Jason, Cailin (NIH/NINDS) [C]

From: Emr, Marian (NIH/NINDS) [E]
Sent: Tuesday, August 18, 2015 11:07 AM
To: Koroshetz, Walter (NIH/NINDS) [E]
Subject: ACTION: Concussion study

I was glad to be on the line when you discussed the applications that we've received in response to the ENH *Sports and Health Research Program* initiative. I am quite concerned about (b) (5)
(b) (5)
(b) (5) so that I can offer assistance and advice.
Also, can you tell me what time this discussion is likely to take place on the agenda? I have to host a presentation at the NIH Communications Directors' meeting between 1:30 and 3:00 on Sept 10th but I don't want to miss the Council discussion of the two grant applications.
Thank you.
Marian

Marian Emr

Director, Office of Communications and Public Liaison/NINDS
31 Center Drive MSC 2540
Building 31, Room 8A07
Bethesda, MD 20892-2540
Phone: (301) 496-5924
Fax: (301) 402-2186
me20t@nih.gov

National Institutes of Health

McMakin, Barbara (NIH/NINDS) [E]

From: McMakin, Barbara (NIH/NINDS) [E]
Sent: Thursday, October 29, 2015 3:22 PM
To: Bellgowan, Patrick (NIH/NINDS) [E]
Subject: RE: NFL concussion grants

Thanks for responding so quickly. Yes, I know this is a very sensitive issue, that's why I wanted to clarify all of the information. I may have additional questions about these grants in the next day or two.

Best.
Barbara

From: Bellgowan, Patrick (NIH/NINDS) [E]
Sent: Thursday, October 29, 2015 3:19 PM
To: McMakin, Barbara (NIH/NINDS) [E]
Subject: RE: NFL concussion grants

(b) (5)

[redacted]

Patrick SF Bellgowan, PhD
Program Director, Repair and Plasticity
NIH/NINDS
301-496-1447
psfb@mail.nih.gov

http://www.ninds.nih.gov/disorders/tbi/tbi.htm

From: McMakin, Barbara (NIH/NINDS) [E]
Sent: Thursday, October 29, 2015 3:08 PM
To: Bellgowan, Patrick (NIH/NINDS) [E]
Subject: RE: NFL concussion grants

Are the funds for 2016 and 2017 guaranteed? And is that public knowledge?

Thanks.
Barbara

From: Bellgowan, Patrick (NIH/NINDS) [E]
Sent: Thursday, October 29, 2015 3:05 PM
To: McMakin, Barbara (NIH/NINDS) [E]
Subject: RE: NFL concussion grants

Yes, they each have about $1.5M per year for 4 years 2014-2017.

Patrick SF Bellgowan, PhD

Program Director, Repair and Plasticity
NIH/NINDS
301-496-1447
psfb@mail.nih.gov

http://www.ninds.nih.gov/disorders/tbi/tbi.htm

From: McMakin, Barbara (NIH/NINDS) [E]
Sent: Thursday, October 29, 2015 3:00 PM
To: Bellgowan, Patrick (NIH/NINDS) [E]
Subject: NFL concussion grants

Hi Pat,

A reporter from CBS News is doing a segment on concussion research, focusing on the NFL-supported grants. I'm pulling together some information for her and had a question for you:
I thought the two cooperative grants (McKee and Gordon) were to be worth $6 million each. They have currently received $3million ($1.5mil/year for 2014 and 2015)—will they receive additional funding in FY2016 and FY2017?

Thanks,
Barbara

Barbara L. McMakin
Science Writer
Office of Communications and Public Liaison
National Institute of Neurological Disorders & Stroke
National Institutes of Health
Building 31, Room 8A07
31 Center Drive MSC 2540
Bethesda, MD 20892-2540
Main Office Line (301) 496-5751
Direct Line (240) 435-2747
Email: mcmakinbl@ninds.nih.gov

McMakin, Barbara (NIH/NINDS) [E]

From: Bellgowan, Patrick (NIH/NINDS) [E]
Sent: Wednesday, December 02, 2015 10:04 AM
To: McMakin, Barbara (NIH/NINDS) [E]
Subject: RE: U01 award press release

Hi Barbara,

The total budget for 7 years is $16.5 million

Patrick SF Bellgowan, PhD
Program Director, Repair and Plasticity
NIH/NINDS
301-496-1447
psfb@mail.nih.gov

http://www.ninds.nih.gov/disorders/tbi/tbi.htm

From: McMakin, Barbara (NIH/NINDS) [E]
Sent: Wednesday, December 02, 2015 6:50 AM
To: Bellgowan, Patrick (NIH/NINDS) [E]
Subject: RE: U01 award press release

Thanks! How much is the grant worth?

Best,
Barbara

From: Bellgowan, Patrick (NIH/NINDS) [E]
Sent: Tuesday, December 01, 2015 4:49 PM
To: McMakin, Barbara (NIH/NINDS) [E]
Subject: RE: U01 award press release

I've asked a couple times but haven't heard. I'll try again tomorrow and get back to you.

Thanks
Pat

Patrick SF Bellgowan, PhD
Program Director, Repair and Plasticity
NIH/NINDS
301-496-1447
psfb@mail.nih.gov

http://www.ninds.nih.gov/disorders/tbi/tbi.htm

From: McMakin, Barbara (NIH/NINDS) [E]
Sent: Tuesday, December 01, 2015 3:18 PM
To: Bellgowan, Patrick (NIH/NINDS) [E]
Subject: U01 award press release

Hi Pat,

I'll be writing the press release announcing Dr. Stern's grant. Do you know when the NOA is going out?

Thanks,
Barbara

Barbara L. McMakin
Science Writer
Office of Communications and Public Liaison
National Institute of Neurological Disorders & Stroke
National Institutes of Health
Building 31, Room 8A07
31 Center Drive MSC 2540
Bethesda, MD 20892-2540
Main Office Line: (301) 496-5751
Direct Line: (301) 435-7747
E-mail: mcmakinbl@ninds.nih.gov

McMakin, Barbara (NIH/NINDS) [E]

From: Emr, Marian (NIH/NINDS) [E]
Sent: Thursday, December 03, 2015 8:48 AM
To: McMakin, Barbara (NIH/NINDS) [E]
Subject: FW: PRIORITY ACTION: Preparation for U01 award press release

FYI only. Meghan is scheduled to call me at 10:30 to discuss.

Marian Emr
Director, Office of Communications and Public Liaison/NINDS
NIH Building 31, Room 8A07
Phone: (301) 496-5924
marian.emr@nih.gov

From: Mott, Meghan (NIH/NINDS) [E]
Sent: Wednesday, December 02, 2015 5:55 PM
To: Emr, Marian (NIH/NINDS) [E]
Cc: Koroshetz, Walter (NIH/NINDS) [E]; Bellgowan, Patrick (NIH/NINDS) [E]
Subject: PRIORITY ACTION: Preparation for U01 award press release

Hi Marian,

Ok to work on the release, but can we hold off on publishing it for now? We are waiting on a few final loose ends to be tied up. Walter will let us know when it is ready to go out. Probably not until next week at the earliest.

Thanks,
Meghan

From: Emr, Marian (NIH/NINDS) [E]
Sent: Tuesday, December 01, 2015 2:15 PM
To: Koroshetz, Walter (NIH/NINDS) [E]; Bellgowan, Patrick (NIH/NINDS) [E]
Subject: RE: Preparation for U01 award press release

OCPL would be happy to work with the grantee Institutions to coordinate an NIH release timed with theirs. Marian

Marian Emr
Director, Office of Communications and Public Liaison/NINDS
NIH Building 31, Room 8A07
Phone: (301) 496-5924
marian.emr@nih.gov

From: Koroshetz, Walter (NIH/NINDS) [E]
Sent: Tuesday, December 01, 2015 2:07 PM
To: Bellgowan, Patrick (NIH/NINDS) [E]
Cc: Emr, Marian (NIH/NINDS) [E]
Subject: ACTION: Preparation for U01 award press release

Yes, I agree that press release would be important. Either NINDS or joint.

Jason, Cailin (NIH/NINDS) [C]

From: Koroshetz, Walter (NIH/NINDS) [E]
Sent: Wednesday, December 09, 2015 10:57 AM
To: Bellgowan, Patrick (NIH/NINDS) [E]; Emr, Marian (NIH/NINDS) [E]; McMakin, Barbara (NIH/NINDS) [E]
Cc: Mott, Meghan (NIH/NINDS) [E]
Subject: ACTION: U01 NS093334-01

Thanks Pat. Will give a call. If free can call now.
310 496(b) (6)
walter

From: Bellgowan, Patrick (NIH/NINDS) [E]
Sent: Wednesday, December 09, 2015 10:49 AM
To: Emr, Marian (NIH/NINDS) [E]; McMakin, Barbara (NIH/NINDS) [E]
Cc: Mott, Meghan (NIH/NINDS) [E]; Koroshetz, Walter (NIH/NINDS) [E]
Subject: RE: U01 NS093334-01

Hi Barbara,

Tia in GMB just informed us that Dr. Stern's U01 will be released on Dec. 12th. Will you be contacting the various organizations PR people?

Thanks
Pat

Patrick SF Bellgowan, PhD
Program Director, Repair and Plasticity
NIH/NINDS
301-496-1447
psfb@mail.nih.gov

http://www.ninds.nih.gov/disorders/tbi/tbi.htm

From: Decoster, Tijuanna (NIH/NINDS) [E]
Sent: Wednesday, December 09, 2015 10:21 AM
To: Bellgowan, Patrick (NIH/NINDS) [E]
Cc: Mott, Meghan (NIH/NINDS) [E]; Koroshetz, Walter (NIH/NINDS) [E]
Subject: FW: U01 NS093334-01

The grant has been released with an issue date of 12/12/15. The issue date is when the grantee will be notified.

