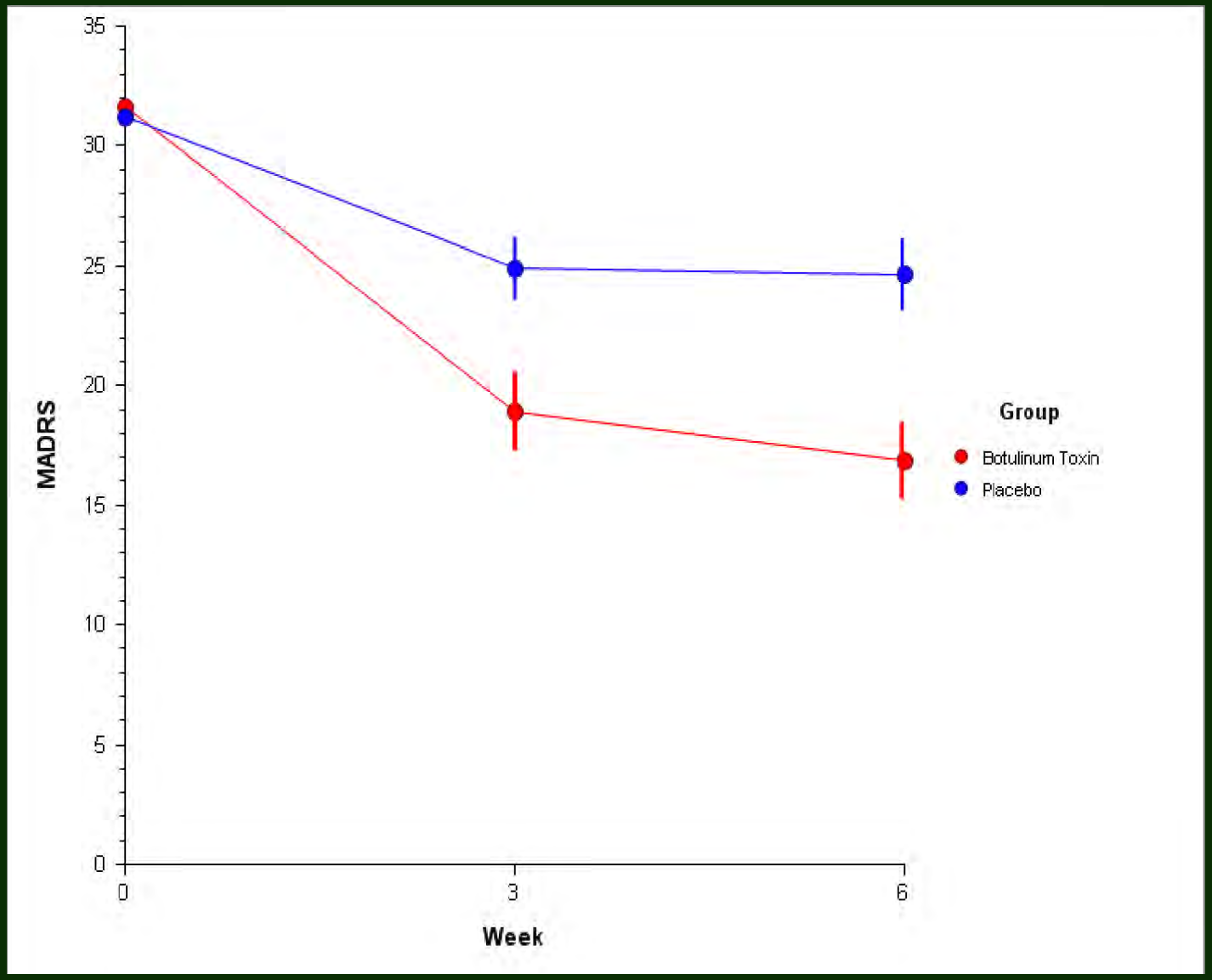
Randomized, Double-Blind Placebo Controlled Trial of OnabotulinumtoxinA(OBA) Inhibition of Frowning for Major Depression

- Major Depressive Disorder- DSM IV
- MADRS score of ≥ 26
- CGI-S ≥ 4
- MADRS score mean = 31
- 121 subjects screened, 85 subjects randomized
- 74 subjects with usable data
- Single treatment with OBA
- Frown score quantification, baseline,6 wks
- MADRS,BDI-II,CGI evaluation 0,3,6 wks

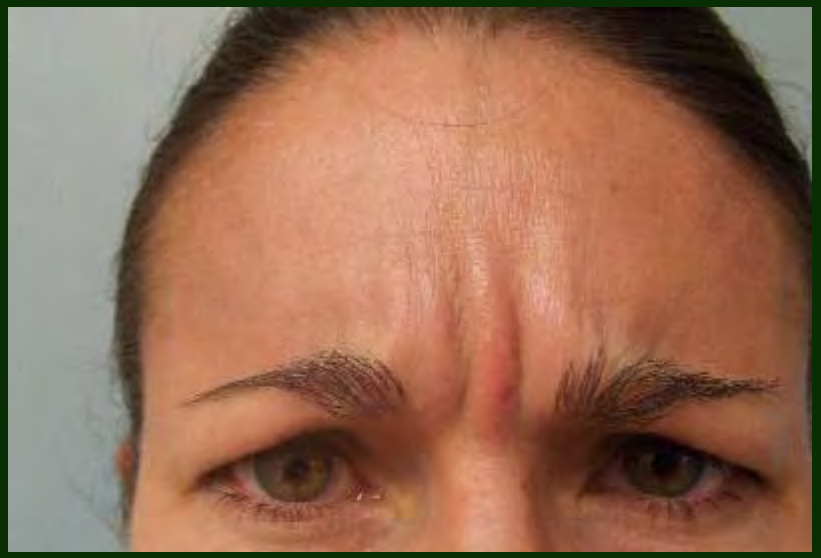
Patient Characteristics

	OBA	Placebo
Age,mean	48 ± 10	49 ± 9
Sex, % Female	96	90
Age of first depressive episode,years	27 ± 12	27 ± 14
Duration of current episode,months	20 ± 19	35 ± 44
Pts currently on antidepressants(%)	42	41
Pts tried on antidepressants (%)	94	78
No. of antidepressants tried	2.2 ± 1.2	1.8 ± 1.3
No. previous depressive episodes	5.9 ± 5.8	6.9 ± 7.8
Recurrent depression (%)	91	80
MADRS, mean	32 ± 3.8	31 ± 3.6
CGI-S, mean	4.6 ± 0.5	4.6 ±0.5

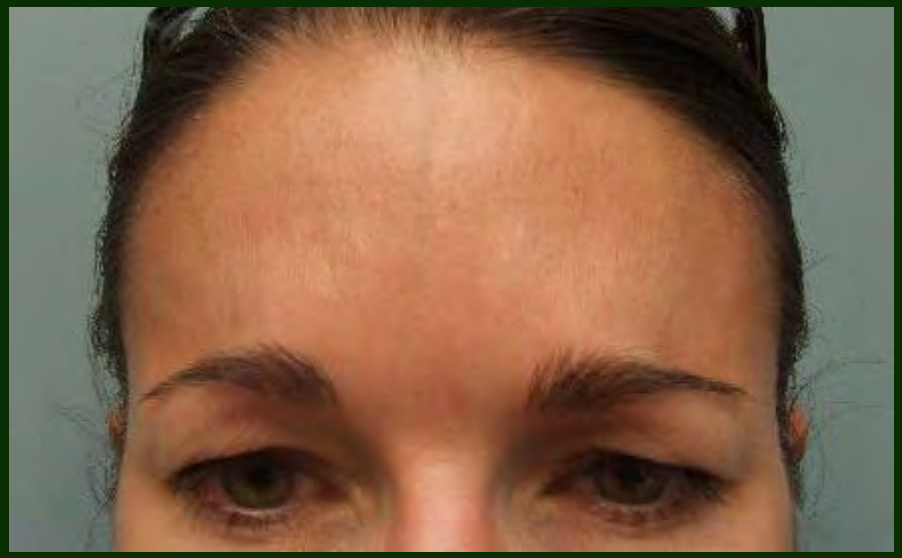
MADRS scores over time(mean ±sem), in the OBA and placebo groups at 3 and 6 weeks versus baseline.



