Role of Intervventional Therapies for Migraine and Headache: Onabotulinum Toxin A, Stimulators, and Nerve Blocks

Moderated by David Dodick, MD

Discussants: Sheena K. Aurora, MD; Peter Goadsby, MD, PhD; Stephen Silberstein, MD

DR. DODICK: Welcome to this roundtable discussion entitled “Role of interventional therapies for migraine and headache: onabotulinum toxin A, stimulators, and nerve blocks.” Once a purely cognitive subspecialty, procedural clinics are today, I think, commonplace in headache medicine practices around the country, where injectable treatments and peripheral nerve stimulation have emerged as potentially viable tools in the management of patients with a variety of primary headache disorders. Today, we’ve assembled a panel of international experts to discuss the role of extracranial nerve blocks, nerve stimulation, and onabotulinum toxin A in headache medicine.

My name is David Dodick. I’m a Professor in the Department of Neurology at the Mayo Clinic in Phoenix, Arizona. On the line with me today are Drs. Sheena Aurora, Peter Goadsby, and Stephen Silberstein. Please take a moment to introduce yourselves and give your academic affiliations.

DR. AURORA: I’m Sheena Aurora. I’m a Clinical Associate Professor at Stanford University in California.

DR. GOADSBY: I’m Peter Goadsby, and I am a Professor of Neurology, University of California, San Francisco.

DR. SILBERSTEIN: I am Stephen Silberstein, Professor of Neurology, Thomas Jefferson University in Philadelphia.

DR. DODICK: We’ll start with a few questions about onabotulinum toxin A. Let’s start with you, Dr.

ABSTRACT

The discussion focused primarily on: 1) The role of extracranial nerve blocks, nerve stimulation, and onabotulinum toxin A in headache medicine; 2) the type of patient that should be considered for onabotulinum toxin A treatment; 3) counseling patients on expected results; 4) the costs associated with onabotulinum toxin A therapy and reimbursements; 5) the mechanism of action for onabotulinum toxin A; 6) extracranial neurostimulation, deep brain stimulation, and transcranial magnetic stimulation as options for migraine therapy; 7) the use of extracranial nerve blocks and occipital nerve block aids for migraine treatment; 8) the use of occipital nerve blocks with ultrasound guidance; 9) costs associated with the use of occipital nerve blocks and reimbursement; and 10) the use of onabotulinum toxin A in pregnant patients. Med Roundtable Gen Med Ed. 2014;1(3):230–239.

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Aurora. We know that within the past 2 years, onabotulinum toxin A has been approved in the United States for the treatment of patients with migraine, who have more than 15 headache days per month. Can you tell us which patients should be considered for treatment with onabotulinum toxin A, and how should patients be counseled with regard to the expectations or results that they might experience?

DR. AURORA: In my opinion, any patient who has had a history of episodic migraine and then has headaches on more than 15 days a month or more than half the time, should be considered for onabotulinum toxin A, but practically, I think what happens is that our patients who have chronic migraines are placed on other oral prophylactic medications, which I think clinically is the practical first step because some of these older medications, although they lack class A evidence, are effective.

In my practice, when I see a patient who has had chronic migraines but already tried other medications, we consider him/her as candidates for onabotulinum toxin A therapy. Suppose a patient comes in who has not had an adequate trial with topiramate, we may choose to start them off with topiramate administration and if they have side effects or failed therapy, then we consider onabotulinum toxin A therapy.

DR. DODICK: So, you believe patients should probably fail one or more conventional oral preventative medications before being tried on onabotulinum toxin A?

DR. AURORA: I think therapy for most patients should be individualized. For example, if I see a patient who has depression, I don’t think that he/she is a good candidate for beta-blockers because sometimes, this class of drugs can worsen depression. But, in general, if I see 10 patients, I would say that most patients have tried one drug or the other, or usually, I try one drug or the other on them, before I start onabotulinum toxin A administration.