From: Conklin, Elizabeth (NIH/NINDS) [E]
Sent: Wednesday, December 09, 2015 10:03 AM
To: Decoster, Tijuanna (NIH/NINDS) [E]; Pree, Nia (NIH/NINDS) [E]
Subject: RE: U01 NS093334-01

Hi Tia,

I just released this award.

Nia, thank you for your careful and thorough work on this one. What a bear!

Liz

From: Decoster, Tijuanna (NIH/NINDS) [E]
Sent: Tuesday, December 01, 2015 11:04 AM
To: Pree, Nia (NIH/NINDS) [E]
Cc: Conklin, Elizabeth (NIH/NINDS) [E]
Subject: U01 NS093334-01

Hi Nia,

Please proceed with getting this grant ready to award. Once you have completed the workup and signed off, please let me know. Liz, please let me know when you release this grant.

Thanks
Tia

Jason, Cailin (NIH/NINDS) [C]

From: Emr, Marian (NIH/NINDS) [E]
Sent: Wednesday, December 09, 2015 10:59 AM
To: Bellgowan, Patrick (NIH/NINDS) [E]
Cc: Mott, Meghan (NIH/NINDS) [E]; Koroshetz, Walter (NIH/NINDS) [E]; McMakin, Barbara (NIH/NINDS) [E]
Subject: ACTION: U01 NS093334-01

As you probably know, we are in a holding pattern awaiting further instructions from Dr. Collins about any press activity. Before hearing from Dr. Collins, we notified the PR staff from BU and the co-PI institutions to hold their publicity so that NIH could take the lead. When the final decision is made by Dr. Collins, we will send an appropriate updated message to each.
Marian

Marian Emr
Director, Office of Communications and Public Liaison/NINDS
NIH Building 31, Room 8A07
Phone: (301) 496-5924
marian.emr@nih.gov

From: Bellgowan, Patrick (NIH/NINDS) [E]
Sent: Wednesday, December 09, 2015 10:49 AM
To: Emr, Marian (NIH/NINDS) [E]; McMakin, Barbara (NIH/NINDS) [E]
Cc: Mott, Meghan (NIH/NINDS) [E]; Koroshetz, Walter (NIH/NINDS) [E]
Subject: RE: U01 NS093334-01

Hi Barbara,

Tia in GMB just informed us that Dr. Stern's U01 will be released on Dec. 12th. Will you be contacting the various organizations PR people?

Thanks
Pat

Patrick SF Bellgowan, PhD
Program Director, Repair and Plasticity
NIH/NINDS
301-496-1447
psfb@mail.nih.gov

http://www.ninds.nih.gov/disorders/tbi/tbi.htm

From: Decoster, Tijuanna (NIH/NINDS) [E]
Sent: Wednesday, December 09, 2015 10:21 AM
To: Bellgowan, Patrick (NIH/NINDS) [E]
Cc: Mott, Meghan (NIH/NINDS) [E]; Koroshetz, Walter (NIH/NINDS) [E]
Subject: FW: U01 NS093334-01

The grant has been released with an issue date of 12/12/15. The issue date is when the grantee will be notified.

Jason, Cailin (NIH/NINDS) [C]

From: Stern, Robert A <bobstern@bu.edu>
Sent: Friday, December 11, 2015 1:59 PM
To: Emr, Marian (NIH/NINDS) [E]
Cc: Wilczewski, Gina Maria; McMakin, Barbara (NIH/NINDS) [E]
Subject: ACTION: Checking in re: U01 Press Release

Hi Marian,
Thanks for the response. I would really prefer that BU (or any other institution) not release individual releases if NINDS will, indeed be having its own release. Is there a reason for the hold up? And, can you possibly provide a timeline so we can make a decision about the timing of any individual releases. I look forward to hearing back from you. Thanks.

Bob

From: Emr, Marian (NIH/NINDS) [E] [mailto:emrm@ninds.nih.gov]
Sent: Friday, December 11, 2015 12:45 PM
To: Stern, Robert A <bobstern@bu.edu>
Cc: Wilczewski, Gina Maria <ginad@bu.edu>; McMakin, Barbara (NIH/NINDS) [E] <mcmakinbi@ninds.nih.gov>
Subject: RE: Checking in re: U01 Press Release

Hi, Bob. Marian Emr, here. I understand your desire to make a statement as soon as possible so it's probably best if you go ahead with your own release and not wait for us. Please ask your folks to observe the NIH requirement that you wait 72 hours after receiving the NGA. Also, I'd appreciate it if Gina could send me a copy of her draft once you clear it.
Congratulations on your new grant. We look forward to working with you and your team going forward to announce your research results.
Marian

Marian Emr
Director, Office of Communications and Public Liaison/NINDS
Building 31, Room 8A07
Bethesda, MD 20892-2540
Phone: (301) 496-5924
marian.emr@nih.gov

From: Stern, Robert A [mailto:bobstern@bu.edu]
Sent: Friday, December 11, 2015 11:32 AM
To: McMakin, Barbara (NIH/NINDS) [E]
Cc: Emr, Marian (NIH/NINDS) [E]; Wilczewski, Gina Maria
Subject: ACTION: Checking in re: U01 Press Release

Thanks, Barbara. Would it be possible for you to provide me with the reasoning behind waiting so long after the NoGA to even have an update on the plans. My colleagues and I will be letting all of the co-investigators, consultants, and advisory board members know about the receipt of the NoGA immediately since everyone has been waiting for this for approximately six months and are eager to get to work. It seems to me that it would be helpful to have the PR come out pretty soon since word will quickly spread once the team is informed of the NoGA. Obviously, I am not a communications/media expert, but I do know that this area of research is the focus of tremendous media attention and I always feel more comfortable when the dissemination of the information is controlled by the communications experts

and not the individual investigators. I apologize if I am being a pest. I just would really like to have a sense of the plans. I hope you understand. Thanks very much.

Bob

From: McMakin, Barbara (NIH/NINDS) [E] [mailto:mcmakinbi@ninds.nih.gov]
Sent: Friday, December 11, 2015 11:21 AM
To: Stern, Robert A <bobstern@bu.edu>
Cc: Emr, Marian (NIH/NINDS) [E] <emrm@ninds.nih.gov>; Wilczewski, Gina Maria <ginad@bu.edu>
Subject: RE: Checking in re: U01 Press Release

Hi Dr. Stern,

Thank you for your email. We should have an update regarding our plans sometime next week.

Best,
Barbara

From: Stern, Robert A [mailto:bobstern@bu.edu]
Sent: Friday, December 11, 2015 11:04 AM
To: McMakin, Barbara (NIH/NINDS) [E]
Cc: Emr, Marian (NIH/NINDS) [E]; Wilczewski, Gina Maria
Subject: Checking in re: U01 Press Release

Hi Barbara,
I am checking in about the status of the CTE U01 Press Release. My understanding is that the Notice of Grant Award is expected to be released tomorrow (12/12/15). When do you anticipate to release the PR? I know you have been working with Gina (cc'd) from our place, as well as the communications folks at the other three institutions. Please let me know if you have any questions or if there is anything I can do to assist.

Regards,

Bob

Robert A. Stern, Ph.D.
Professor of Neurology, Neurosurgery, and Anatomy and Neurobiology
Clinical Core Director, BU Alzheimer's Disease and CTE Center
Boston University School of Medicine

72 East Concord Street, B7800
Boston, MA 02118

Dir. Tel: 617-638-5678 * Nicole Gullotti (Admin. Asst.): 617-414-1195
Fax: 617-638-5679

Email: bobstern@bu.edu
Web: www.sternneurolab.org

Jason, Cailin (NIH/NINDS) [C]

From: McMakin, Barbara (NIH/NINDS) [E]
Sent: Monday, December 14, 2015 8:30 AM
To: Emr, Marian (NIH/NINDS) [E]
Subject: ACTION: CTE grant

Hi Marian,

Gina from BU's press office is asking for PIO contact info from the other institutions involved in the grant. Can I share the info with her or hold off on sending her anything?

Thanks,
Barbara

Barbara I. McMakin
Science Writer
Office of Communications and Public Liaison
National Institute of Neurological Disorders & Stroke
National Institutes of Health
Building 31, Room 8A07
31 Center Drive MSC 2540
Bethesda, MD 20892-2540
Main Office Line: (301) 496-5751
Direct Line: (301) 435-7747
Email: mcmakinbi@ninds.nih.gov

Jason, Cailin (NIH/NINDS) [C]

From: McMakin, Barbara (NIH/NINDS) [E]
Sent: Wednesday, December 16, 2015 12:15 PM
To: 'Wilczewski, Gina Maria'
Cc: Emr, Marian (NIH/NINDS) [E]
Subject: PRESS: Preparation for U01 award press release

Sounds good! Thank you for the update.

Best,
Barbara

From: Wilczewski, Gina Maria [mailto:ginad@bu.edu]
Sent: Wednesday, December 16, 2015 12:13 PM
To: McMakin, Barbara (NIH/NINDS) [E]
Cc: Emr, Marian (NIH/NINDS) [E]
Subject: RE: Preparation for U01 award press release

Still working that out but it looks like we'll send out early next week.
I will keep you posted.