FROWN EXPRESSION BEFORE AND AFTER OBA



Before



After

Patient went into remission

Statistical Analysis

- Response rate at 6 weeks, 52% OBA, 15% placebo
- (Chi-Square(1)=11.2, $p < 0.001$, Fisher $p < 0.001$
- Remission rate at 6 weeks, 27% OBA , 7% placebo,(Chi-square(1) = 5.1, $p < 0.02$)
- Effect size = 0.95 - high
- Mixed model ANOVA $F(2,139) = 10.03$, $p < 0.0001$
- 47% reduction in MADRS scores in OBA, 21% placebo, Mann-Whitney U, $p < 0.0005$
- BDI, CGI – similar results
- Observable frown at initial visit not predictive of response to OBA

Conclusions

- A single treatment of the glabellar region with OBA induces a strong and sustained alleviation of symptoms in a broadly defined group with major depression.
- An observable frown at rest is ***not*** necessary for improvement in depression.
- Frowning in and of itself may be depressogenic.

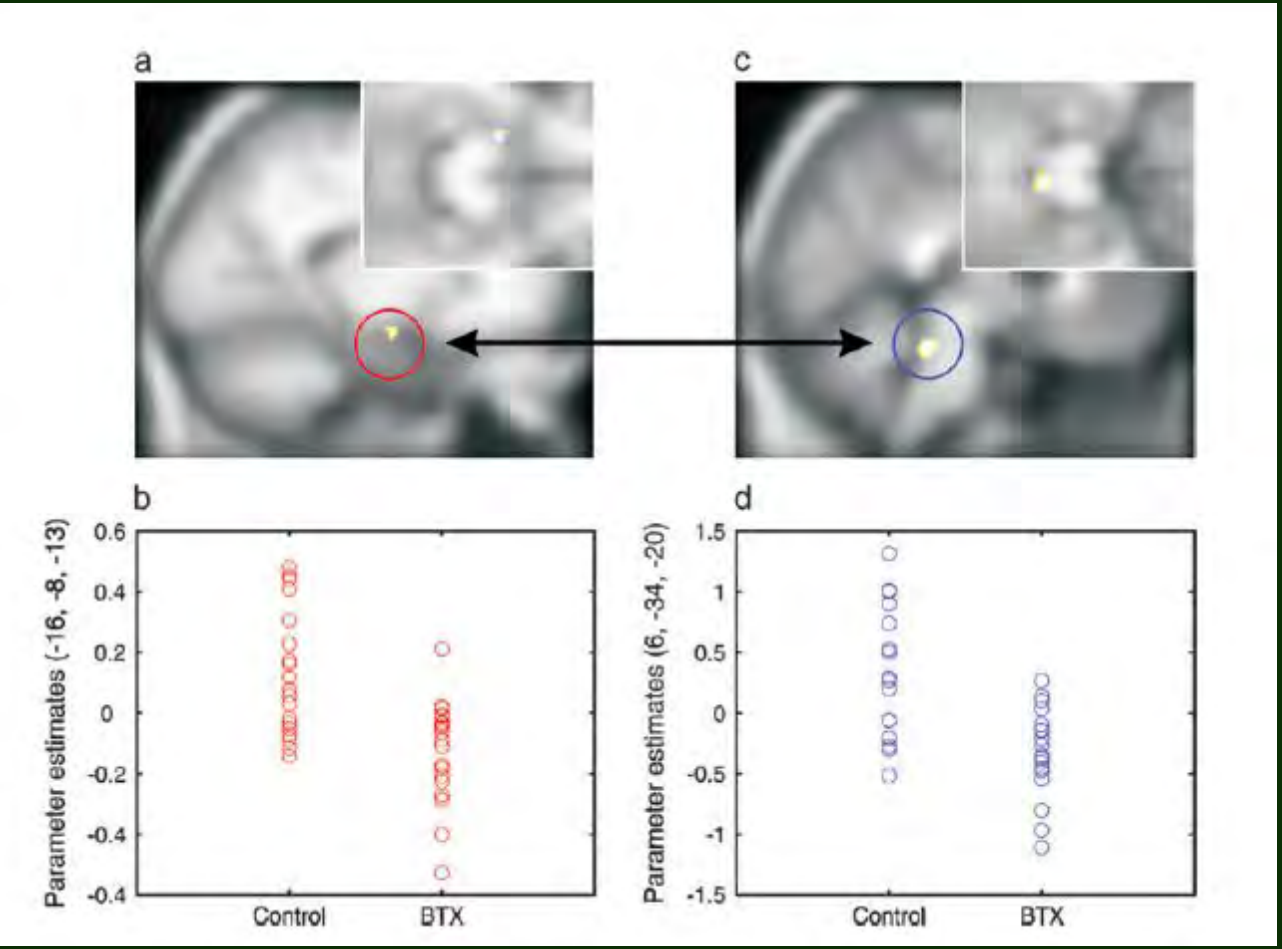
Mechanism of Action

- Emotional Proprioception – the brain measures your emotional temperature thru facial muscle feedback.
- Facial muscles send afferent information to the brain via the trigeminal or facial nerve.
- Facial expressions relay, in real time, our emotional state to our brain
- Silent feedback from facial muscles about their state of contraction help embody our emotions

Mechanism of Action

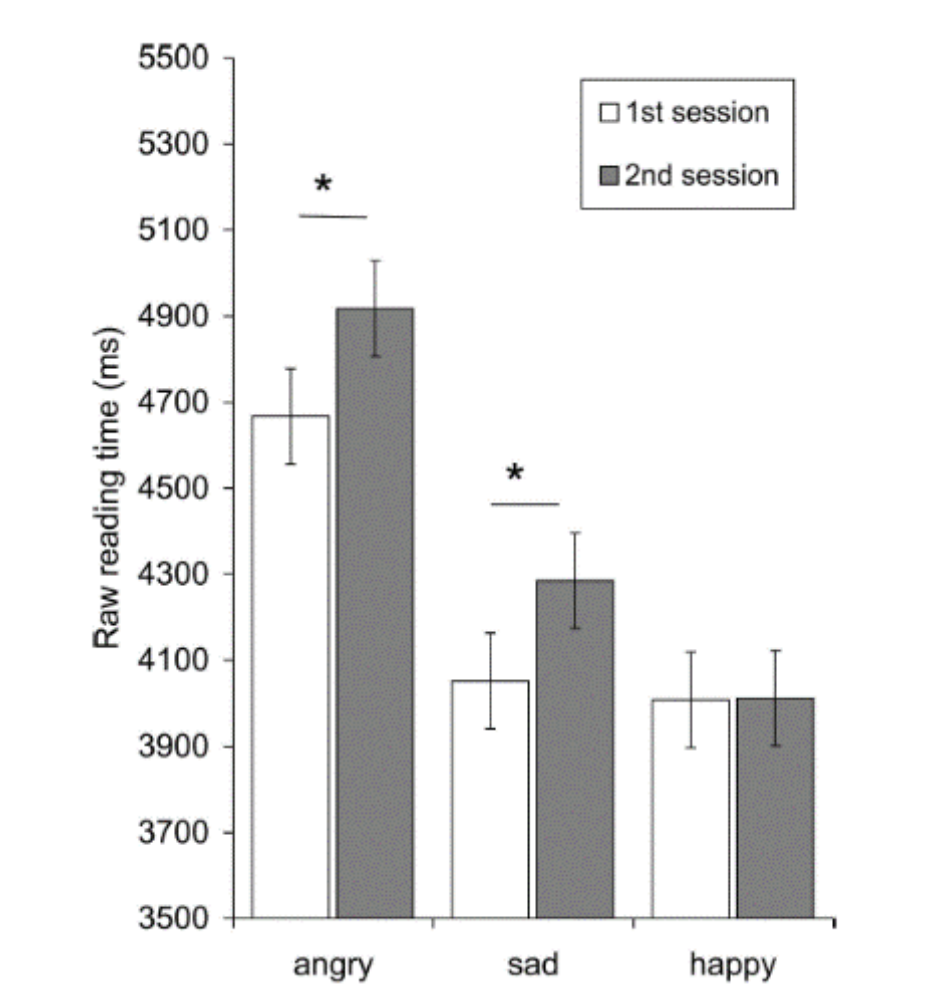
- Motor deenervation of corrugator muscles reduces afferent sensory information to the brain stem and left amygdala.
- OBA injection into the frown muscles in normal subjects decreases left amygdala activity when mimicking angry faces.
  Hennenlotter et al, Cerebral Cortex,2009,19(3):537-542.