DR. DODICK: Dr. Goadsby, the results of the clinical trials that have evaluated the effectiveness of onabotulinum toxin A for chronic migraine have not been without some controversy. In particular, some feel that the difference in the reduction of days with headache per month between the active and placebo groups was not clinically meaningful. What’s your opinion on this and your assessment of the data?

DR. GOADSBY: When it is said that the reduction of a few days a month is not clinically meaningful, I think the statement belies a lack of understanding of what a clinical trial delivers. A clinical trial looks at the changes between treated groups, in this case, placebo and onabotulinum toxin. It looks at what one could call “herd response” in the cohort of people who received onabotulinum toxin and who, in this study, had somewhat less headache days than those who received the placebo.

Primary outcome data that summarize group responses are not clinically meaningful, useful, or actually applicable because we don’t treat herds or groups, we treat individuals. The patient who you treat in front of you is either going to achieve a response that is satisfactory to them or not. So, from a clinical perspective, I find it more useful to use 50% or 75% responder rates to give patients an idea of their chances of reducing half or three-quarters of their headache days. I find that information easier to communicate, and I think it is fair to say it is clinically meaningful.

I think the controversy around the number of days reduced here conflates the issues of clinical significance versus economic significance. Is it valuable to society, broadly speaking, to reduce the number of days in the chronic headache population? I don’t think that is necessarily a question well asked by physicians, particularly if they don’t have health economics training. I think the controversy is simply a conflation between 2 related, but not equal issues.

DR. DODICK: Well that’s a good segue; one of the points you made to this question is regarding cost effectiveness. Dr. Silberstein, onabotulinum toxin is an expensive therapy. Do you believe that it can be cost effective?
effective, and what can you tell clinicians about the status of reimbursement in clinical practice?

DR. SILBERSTEIN: Let me just comment on one more thing about what Dr. Goadsby said. I think the issue of clinical meaningfulness is different in a clinical trial and the patient population. In a clinical trial, we look at the herd response to show a difference from placebo. We’re treating both responders and nonresponders. As Dr. Goadsby clearly said, in real life, we’re treating individuals.

I’ll give you a very simple example. Probably the only other reasonably large trial of responsiveness in the chronic migraine population that was done involved topiramate, and if you just look at the topiramate trials compared to the botulinum type A trials, response to botulinum toxin type A is superior in efficacy to that of topiramate. This is relevant because topiramate is one of the most commonly used drugs today for both migraines and chronic migraines.

DR. GOADSBY: If we go back for a moment to the triptans, I think most people who think about headaches, most neurologists, and probably physicians who practice would say that they were a spectacular step forward in the management of migraine. However, the 2-hour, pain-free rates of oral triptans are around 30%, which is hardly wonderful.

That’s clinical trial data, and it’s very solid clinical trial data. However, I think when you focus on just the clinical trial numbers, which are designed to prove the hypothesis in a population, and put them directly into a clinical practice, it is unhelpful. They’re not designed that way, and so you can make cheap criticisms if you’re not careful with the way you use the data. You could say 30% is quite a bad number, but that’s 100 mg of sumatriptan, and it revolutionized practice.

DR. DODICK: Regarding the expense of this therapy, do you think it is cost effective, and what’s the status of reimbursement for clinicians out there?

DR. SILBERSTEIN: I think it’s clearly cost effective, and I think that most insurance carriers today, paradoxically, require that you fail pre-emptively, that you fail preventively treatments with 2 drugs that have never been approved for a chronic migraine indication. If I wanted to use those drugs for off-label treatments, which they require, the carrier would probably deny it.

From the reimbursement point of view, you need to demonstrate that the patient has chronic migraines and, depending on the insurance carrier, that they have failed 2 or 3 different migraine preventive treatments. They may even require that they fail acute medications, which makes absolutely no sense. Then, the carrier will reimburse it.

We all have certain patients who have chronic intractable headaches. If they wind up in the emergency room for treatment and have a computed tomography scan and magnetic resonance imaging, it can cost more than it would to use onabotulinum toxin A for almost a year. If you determine the cost of this treatment for a year and how it relieves the headache burden and gets the patient back to daily life and work, I think it makes sense to use it.