Gina DiGravio-Wilczewski
Media Relations Manager
Boston University School of Medicine
617-638-8480 (O)
617-224(b) (6)(M)
ginad@bu.edu

From: McMakin, Barbara (NIH/NINDS) [E] [mailto:mcmakinbi@ninds.nih.gov]
Sent: Wednesday, December 16, 2015 12:07 PM
To: Wilczewski, Gina Maria
Cc: Emr, Marian (NIH/NINDS) [E]
Subject: RE: Preparation for U01 award press release

Hi Gina,

What is the timing of your statement? Have you set an embargo for the release?

Thanks,
Barbara

From: Wilczewski, Gina Maria [mailto:ginad@bu.edu]
Sent: Tuesday, December 15, 2015 9:25 AM
To: McMakin, Barbara (NIH/NINDS) [E]
Cc: Emr, Marian (NIH/NINDS) [E]
Subject: RE: Preparation for U01 award press release

Yes, that is my plan.

Gina DiGravio-Wilczewski
Media Relations Manager

Boston University School of Medicine
617-638-8480 (O)
617-224(b) (6) (M)
ginad@bu.edu

From: McMakin, Barbara (NIH/NINDS) [E] [mailto:mcmakinbi@ninds.nih.gov]
Sent: Tuesday, December 15, 2015 9:22 AM
To: Wilczewski, Gina Maria
Cc: Emr, Marian (NIH/NINDS) [E]
Subject: RE: Preparation for U01 award press release

You're welcome! Would you be willing to share a draft of your release with us?

Thanks,
Barbara

From: Wilczewski, Gina Maria [mailto:ginad@bu.edu]
Sent: Tuesday, December 15, 2015 8:55 AM
To: McMakin, Barbara (NIH/NINDS) [E]
Cc: Emr, Marian (NIH/NINDS) [E]
Subject: RE: Preparation for U01 award press release

Thanks Barbara. You are right, it wasn't NYU--my mistake!
I'm all set now.

Gina DiGravio-Wilczewski
Media Relations Manager
Boston University School of Medicine
617-638-8480 (O)
617-224(b) (6) (M)
ginad@bu.edu

From: McMakin, Barbara (NIH/NINDS) [E] [mailto:mcmakinbi@ninds.nih.gov]
Sent: Tuesday, December 15, 2015 8:22 AM
To: Wilczewski, Gina Maria
Cc: Emr, Marian (NIH/NINDS) [E]
Subject: RE: Preparation for U01 award press release

Hi Gina,

I apologize for not getting back to you yesterday. The PR contact at Cleveland Clinic Lou Ruvo is Halle Bishop (bishoph@ccf.org). I wasn't aware that NYU Langone Medical Center is involved in the grant; I thought the fourth institution was Banner Health. I left a couple of voicemails with Banner's PR office, but nobody called me back.

Thanks,
Barbara

From: Wilczewski, Gina Maria [mailto:ginad@bu.edu]
Sent: Monday, December 14, 2015 8:08 AM
To: McMakin, Barbara (NIH/NINDS) [E]
Subject: RE: Preparation for U01 award press release
Importance: High

Good morning Barbara,

Would you be willing to share the names and email addresses to the PIOs at Cleveland Clinic Lou Ruvo Center and New York University Langone Medical Center?
Thank you.

Gina DiGravio-Wilczewski
Media Relations Manager
Boston University School of Medicine
617-638-8480 (O)
617-224(b) (6) (M)
ginad@bu.edu

From: Wilczewski, Gina Maria
Sent: Thursday, December 03, 2015 8:42 AM
To: 'McMakin, Barbara (NIH/NINDS) [E]'
Cc: Ober, Maria Pantages (mpober@bu.edu)
Subject: RE: Preparation for U01 award press release

Sounds good Barbara.
Please follow the directions below for the conference call:
Outside callers should call either the local telephone number, 617-414(b) (6) or toll free telephone number, 855-708-(b) (6) then follow the voice prompts. When asked, Attendees should enter Code (b) (6) and the # key. You will be connected to the conference if your Participant Code is correct. If you are disconnected for any reason, repeat instructions above.
Thank you

Gina DiGravio-Wilczewski
Media Relations Manager
Boston University School of Medicine
617-638-8480 (O)
617-224(b) (6) (M)
ginad@bu.edu

From: McMakin, Barbara (NIH/NINDS) [E] [mailto:mcmakinbi@ninds.nih.gov]
Sent: Thursday, December 03, 2015 8:19 AM
To: Wilczewski, Gina Maria
Subject: RE: Preparation for U01 award press release

Hi Gina,

My director Marian will be on the call as well. Why don't we call you? What number should we dial?

Best,
Barbara

From: Wilczewski, Gina Maria [mailto:ginad@bu.edu]
Sent: Wednesday, December 02, 2015 3:38 PM
To: McMakin, Barbara (NIH/NINDS) [E]
Subject: RE: Preparation for U01 award press release

Yes, 11:30 am works for us. My director Maria Ober will also be on the call.
Should we call your direct line: (301) 435-7747?

Gina DiGravio-Wilczewski
Media Relations Manager

Boston University School of Medicine
617-638-8480 (O)
617-224(b) (6)(M)
ginad@bu.edu

From: McMakin, Barbara (NIH/NINDS) [E] [mailto:mcmakinbi@ninds.nih.gov]
Sent: Wednesday, December 02, 2015 1:56 PM
To: Wilczewski, Gina Maria
Subject: RE: Preparation for U01 award press release

How about 11:30?

From: Wilczewski, Gina Maria [mailto:ginad@bu.edu]
Sent: Wednesday, December 02, 2015 1:52 PM
To: McMakin, Barbara (NIH/NINDS) [E]
Subject: RE: Preparation for U01 award press release

Tomorrow is fine, just let me know what works for you.

Gina DiGravio-Wilczewski
Media Relations Manager
Boston University School of Medicine
617-638-8480 (O)
617-224(b) (6)(M)
ginad@bu.edu

From: McMakin, Barbara (NIH/NINDS) [E] [mailto:mcmakinbi@ninds.nih.gov]
Sent: Wednesday, December 02, 2015 1:50 PM
To: Wilczewski, Gina Maria
Subject: RE: Preparation for U01 award press release

I'll be out of the office starting at 3, but I should be available tomorrow. Would that work for you?

From: Wilczewski, Gina Maria [mailto:ginad@bu.edu]
Sent: Wednesday, December 02, 2015 1:48 PM
To: McMakin, Barbara (NIH/NINDS) [E]
Subject: RE: Preparation for U01 award press release

Ok, great, thanks.
Could we chat maybe later today?
Say after 3 pm?

Gina DiGravio-Wilczewski
Media Relations Manager
Boston University School of Medicine
617-638-8480 (O)
617-224(b) (6)(M)
ginad@bu.edu

From: McMakin, Barbara (NIH/NINDS) [E] [mailto:mcmakinbi@ninds.nih.gov]
Sent: Wednesday, December 02, 2015 1:44 PM
To: Wilczewski, Gina Maria
Subject: RE: Preparation for U01 award press release

Hi Gina.

Yes, this is the same thing. I reached out to the other institutes yesterday and am still waiting to hear back from Banner.

Best,
Barbara

Barbara I. McMakin
Science Writer
Office of Communications and Public Liaison
National Institute of Neurological Disorders & Stroke
National Institutes of Health
Building 31, Room 8A07
31 Center Drive MSC 2540
Bethesda, MD 20892-2540
Main Office Line: (301) 496-5751
Direct Line: (301) 435-7747
Email: mcmakinbi@ninds.nih.gov

From: Wilczewski, Gina Maria [mailto:ginad@bu.edu]
Sent: Wednesday, December 02, 2015 1:39 PM
To: McMakin, Barbara (NIH/NINDS) [E]
Subject: FW: Preparation for U01 award press release

Barbara,
Thanks for your email and call yesterday. Jenny did pass it along to me.
Please see the email trail below. Is this all the same thing?

Gina DiGravio-Wilczewski
Media Relations Manager
Boston University School of Medicine
617-638-8480 (O)
617-224(b)(6) (M)
ginad@bu.edu

From: Ober, Maria Pantages
Sent: Tuesday, December 01, 2015 10:02 PM
To: Stern, Robert A
Cc: Bellgowan, Patrick (NIH/NINDS) [E]; Emr, Marian (NIH/NINDS) [E]; Wilczewski, Gina Maria
Subject: Re: Preparation for U01 award press release

Thanks for connecting us, Bob.
Marian, my media relations manager Gina DiGravio will actually be handling this effort for us. I've copied her here. She's well-versed in this type of coordination between multiple institutions and the award-granting agency. That said, Gina and I would be happy to hop on a call to start things rolling. Please let us know when you'd like to do this...Do we have a timetable for the release?