Downregulation of amygdala activity after BTX Imaging during imitation of angry facial expression



Hennenlotter et al. 2009
Cerebral Cortex

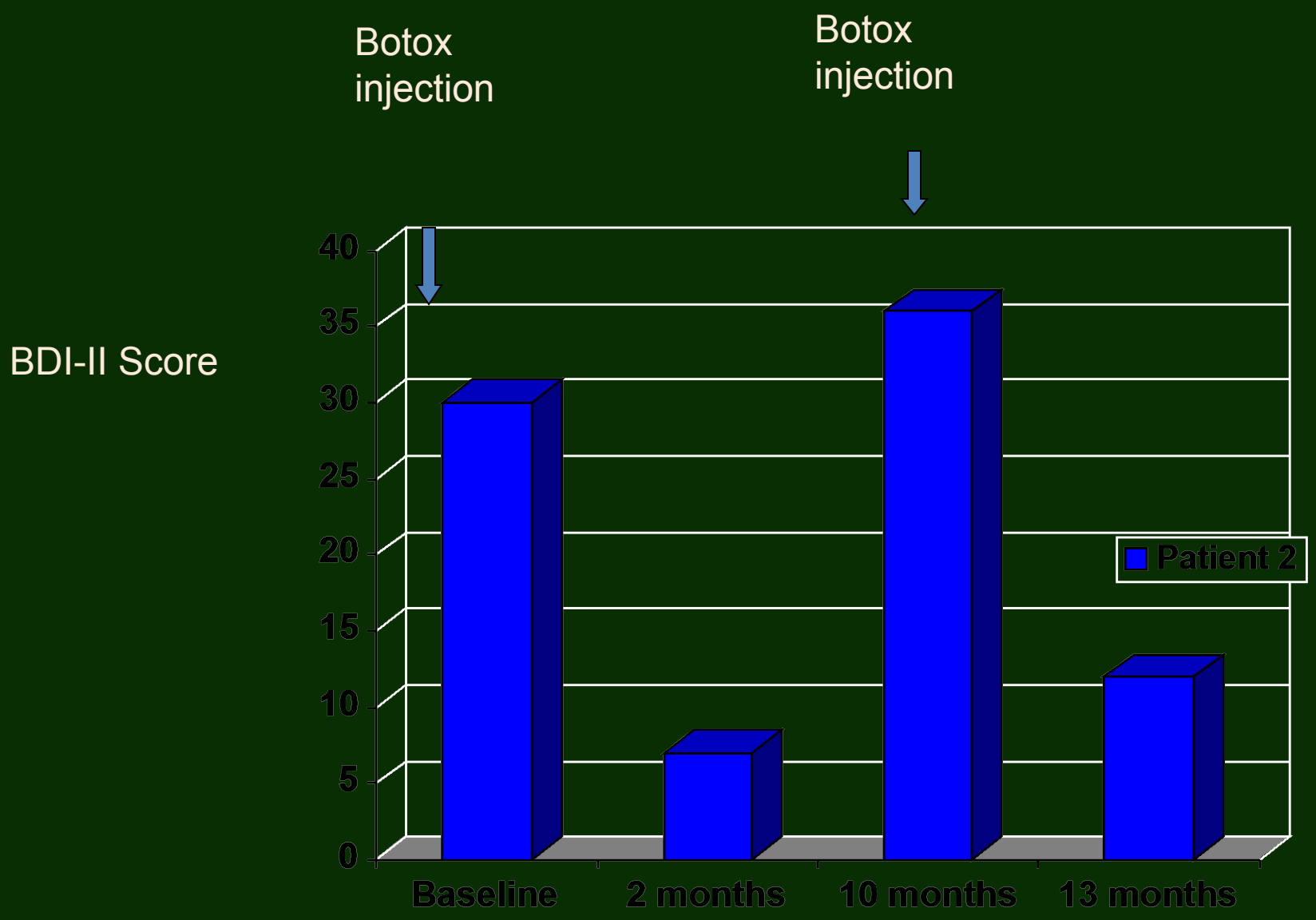
BLOCKING THE CORRUGATOR MUSCLE SLOWS COMPREHENSION OF NEGATIVE EMOTIONS



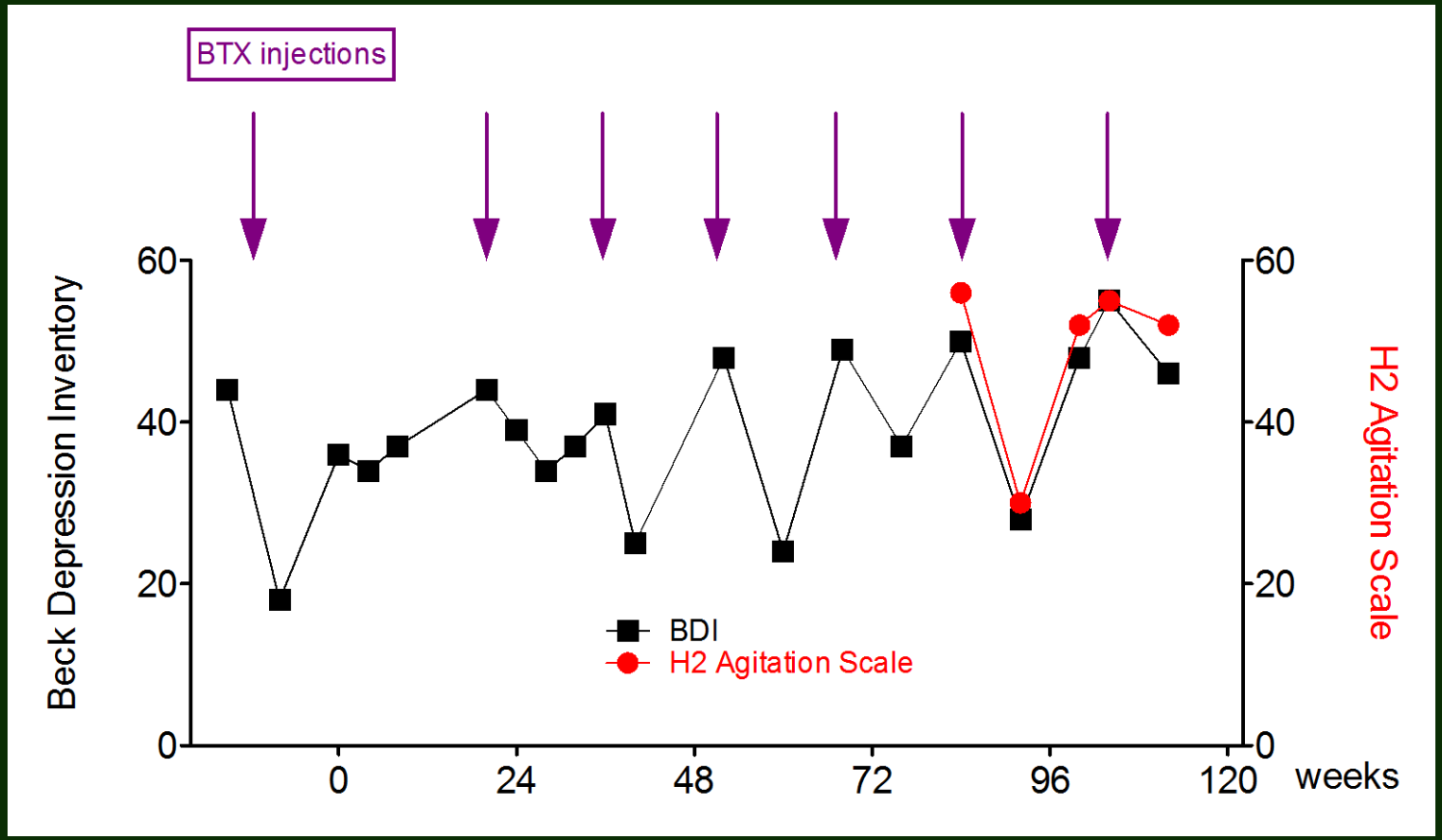
Havas et al
Psychological Science 2010

What Happens When OBA Wears Off

- Depressive symptoms return.
- Reinjection improves depressive symptoms again.


Botox injection
Botox injection
BDI-II Score
40
35
30
25
20
15
10
5
0
Baseline
2 months
10 months
13 months
Patient 2

D.P., 54 yr old female with therapy resistant chronic MDD and repeated BTX injections



Kruger & Wollmer 2014

Contents lists available at SciVerse ScienceDirect

Journal of Psychiatric Research

journal homepage: www.elsevier.com/locate/psychires

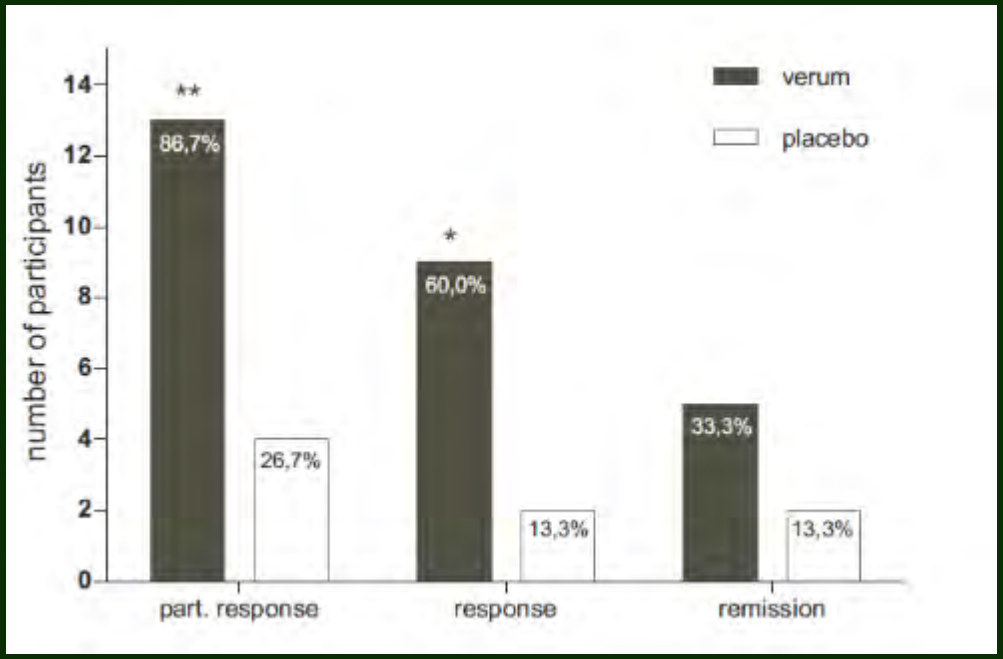
Facing depression with botulinum toxin: A randomized controlled trial

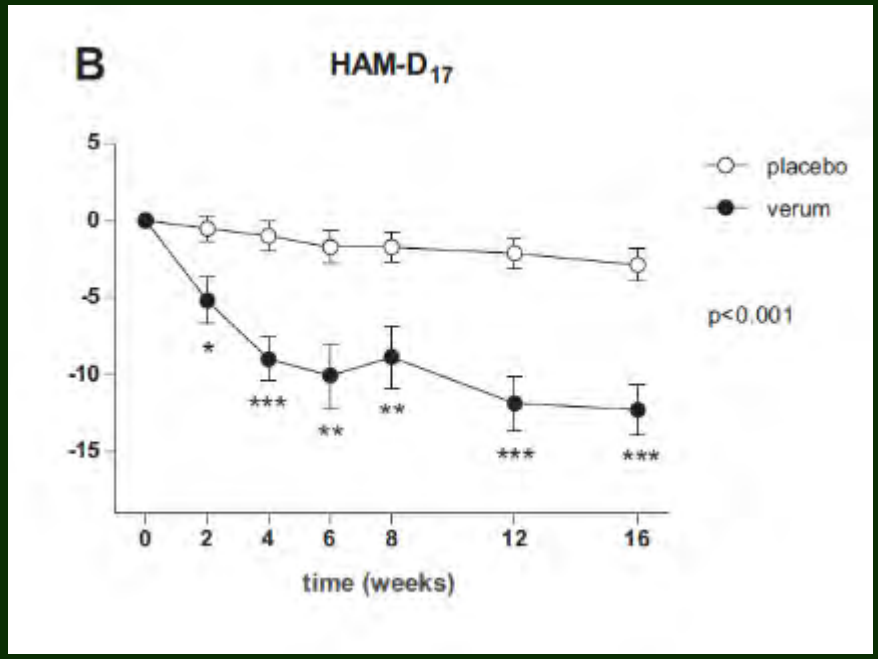