One, you reduce the cost of neuroimaging. Two, you reduce the cost of emergency room visits. Three, you get the patient back to life, and the total healthcare costs is reduced.

DR. GOADSBY: Dr. Silberstein, about the third thing you said, ie, getting them back to life, unfortunately, insurers and payers worldwide and especially some physicians don’t really see the value—they don’t see the cost of the person sitting at home, life and activities ruined.

DR. SILBERSTEIN: Let’s think about another disorder like multiple sclerosis, where the drug treatments are $20,000 to $40,000 a year. Depending on the cocktail, the benefits are minimal, and you’re just prolonging the agony. The treatment will not reverse disability, yet people don’t consider not paying for multiple sclerosis drugs, and the 4 of us have seen patients that have undergone magnetic
resonance imaging for their migraines, come in with a few white spots, and start on multiple sclerosis drugs without any problems. Then, we want to treat them with botulinum toxin and cut the cost of the treatments by one-third or one-quarter, and yet we get resistance. That’s the irony.

DR. AURORA: Yes, I also want to say that the Headache Impact Test (HIT-6) was one of the endpoints and has been shown to be validated as a measure for change that the therapy created, and there was a shift of more than 2.3 (score), which is clinically meaningful.

DR. DODICK: Dr. Aurora, can you just tell us again what HIT-6 is?

DR. AURORA: HIT-6 is a 6-item questionnaire that measures patients’ ability to function. The questions are rated from 0 to 60, each, which is the minimum. So, the minimum HIT-6 is 36, and it can go up to 108. In the Phase III REsearch Evaluating Migraine Prophylaxis Therapy (PREEMPT) studies, most of the patients at baseline had an HIT-6 that was severe; on an average, the score was greater than 90. These patients in the placebo-control trials showed a difference in HIT-6 of greater than 2.3. HIT-6 takes into account how the patient is functioning.2

DR. DODICK: I have just 2 more brief questions and then we’ll move onto another topic. You enlightened us, Dr. Aurora, on who the target patient population is. Can you tell us now, within that population, if there is anything about a particular patient that identifies them as being likely to respond or not respond to botulinum toxin?

DR. AURORA: Whenever anybody asks me that question, I always ask him/her whether we have this question answered for any other therapies or, for that matter, any other clinical indications. What I tell clinicians is that anybody who meets the criteria for chronic migraine should probably have a trial, and, as Dr. Goadsby said, only those patients who respond should continue. One subset of patients who did well in the trial included those who were overusing acute medications for migraine, and these were randomized investigator sites.

DR. DODICK: Final question here, Dr. Goadsby, we’re often asked this: What is the potential mechanism of action by which onabotulinum toxin works in chronic migraine; do we know that yet or can you speculate?

DR. GOADSBY: That’s the “easiest” question: physiology. I don’t really think we have a good idea certainly in comparison to other therapies that we have, but I’d like to think that its effect is on large-fiber sensory nerves or even cranial parasympathetic sensory nerves. I think it’s unlikely that it’s a muscle effect or an exclusively peripheral effect at the end of the day, but I don’t think we’ve spent nearly enough time even starting to ask the questions, and I don’t really think that what’s being done in the general pain area is going to be terribly informative because it hasn’t been informative about any of the other migraine treatments. It’s an exciting work in progress.

DR. DODICK: Dr. Goadsby, I’m going to switch topics now and ask you a question about neurostimulation techniques that have been evaluated for the treatment of a wide variety...
of primary headache disorders. Speaking specifically about extracranial neurostimulation, do you actually see neurostimulation as a viable treatment option? And if you do, which modalities do you think look most promising?

**DR. GOADSBY:** Yes, I think extracranial stimulation is a viable modality. I don’t think that it’s been adequately proven certainly in the migraine sphere. The need for better-designed studies is obvious, and the difficulties with the perception and stimulation potentially influencing the placebo response are extremely important. In general, the less-invasive treatments are, the more excited I am, because the simpler they are to deploy, the more likely it is that they’ll be used more widely.