Maria

On Dec 1, 2015, at 9:47 PM, Stern, Robert A <bobstern@bu.edu> wrote:

> Thanks Pat. Good to meet you Marian.
> I am cc'ing Maria Pantages Ober, Director of the Office of Communications at BU School of Medicine. Since BU is the recipient institution, Maria will hopefully be able to coordinate efforts between NINDS, BU, and the institutions of the other three PIs: Dr. Cummings (Cleveland Clinic), Dr. Reiman (Banner Alzheimer's Institute), and Dr. Shenton (Brigham and Women's Hospital). Perhaps a starting point would be for Marian and Maria to connect. To get everyone on the same page, I have attached the a summary of the project along with a listing of the investigator team. I am not sure when the Notice of Grant Award will be received (Pat, any word on your end?), but given all that has been going in the media regarding CTE (e.g., Frank Gifford's diagnosis, the upcoming Will Smith "Concussion" movie), it may be helpful to move somewhat quickly on this. Marian and Maria, please let me know if you would like to schedule a time for a conference call. If not, let me know if you have any questions. Thanks very much, everyone!
>
> Regards,
>
> Bob
>
> Robert A. Stern, Ph.D.
> Professor of Neurology, Neurosurgery, and Anatomy & Neurobiology
> Director, Clinical Core, BU Alzheimer's Disease and CTE Center
> Boston University School of Medicine
>
> 72 East Concord Street, B7800
> Boston, MA 02118
>
> Tel: 617-638-5678
> Fax: 617-638-5679
> Email: bobstern@bu.edu
> www.sternneurolab.org

From: Bellgowan, Patrick (NIH/NINDS) [E] [mailto:patrick.frostbellgowan@nih.gov]
Sent: Tuesday, December 01, 2015 2:52 PM
To: Emr, Marian (NIH/NINDS) [E] <emrm@ninds.nih.gov>; Stern, Robert A <bobstern@bu.edu>
Subject: RE: Preparation for U01 award press release

Hi Bob,

Marian Emr is the Director of the Office of Communications and Public Liaison for NINDS and can work with your and/or the PR people from each of your institutes to help produce a Press release for the U01 award on Diagnosing CTE. Please contact her and she can lead the group through the NIH process.

Best wishes
Pat

Patrick SF Bellgowan, PhD

Program Director, Repair and Plasticity
NIH/NINDS
301-496-1447
psfb@mail.nih.gov

http://www.ninds.nih.gov/disorders/tbi/tbi.htm

From: Koroshetz, Walter (NIH/NINDS) [E]
Sent: Tuesday, December 01, 2015 2:17 PM
To: Emr, Marian (NIH/NINDS) [E]; Bellgowan, Patrick (NIH/NINDS) [E]
Subject: Re: Preparation for U01 award press release

Thanks Marian. Pat, want to hook Marian up with Bob.
Walter

From: Marian Emr <emrm@ninds.nih.gov>
Date: Tuesday, December 1, 2015 at 2:15 PM
To: "Koroshetz, Walter (NIH/NINDS) [E]" <koroshetzw@ninds.nih.gov>, Patrick Bellgowan <patrick.frostbellgowan@nih.gov>
Subject: RE: Preparation for U01 award press release

OCPL would be happy to work with the grantee Institutions to coordinate an NIH release timed with theirs.
Marian

Marian Emr
Director, Office of Communications and Public Liaison/NINDS
NIH Building 31, Room 8A07
Phone: (301) 496-5924
marian.emr@nih.gov

From: Koroshetz, Walter (NIH/NINDS) [E]
Sent: Tuesday, December 01, 2015 2:07 PM
To: Bellgowan, Patrick (NIH/NINDS) [E]
Cc: Emr, Marian (NIH/NINDS) [E]
Subject: ACTION: Preparation for U01 award press release

Yes, I agree that press release would be important. Either NINDS or joint.
Walter

From: Patrick Bellgowan <patrick.frostbellgowan@nih.gov>
Date: Tuesday, December 1, 2015 at 1:51 PM
To: Bob Stern <bobstern@bu.edu>, "Koroshetz, Walter (NIH/NINDS) [E]" <koroshetzw@ninds.nih.gov>, Debra Babcock <dbabcock@ninds.nih.gov>
Cc: Marian Emr <emrm@ninds.nih.gov>
Subject: RE: Preparation for U01 award press release

Hi Bob,
It appears that there was a Press release when the 1st wave of grants were awarded. I think that with the whirlwind around CTE presently it would be great to let people know that NINDS is funding a project aimed at developing a ante-mortem diagnosis but this decision is above my pay-grade.

Thanks

pat

Patrick SF Bellgowan, PhD
Program Director, Repair and Plasticity
NIH/NINDS
301-496-1447
psfb@mail.nih.gov

http://www.ninds.nih.gov/disorders/tbi/tbi.htm

From: Stern, Robert A [mailto:bobstern@bu.edu]
Sent: Tuesday, December 01, 2015 12:01 PM
To: Koroshetz, Walter (NIH/NINDS) [E]; Bellgowan, Patrick (NIH/NINDS) [E]; Babcock, Debra (NIH/NINDS) [E]
Subject: Preparation for U01 award press release

Hi everyone,
I hope your Thanksgivings were wonderful. Now that it is December 1, my co-PI's and I are eagerly anticipating the NoGA for the CTE U01. All four institutions (Cleveland Clinic, Banner, Brigham & Women's, and BU) are, therefore, hoping to work with NINDS if a press release will be developed and released. Or, if NINDS will not be doing a press release on the award, the four individual sites would like to do their own. Do you know if this is the type of grant for which NINDS/NIH would be issuing a press release? If so, is it appropriate timing for the Communications offices at the four institutions to be communicating with the NIH folks in anticipation of the award? Let me know when you can. Thanks much.

Regards,

Bob

Robert A. Stern, Ph.D.
Professor of Neurology, Neurosurgery, and Anatomy and Neurobiology
Clinical Core Director, BU Alzheimer's Disease and CTE Center
Boston University School of Medicine

72 East Concord Street, B7800
Boston, MA 02118

Dir. Tel: 617-638-5678 * Nicole Gullotti (Admin. Asst.): 617-414-1195
Fax: 617-638-5679

Email: bobstern@bu.edu

<CTE U01 Summary - 12-1-15.docx>

Jason, Cailin (NIH/NINDS) [C]

From: Wilczewski, Gina Maria <ginad@bu.edu>
Sent: Thursday, December 17, 2015 11:58 AM
To: Emr, Marian (NIH/NINDS) [E]
Cc: McMakin, Barbara (NIH/NINDS) [E]
Subject: ACTION: UO1 press release

Follow Up Flag: Follow up
Flag Status: Flagged

Just following to make sure you did receive the email I sent you late yesterday afternoon with the draft.

Gina DiGravio-Wilczewski
Media Relations Manager
Boston University School of Medicine
617-638-8480 (O)
617-224-8962 (M)
ginad@bu.edu

From: Wilczewski, Gina Maria
Sent: Wednesday, December 16, 2015 4:30 PM
To: Emr, Marian (NIH/NINDS) [E]
Cc: Ober, Maria Pantages (mpober@bu.edu); Stern, Robert A; 'McMakin, Barbara (NIH/NINDS) [E]'
Subject: UO1 press release

Marian,
As per Dr. Stern's discussion with Dr. Koroshetz last week, we are taking the lead on issuing a press release announcing the receipt of this grant. We understand the NIH will not be issuing anything.

The attached release was collaboratively developed with the four PIs and their public information officers.
We feel it is ready for release but are sending it to you for your review.
We would appreciate receiving your feedback by this Friday (12/18) morning.
Our current plan is to distribute it widely on Monday (12/21) morning.
In anticipation of this announcement, we shared an earlier draft version of the release with two ESPN reporters, with whom we have had a longstanding relationship, to allow them the opportunity to include the other PIs in their story.
Look forward to hearing from you.
Thank you

Gina DiGravio-Wilczewski
Media Relations Manager
Boston University School of Medicine
617-638-8480 (O)
617-224(b) (6)(M)
ginad@bu.edu

DRAFT **DRAFT** **DRAFT** **DRAFT**

FOR IMMEDIATE RELEASE, date
Contact: Gina DiGravio, 617-638-8480, ginad@bu.edu

NIH/NINDS Grant Awarded to Develop Methods for Diagnosing Chronic Traumatic Encephalopathy (CTE) During Life

(Boston)—Researchers from Boston University, the Cleveland Clinic, Banner Alzheimer's Institute and Brigham and Women's Hospital in Boston, have been awarded a $16 million grant from the National Institutes of Health/National Institute of Neurological Disorders and Stroke (NIH/NINDS). This seven-year, multi-center grant will be used to create methods for detecting and diagnosing chronic traumatic encephalopathy (CTE) during life as well as examining risk factors for CTE.

CTE is a degenerative brain disease characterized by changes in behavior, mood and cognition, including the development of dementia. Currently it can only be diagnosed post-mortem through examination of an abnormal form of tau protein. CTE has been found most often in professional contact sport athletes (e.g., boxers, football players) who have been subjected to repetitive blows to the head resulting in symptomatic concussive and asymptomatic subconcussive trauma. Neuropathologically-confirmed CTE has been reported in individuals as young as 17 and in athletes who only played sports through high school or college. It also has been found in non-athletes who experienced repetitive head impacts, including military service members.

According to the researchers, although the neuropathological features of CTE have become further clarified in recent years, the clinical presentation of CTE is still not well characterized and there remains no method to diagnose it before death. "There are so many critical unanswered questions about CTE. We are optimistic that this project will lead to many of these answers, by developing accurate methods of detecting and diagnosing CTE during life, and by examining genetic and other risk factors for this disease." explained lead principal investigator, Robert Stern, PhD, professor of neurology, neurosurgery, and anatomy & neurobiology at Boston University School of Medicine, where he is Clinical Core director of the Boston University Alzheimer's Disease and CTE Center.

Through this grant, NINDS is funding a longitudinal study of former NFL players, former college football players, and a control group of individuals without any history of contact sports or brain injury. Participants will be examined at one of four centers across the country, including Boston University School of Medicine; Cleveland Clinic Lou Ruvo Center for Brain Health in Las Vegas; Mayo Clinic in Scottsdale, Ariz; and New York University Langone Medical Center, New York City.

Participants in the study will undergo extensive clinical examinations, as well as state-of-the art PET scans, advanced MRI scans, experimental blood tests and other potential methods of detecting changes in the brain associated with CTE. Researchers also will refine and validate specific criteria for clinical diagnosis of the disease and will investigate genetic and head impact exposure risk factors for CTE in order to begin to determine why some people are more prone to get CTE than others. Project data will be shared with researchers across the country and abroad to facilitate a more complete understanding of this disease, ultimately leading to successful methods of preventing and treating CTE.