M. Axel Wollmer[a,*], Claas de Boer[b], Nadeem Kalak[a], Johannes Beck[a], Thomas Götz[a], Tina Schmidt[b], Muris Hodzic[c], Ursula Bayer[a], Thilo Kollmann[a], Katja Kollewe[d], Daniela Sönmez[b], Katja Duntsch[b], Martin D. Haug[e], Manfred Schedlowski[f], Martin Hatzinger[g], Dirk Dressler[d], Serge Brand[a], Edith Holsboer-Trachsler[a], Tillmann H.C. Kruger[b]

- 30 Patients age 25-65. Double-blind Placebo controlled.
- 15 Received Botulinum and 15 Received Placebo in Glabellar region.
- Depression diagnosis based on SCID and Ham D-17 >14.
- Moderate to severe frown lines
- Women received 29 units; Men received 39 units.
- Exclusion: Psychosis, significant Axis II, migraines, previous Botulinum treatment
- 0-2 medications. Were not allowed to change them during the first six weeks of the trial
- **Primary outcome: Ham D response (50% reduction in score) and remission (≤ 7 score) at 6 weeks**
- BDI and CGI-S also used for evaluation

Wollmer et al. Facing Depression wih Botulinum Toxin. A randomized controlled trial. Journal of psychiatric research. 2012

Results





Ham D-17 Response: 60% vs. 13.3%
(>50% reduction in Ham-D)

Ham D-17 Remission: 33.3% vs. 13.3%
(Ham D ≤7)

Ham D-17 change: -47.1% vs. -9.2%

- Botulinum: 10 point drop (47.1%)
- Placebo: 1.73 point drop (9.2%)

