CLINICAL INQUIRIES

Q/Which injections are effective for lateral epicondylitis?

EVIDENCE-BASED ANSWER

A PLACEBO INJECTIONS actually improve lateral epicondylitis at high rates. No other injections convincingly improve it better than placebo.

Corticosteroid injection is not superior to saline or anesthetic injection (strength of recommendation [SOR] **A**, systematic review of randomized controlled trials [RCTs]). Platelet-rich plasma (PRP) injection is not superior to saline injection (SOR **A**, meta-analysis of RCTs).

Botulinum toxin injection, compared to saline injection, modestly improved pain in lateral epicondylitis, but with

Evidence summary

Neither corticosteroids nor platelet-rich plasma are superior to placebo

A 2014 systematic review of RCTs of nonsurgical treatments for lateral epicondylitis identified 4 studies comparing corticosteroid injections to saline or anesthetic injections.¹ In the first study, investigators followed 64 patients for 6 months. Both groups significantly improved from baseline, but there were no differences in pain or function at 1 or 6 months. Skin discoloration occurred in 2 patients who received lidocaine injection and 1 who received dexamethasone.²

In a second RCT of patients with symptoms for > 4 weeks, 39 participants were randomized to either betamethasone/bupivacaine or bupivacaine-only injections. Inperson follow-up occurred at 4 and 8 weeks and telephone follow-up at 6 months. Both groups statistically improved from baseline to 6 months. No differences were seen between groups in pain or functional improvement at 4, 8, or 26 weeks, but the betamethasone short-term grip-strength weakness (SOR **A**, meta-analysis of RCTs). Prolotherapy injection, compared to saline injection, improved pain at 16-week, but not at 8-week, follow-up (SOR **B**, one small pilot RCT).

Hyaluronic acid injection, compared to saline injection, resulted in a statistically significant pain reduction (6%) but did not achieve the minimum clinically important difference (SOR **B**, single RCT). Autologous blood injection, compared to saline injection, did not improve disability ratings (SOR **B**, one small RCT).

group showed statistically greater improvement on the Visual Analog Scale (VAS) from 8 weeks to the final 6-month telephone follow-up. No functional assessments were reported at 6 months.³

The third RCT of 165 patients with lateral epicondylitis for > 6 weeks evaluated 4 intervention groups: corticosteroid injection with/without physiotherapy and placebo (small-volume saline) injection with/ without physiotherapy. At the end of 1 year, the corticosteroid injection groups had less complete recovery (83% vs 96%; relative risk [RR] = 0.86; 99% CI, 0.75-0.99) and more recurrences (54% vs 12%; RR = 0.23; 99% CI, 0.10-0.51) than the placebo groups.⁴

The fourth RCT randomized 120 patients to either 2 mL lidocaine or 1 mL lidocaine plus 1 mL of triamcinolone. At 1-year follow-up, 57 of 60 lidocaine-injected patients had an excellent recovery and 56 of 60 triamcinolone plus lidocaine patients had an excellent recovery.⁵

■ Platelet-rich plasma. A meta-analysis⁶ of RCTs of PRP vs saline injections included

Brian Vukelic, MD; Rebecca Abbey, MD; Jordan Knox, MD University of Utah Family Medicine Division, Salt Lake City

Alyssa Migdalski, MLIS Schusterman Library, University of Oklahoma, Tulsa

ASSISTANT EDITOR

Richard Guthmann, MD, MPH Advocate Illinois Masonic Family Medicine Residency, Chicago

doi: 10.12788/jfp.0308

5 trials and 276 patients with a mean age of 48 years; duration of follow-up was 2 to 12 months. No significant differences were found between the groups for pain score measured by VAS or the Patient-Rated Tennis Elbow Evaluation (PRTEE)—(standardized mean difference [SMD] = -0.51; 95% CI, -1.32 to -0.30) nor for functional score (SMD = 0.07; 95% CI, -0.46 to 0.33). Two of the trials reported adverse reactions of pain around the injection site: 16% to 20% in the PRP group vs 8% to 15% in the saline group.

Corticosteroids and PRP. A 2013 3-armed RCT⁷ (n = 60) compared 1-time injections of PRP, corticosteroid, and saline for treatment of lateral epicondylitis. Pain was evaluated at 1 and 3 months using the PRTEE. Compared to saline, corticosteroid showed a statistically significant, but not a minimum clinically important, reduction (8% greater improvement) at 1 month but not at 3 months. PRP pain reduction at both 1 and 3 months was not significantly different from placebo. Importantly, a small sample size combined with a high dropout rate (> 70%) limit validity of this study.

Botulinum toxin shows modest pain improvement, but ...

A 2017 meta-analysis⁸ of 4 RCTs (n = 278) compared the effectiveness of botulinum toxin vs saline injection and other nonsurgical treatments for lateral epicondylitis. The studies compared the mean differences in pain relief and hand grip strength in adult patients with lateral epicondylitis symptoms for at least 3 months. Compared with saline injection, botulinum toxin injection significantly reduced pain to a small or medium SMD, at 2 to 4 weeks post injection (SMD = -0.73; 95% CI, -1.29 to -0.17); 8 to12 weeks post injection (SMD = -0.45; 95% CI, -0.74 to -0.15); and 16+ weeks post injection (SMD = -0.54; 95% CI, -0.98 to -0.11). Harm from botulinum toxin was greater than from saline or corticosteroid, with a significant reduction in grip strength at 2 to 4 weeks (SMD = -0.33; 95% CI, -0.59 to -0.08).