The other principal investigators are Jeffrey Cummings, MD, ScD, (director, Cleveland Clinic Lou Ruvo Center for Brain Health in Las Vegas and Cleveland; the Camille and Larry Ruvo Chair of the Neurological Institute of Cleveland Clinic; and professor of medicine, Cleveland Clinic Lerner College of Medicine at Case Western Reserve University); Eric Reiman, MD (executive director of the Banner Alzheimer's Institute, Phoenix) and Martha Shenton, PhD (director, Psychiatry Neuroimaging Laboratory and senior scientist, Brigham and Women's Hospital; professor of psychiatry and radiology, Harvard Medical School). The project involves a group of approximately 50 investigators, representing 17 research institutions.

"There is an urgent need to clarify the clinical and biological consequences of repetitive head impacts in athletics and to use this information to find the best ways to treat and prevent those consequences," said Reiman. "It is both a great privilege and responsibility to help in that endeavor."

"This research is an exciting and important opportunity to acquire new information about the potential devastating consequences of repetitive head impact including CTE," said Shenton. "We hope that by gaining this knowledge, new avenues of treatment will emerge for those who experience debilitating symptoms from repetitive brain trauma."

"We currently have no method to diagnosis CTE during life and it is crucial to take the next steps to better understand this disease," said Cummings. "This grant will allow us to take what we know about CTE and move to the next level of research, with the end goal of diagnosing these athletes at early stages of the illness when treatments may help prevent the progression of the disease."

Editors Note:
The exact amount of this grant is $15,859,906.

Jason, Cailin (NIH/NINDS) [C]

From: Bellgowan, Patrick (NIH/NINDS) [E]
Sent: Thursday, December 17, 2015 2:29 PM
To: Emr, Marian (NIH/NINDS) [E]
Subject: ACTION: U01 press release

Looks fine to me.

Patrick SF Bellgowan, PhD
Program Director, Repair and Plasticity
NIH/NINDS
301-496-1447
psfb@mail.nih.gov

http://www.ninds.nih.gov/disorders/tbi/tbi.htm

From: Emr, Marian (NIH/NINDS) [E]
Sent: Thursday, December 17, 2015 2:20 PM
To: Koroshetz, Walter (NIH/NINDS) [E]; Bellgowan, Patrick (NIH/NINDS) [E]
Cc: Mott, Meghan (NIH/NINDS) [E]; McMakin, Barbara (NIH/NINDS) [E]
Subject: U01 press release
Importance: High

Attached is BU's draft release announcing the new CTE grant. Their plan is to distribute it to the press on Monday morning. I think the draft looks quite good but please take a look at it and let me know if you have any comments or suggestions for changes. I have already asked them to add the grant number in accordance with NIH policy.
BU has already shared the draft with two trusted ESPN reporters (on an embargoed basis). We are trying to arrange a time on Monday at noon for Walter to speak with Steve Fainaru.
Walter: Do you have 5 minutes to discuss before you head over to the DIR holiday party?
Marian

Marian Emr
Director, Office of Communications and Public Liaison/NINDS
NIH Building 31, Room 8A07
Phone: (301) 496-5924
marian.emr@nih.gov

Jason, Cailin (NIH/NINDS) [C]

From: McMakin, Barbara (NIH/NINDS) [E]
Sent: Thursday, December 17, 2015 3:01 PM
To: Emr, Marian (NIH/NINDS) [E]
Subject: ACTION: CTE talking points

Hi Marian,

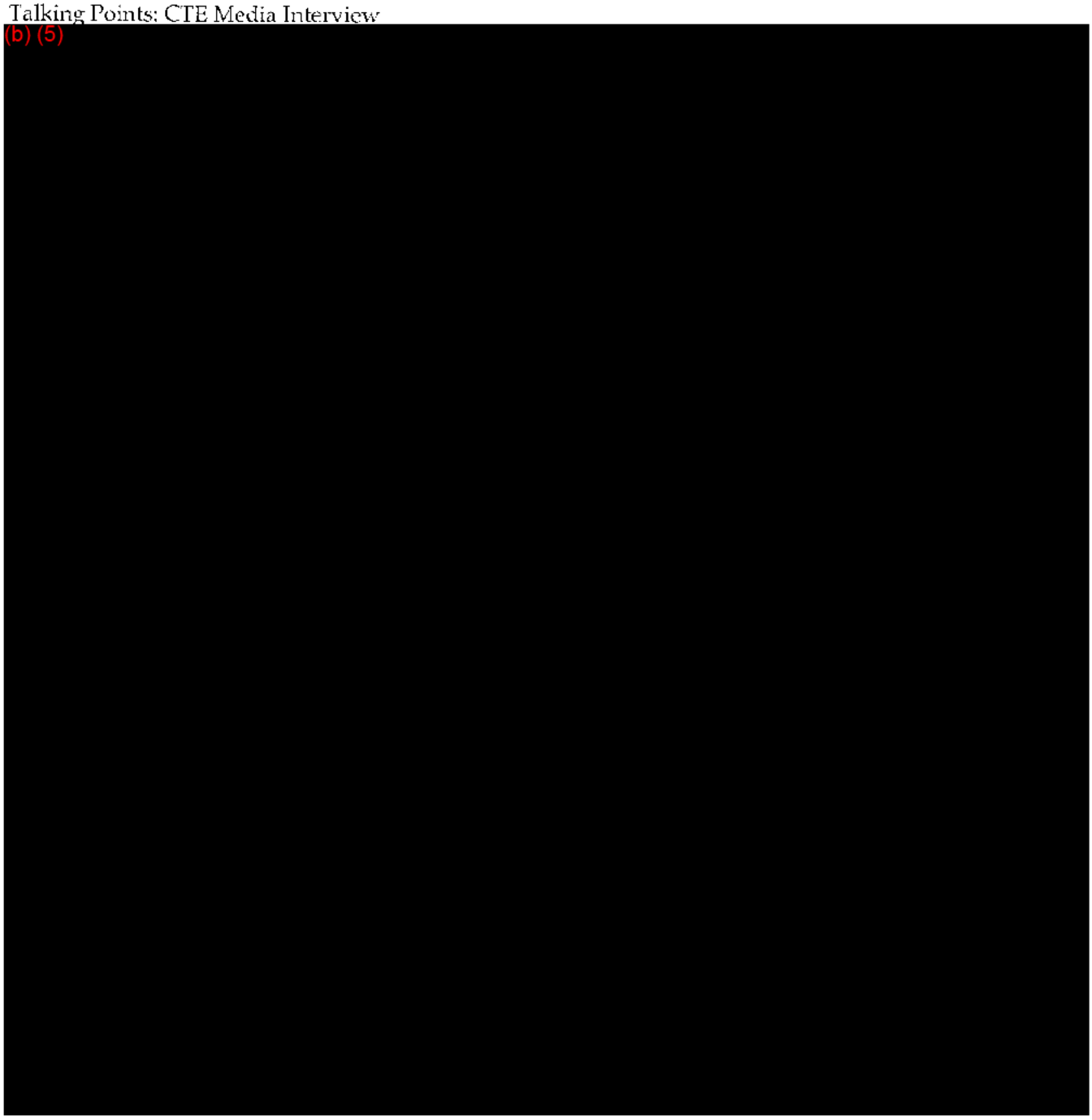
Attached is what I have so far for talking points. Am I on the right track with this; is this what Building 1 is expecting?

Thanks,
Barbara

Barbara I. McMakin
Science Writer
Office of Communications and Public Liaison
National Institute of Neurological Disorders & Stroke
National Institutes of Health
Building 31, Room 8A07
31 Center Drive MSC 2540
Bethesda, MD 20892-2540
Main Office Line: (301) 496-5751
Direct Line: (301) 435-7747
Email: mcmakinbi@ninds.nih.gov

Talking Points: CTE Media Interview

(b) (5)



Jason, Cailin (NIH/NINDS) [C]

From: Ober, Maria Pantages <mpober@bu.edu>
Sent: Friday, December 18, 2015 1:49 PM
To: McMakin, Barbara (NIH/NINDS) [E]
Cc: Stern, Robert A; Wilczewski, Gina Maria; Emr, Marian (NIH/NINDS) [E]
Subject: PRESS: UO1 press release

Thank you, Marian...we will move forward as outlined below.

From: McMakin, Barbara (NIH/NINDS) [E] [mailto:mcmakinbi@ninds.nih.gov]
Sent: Friday, December 18, 2015 1:47 PM
To: Ober, Maria Pantages <mpober@bu.edu>
Cc: Stern, Robert A <bobstern@bu.edu>; Wilczewski, Gina Maria <ginad@bu.edu>; Emr, Marian (NIH/NINDS) [E] <emrm@ninds.nih.gov>
Subject: RE: UO1 press release

Hi Maria,

Thank you for honoring our request to push back the embargo on the release.

Other than the grant number, we have no additional changes to your release.

Best,
Barbara

From: Ober, Maria Pantages [mailto:mpober@bu.edu]
Sent: Friday, December 18, 2015 1:34 PM
To: Emr, Marian (NIH/NINDS) [E]
Cc: Stern, Robert A; Wilczewski, Gina Maria; McMakin, Barbara (NIH/NINDS) [E]
Subject: RE: UO1 press release

Marian, Barbara:
Totally understand things from your perspective. We will embargo the announcement for **9 a.m. EST Tuesday, Dec. 22.**
How does that sound?
If you're fine with that, please let me know and we will notify the PIs and communications colleagues (and the Fainaru bros).