I try to discourage open-label random use of peripheral stimulation in just a few patients in any center. I don’t think that helps anybody, although I do look forward to the day we will have a better idea of how it might work and how to conduct the control trials that’ll convince regulatory authorities and us that this is the right way forward. It’s like the Mars lander; it’s almost inconceivable that we are driving around Mars with a 1-ton vehicle. Five years ago, that would have been unbelievable, but there’s someone driving around Mars with a 1-ton vehicle today.

**DR. DODICK:** Yes, Dr. Silberstein, for example, the use of an implantable stimulator that stimulates the occipital nerves is fairly invasive and costly. So, in which patients would you consider neurostimulation, and are there any clinical features, for example, a response to an occipital nerve block, that might identify patients who are likely to respond?

**DR. SILBERSTEIN:** Let me start with the second half of the question first, Dr. Dodick. In the first trial, based on open-label data, patients were administered an occipital nerve block. Those patients who achieved a response from an occipital nerve block were then administered an occipital neurostimulator. In our trial, we strongly argued that this relationship had never been proven. We created an auxiliary group of patients who

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Stephen Silberstein

**DR. DODICK:** Would any of you consider performing deep brain stimulation in any patient population, and in particular, in a patients with cluster headache, prior to at least a trial of occipital nerve stimulation?

**DR. SILBERSTEIN:** I would say yes. If you have a patient with a severe intractable cluster headache, in whom all treatment has failed, everything including invasive procedures, I might consider deep brain stimulation if the patient’s life is so impaired that their alternative is what we call these patients’ suicide headaches. I realize there’s a lot of controversy, but again, although I’ve never done it, if I had a patient like that, in whom all treatment has failed including peripheral stimulation, even using the new device for sphenopalatine ganglion stimulation, I might consider deep brain stimulation.

**DR. DODICK:** But you wouldn’t consider deep brain stimulation in advance of or prior to peripheral nerve stimulation.

**DR. SILBERSTEIN:** That is absolutely correct.

**DR. DODICK:** I gather my colleagues would agree with that?

**DR. AURORA:** Yes.

**DR. GOADSBY:** Yes, I certainly would. I think that the risk of the brain stimulation and the benefit
have to be considered. It’s not that everyone responds to deep brain stimulation. The best experience comes from the study by the Milan group, Leone, Bussoni, and Franzini, who have the most experience in the world. They would not say that 100% of their patients respond; their published results are about two-thirds.

Two-thirds is reasonable, but I don’t think, in the context of having a less-invasive procedure, that is it is the first choice. There are new procedures underway and new devices, such as the sphenopalatine stimulator approach, that are now in trials in Europe, reportedly with success. So, there are so many solutions being developed that it’s not time to think about deep-brain stimulation until all the peripheral options have been tried.

DR. DODICK: One of those peripheral procedures is transcranial magnetic stimulation, for which a trial has been conducted and completed in the United States, and I know that it’s been approved in the United Kingdom. Do any of you have any experience with transcranial magnetic stimulation in patients with migraine? What’s your take on this treatment modality? Since you used to practice in the United Kingdom, Dr. Goadsby, let’s start with you.

DR. GOADSBY: Yes, I’ve spoken to a number of patients who have used this device open label in the United Kingdom. There’s a cohort, not all, who think it is useful to avoid attacks and reduce the severity of attacks. It almost seems too simple to be true, but as you know, we’ve done some laboratory work, and indeed, it seems a very good basis for what’s happening on the experimental side. We did some laboratory studies to examine the ability of a scaled-down version of the human stimulator that would produce the same Tesla field, the magnetic field, to affect cortical spreading depression. Indeed, in anesthetized rats and cat, this device could block the passage of induced cortical spreading depression. We have done additional work to determine the mechanism by which this device can interrupt thalamo-cortical relay circuits that are activated by trigeminal pain. So, there seems to be at least a few potential mechanisms.

DR. DODICK: Does that mean it might be effective in patients who have migraine without aura, in addition to those who have aura?