Prolotherapy needs further study

A 2008 RCT⁹ of 20 adults with at least 6 months of lateral epicondylitis received

either prolotherapy (1 part 5% sodium morrhuate, 1.5 parts 50% dextrose, 0.5 parts 4% lidocaine, 0.5 parts 0.5% bupivacaine HCl, and 3.5 parts normal saline) injections or 0.9% saline injections at baseline, 4 weeks, and 8 weeks. On a 10-point Likert scale, the prolotherapy group had a lower mean pain score at 16 weeks than the saline injection group (0.5 vs 3.5), but not at 8 weeks (3.3 vs 3.6). This pilot study's results are limited by its small sample size.

Hyaluronic acid improves pain, but not enough

A 2010 double-blind RCT¹⁰ (n = 331) compared hyaluronic acid injection vs saline injection in treatment of lateral epicondylitis in adults with > 3 months of symptoms. Two injections were performed 1 week apart, with follow-up at 30 days and at 1 year after the first injection. VAS score in the hyaluronic acid group, at rest and after grip testing, was significantly different (statistically) than in the placebo group but did not meet criteria for minimum clinically important improvement. Review of the literature showed limited follow-up studies on hyaluronic acid for lateral epicondylitis to confirm this RCT.

Autologous blood has no advantage over placebo

The only RCT of autologous blood compared to saline injections¹¹ included patients with lateral epicondylitis for < 6 months: 10 saline injections vs 9 autologous blood injections. Patient scores on the Disabilities of the Arm, Shoulder, and Hand scale (which measures symptoms from 0 to 100; lower is better) showed no difference but favored the saline injections at 2-month (28 vs 20) and 6-month (20 vs 10) follow-up.

Editor's takeaway

Limiting the evidence review to studies with a placebo comparator clarifies the lack of effectiveness of lateral epicondylitis injections. Neither corticosteroid, platelet-rich plasma, botulinum toxin, prolotherapy, hyaluronic acid, or autologous blood injections have proven superior to saline or anesthetic injections. However, all injections that contained

All injections that contained "placebo" significantly improved lateral epicondylitis.

STATEMENT OF OWNERSHIP

"placebo" significantly improved lateral epicondylitis. JFP

References

- 1. Sims S, Miller K, Elfar J, et al. Non-surgical treatment of lateral epicondylitis: a systematic review of randomized controlled trials. Hand (NY). 2014;9:419-446. doi: 10.1007/s11552-014-9642-x
- 2. Lindenhovius A, Henket M, Gilligan BP, et al. Injection of dexamethasone versus placebo for lateral elbow pain: a prospec-tive, double-blind, randomized clinical trial. J Hand Surg Am. 2008;33:909-919. doi: 10.1016/j.jhsa.2008.02.004
- 3. Newcomer KL, Laskowski ER, Idank DM, et al. Corticosteroid injection in early treatment of lateral epicondylitis. Clin I Sport Med. 2001;11:214-222. doi: 10.1097/00042752-200110000-00002
- 4. Coombes BK, Bisset L, Brooks P, et al. Effect of corticosteroid injection, physiotherapy, or both on clinical outcomes in patients with unilateral lateral epicondylalgia: a randomized controlled trial. IAMA. 2013;309:461-469. doi: 10.1001/jama.2013.129
- 5. Altay T, Gunal I, Ozturk H. Local injection treatment for lateral epicondylitis. Clin Orthop Relat Res. 2002;398:127-130.
- 6. Simental-Mendía M. Vilchez-Cavazos F. Álvarez-Villalobos N. et al. Clinical efficacy of platelet-rich plasma in the treatment of lateral epicondylitis: a systematic review and meta-analysis of randomized placebo-controlled clinical trials. Clin Rheumatol. 2020;39:2255-2265. doi: 10.1007/s10067-020-05000-y
- 7. Krogh T, Fredberg U, Stengaard-Pedersen K, et al. Treatment of lateral epicondylitis with platelet-rich-plasma, glucocorticoid, or saline: a randomized, double-blind, placebo-controlled trial. Am J Sports Med. 2013;41:625-635. doi:10.1177/0363546512472975
- 8. Lin Y. Wu W. Hsu Y. et al. Comparative effectiveness of botulinum toxin versus non-surgical treatments for treating lateral epicondylitis: a systematic review and meta-analysis. *Člin Rehabil*. 2017;32:131-145. doi:10.1177/0269215517702517
- 9. Scarpone M, Rabago DP, Zgierska A, et al. The efficacy of prolotherapy for lateral epicondylosis: a pilot study. Clin J Sports Med. 2008;18:248-254. doi: 10.1097/JSM.0b013e318170fc87
- 10. Petrella R, Cogliano A, Decaria J, et al. Management of tennis elbow with sodium hyaluronate periarticular injections. Sports Med Arthrosc Rehabil Ther Technol. 2010;2:4. doi: 10.1186/ 1758-2555-2-4
- 11. Wolf JM, Ozer K, Scott F, et al. Comparison of autologous blood, corticosteroid, and saline injection in the treatment of lateral epicondylitis: a prospective, randomized, controlled multicenter study. J Hand Surg Am. 2011;36:1269-1272. doi: 10.1016/ j.jhsa.2011.05.014

WE WANT TO HEAR **FROM YOU!**

Have a comment on an article, editorial, or department? You can send it by:

1. E-MAIL: jfp.eic@gmail.com

2. FAX: 973-206-9251 or

3. MAIL: The Journal of Family Practice, 7 Century Drive, Suite 302, Parsippany, NJ 07054



LETTERS SHOULD BE 200 WORDS OR LESS. THEY WILL BE EDITED PRIOR TO PUBLICATION.