We've added the grant number to the release in the editor's note; other than that. I would like your confirmation that you had no other content suggestions.

Thank you.
maria

From: Emr, Marian (NIH/NINDS) [E] [mailto:emrm@ninds.nih.gov]
Sent: Friday, December 18, 2015 11:06 AM
To: Ober, Maria Pantages <mpober@bu.edu>
Cc: Stern, Robert A <bobstern@bu.edu>; Wilczewski, Gina Maria <ginad@bu.edu>; McMakin, Barbara (NIH/NINDS) [E] <mcmakinbi@ninds.nih.gov>
Subject: RE: UO1 press release

Your release is very well written. We would only ask that you include the grant number somewhere in the release (a footnote will do) so that it is picked up by the NIH RePORTER search algorithm.
Hoping you will consider our request to allow time for Dr. Koroshetz to speak with Steve before you release. I wouldn't be surprised if you receive the same request for consideration from him.
Marian

From: Ober, Maria Pantages [mailto:mpober@bu.edu]
Sent: Friday, December 18, 2015 10:57 AM
To: McMakin, Barbara (NIH/NINDS) [E]; Wilczewski, Gina Maria
Cc: Emr, Marian (NIH/NINDS) [E]; Stern, Robert A
Subject: UO1 press release

Barbara
We will confer on our end and get back to you this afternoon.

Meanwhile, any feedback on the release or is that good to go? Please send the grant number so that we can include that.

Thank you,
maria

From: McMakin, Barbara (NIH/NINDS) [E] [mailto:mcmakinbi@ninds.nih.gov]
Sent: Friday, December 18, 2015 10:52 AM
To: Wilczewski, Gina Maria <ginad@bu.edu>
Cc: Emr, Marian (NIH/NINDS) [E] <emrm@ninds.nih.gov>; Ober, Maria Pantages <mpober@bu.edu>; Stern, Robert A <bobstern@bu.edu>
Subject: RE: UO1 press release

Hi Gina,

I just spoke with Marian. We're dealing with pressure on our end regarding the timing of your statement and Dr. Koroshetz's interview with the Fainara brothers. Dr. Koroshetz is scheduled to speak with them at noon on Monday. Would you reconsider delaying your release until Monday afternoon or Tuesday morning?

Best,
Barbara

From: Wilczewski, Gina Maria [mailto:ginad@bu.edu]
Sent: Thursday, December 17, 2015 3:58 PM
To: Emr, Marian (NIH/NINDS) [E]; Ober, Maria Pantages; Stern, Robert A
Cc: McMakin, Barbara (NIH/NINDS) [E]
Subject: RE: UO1 press release

Marian,
We need to go forward with the dissemination of the release on Monday (12/21) morning as planned.
As Dr. Stern and Maria have both explained we are feeling pressure to proceed with the announcement.

Gina DiGravio-Wilczewski
Media Relations Manager
Boston University School of Medicine
617-638-8480 (O)
617-224(b) (6)(M)
ginad@bu.edu

From: Emr, Marian (NIH/NINDS) [E] [mailto:emrm@ninds.nih.gov]
Sent: Thursday, December 17, 2015 2:42 PM
To: Ober, Maria Pantages; Stern, Robert A
Cc: McMakin, Barbara (NIH/NINDS) [E]; Wilczewski, Gina Maria
Subject: RE: UO1 press release

Steve has contacted us, as well, but I can't get him time to speak with Walter until noon on Monday which is why I was asking for some leeway in the release time.
Marian

Marian Emr
Director, Office of Communications and Public Liaison/NINDS
NIH Building 31, Room 8A07
Phone: (301) 496-5924
marian.emr@nih.gov

From: Ober, Maria Pantages [mailto:mpober@bu.edu]
Sent: Thursday, December 17, 2015 2:39 PM
To: Stern, Robert A; Emr, Marian (NIH/NINDS) [E]; Wilczewski, Gina Maria
Cc: McMakin, Barbara (NIH/NINDS) [E]
Subject: RE: UO1 press release

Thank you. Bob... I'll respond from our communications point of view and echo what you are saying. We are getting pressure to announce with adequate time before the holidays so that PIs are available to do interviews. Monday morning works for everyone.

Regarding ESPN, we are dealing with the Fainaru brothers, Steve and Mark.

maria

From: Stern, Robert A
Sent: Thursday, December 17, 2015 2:35 PM
To: Emr, Marian (NIH/NINDS) [E] <emrm@ninds.nih.gov>; Wilczewski, Gina Maria <ginad@bu.edu>
Cc: Ober, Maria Pantages <mpober@bu.edu>; McMakin, Barbara (NIH/NINDS) [E] <mcmakinbi@ninds.nih.gov>
Subject: RE: UO1 press release

Thanks Marian. I'm not sure if Gina has responded yet, but I wanted to give my input about the timing. My co-PIs and their teams are really wanting to move forward with the announcement; a combination of pressure from their institutions, a desire to get the word out quickly, and also with the holidays coming up, they would like to make sure that the announcement is widely disseminated before people go on vacation. For me personally, I will be going out of the country for a week starting on the 24th, and so I want to make sure I am available for interviews following the release. For all these reasons, I would very much like to keep to the Monday morning release. I hope you understand.

Regards,

Bob

From: Emr, Marian (NIH/NINDS) [E] [mailto:emrm@ninds.nih.gov]
Sent: Thursday, December 17, 2015 2:09 PM
To: Wilczewski, Gina Maria <ginad@bu.edu>
Cc: Ober, Maria Pantages <mpober@bu.edu>; Stern, Robert A <bobstern@bu.edu>; McMakin, Barbara (NIH/NINDS) [E] <mcmakinbi@ninds.nih.gov>
Subject: RE: UO1 press release

Gina: Thanks for sharing your draft with us. We've asked a few people to take a look at it (on very close hold, of course) and will get back to you by tomorrow. One thing that we will need you to do is to add the grant number somewhere on the release. A footnote will do.
I wonder if you would be willing to hold on your release until Tuesday morning since we're trying to find availability for Dr. Koroshetz to speak with reporters who have questions about the grant. Also, can you tell us who you've spoken with at ESPN?
Marian

Marian Emr
Director, Office of Communications and Public Liaison/NINDS
NIH Building 31, Room 8A07
Phone: (301) 496-5924
marian.emr@nih.gov

From: Wilczewski, Gina Maria [mailto:ginad@bu.edu]
Sent: Wednesday, December 16, 2015 4:30 PM
To: Emr, Marian (NIH/NINDS) [E]
Cc: Ober, Maria Pantages; Stern, Robert A; McMakin, Barbara (NIH/NINDS) [E]
Subject: ACTION: UO1 press release

Marian,
As per Dr. Stern's discussion with Dr. Koroshetz last week, we are taking the lead on issuing a press release announcing the receipt of this grant. We understand the NIH will not be issuing anything.

The attached release was collaboratively developed with the four PIs and their public information officers.
We feel it is ready for release but are sending it to you for your review.
We would appreciate receiving your feedback by this Friday (12/18) morning.
Our current plan is to distribute it widely on Monday (12/21) morning.
In anticipation of this announcement, we shared an earlier draft version of the release with two ESPN reporters, with whom we have had a longstanding relationship, to allow them the opportunity to include the other PIs in their story.
Look forward to hearing from you.
Thank you

Gina DiGravio-Wilczewski
Media Relations Manager
Boston University School of Medicine
617-638-8480 (O)
617-224(b) (M)
ginad@bu.edu

Jason, Cailin (NIH/NINDS) [C]

From: Bellgowan, Patrick (NIH/NINDS) [E]
Sent: Friday, December 18, 2015 2:59 PM
To: McMakin, Barbara (NIH/NINDS) [E]
Cc: Emr, Marian (NIH/NINDS) [E]
Subject: PRESS: CTE grant: Banner Health release

Maybe a bit long but very good.

Patrick SF Bellgowan, PhD
Program Director. Repair and Plasticity
NIH/NINDS
301-496-1447
psfb@mail.nih.gov

http://www.ninds.nih.gov/disorders/tbi/tbi.htm

From: McMakin, Barbara (NIH/NINDS) [E]
Sent: Friday, December 18, 2015 1:56 PM
To: Bellgowan, Patrick (NIH/NINDS) [E]
Cc: Emr, Marian (NIH/NINDS) [E]
Subject: CTE grant: Banner Health release

Hi Pat,

Attached is a draft release from Banner Health. Please take a look at it and let me know if you have any edits or comments.

Thanks,
Barbara

Barbara I. McMakin
Science Writer
Office of Communications and Public Liaison
National Institute of Neurological Disorders & Stroke
National Institutes of Health
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31 Center Drive MSC 2540
Bethesda, MD 20892-2540
Main Office Line (301) 496-5751
Direct Line (301) 435-7747
Email: mcmakinbi@ninds.nih.gov

DRAFT 12 18 15

Banner
Alzheimer's
Institute

MAYO
CLINIC

Contact:
Sarah Boggan, Banner Alzheimer's Institute
sarah.boggan@bannerhealth.com

Jim McVeigh, Mayo Clinic
Mcveigh.jim@mayo.edu

FOR IMMEDIATE RELEASE

Banner Alzheimer's Institute and Mayo Clinic Arizona to Participate in Multi-Center Study of Chronic Traumatic Encephalopathy in Former Football Players

Researchers awarded $16 million to advance detection of serious brain disease

PHOENIX (December XX, 2015) – Researchers from Phoenix-based Banner Alzheimer's Institute (BAI) and Mayo Clinic Arizona will participate in a new $16 million federally funded study of former professional and college football players, attempting to create methods to detect and diagnose a serious brain disease known as chronic traumatic encephalopathy (CTE) before death.