ORIGINAL RESEARCH

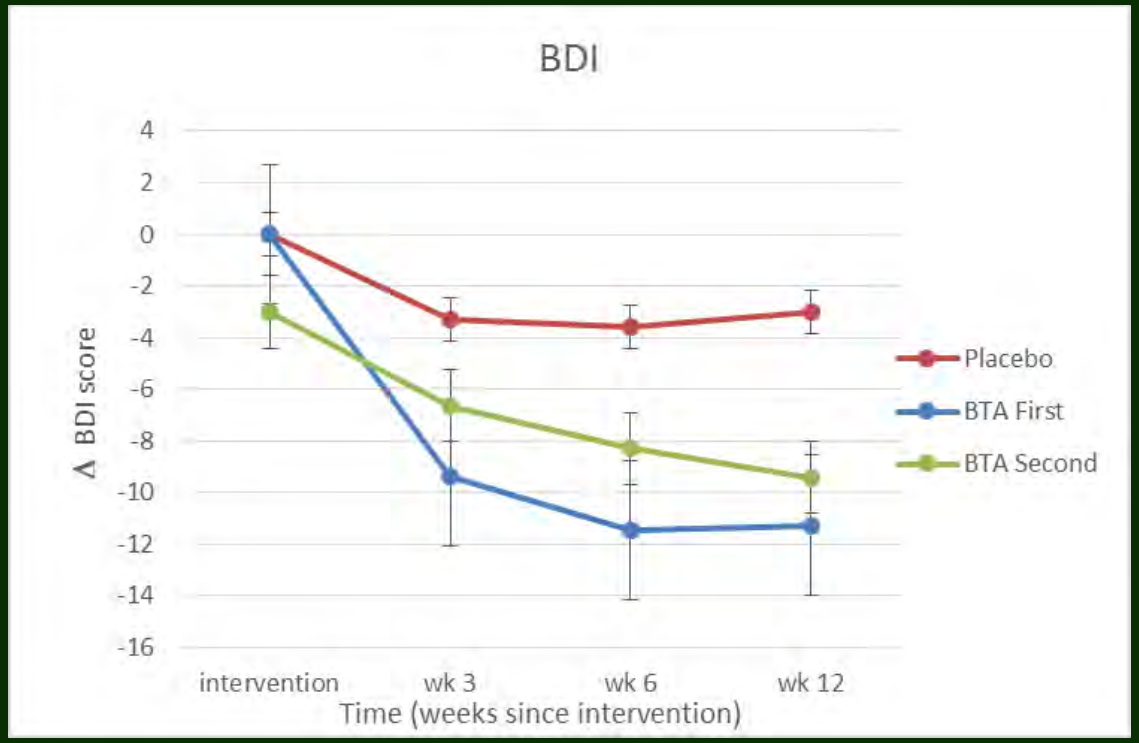
Treatment of Major Depressive Disorder Using Botulinum Toxin A: A 24-Week Randomized, Double-Blind, Placebo-Controlled Study

Michelle Magid, MD; Jason S. Reichenberg, MD; Poppy E. Poth, BS; Henry T. Robertson, PhD; Amanda K. LaViolette, MD, MPH; Tillmann H. C. Kruger, MD; and M. Axel Wollmer, MD

- 30 Patients age 18-65
- 11 received botulinum and 19 received Placebo in Glabellar region.
- **At week 12, the groups were switched!**
- Depression diagnosis based on MINI and Ham D-21 >14
- Moderate to severe frown lines
- Women received 29 units; Men received 39 units.
- Exclusion: Psychosis, significant axis II, previous botulinum treatment, substance abuse
- 0-3 psychotropic medications. No med changes 2 months prior to trial
- **Primary outcome: Ham D response (>50% reduction) at 6 weeks**
- Secondary outcomes: Ham D remission (score ≤ 7), BDI response (>50% reduction) BDI remission (score ≤ 9), PHQ-9 scores at 6 weeks

Magid M, Reichenberg J, Poth P, et al. The Treatment of Depression using Botulinum Toxin A: A 24 week randomized double blind, placebo controlled study. Journal of Clinical Psychiatry, In press Feb 2014.

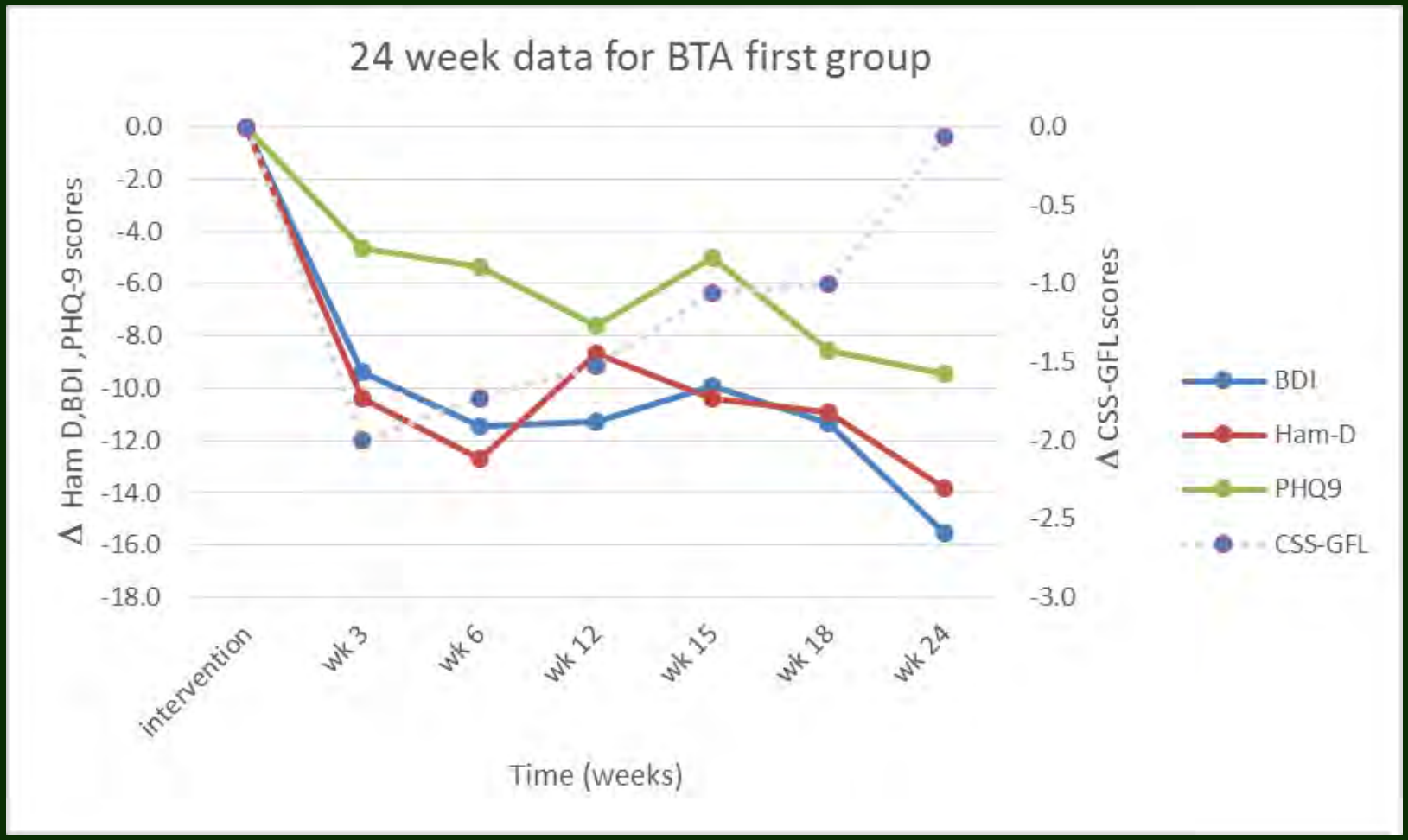
Results



BDI -42% vs. -35% vs. -15%

- Botulinum 1st: 27.5-16 = 11.5 point drop (42%)
- Botulinum 2nd: 23.7-15.4 = 8.3 point drop (35%)
- Placebo: 23.7- 20.1= 3.6 point drop (15%)