The local	Title	Temix Practice	2. Public	cation	Numb	er		-	_	3. Filing	Date
. ne Journi	nev		5. Num	9 ser of	4 Issues	Pu	blished	0 LAnnua	9 ily	6. Annua	I Subscription Price
Nonthly (except	con	bined January/February and July/August issues)	10							(# any \$169	9
. Complete Ma Frontline Medici	t, city, county, state, and 2/P+4*9 (, Morris County, NJ 07054-4509						Contact Person Jared Sonners				
3. Complete Ma	uiling	Address of Headquarters or General Business Office of Pr	ublisher	(Not p	rister)	_				973-206-	-8091
7 Century D	rive,	Suite 302, Parsippany, NJ 07054-4609									
9. Full Names a Publisher (Nam	nd C e an	complete Mailing Addresses of Publisher, Editor, and Mana d complete mailing address)	iging Ed	tor (D	o not a	eev	e blani	0			
Geoff Watkin	s, 7	Century Drive, Suite 302, Parsippany, NJ 07054-460	99								
iditor (Name ar Marya Ostrov	norica Niski	mplete mailing address) , 7 Century Drive, Suite 302, Parsippany, NJ 07054-4	4609								
Managing Edito	e (N	une and complete mailing address)									
N/A 0. Owner (Do	not k	save blank. If the publication is owned by a corporation, giv	e the na	me ar	id add	ne si	s of the	corpor	ation	immedial	ely followed by the
names and names and each individ	addh addh lual e	esses of all stockholders owning or holding 1 percent or m esses of the individual owners. If owned by a pertnership o wner. If the publication is published by a nonprofit organiz.	ore of th ir other i ation, gi	e total minco re its r	porate ame a	nt o ad f and	f stock im, giv addres	e its na is.)	owne ime a	d by a co nd addre	rporation, give the ss as well as those of
ull Name	-	ommunications for	Compl	ite Ma	illing A	Add	ress	Darri		- NI 07	054,4600
and the media	an c	cininencadoris inc.	7 cent	uryb	1146, 5	Sun	10 302	, rais	ppar	iy, na 07	034-4605
	_										
1. Known Bon Other Secu	dhole	sers, Mongagees, and Other Security Holders Owning or H If none, check box.	rolding 1	Perci	None	vior b	e of To	tel Amo	ount o	T Bonds,	Montgages, or
uiname	_		compl	ice Ma	ang /	-dd	e 1955		_		
						_					
12. Tax Status (For	completion by nonprofit organizations authorized to mail at	nonprof	it rates	i) (Che	eck.	one)				
The purpose	cha	action, and nonprofit status of this organization and the exe nged During Preceding 12 Months	mpt stal	us for	feciera	l in	come to	ax purp	oses		
S Form 3526-	R, J	a using Proceeding 12 Months (Publisher must submit exp dy 2014 (Page 1 of 4 (See instructions page 4)) PSN: 7530	-09-000	ar chi 8855	PRI	an I IVA	CY NO	TICE	/ See o	ur privacy	policy on www.uspe.c
cation Title Iournal of Fam						_	let	ue Del	te for	Circulati	on Data Below
Journal of Family Practice Extent and Nature of Circulation							Se	ptemb	er 20	21	
Extent and Na	ture	of Circulation					Av	erage ch Iss	No. C	21 Copies uring	No. Copies of Sing Issue Published
Extent and Na	ture ture	of Circulation Copies (Net press run)					Se Av Ea Pr	erage ch Iss ecedin 10	er 20 No. (ue Di g 12 4,20	21 Copies uring Months 08	No. Copies of Sing Issue Published Nearest to Filing 0 104,029
Extent and Na	ture r of	and Circulation Occess (Mel press run) Codes (Mel press run) Occused (Codes) Palotimeousered Mail Buberciptions at executed from recipient, part public public policy, and excit enguests from recipient, part public public policy, and excit enguests and excit public in policy and excit.enguests and excit	ated on i eting, ar ominal r bange ci	PS Fo Id Inte Inte su Inte su	rm 35- rnet biscript	41. 6ion	Se Av Ea Pr	erage ch Iss ecedin 10	er 20 No. (us Di g 12 14,2(1,99	21 Coples uring Months 08 0	No. Copies of Sing Issue Published Nearest to Filing D 104,029 51,975
Extent and Na . Total Numbe . Legitimate Paid and/or Requested Distribution (By mail and	(1)	adole of Circulation Copies (Intramentary) Copies (Intramentary) Could County Parolineousetta Mail Subscriptions and county County Parolineousetta Mail Subscriptions requests from recipient, pairt Justorphilos including in anglayer mequatis Advertismer parol county, and excellent Pocounty Parolineousetta Mail Subscriptions exaiting in County Parolineousetta Mail Subscriptions including requests from recipient pairt autorphilos including in County Parolineousetta Mail Subscriptions exaiting requests from recipient pairt autorphilos including requests from recipient pairt autorphilos in including requests from recipient pairt autorphilos in including in major recipient autorphilose in including	ited on l eting, ar ominal r hange or n PS Fo eting, ar ominal r hange or	PS Fo d Inte apies J m 35 d Inte ate su apies J	rm 35- rnet bacripi 41. rnet bacripi	41. 6ion	Av Ea Pro	erage ch Iss seedin 10 5:	er 20 No. 0 g 12 44,20 1,99	21 Coples uring Months 08 0	No. Copies of Sing Issue Published Nearest to Filing 104,029 51,975