Under a seven-year, multi-center grant from the National Institutes of Health/National Institute of Neurological Disorders and Stroke (NIH/NINDS), the two Arizona research facilities will work with physicians and scientists from Boston University, the Cleveland Clinic and New York University.

"There is an urgent need to clarify the clinical and biological consequences of repetitive head injuries, as well as the factors that lead some but not all athletes to develop chronic traumatic encephalopathy, and to use this information to find the best ways to treat and prevent this condition," said Eric Reiman, MD, executive director of BAI and one of the four multi-center principal investigators for the grant.

Mayo Clinic will conduct extensive clinical examinations, advanced MRI scans, experimental blood tests and other tests in an effort to detect the changes in the brain associated with CTE on study participants. BAI will conduct state-of-the art PET scans in the same research participants, including information about the accumulation of an abnormal tau protein, a characteristic feature of this disease seen in the brains of autopsied individuals, and assist in the analysis of the brain imaging data.

CTE is a degenerative brain disease that occurs in individuals with repetitive head injuries and is characterized by changes in behavior, mood and memory, and may lead to the development of dementia and Parkinson's disease. It has been described most extensively in boxers and football players, but has also been reported in individuals who have played in other contact sports and in some military veterans. Many cases have been diagnosed in deceased former professional football players, and currently CTE can only be diagnosed by autopsy.

The grant will fund a study in which former professional football players, former college football players and a control group of individuals without any history of contact sports or brain injury will be examined over a few years' time.

"Although we've made some progress in understanding CTE, the clinical presentation of this disorder is still not well characterized," said Charles Adler, MD, PhD, professor of neurology at the Mayo Clinic and principal investigator for the study's combined Arizona site. "The main goal of our study is to identify biomarkers that predict which individuals will have CTE, as currently we are only able to make the diagnosis after death."

David Dodick, MD, professor of neurology and director of the Mayo Clinic Sports Neurology and Concussion Program, will provide his extensive clinical expertise in CTE to the research team. Dodick said, "This study will bring together many of the nation's foremost experts who will use their clinical expertise and the most advanced tools to develop diagnostic and prognostic markers of CTE. Ultimately, the ability to identify who is at risk and what the earliest manifestations of the disease are will enable strategies aimed at preventing the disease before it develops or treating the disease after it's begun."

Adler added that by finding tests to predict who may develop CTE during life, we then expect to find treatments to stop this devastating disease.

Drs. Reiman, Adler and Dodick all maintain that it is both a great privilege and responsibility for BAI and Mayo Clinic researchers to partner with leading experts from around the U.S. to help find solutions to this devastating neurological disease.

Banner Alzheimer's Institute and Mayo Clinic's collaboration in this study is part of their commitment to furthering Arizona's leadership position in scientific advancement. They are key members of the Arizona Alzheimer's Consortium, the nation's leading model of statewide collaboration in Alzheimer's disease research, and the Arizona Parkinson's Disease Consortium, a collaboration in Parkinson's disease research.

"There are so many critical unanswered questions about CTE," explained lead principal investigator, Robert Stern, PhD, clinical core director of the Boston University Alzheimer's Disease and CTE Center. "We are optimistic that this project will lead to many of these answers, by developing accurate methods of detecting and diagnosing CTE during life, and by examining genetic and other risk factors for this disease."

The researchers will characterize the clinical features of CTE and develop clinical criteria for the disorder. They will also seek to clarify the nature and extent of head injuries and genetic factors that lead some but not all football players to develop clinical and biological features of CTE.

Project data will be shared with researchers around the world to promote understanding of this disease, ultimately leading to successful methods of preventing and treating CTE.

###

About the Banner Alzheimer's Institute

Banner Alzheimer's Institute (BAI) is a nonprofit organization dedicated to the goal of ending Alzheimer's disease without losing another generation. It is helping to launch a new era of Alzheimer's research—detection, treatment and prevention at the pre-symptomatic stage—and to establish a comprehensive model of care that can be the national standard. BAI was founded in 2006 by Phoenix-based Banner Health, one of the country's largest nonprofit healthcare systems. For more information, go to www.banneralz.org.

About Mayo Clinic

Recognizing 150 years of serving humanity in 2014, Mayo Clinic is a nonprofit worldwide leader in medical care, research and education for people from all walks of life. The Neurology Department at Mayo Clinic Arizona is one of the largest in the Southwest United States and specializes in the treatment of athletes suffering from concussion as well as dementia and Parkinson's disease. For more information, visit 150years.mayoclinic.org, www.mayoclinic.org and newsnetwork.mayoclinic.org.

About the Arizona Alzheimer's Consortium

The Arizona Alzheimer's Consortium (AAC) is the nation's leading model of statewide collaboration in Alzheimer's disease research. Established in 1998, the Consortium capitalizes on its participating institutions' complementary strengths in brain imaging computer science, genomics, the basic and cognitive neurosciences and clinical and neuropathology research to promote the scientific understanding and early detection of Alzheimer's disease and find effective disease-stopping and prevention therapies. It also seeks to educate Arizona residents about Alzheimer's disease, research progress in the state and the resources needed to help patients, families and professionals manage the disease. The Consortium is determined to find effective treatments to halt the progression and prevent the onset of Alzheimer's disease in the next 12 years.

About the Arizona Parkinson's Disease Consortium

The Arizona Parkinson's Disease Consortium (APDC) is a unique collaboration of Arizona researchers performing a longitudinal clinicopathological study of patients with Parkinson's disease and similar disorders. The clinical component is called the Arizona Study of Aging and Neurodegenerative Disorders and all participants have agreed to be autopsied at the end of life providing a valuable resource of tissue for scientists around the world to study this disease. The goals of the APDC include finding the cause of Parkinson's disease as well as treatments to improve symptoms and eventually stop the progression of disease.

Jason, Cailin (NIH/NINDS) [C]

From: Emr, Marian (NIH/NINDS) [E]
Sent: Monday, December 21, 2015 8:12 AM
To: Burklow, John (NIH/OD) [E]
Subject: PRIORITY ACTION: CTE talking points

Importance: High

Follow Up Flag: Follow up
Flag Status: Flagged

Good morning, John. Do you and Kathy want any changes in the talking points we put together for Walter's noon interview with Steve Fainaru? I am getting ready to brief him and would like him to take a look at them.
Marian

Marian Emr
Director, Office of Communications and Public Liaison/NINDS
NIH Building 31, Room 8A07
Phone: (301) 496-5924
marian.emr@nih.gov

From: Emr, Marian (NIH/NINDS) [E]
Sent: Thursday, December 17, 2015 4:24 PM
To: Burklow, John (NIH/OD) [E]
Cc: Myles, Renate (NIH/OD) [E]; McMakin, Barbara (NIH/NINDS) [E]
Subject: CTE talking points

John: Walter is scheduled to speak with Steve Fainaru on Monday shortly after noon. We will take the call in his conference room (31/8A-52). Attached are some draft talking points and background information for your review. Barbara can make any changes you want (and will also send a request for interview approval) tomorrow morning.
Also attached for your information is a paper published this week highlighting the results of the NIH-run (SHRP- funded) consensus meeting on the pathological diagnosis of CTE.
Marian

Marian Emr
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Jason, Cailin (NIH/NINDS) [C]

From: McMakin, Barbara (NIH/NINDS) [E]
Sent: Monday, December 21, 2015 8:50 AM
To: Emr, Marian (NIH/NINDS) [E]
Subject: PRESS: 2013 CTE press release

Hi Marian,

The 2013 press release can be found here:
http://www.ninds.nih.gov/news_and_events/news_articles/pressrelease_nfl_tbi_12162013.htm
I have also attached a copy of the release.

Thanks,
Barbara

Barbara I. McMakin
Science Writer
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National Institute of Neurological Disorders & Stroke
National Institutes of Health
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U.S. Department of Health and Human Services
NIH News
National Institutes of Health

National Institute of Neurological Disorders and Stroke (NINDS)
www.ninds.nih.gov

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December 16, 2013
9:00 am EST

CONTACT:
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NIH and NFL tackle concussion research

NIH announces research projects funded largely by donation from the NFL

The National Institutes of Health has selected eight projects to receive support to answer some of the most fundamental problems on traumatic brain injury, including understanding long-term effects of repeated head injuries and improving diagnosis of concussions.

Funding is provided by the Sports and Health Research Program, a partnership among the NIH, the National Football League, and the Foundation for the National Institutes of Health (FNIH). In 2012, the NFL donated $30 million to FNIH for research studies on injuries affecting athletes, with brain trauma being the primary area of focus.

Traumatic brain injury (TBI) is a major public health problem that affects all age groups and is the leading cause of death in young adults. Recently, concern has been raised about the potential long-term effects of repeated concussion, particularly in those most at risk: young athletes and those engaged in professions associated with frequent head injury, including men and women in the military. Current tests cannot reliably identify concussions, and there is no way to predict who will recover quickly, who will suffer long-term symptoms, and which few individuals will develop progressive brain degeneration, called chronic traumatic encephalopathy (CTE).

"We need to be able to predict which patterns of injury are rapidly reversible and which are not. This program will help researchers get closer to answering some of the important questions about concussion for our youth who play sports and their parents." said Story Landis, Ph.D., director of the National Institute of Neurological Disorders and Stroke (NINDS), part of NIH.