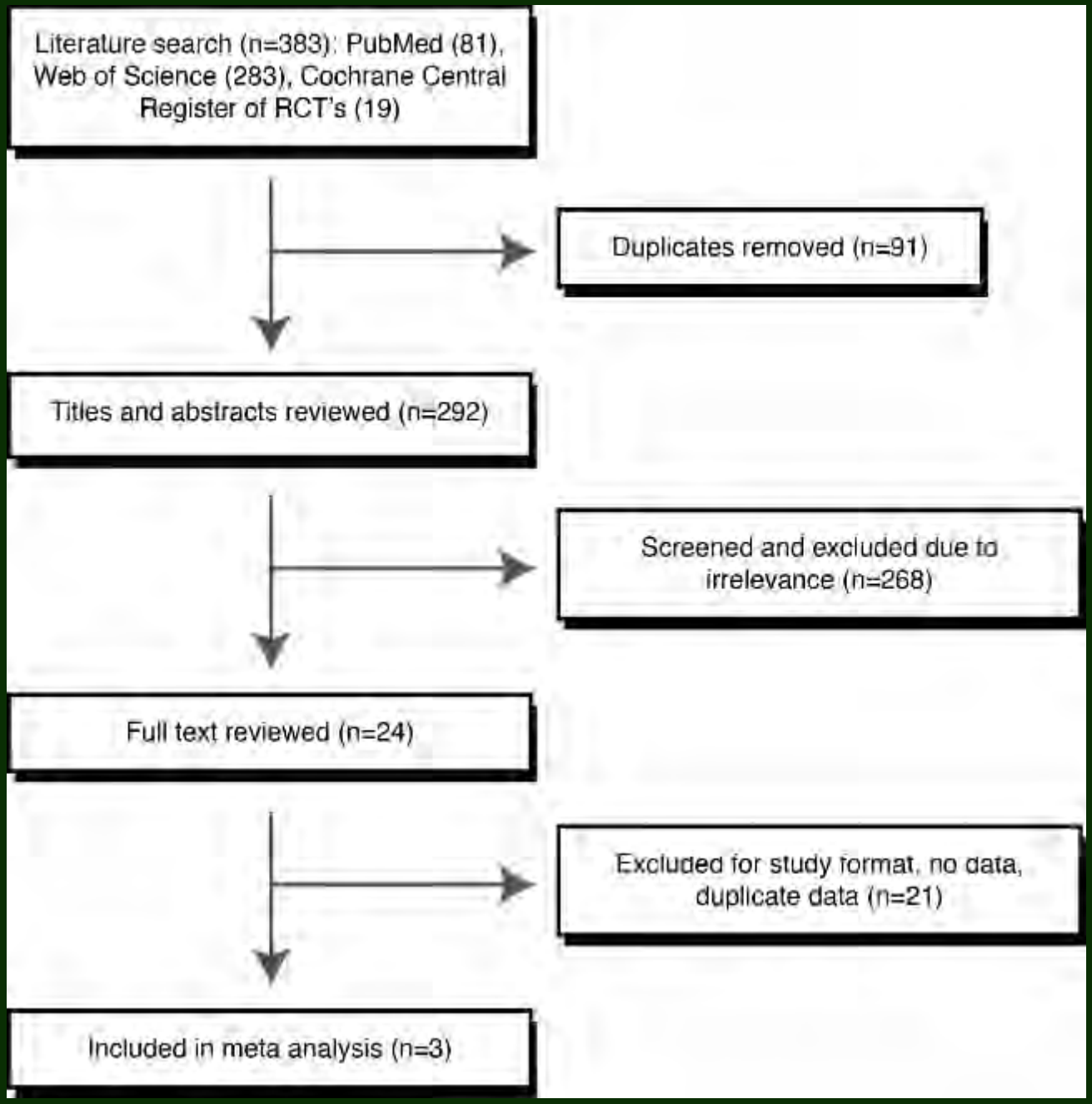
Response: 45% vs. 33% vs. 5% (>50% reduction in BDI)
Remission: 27% vs. 33% vs. 5% (BDI ≤7)



At week 24, the mean frown score (CSS-GFL) in the BTA first group was back to baseline (baseline score= 2.7; wk 24 score= 2.7), indicating that the botulinum toxin had worn off. Nonetheless, all three measurement scales showed continued reduction in depression MDD scores throughout the 24 weeks, indicating that mood continued to improve despite the BTA effects wearing off.

Blinding

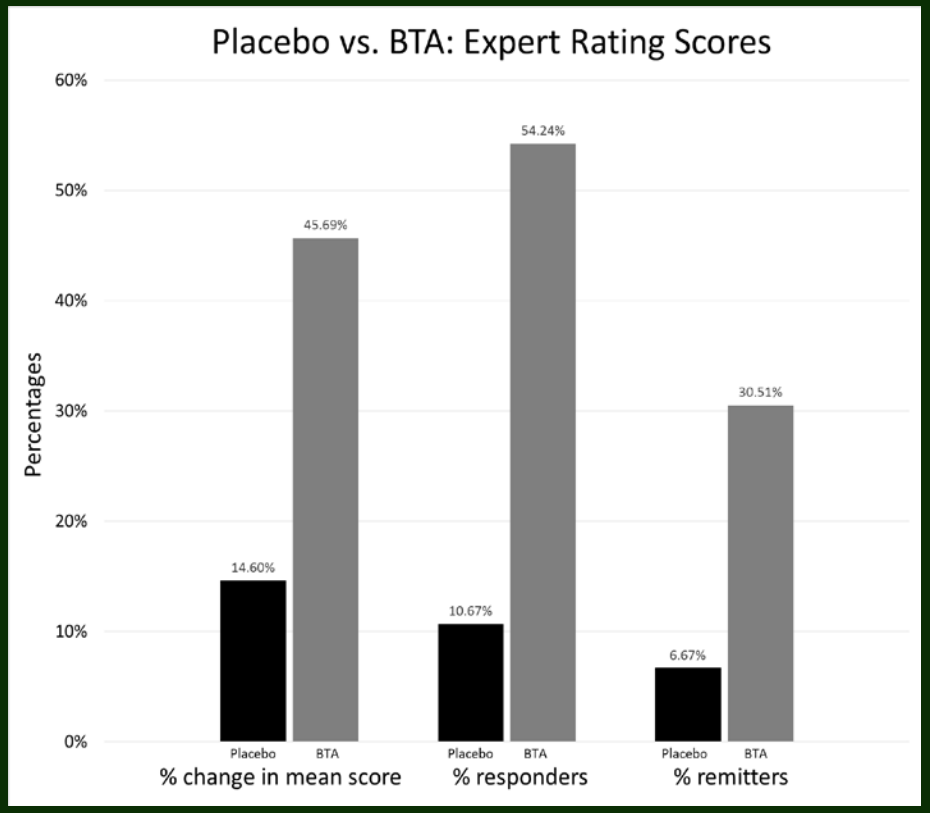
Staff member demonstrating blinding technique.
Consent given to use her image.