Extent and Na . Total Numbe Paid and/or Requested Distribution (By mail and outside the mail	(1) (2) (3)	adole of Circulation Copies (Mel press run) Copies (Copier) PulloTecuested Mail Subscriptions st include direct water imposit from recipient, lateriarius requests from recipient, pull subscriptions relation pulloyer insupuel, advertismin z prod copies, and excli- im-County PueltRecuested Mail Subscriptions stated module Advertismin z prod copies, and excli- michaet and advertismin z prod copies, and excli- michaet advertismin z prod copies, and excli- minipative requests. Advertismin z prod copies, and excli- satismic Through Destima and Contrars. Street Venders, and Seise Through Chesters and Contrars.	ated on I eting, ar ominal r hange of eting, an ominal r hange of Counter ide USP	PS Fo of Inte operations of Inte stering Inter stering ST	rm 35- rnet bscripr 41. 41.	41. 601	Se Av Pro	erage ch Iss ocedin 10 5:	er 20 No. (g 12 4,2(1,99	21 Copies uring Months 08 0	No. Caples of Sin; Issue Published Nearest to Filing to 104,029 51,975 - -
Extent and Na Total Numbe Legtimate Paid and/or Requested Distribution (By mail and outside the mail)	r of (1) (2) (3) (4)	adole of Circulation Copies (Met preserva) Outside Copyly Paul/Requested Mail Subscriptions star requests from recipient, part studentistice in the mapper requests durities in profice and and and impound in the subscriptions stated on impound the subscription of the subscriptions stated impound in the subscription of the subscriptions stated impound in the subscription in the subscriptions stated in County Paul/Requested Mail Subscriptions stated in County Paul/Requested Mail Subscriptions stated in County Paul/Requested Mail Subscriptions stated subscriptions and subscriptions request the mapper request, and statements and county and sales. In those that of Requested Subscriptions that and Requested Copers Durithdent by Other Mail Cosess 1 Requested Copers Durithdent by Other Mail Cosess 1 (a) Figure State Mail N	ated on I eting, ar ominal / hange of eting, ar ominal / hange of Counter ide USP	PS Fo id Inte site su pples.j id Inte site su sples.j S ^{III} the U	rm 35/ rnet boorip 41. rnet boorip SPS	41. 60n	Se Av Pr	erage chissi codin 10 5:	er 20 No. (ue D g 12 4,2(1,99 -	21 Coples uring Months X8 0	No. Copies of Sin Issue Published Nearest to Filing t 104,029 51,975
Extent and Na . Total Numbe Paid and/or Requested Distribution (By mail and cutside the mail)	r of (1) (2) (3) (4)	addie of Circulation Copies (Mit preserva) Copies (Mit preserva) Copies (Mit preserva) Copies (Mit preserva) Copies (Mit preserva) Copies (Mit preserva) Copies (Mit preserva) Mit Copies (Mit preserva)	ated on 1 eting, ar ange ci n PS Fc annage ci annage ci counter Counter Through	PS Fo d Inte spies.j m 35 d Inte ste su spies.j S ^{III} the U	rm 35/ rnet booripr 41. rnet booripr SPS	41. 60n	ي ج ا ب ب ب ب ب ب ب ب ب ب ب ب ب ب ب ب ب ب	erage chission international i	er 20 No. (up Di g 12 4, 20 1,99	21 Copies uring Months)8 0	No. Copies of Sin Issue Published Nearest to Filing I 104,029 51,975
Extent and Na . Total Numbe . Legilimate Paid and/or Paid and/or Requested Distribution (B) mail and cutside the mail) . Total Paid ar	r of (1) (2) (3) (4)	addie of Circulation Copies (Mit preserve) Copies (Mit preserve) Copies (Mit preserve) Copies (Mit preserve) Copies (Mit preserve) Copies (Mit preserve) Mitorial (Mitorial Mitorial Mitorial Regested Copies Distributed Differ Mitorial Copies Mitorial (Mitorial Preserve) Mitorial (Mitorial Preser	ated on i eting, ar angle c angle c angle c counter counter through p orm 354 loced by	PS Fee of Inte su aples.) of Inte aples.) S ^{III} the U	rm 35- rrnet boorijp 411. rrnet boorijp SPS	41. 6ion	Se Average and Ave	erage chission 10 5: 5:	er 20 No. (ue Di 9 12 4,20 1,99 - - - 1,99 2,09	Copies uring Months 38 0 0	No. Copies of Sing Issue Published Nourest to Filing 2 104/029 51,975 - - - 51,975 51,975 51,933
Extent and Na . Total Number . Legtimate Paid and/or Requested Distribution (g)/ mail and outside tote mail() . Total Paid an	(1) (2) (3) (4)	adde of Circulation Copies (Met preserve) Copies (Met preserve) Copies (Met preserve) Copies (Met preserve) Copies (Met preserve) Copies (Met preserve) Copies (Met and Preserve) Methods effect (Methoder) and Copies (Methoder Methode (Methoder) and Copies (Methoder Methoder (Methoder) and Copies (Methoder Methoder) Methoder (Methoder) and Copies (Methoder Methoder) Methoder (Methoder) Sales Through Dealers and Copies (Methoder Methoder) Requested Copies Duithdeatby Other Methoder Sales Through Dealers and Copies (Methoder) Requested Copies Duithdeatby Other Methoder Methoder (Copies Duithdeatby Other Methoder) Requested Copies Duithdeatby Other Methoder Sales Copies Duithdeatby Other Methoder Sales Copies Copies Salest on 9 Jar A	ated on 1 being, an annhai / / n PS Fer annhai / / annge cu counter co	PS Fo of Inte ste su spies.) of Inte ste su spies.) ST the U	rm 35- rnet bscript 41. SPS SPS	41. 6ion	it,	erage chission condition of the chission of the chission of the condition of the chission of t	er 20 No. (ue D g 12 44,2(1,99 - - - - - - - - - - - - -	Copies uring Months 38 0 0	No. Copies of Binn Issue Published Neurost for Filing (104,027) 51,975 - - 51,975 51,975 51,933