DR. GOADSBY: Yes, and I think that was the driving factor to start examining thalamic-cortical mechanisms, because there are patients who, both in the clinical trials and certainly in the open-label work, report, not an exclusive effect on their aura, but certainly an effect on pain, and indeed, patients without an aura at all report an effect on pain, which needs to be explained. One way of explaining that effect would be to think about the involvement of the cortical relays in the action of this modality.

DR. DODICK: Okay, now the third and final topic: extracranial nerve blocks. Dr. Silberstein, I’ll start with you this time. Off-label treatment is common in clinical practice for most physicians by necessity. But there are few treatments that clinicians feel so passionately in favor of, despite the absence of evidence as extracranial nerve blocks and, in particular, occipital nerve blockade. So, if you can tell us, in which primary headache disorders do we actually have any evidence to support the use of occipital nerve block?

DR. SILBERSTEIN: I think the best scientific evidence for occipital nerve block with a local anesthetic in combination with corticosteroids is for cluster headache. Other people have conducted clinical trials to show that the combination works in comparison to placebo injection. If you look at the data for occipital nerve block, it’s very difficult to control for an anesthetic. One can argue that perhaps, you’ll use a short-acting versus a long-acting anesthetic, but the problem is that the duration of response often exceeds the duration of anesthesia.

We did a trial asking whether the addition of corticosteroids makes any difference in migraine as opposed to cluster headache, and we found no difference. I think we can say that steroids don’t make any difference, but it’s very difficult to control for a local anesthetic if people have had it for other simple procedures, like having teeth removal or a laceration on the skin. I cannot yet envision how to set up a clinical trial where the duration of the response exceeds the duration of action of the drug.

Bogduk, in a series of sophisticated experiments aimed at determining the cause of pain in the neck, used differential blocks with local anesthetics of different duration. But, in his clinical trials, the duration of response was equal to the duration of action of the local anesthetic, and when we perform occipital nerve blocks in humans, with problems in that area, we do not find that correlation.

Psychologists would use waiting-room controls, but I think we’ve all seen patients who have come into the office with severe significant pain and exacerbation of headaches, and when we perform a nerve block, their pain disappears.
for a month or may never come back. Others last for the duration of the anesthesia. So, I believe that it works, but I can’t conceive, yet, of how to do a trial to prove it works.

DR. DODICK: So, Dr. Aurora, I’m going to assume that you, at least for some patients, use occipital nerve blocks as a treatment option. Can you tell us what you use and do you use it for acute therapy to terminate an attack? Do you use it for prophylaxis? Can you give us an idea of which patients you use it for and in what setting?

DR. AURORA: We mostly use this for trying to prevent further attacks, but I have used it for acute treatment as well. I find that cluster headache patients actually respond very well to it. In terms of what I use, for cluster headache patients, I use some kind of a steroid in conjunction; most commonly, I use bupivacaine (or Marcaine), but it’s really quite arbitrary how I came to that choice.

Recently, when I worked at the pain center in Seattle, I used ultrasound guidance for some of these patients and found that some patients who didn’t respond to the blind procedure seemed to respond better to ultrasound guidance. I find it very useful in pregnancy because, as you know, most of the medications are of category C, and patients cannot take preventive medications when they’re pregnant. I find that using it as a prophylaxis during pregnancy works as well.

DR. DODICK: For both migraine and cluster?

DR. AURORA: For both migraine and cluster; just anecdotally, I’ve seen that patients who have a lot of neck triggers, where they’ve been categorized as having cervicogenic headache, although clearly, they have a history of migraine, which is triggered from the neck. Those patients seem to respond well to occipital nerve block.

DR. DODICK: A question for Dr. Goadsby: I, too, have had a clinical experience, whether there is a placebo or not, wherein for patients with cluster headache or migraine, you can terminate an attack rather abruptly with an occipital nerve block. Can you speculate the potential mechanism of action of that response?