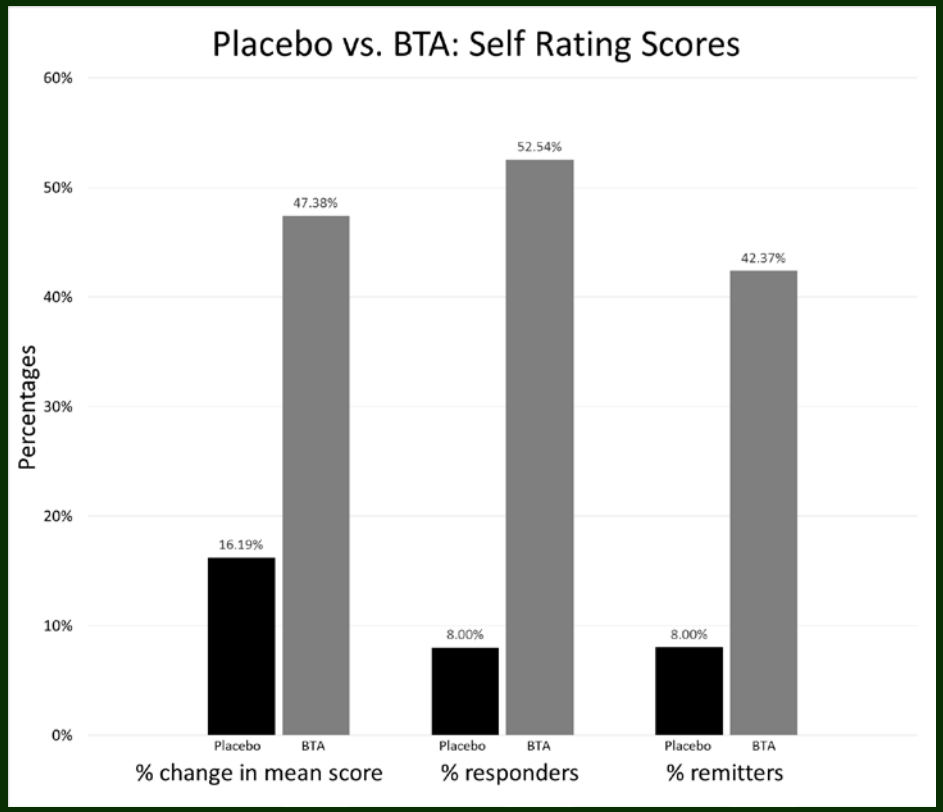

Literature search (n=383): PubMed (81), Web of Science (283), Cochrane Central Register of RCT's (19)
Duplicates removed (n=91)
Titles and abstracts reviewed (n=292)
Screened and excluded due to irrelevance (n=268)
Full text reviewed (n=24)
Excluded for study format, no data, duplicate data (n=21)
Included in meta analysis (n=3)

STUDY	WOLLMER et al. 2012		FINZI et al. 2013		MAGID et al. 2014	
# of Patients	30		74		30	
Sex	Females and Males		Females and Males		Females and Males	
Age	25-65		18-65		18-65	
Units of BTA Given	29 Female, 39 Male		29 Female, 40 Male		29 Female, 39 Male	
Baseline CSS-GFL score[a]	2.3		1.7		2.6	
Measurement Scale	HAM D-17	BDI	MADRS	BDI-II	HAM D-17	BDI
Mean Baseline Score	20.1	25.3	31.4	29.3	20.8	25.1
Botulinum Response Rate	60%	40%	52%	61%	55%	45%
Placebo Response Rate	13%	0%	15%	12%	0%	5%
Botulinum Percent Change in Score	-47%	-40%	-47%	-55%	-50%	-42%
Placebo Percent Change in Score	-9%	3%	-21%	-28%	-6%	-15%
Botulinum Remission Rate	33%	33%	27%	48%	36%	27%
Placebo Remission Rate	13%	0%	7%	12%	0%	5%
Length of trial in weeks	16		6		24	
Moderate-severe frown lines needed for inclusion?	Yes		No		Yes	
Medications	0-2 No change x 1 month		Not failed ≥3 trials No change x 1 month		0-3 No change x 2 months	
Guessed intervention correctly?	90% Participants 60% Raters		≈50% Participants 73% Raters		N/A	
Augmentation or Primary treatment?	Augmentation		Both		Both	

Category	Variable	Placebo (N=75)	Botulinum (N=59)	P-value
Demographics	Age	49.35	49.14	0.90
	Sex, % Female	86.67%	93.22%	0.38
	# of years with depression, mean	19.72	18.78	0.69
	Duration of current episode in months, mean	28.91	19.81	0.08
	% of patients on current antidepressants	64.00%	64.41%	0.96
	# of current antidepressants, mean	0.89	0.85	0.74
	# of previous episodes, mean	5.65	6.93	0.09
	% of patients with recurrent depression	84.00%	86.44%	0.64
	% of patients with mild depression	13.33%	8.47%	0.38
	% of patients with moderate depression	46.67%	45.76%	0.92
	% of patients with severe depression	38.67%	44.07%	0.53
BDI	Baseline score, mean	26.28	28.98	0.09
	Week 6 score, mean	21.23	14.73	<.0001
	Change in score, mean	5.05	14.25	<.0001
	% change in score	-16.19%	-47.38%	<.0001
	% patient responders	8.00%	52.54%	<.0001
	% patient remitters	8.00%	42.37%	<.0001
HAM-D / MADRS	% change in score	-14.60%	-45.69%	<.0001
	% patient responders	10.67%	54.24%	0.001
	% patient remitters	6.67%	30.51%	0.03
CSS-GFL	Baseline frown score, mean	2.08	2	0.589
	Week 6 frown score, mean	2.20	0.73	<.0001

Meta-analysis Results

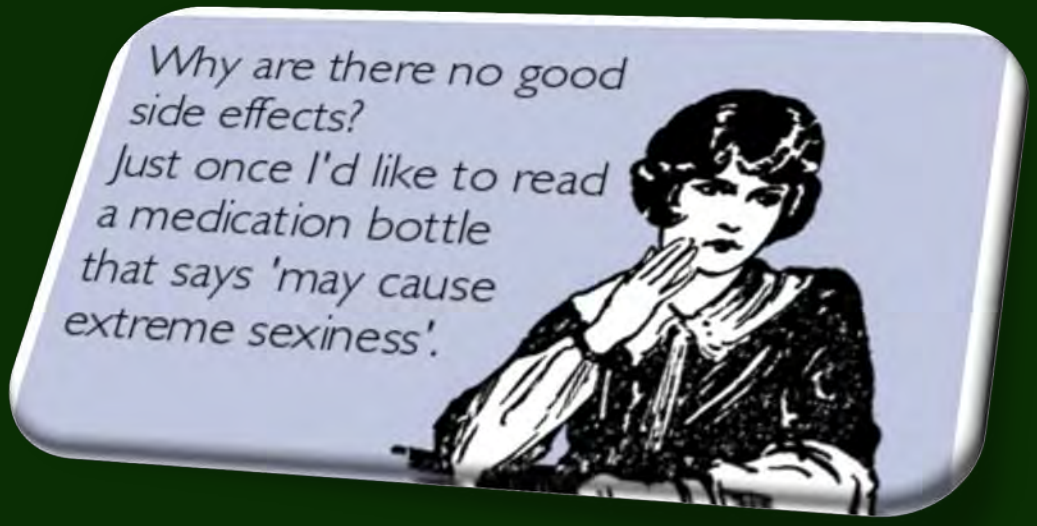




Placebo N=75 Botulinum N=59

Is botulinum toxin safe?

- No severe adverse reactions were reported in the trials.
- 11.8% (n=7) of the botulinum group
- 8.0% (n=6) of the placebo group
- Mild adverse reactions including temporary headaches and local irritation immediately after injection) (P-value=0.46).



Is botulinum better as a monotherapy or an augmentation strategy?

Number and % of patients taking antidepressants who were responders, according to Patient Rating Scales	Number (%) of patient responders	
	BTA (n=59)	**Placebo (n=75)**
Taking Antidepressants	19/38 (50%)	3/48 (6%)
Not taking antidepressants	12/21 (57%)	3/27 (11%)

The was no statistically significant difference in the response rates for patients using the botulinum as a monotherapy (patients on no psychotropic medication) vs. an adjunct agent (patients on 1-3 psychotropic medications), indicating that BTA was similarly effective as both a monotherapy and adjunctive therapy.

Does it work better in women than in men?

- There was no statistical difference in efficacy between men (n = 14) and women (n=120)
- Larger studies with a higher number of male participants are warranted.