Extent and Na Total Number Legtimale Paid and/or Requested Distribution outside the mail Non- requested Distribution (8) mail and (8) mail and (8) mail (8) mail	r of (1) (2) (3) (4) (2)	adde of Circulation Copies (Mit preserve) Copies (Mit preserve) Copies (Mit preserve) Copies (Mit preserve) Copies (Mit preserve) Copies (Mit preserve) Mitorial (Mitorial Interpretation (Mitorial Mitorial (Mitorial Interpretation (Mitorial Mitorial Mitorial Interpretation (Mitorial Regested Copies Dutitude) Other Mitorial Copies Mitorial Mitorial Interpretation (Mitorial Mitorial Interpretation (Mitorial Interpretation Mitorial Mitorial Interpretation (Mitorial Interpretation Mitorial Interpretation (Mitorial Interpretation Mitorial Interpretation (Mitorial Interpretation Mitorial Interpretation (Mitorial Interpretation) Mitorial Interpretation) Mitorial Interpretation (Mitorial Interpretation) Mitorial Interpretation (Mitorial Interpretation) Mitorial Interpretation (Mitorial Interpretation) Mitorial Interpretation (Mitorial Interpretation) Mitorial Interpretation) Mitorial Interpretation (Mitorial	ated on 1 teting, ar n PS For ting, ar hange ci counter Counter Counter Through 7 Through 7 Through 7 S41 (inc	PS Fo d inte sples.j m 35 ste sus sples.j S T (ince i obtain lude s inm, t inm, t	rm 35- rnet bscrip 41. rnet bscrip 41. spsrip scrip scrip scrip scrip bscrip bscrip scrip	41. 6ion	ري بر بر بر بر بر بر بر	ste bank	er 20 No. G g 12 44,20 1,99 - - - 1,99 2,09 -	Copies uring 000000000000000000000000000000000000	No. Capito of Sin No. Capito of Market No. 2014 104,029 51,975 - - - - - - - - - - - - - - - - - - -
Extent and Na Total Number Production Production Production (By mail the road) Total Paid an Total Paid an Neon- requested Distribution (By mail and cutstie be road)	r of (1) (2) (4) (1) (2) (3) (3)	addie of Circulation Copies (<i>Ihti press run</i>) Copies (<i>Ihti press run</i>) Fourth PuictRepareted Mail Bubarcipies including anglager meujatis downtiamer (<i>prod copies</i> , and <i>each</i> <i>Ihtighter meujatis</i>) <i>Ihtighter anglaget including</i> Copies (<i>Ihtighter anglaget including</i>) Repareted Copies Paid & Repert Vendos I. Sales, and Repert Vendos I. Sales, and Copies Paid & Repert Vendos I. Sales, and Repert Vendos I.	ated on i teting, ar primary i n PS For Counterr Counterr Counterr Counterr S41 (incough S41 (incough S4	PS Fo Inte su sples.) of Inte sples.) of Inte sples.) S ^m I (inco <i>s</i> pre- solution sples.) Classi ess of	rm 35- rret boorip 1 41. rret boorip boorip 1 8PS serve serve tota form	41. 6ion		strenge erage ocedin 10 5: 5: 5:	er 20 No. (ue D g 12 4,2(1,99 - - - - - - - - -	221 Copies uring 08 0 0 0 4	No. Capies of Bini Issue Published Neurosci 104,022 51,975 - - 51,975 51,975 51,975 - - -
Extent and Na Total Number Pad ander Pad ander Pad ander Pad ander Pad ander Pad ander Pad ander Pad ander Strate Distribution der Strate Stra	r of (1) (2) (3) (4) (2) (3) (4) (2) (3) (4)	addie of Circulation Copies (Mel press nun) Outside Copies (Mel press nun) Outside Occurry Pulicifieousteeld Mail Subscriptions st requests from recipient, pairt subscriptions, betwends requests from recipient, pairt subscriptions, stelled of the County Pulicifieousteeld Mail Subscriptions stelled on requests from recipient, pairt subscriptions, stelled of the County Pulicifieousteeld Mail Subscriptions stelled on requests from recipient, pairt subscriptions, stelled of temployer frowerski and externs in Steller steller and extern requests from recipient pairt subscriptions inclusion requests from recipient pairt subscriptions inclusion requests from recipient pairt subscriptions inclusion Sales Through Destins and Carters. Steller Venders, Requested Counted on Pairt and Oracle and exit Requested Counted Carters Steller Venders, Requested Counted Carters and Recipients and exit in County Norrequested Operational Advections of the subscription State and requested Distributed Theory In County Norrequested Copies Stated on PS From 35 requests and requests including a sociation request in County Norrequested Copies Stated on PS From 30 in Theory Table Mail Carters and the succession In County Norrequested Copies Stated on PS From 30 in Theory Table Mail Carters and the succession Norrequested Copies Distributed Through the USP It Mail (ag., FracCopies Distributed Charles Copies Intervention Staters and St	ated on 1 eting, ar primary of the stange of	PS Fo d'Inte ste su spies.j S ^m the U 1 (incl s pre sobtai inn, 1 inned 1 Classi ess of kup s	m 35- rnet borip 1 41. rnet borip borip SPS ses ses tom tom tom	41. 6ion	ري بر بر بر بر بر بر	5: 5: 5:	er 20 No. (ue D g 12 4,2(1,99 - - - - - - - - - - - - -	Copies uring 38 0 0 4	No. Capies of Bin Issue Published Necessaria 104,029 51,975 - - - 51,975 51,975 51,933 - -