DR. GOADSBY: Well, I think the acting mechanism of action in occipital nerve blocks is to modulate cervical neurons sufficient for the brain processes involved in migraine, cluster, or any of the primary headaches, to take their normal course of action, which is to terminate them. If you look at migraine, it’s been defined as an episodic headache and cluster headache quintessentially. They are chronic versions, and typically, when the version is chronic, they have episodes over that as well, so there are clearly mechanisms in the brain that either exhaust or actively terminate acute migraine.

I think by stimulating these trigeminocervical neurons, either these mechanisms are exhausted or mechanisms normally turning the attack off are allowed to gain a foothold.

DR. SILBERSTEIN: If I can suggest an impossible-to-do trial, Dr. Dodick, it’s penicillin for pneumococcal pneumonia. I don’t think you can do it.

DR. DODICK: I hope that someone will find a way to do this trial because as we know, it’s becoming increasingly difficult for clinicians to do this in practice because there is no reimbursement for it. So, clinicians are not able to implement what they see as a very useful tool in their therapeutic armamentarium, because in the absence of evidence, insurers are not willing to cover it. So, I’m hopeful that we’ll see a trial soon that will compel third-party payers to at least reimburse.

DR. SILBERSTEIN: Dr. Dodick, I believe the issue arose because people outside the headache field have patients come back on a weekly basis for blocks. That’s what they do for a living, but I think that’s the problem. I think all of us agree it works, but the problem and the way to maybe do a trial would be to compare once per week, once per month, and once every 3 months and look for outcomes. I think that might be the way to do it, because I think the issue, from the carrier’s point of view, is cost. When it’s done under fluoroscopic guidance, the cost can be astronomically high, and that’s what they’re reacting to.

I think one of the ways to do it is just take it to the carrier and say, this is what we’d like to do, finance it or get the federal government to finance a study, and find out what their objections are.

My strongest objection is not the procedure, but the need for fluoroscopy and frequent repetitive blocks. The other issue that really bothers me is that you may want to see if the block is effective at all, or we could use a block instead of an ED transfer or admission. Permission should not be needed for diagnostic or emergency blocks.

DR. GOADSBY: If it’s true that it has a modulating effect, it’s likely
On extracranial stimulation may be effective for patients unresponsive to oral medications or botulinum toxin.

Clinical Implications

▶ Patients who fit the criteria for chronic migraine should be considered for onabotulinum toxin A.
▶ Most patients fail one or more conventional medications before trying onabotulinum toxin A.
▶ Extracranial stimulation may be effective for patients unresponsive to oral medications or botulinum toxin.
▶ Occipital nerve blocks are widely used to prevent future attacks as well as for acute treatment, but developing a clinical trial to isolate their effectiveness from the use of anesthetic is a challenge.
▶ Occipital nerve blocks can be particularly valuable as prophylaxis in pregnancy, when most medications cannot be administered.
When we looked systematically at occipital nerve blocks, we found an interesting phenomenon that slightly mirrors the effect of dihydroergotamine infusions: if you perform occipital nerve block—peri-occipital nerve injection might be a better way to put it—you might well see effects that take 5 to 7 days to have their onset, and that will confuse the outcome of further blocks done on the day. I don’t really think that the examination of multiple blocks has been done in a systematic fashion.

**DR. SILBERSTEIN:** When the patient is in my office, outside of a trial, I try to give them the best benefit that I can. But, I agree with you in the case of a systematic study. In fact, when we started the steroid study, we actually did what you suggested. We localized the blocks and only performed them in those certain areas so we could compare outcomes.

**DR. DODICK:** Since you’re an advocate, Dr. Silberstein, of, let’s say, supra-orbital nerve blocks in some patients, if a patient came in with exclusively anterior pain, vertex or frontal, do you believe that an occipital nerve block can be effective for him/her, and would you preferentially perform a supraorbital nerve block in those patients? In other words, does the location of the pain guide you in terms of which nerve you block?