Future Directions

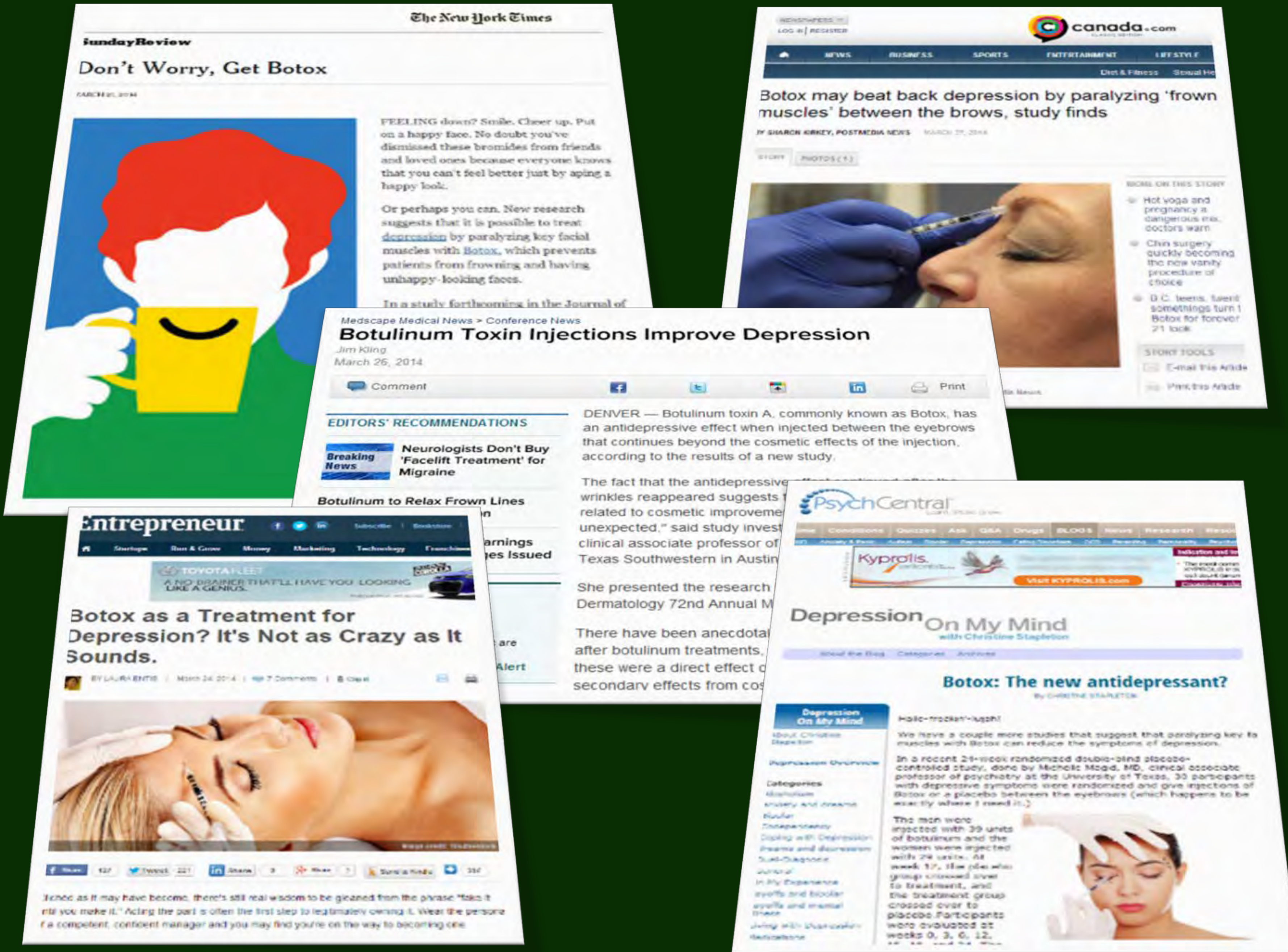
- FMRI imaging before and after treatment of depressives with OBA .
- Phase II Clinical Trial of Botox for Depression at Allergan
- The corrugator muscle is activated in facial expressions of anger, fear and sadness.
- Can OBA help in other disorders where anger and/or fear is prominent?
- Social Anxiety Disorder
- Post-Traumatic Stress Disorder
- Preliminary evidence for OBA helping with both.

Case 1 -Social Anxiety Disorder

- A.R. is a 28 year old Caucasian female with a history of severe social anxiety disorder that had been diagnosed in college. She took no medications. Her brother also suffered from social anxiety disorder, and had become a drug addict. She was an excellent student and went on to receive a masters in chemical engineering. She was currently employed at a large chemical company in Virginia.
- She was extremely good-looking but could not recall the last time that she had dated. She stated that going out on dates caused too much anxiety. Any group interaction with strangers also caused her undue anxiety. In particular, she experienced extreme emotional difficulty with group office meetings. Unfortunately this was a common occurrence in her current work. Just prior to, and during any office meeting with coworkers, emotions of fear and anxiety would flood her mind, to the extent that she could not focus during the meeting, She complained of how her fear of group meetings completely prevented her from advancing in the company, and made her time there very stressful.
- Although she had many ideas to contribute, any group meeting would prevent her from speaking up. She was incapable of any open disagreement with colleagues, or giving a presentation to the group, in spite of her desire to so.
- She received 29 units of botulinum toxin A to her frown muscles. At her 6 week follow up she stated that her anxiety in her workplace had greatly diminished; she was now able to speak up at office meetings without anxiety. She stopped viewing her work as very stressful. At her 3 month follow up she spontaneously related that she had had 3 dates in the past 2 weeks-more than she had had in the past 2 years. She no longer trembled at the thought of dating a stranger. Her social anxieties had greatly diminished and she felt in much better control of her life.

Case 2- PTSD

- 22 y.o., raped at age 14
- Anxiety and fear triggered by dating
- Depression partially controlled by Escitalopram
- Dx of PTSD at age 17
- Remission of both PTSD and Depression after 29 units of Botox to frown region



The New York Times

SundayReview

Don't Worry, Get Botox

FEELING down? Smile. Cheer up. Put on a happy face. No doubt you've dismissed these bromides from friends and loved ones because everyone knows that you can't feel better just by aping a happy look.

Or perhaps you can. New research suggests that it is possible to treat depression by paralyzing key facial muscles with Botox, which prevents patients from frowning and having unhappy-looking faces.

In a study forthcoming in the Journal of

canada.com

Botox may beat back depression by paralyzing 'frown muscles' between the brows, study finds

BY SHARON KIRKEY, POSTMEDIA NEWS

Medscape Medical News > Conference News

Botulinum Toxin Injections Improve Depression

Jim Kling

March 26, 2014

Comment | Print

EDITORS' RECOMMENDATIONS

Breaking News — Neurologists Don't Buy 'Facelift Treatment' for Migraine

Botulinum to Relax Frown Lines

DENVER — Botulinum toxin A, commonly known as Botox, has an antidepressive effect when injected between the eyebrows that continues beyond the cosmetic effects of the injection, according to the results of a new study.

The fact that the antidepressive ... wrinkles reappeared suggests ... related to cosmetic improveme... unexpected," said study invest... clinical associate professor of ... Texas Southwestern in Austin

She presented the research ... Dermatology 72nd Annual M...

There have been anecdotal ... after botulinum treatments, ... these were a direct effect o... secondary effects from cos...

Entrepreneur

Botox as a Treatment for Depression? It's Not as Crazy as It Sounds.

PsychCentral

Depression On My Mind

Botox: The new antidepressant?

Conclusions

- Further clinical trial data is necessary to establish the safety and efficacy of botulinum toxin A in the treatment of depression and other disorders of mental health.

Acknowledgements/Disclosure

- We are grateful to Norman E Rosenthal, Joshua Z. Rosenthal, Khursheed K. Khine, Eduardo Romano, and John Bartko for help with the controlled trial.
- We thank our colleagues Michelle Magid, Tillman Kruger , Jason Reichenberg and Axel Wollmer for meta-analysis and patient data.

- Eric Finzi has received a US patent for treating depression with botulinum toxin. Funding for this trial was provided by Chevy Chase Cosmetic Center.