Extent and Na . Total Number . Legismate Pad and/or Distribution (By mail and the mail) . Total Paid an . Non- . requested Distribution (By mail and . Non- . requested Distribution (By mail and . Non- . requested Distribution . State State . State . State State . S	r of (1) (2) (3) (4) (2) (3) (4) (2) (3) (4)	addie of Circulation Copies (Met press run) Copies (Met press run) Copies (Copier) Publisheouseded Mail Subscriptions du requests from recipient, paid subscriptions, telemotic requests from recipient, paid subscriptions, stated mitogener requests and experiments of the subscriptions mitogener requests and experiments of the subscriptions manager requests during as proceedings, and exit in-County Publisheouseted Mail Subscriptions dated on manager requests during as processes, and exit subscriptions and and a subscriptions of the subscriptions subscriptions and the subscription of the subscriptions dates Through Destins and Counters, Street Vendors, Requested Counter Subscriptions and exit Bales Through Destins and Counters Stated on PS Feed Requested Counters, Bland of the subscription and the subscription of the subscription and the subscription of the subscription of the subscription of the subscription of the subscription of the subscription of the subscription of the bit Subscription of the subscription of the subscription bit Subscription of the subscription of the subscription of the subscription of the subscription of the subscription of the Mail and and additional of the subscription of the subscription of the Nonrequested Copies Distributed Dutise the Mail Mail Nonrequested Copies Distributed Dutise the Mail Mail Mail Ad	ated on in eting, an ange or eting, at ange or counter through Through orm 354 funced by through throu	PS Fo of Inte su poles.) m 35 of Inte ste su fill inte second second classic ess of classic ess of kup s	rm 35- rnet bacripi 1 41. rnet seripi seripi seripi tom tes of ample tom tom	60n		strenge chission coolin 10 5: 5: 5: 5:	er 200 No. (ue Dr g 12 44,20 1,99 - - - - - - - - - - - - -	221 Copies Months 38 0 0 0 4	No. Capies of Binn Issue Published Neurosen 104,029 51,975 51,975 51,975 51,933 - - - - 51,933
Extent and Na Total Number Legismale Page angly Distribution Strongen Total Paid and Strongen Total Number Non- requested Distribution Total Paid and Strongen Total Number Strongen	(1) (2) (3) (4) (2) (3) (4) (2) (3) (4) (2) (3) (4) (3) (4) (3) (4) (3) (4) (3) (4) (3) (4) (3) (4) (3) (4) (4) (4) (4) (4) (4) (4) (4) (4) (4	addie of Circulation Copies (Met press nut) Copies (Met press nut) Copies (Copier) Paid/Requested Mail Subscriptons du include drect waterness if on orcepant, baienda include in the waterness if on orcepant, baienda baies in thome proget for on orcepant, baienda baies in thome or baiend in the second baies. Introduct hard in Reserved Data in the second Respective Copies Data Chaines data on the second baies and other baies and Copies Stated on PS (m), do, and the second or or parts and courses and baies and regrets including a sociation regeets in baies and other in the sociation of the ourced baies and regrets including a sociation regeets in baies and regrets including a sociation regeets in the social in the social in the social in the social baies and regrets including a sociation regeets in the social in the social in the social in the social baies and regrets in baies and regrets baies and the social baies and regrets in baies and the social in the social baies and regrets in the social in the socia	ated on in eting, any annual is n PS Foc forg, at your annual is ange of the second by orm 3.5541 (second by orm 3.5541 (second by or of the second by of the second by of the second by of the second by of the second by of the second by of the second by of the second by of the second by of the second by of the second by of the second by of the second by of the second by of the secon	PS Fo d inte supers pres pres pres spres the U f (ince spres class item, t class class item, t kup s	rm 35- rnet bacrip 1 1 41. rnet bacrip bacrip 1 5 SPS bacrip 1 5 SPS bacrip 1 5 SPS bacrip 1 1 7 5 6 1 1 7 6 6 1 1 7 6 6	60n	ري بر در در در در	sceeding of the second	er 20 No. (ue Di g 12 44,20 1,99 - - - 1,99 2,09 - - - 2,09 44,00	221 Copies Months 308 0 0 0 4 4	No. Capies of Binn Issue Publishing Neuroscience 10, 104,029 51,975 51,975 51,975 51,933 - - - 51,933 103,908
Extent and Name Total Number Legismale Page and/or Distriction Total Pad as Distriction Total Pad as Distriction Total Pad ad Total Num	(1) (2) (3) (4) (2) (3) (4) (2) (3) (4) (2) (3) (4) (3) (4) (3) (4) (3) (4) (3) (4) (3) (3) (4) (3) (4) (3) (3) (3) (4) (3) (4) (3) (4) (3) (4) (3) (4) (4) (3) (4) (4) (3) (4) (4) (4) (4) (4) (4) (4) (4) (4) (4	adde of Circulation Copies (Met press nut) Copies (Met press nut) Copies (Copier) Pail/Requested Mail Subscriptions due trequests from recipient, paid subscriptions stated mighter insuest. A contraction of the subscriptions in County Pail/Requested Mail Subscriptions stated in County Pail/Requested Mail Subscriptions stated in County Pail/Requested Mail Subscriptions stated mighter insuest. A contract is provided in the majour requests downter in sport Counts, and eccl Sales Through Destins and Counts. States Hereit Requested Coges Dublished Reguest Data Requested Coges Dublished Coges States and Pail Requested Coges Dublished Coges States and Pail Double and requests including association request, in on Losses at directions. It is and direct expected the sales and requests including association request, and built and regrets including association request, and humoregrets coges State and P F and assist and contract and and and Nonrequested Cogies Distributed Through the USPS Is and in travel of Standord Mail" or Palsage Services ratio and association (Sum of 150 (1), (2), (3) and (4) In Count 15c and effect totad (Stee Instructors to Publishers H, (jege #2))	ated on 1 telong, an n PS Fcing, at angre ci commark of the commark of the commar	PS Fo d Inte suples.j m 35 d Inte suples.j S ^{III} the U 1 (inco s pre obbiai Unde s ison d Classi ess of kup s	m 35 rret bacrip 41. rret bacrip bacrip service service tom tom tom tom tom tom tom tom	441. 