**DR. SILBERSTEIN:** If people have nummular headache, I’ll go to the nummular area. But, often what we see are patients who have pain in a wider area of distribution in the front. I think as Dr. Goadsby says, we’re modulating the central terminal. What I might do the first time I see the patient is to try the occipital nerve block therapeutically, diagnostically, and mechanically. If it doesn’t work, I will go anteriorly, and will then see how they do afterwards. I don’t think I know the answers to those questions. My exception to the rule would be nummular headache, but I would only go to that area.

**DR. GOADSBY:** It is interesting when you look at the cluster headache data; for occipital nerve injection, the only place where randomized control trials have been done is cluster headache, and it is an anterior pain. I think it’s probably the most sound systematic clinical trial evidence we have to show that the effect of the procedure is on a central basis. The reason I raise this multiple cranial nerve block matter is that if we’re going to be asking payers of any form to approve these procedures, we have to be quite systematic in the procedures we describe and in the way we collect our evidence, because I can’t imagine that payers are going to allow or want confused, randomly localized injections. That’s part of the problem.

**DR. DODICK:** Well that’s sage and wise advice.

**DR. DODICK:** I want to thank my colleagues for willing to share their expertise. I can’t imagine 3 more authoritative voices in the field of headache to speak on these issues than the ones we’ve had today, and I want to thank them.

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**FACULTY DISCLOSURES:**

Within the past 4 years, Dr. Dodick serves on advisory boards, has consulted for, and received travel reimbursement from Allergan, Alder, Pfizer, Merck, Coherex, Ferring, Neurocore, Neuralive, Neuraxon, NuPathie Inc., MAP, SmithKlineBeecham, Boston Scientific, Medtronic, Inc., Nautilus, Eli Lilly & Company, Novartis, Colucid, GlaxoSmithKline, Autonomic Technologies Inc., MAP Pharmaceuticals, Inc., Zogenix, Inc., Impax Laboratories, Inc., Bristol Myers Squibb, Neuro Corporation, and Arteus. Within the past 4 years, Dr. Dodick has received funding for travel, speaking, or editorial activities from the following: CogniMed, Scientiae, Intramed, SAGE Publishing, Lippincott Williams and Wilkins, Oxford University Press, Cambridge University Press, Miller Medical, and Annenberg for Health Sciences; he serves as Editor-in-Chief and on the editorial boards of The Neurologist, Lancet Neurology, and Postgraduate Medicine; and has served as Editor-in-Chief of Headache Currents and as an Associate Editor of Headache; receives publishing royalties for Wolff’s Headache and Other Head Pain, 8th edition (Oxford University Press, 2009) and Handbook of Headache (Cambridge University Press, 2010), and Comorbidity in Migraine (Wiley-Blackwell). Within the past 3 years, Dr. Dodick has received research grant support from the following: Advanced Neurostimulation Systems, Boston Scientific, St. Jude Medical, Inc., Medtronic, NINDS/NIH, and Mayo Clinic.

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Dr. Peter Goadsby received an honorarium from Allergan; is a paid board member of Allergan, CoLucid, MAP, MSD, eNeura, NeurAxon Inc., Autonomic Technologies Inc., Boston Scientific, Eli-Lilly, Medtronic, Linde Gases, Bristol-Myers Squibb; is a paid consultant for Pfizer; has provided paid expert testimony for Medico-Legal advice regarding headache; has received grants from GlaxoSmithKline, MAP, MSD, eNeura, Amgen, Allergan; has received honoraria for lectures from MSD, Pfizer, Allergan, Menarini; and has received payment for developing educational presentations for the American Headache Society.

Dr. Silberstein is on the advisory panel of and receives honoraria from Allergan, Amgen, Capnia, Coherex, GlaxoSmithKline, Iroko Pharmaceuticals, Lilly, MAP, Medtronic, Merck, Neuralieve Inc, The National Institute of Neurological Disorders and Stroke, NuPath, Pfizer, and St. Jude Medical. He serves as a consultant for and receives honoraria from Amgen, MAP, Nautilus, Novartis, OptiNose, and Zogenix. His employer receives research support from Allergan, BMS, Cumberland, ElectroCore, Lilly, Merck, OptiNose, St. Jude Medical, and Troy Healthcare.

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