60m		scending ch issue coeding 10 5: 5: 5: 5: 5: 10	er 200 No. G up Di g 12 4,20 1,99 - - - - 2,09 44,00 - - - - - - - - - - - - -	221 Copies Mining Monthis D8 0 0 0 4 4	No. Capies of Binn Issues to Filling Normal To Filling States of the States States of States of States States of States of States States of States of States of States States of States of States of States of States States of States of States of States of States States of States of States of States of States of States States of States of State
Extent and Name Total Number Legitime Records Distriction Costs Distriction Total Part and Total Nume Total District Copes and Total District Copes and Total Copes and Total (Sum	(1) (2) (3) (4) (2) (3) (4) (2) (3) (4) (2) (3) (4) (2) (3) (4) (3) (4) (3) (4) (3) (4) (3) (4) (3) (4) (3) (4) (3) (4) (4) (4) (5) (4) (5) (5) (6) (6) (7) (7) (7) (7) (7) (7) (7) (7) (7) (7	adde of Circulation Copies (Mit press run) Coticide Copier Parison request for mediation request for requests from recipient, paris studentistics and en- requests from recipient, paris studentistics and en- diculate different studentistics and en- sites. Through Desters and Carriers, Breef Vendors, Bales, Through Desters and Carriers, Breef Vendors, Requested Copies Durithated by Other Misl Classes 1 Requested Copies Durithated by Other Misl Classes 1 Destude Copies Durithated by Other Misl Classes 1 Destude Copies Durithated by Other Misl Classes 1 Destude and requests including association request, and and and requests including association request, and able ablests including association request, and able ablests and requests including association request, and able ablests and ablest ablests and ablest and ablest abl	ated on in storg, ar ange or ontad / of ange or ontad / of ange or counter counter of a prem mes obli- tion of a prem tion of a premtion of a p	PS Fod International Internati	rm 355 service 41 rnet bacripe 1 SPS unde mount ned ample trong	41. 60m		stemble erage chissis coedin 10 5: 5: 5: 5: 5: 10 10	er 200 No. 6 up Di 12 4,20 1,99 - - - - - - - - - - - - -	221 Copies uring Months 38 0 0 0 4 4 4 4 4 4	No. Capito of Bin Iteration of Bin Normal To Filling 104,029 51,975 51,975 51,933 - - 51,933 103,908 1221 104,029
Extent and Na Total Number Lagrande Angemet	(1) (2) (3) (4) (4) (2) (3) (4) (4) (4) (4) (4) (4) (4) (4) (4) (4	adde of Circulation Copies (Mit press run) Copies (Mit press run) Mitopolitika (Mitopolitika) Mitopolitika (Mitopolitika) Mitopolitika (Mitopolitika) Mitopolitika (Mitopolitika) Mitopolitika (Mitopolitika) Mitopolitika (Mitopolitika) Mitopolitika (Mitopolitika) Mitopolitika (Mitopolitika) Mitopolitika (Mitopolitika) Mitopolitika Mit	alad on in PS For any of the second s	PS Fo interview mm 35 id interview mm 35 id id interview mm 35 id id id interview mm 35 id i	rm 35- rrret 6sorip 41. rrret SPS born born red ample suit form lands, lands,	441. 60m		steel set	er 20 No. G up D g 12 H4,20 - - - - - - - - - - - - -	221 Copies uring Months 38 0 0 0 4 4 4 4 4 4 4 4 4 4 4 4 4 6 6	No. Capito et Bin No. Capito et Bin No. Capito et Bin No. Capito et Bin 104,029 51,975 51,975 51,933 - - - - - - - - - - - - -
Extent and Na Total Number Pagemete Pagemet	(1) (2) (3) (4) (4) (2) (3) (4) (4) (4) (4) (4) (4) (4) (4) (4) (4	adole of Circulation copies (Mit press run) Requested Copies Distribution (Mit press Mit press run) Copies (Mit pr	ated on in PS Fig. and a second secon	PS Fo of inste spies.j	ic cop	41. 607	See	speemb wrage ch issi into seedin i i i i i i i i i i i i i i i i i	er 200 No. 0. Hore to the pro- Hore to the pr	21 Copies Months 38 0 0 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4	No. Capito of Bing Internet to Filling (Internet to Filling (Int
Extent and Na . Total Number . Total Number . Sources . Total Pard as . Non- . Total Pard as . Total Pard as . Non- . Total Pard as . Total Pard as . Total Pard as 	(1) (2) (3) (4) (4) (4) (2) (3) (4) (4) (4) (4) (4) (4) (4) (4) (4) (4	adole of Circulation copies (Mit press run) Coticide County PailofRequested Mail Subscriptons takenow provide from recipient, paid subscriptons recipient provide from recipient, paid subscriptons stated provide from recipient, paid subscriptons provide from recipient and from recipient, paid provide from recipient and from recipient, paid provide from recipient and from recipient, paid provide from recipient, paid subscriptons paid and regulation (Sum of 156 (1), (2), (3), (3), (4), (4), (4) provide from recipient, paid subscriptons paid and regulation (Sum of 156 (1), (2), (3), (4), (4), (4), (4), (4), (4), (4), (4	ated on n esting, an in PIS Feing, at a command is an angle of counter of the USP or 3544 (dime of the use of the use of the use of the use of the use of the use of the use of the use of the use of the use of the of the use of the use of the use of the use of the use of the use of the of the use of the use	PS Fo d / inte supers.) mm 35 Sm the supers.) Sm the U spies.) Sm the Spies.) Sm the Spies.)	In 35- In a sport of the sport	441. 6007	Step 1	steend erage ch issue 10 5 5 5 5 5 5 5 5 5 5 5 5 5	er 20 00 No. C. 10 UB DI	21 Copies uning Monthus 8 0 0 0 0 4 4 4 4 4 4 4 4 4 4 4 5 6 5 10 10 10 10 10 10 10 10 10 10	No. Capito of Bing Intervent to Filling Intervent to Filling Statement to Filling 104,029 51,975 51,975 51,975 51,975 51,975 51,975 51,975 51,975 51,975 51,975 51,975 51,933 103,908 121 104,029 50.0% Circulation theshed on thethed on thethed
Extent and Na . Total Number Langemede Langemede Langemede Langemede Destruction (d) mail Destruction (d) mail (d) ma	(1) (2) (3) (4) (4) (2) (3) (4) (4) (4) (4) (4) (4) (4) (4) (4) (4	adole of Circulation copies (Mit press run) Requested Copies Durbitation (Mit press run) Copies (Mit press run) Copies (Mit press run) Requested Copies Durbitation (Mit press run) Copies (Mit press run) Cop	ated on in terting, and in PS FL manage or manage or counter or a prema of the USP Through or m 364 for end of the e	PS Food Internet of Internet SP The Supervised SP The U	International antiple	ies an	Step 1	steend erage ch issue 10 5: 5: 5: 5: 5: 5: 5: 5: 5: 5: 5: 5: 5:	er 200 No. 6. Un D D Un D D D D D UN D D D D D UN D D D D D D D D D D D D D D D D D D D	21 Copies of the second secon	No. Capiti of Bing Intervent to Filling Intervent to Filling Statement to Filling Statement to Filling Statement to Filling Statement to Filling Statement Statemen
Extent and Na . Total Number Langemede ander ander Received Distribution (f) outside the musical . Non- internation (f) . Total Pard au . Non- internation (f) . Total Pard au . Non- . Total Pard au . Total Non- . Total N	(1) (1) (2) (3) (4) (4) (4) (4) (4) (4) (4) (4) (4) (4	addee of Circulation copies (Mit press run) Requested Copies Durbinder (Mit press run) Requested Copies Durbinder (Mit press run) Requested Copies Durbinder (Mit press run) Mit press run) Copies (Mit press run) Requested Copies Durbinder (Mit press run) Mit press run) Mit press run (Mit press run) Mit press run) Requested Copies Durbinder (Mit press run) Mit press run) Mit press run (Mit press run) Mit press run) Mit press run (Mit press run) Mit press run) Mit press run (Mit press run) Mit press run) Mit press run (Mit press run) Mit press run) Mit press run (Mit press run) Mit press run) Mit press run (Mit press run) Mit press run) Mit press run (Mit press run) Mit press run) Mit press run (Mit press run) Mit press run) Mit press run (Mit press run) Mit press run) Mit press run (Mit press run) Mit press run) Mit press run (Mit press run) Mit press run (Mit press run) Mit press run) Mit press run (Mit press run) Mit press run) Mit press run (Mit press run) Mit press run) Mit press run (Mit press run) Mit press r	ated on in tetrog, and manage or manage o	PS Food Jinks of Jinks sples; j the U sples; j the U sples; j shinks sples; j sples; j	In 35- rinet bearip 41 rinet bearip bearin bearip bearip bearip bearip bearip bearip bearip bearip bearip bearip bearip bearip bearip bearip bearip bearip bearip bearip bearip bearin bear	607 607	step b step b	steen line 1 see 1 se	er 200 No. c. No. c. V. J. V.	21 Copies Microbis Microbis 0 0 0 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4	No. Caption of Bing teachers of the process of the proces
Extent and Na Total Number Pada Inder Pada Inder P	(1) (1) (2) (3) (4) (4) (1) (2) (3) (4) (4) (1) (1) (2) (2) (3) (4) (4) (1) (2) (2) (3) (4) (4) (4) (2) (2) (2) (3) (4) (4) (4) (4) (4) (4) (4) (4) (4) (4	addee of Circulation copies (Mit press run) Cotisie (County Pars/Requested Mai Subscriptons ta production decision request for necession between requests from recipient; puid subscriptons stated states, and Cher Pars and Cherners, Street Vendors; Requested Coreals Durithouted by Other Mai Classes requests and requests including association request; no requests and requests for colleges, and recipient and requests including association request; no colleges, request are requests for the state on P BF and requests including association request; no states and requests including association states and requests including association states and requests including association states and requests states and requests including association states and re	ated on in tetrog, and minimal / manage or another of tetrog and another of a preme of a preme d la USP manage of a preme d la USP for a preme d	SS 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5	In 3-5- rinet descripe 41. rinet descripe 41. special second ampale descripe bescripe bescripe ampale descripe bescr	441. 6007	skip I skip I skip I skip I Average	steer seter s	er 20 No. 6. No. 6. De Di	4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4	No. Capito of Single Internet for Filing (Internet for Filing (

GM/SVP Operations

I certify that all information furnished on this form is true and complete. I understand that anyone who furnishes false or or who centils material or information requested on the form may be subject to criminal sandions (including fines and ins including only certailises).

09/29/21