Two ($6 million each) are large, cooperative agreements focused on defining the scope of long-term changes that occur in the brain years after a head injury or after multiple concussions. The cooperative awards form a partnership between NINDS, the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD) and multiple academic medical centers.

NIH also will fund six pilot projects totaling just over $2 million that will last up to two years and are designed to provide support for the early stages of sports-related concussion projects. If the

early results are encouraging, they may become the basis of more comprehensive projects. The NIH institutes responsible for managing these grants are NINDS, NICHD, and the National Institute on Deafness and Other Communication Disorders (NIDCD).

The eight projects were selected by the NIH following a rigorous scientific review process.

The cooperative awards bring together two teams of independent scientists to study and compare the brains of donors who were at high or low risk for developing long-term effects of TBI. Ten neuropathologists from eight universities will coordinate to describe the chronic effects of head injury in tissue from hundreds of individuals in order to develop standards for diagnosis.

The project includes four teams that will correlate brain scans with changes in brain tissue, using a variety of techniques. This may open the possibility of using these advanced brain imaging techniques to diagnose chronic effects of TBI in living individuals. The investigators in the two projects will also help NIH develop a registry dedicated to enrolling individuals with a history of TBI who are interested in donating brain and spinal cord tissue for study after their death. The new NIH Neurobiobank (https://neurobiobank.nih.gov) will coordinate the tissue collection, data gathering, and also distribute biospecimens, along with relevant information to enable other scientists to access this valuable tissue.

The two cooperative agreements are:

• CTE and Post-traumatic Neurodegeneration: Neuropathology and Ex Vivo Imaging
Principal Investigator: Ann C. McKee, M.D., Boston University School of Medicine and U.S. Department of Veterans Affairs

At present, the diagnosis of CTE is made by examining the brain after death; however, the range of specific features that identify this disorder has not been established. One goal of Dr. McKee's project is to define a clear set of criteria for the various stages of CTE and to distinguish it from Alzheimer's, amyotrophic lateral sclerosis, and other neurodegenerative disorders in post-mortem brain tissue. Once these characteristics have been defined in brain tissue, the imaging teams at Washington University in St. Louis and Massachusetts General Hospital in Boston will correlate them with brain scans to identify features that might eventually be used to diagnose CTE in individuals during their lifetimes.

• Neuropathology of CTE and Delayed Effects of TBI: Toward In Vivo Diagnostics
Principal Investigator: Wayne Gordon, Ph.D., Mount Sinai Hospital, New York City

The goal of Dr. Gordon's project is to identify and describe the chronic effects of mild, moderate and severe TBIs and compare these with the features of CTE. Dr. Gordon and his colleagues at the University of Washington in Seattle will comprehensively evaluate brain tissue obtained from an ongoing study of thousands of people, the Adult Changes in Thought (ACT) study, funded by the National Institute of Aging. They also will examine brain tissue from donors who suffered severe TBI and were cared for in the TBI Model Systems program funded by the Department of Education's National Institute on Disability and Rehabilitation Research. In Dr. Gordon's project, neuroimaging teams at Massachusetts General Hospital, Oregon Health Sciences University in Portland, and the University of Washington will use a variety of sophisticated brain scanning

techniques in patients with a range of head injuries, as well as on post-mortem tissue, to identify potential markers that may eventually be used to diagnose the degenerative effects of TBI in people.

"The investigators will collaborate to develop diagnostic criteria for identifying the chronic features of the entire scope of brain trauma ranging from mild TBI to full-blown CTE, and then work to extend these criteria to living humans using some of the most advanced neuroimaging tools available," said Walter Koroshetz, M.D., deputy director of NINDS.

"Although the two cooperative agreements focus on different aspects of TBI, their combined results promise to answer critical questions about the chronic effects of single versus repetitive injuries on the brain, how repetitive TBI might lead to CTE, how commonly these changes occur in an adult population, and how CTE relates to neurodegenerative disorders like Alzheimer's disease," Dr. Landis said.

The pilot studies will focus on improving the diagnosis of concussion and identifying potential biomarkers that can be used to track a person's recovery. The six pilot grants are:

• Cortical GABA in Pediatric Sports Concussion
Principal Investigator: Jeffrey G. Ojemann, M.D., Seattle Children's Hospital

The brain contains numerous chemicals such as gamma-amino butyric acid (GABA), which is important for many brain functions, including cognition and movement, and may be altered by traumatic brain injury. Magnetic resonance (MR) spectroscopy is a scanning technique that can measure a variety of brain chemicals, including GABA. The goal of Dr. Ojemann's project is to use MR spectroscopy to monitor GABA levels in adolescents who have sports-related concussions and compare those levels to uninjured controls. The researchers also will conduct preliminary comparisons of GABA levels with existing cognitive measures such as memory tests and structural brain imaging. Diagnostic tools that can reliably detect when the brain is injured and when it has recovered following a concussion are essential for determining when it is safe to resume normal activities.

• Evaluation of Spot Light: A Concussion Injury Management App for Youth Sports
Principal Investigators: Lara McKenzie, Ph.D., Center for Injury Research and Policy, The Research Institute at Nationwide Children's Hospital, Columbus, Ohio and Dawn Comstock, Ph.D., Colorado School of Public Health, University of Colorado, Denver

Guidelines exist to help doctors diagnose and manage sports-related concussions, but guidelines are not fully supported by evidence-based research, are applied inconsistently, and those responsible for the care of injured athletes do not always fully communicate with each other. The goal of Drs. McKenzie and Comstock's project is to test the effectiveness of Spot Light, an easy-to-use mobile application (or app), developed by Inlightened, LLC. This app was designed to help doctors, coaches, athletic trainers and parents of young football players track the progress of a young athlete from the time of a concussion injury until they are cleared to return to play. The researchers want to know if the app will result in more concussions being reported, a greater number of referrals to doctors and better adherence to return-to-play guidelines. The goal is to improve diagnosis of concussions that are occurring among young athletes, and ensure that they are receiving appropriate care and are fully recovered before getting back on the field.

• Eye Movement Dynamics: A Rapid Objective Involuntary Measure of Concussion/Mild Traumatic Brain Injury
Principal Investigators: Nicholas Port. Ph.D. and Steven Hitzeman, O.D., Indiana University School of Optometry, Bloomington

People can choose where to look, but they do not have much control over some of the intricate eye muscle movements that are usually made without thinking. Studies have shown that eye movement problems are common in mild traumatic brain injury patients. Drs. Port and Hitzeman, in collaboration with team trainers and physicians at Indiana University and local high schools, plan to take advantage of the involuntary, reflex nature of eye movements. They will develop a portable eye tracking instrument that can be used to help diagnose concussions on the sidelines and to monitor injury progression in high school and college athletes. Drs. Port and Hitzeman will compare the eye tracking data to results from a commonly used cognitive test to determine if changes in eye movement can serve as a biomarker for sports-related mild traumatic brain injury. If successful, this study will help provide an objective and more reliable measure to detect traumatic brain injury than is currently available.

• Imaging and Biomarkers in Adolescents Cleared for Return to Play After Concussion
Principal Investigator: Harvey Levin, Ph.D., Baylor College of Medicine, Houston

Sports concussions may cause persistent long-term effects in young athletes -- in some cases, even after they have been allowed to return to play. Using a variety of neuroimaging techniques, Dr. Levin and his group will look at the effects of sports-related concussions on brain structure and function one month following injury in adolescents who have been cleared to play. In addition, this project will evaluate microRNAs (miRNAs) as potential biomarkers for concussions and recovery. These are small portions of RNA (a molecule that is similar to DNA, which contains our genetic code) that play a role in turning genes on or off. The researchers plan to measure levels of specific miRNAs and determine if they correspond with cognitive test results and neuroimaging data.

• Somatosensory Processing — Assessing Youth Sport-Related Concussion and Recovery
Principal Investigator: Stacy Jennifer Marcus Suskauer, M.D., Kennedy Krieger Institute, Baltimore

The somatosensory system provides information about our environment — for example, what an object feels like to the touch — and may be affected by brain injury. Dr. Suskauer and her colleagues will investigate whether somatosensory system information processing (SSIP) could be used as a biomarker for concussion and recovery in youth aged 13-17. For these experiments, the researchers will use a new portable device that delivers vibrations to fingertips. Perception of the vibrations reflects activity of sensory neurons in the brain, thereby providing a measure of SSIP. The researchers will also investigate whether changes in SSIP are related to differences in certain brain chemicals after head injury.

• Characterization of the Brain and Serum Metabolome in Mouse Models of Concussion
Principal Investigator: Michael J. Whalen, M.D., Massachusetts General Hospital, Boston

Metabolites are small molecules formed in the body as a result of the normal breakdown of proteins, drugs and other large molecules. The collection of all metabolites in the body is the metabolome. Studies have suggested that head injury may change levels of various brain byproducts, but this has

not been researched in a systematic way. Dr. Whalen and his group plan to use an experimental model of traumatic brain injury to conduct a detailed analysis of changes in the brain metabolome following concussion. The researchers will compare those differences with serum byproducts to determine if the changes can be revealed in blood samples. The results of this project may uncover metabolites that contribute to serious effects of traumatic brain injury and may help identify potential targets for detecting and treating concussions.

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The NINDS (http://www.ninds.nih.gov) is the nation's leading funder of research on the brain and nervous system. The NINDS mission is to reduce the burden of neurological disease – a burden borne by every age group, by every segment of society, by people all over the world.

The NICHD (http:www.nichd.nih.gov) sponsors research on development, before and after birth; maternal, child, and family health; reproductive biology and population issues; and medical rehabilitation.

The NIDCD (http://www.nided.nih.gov) supports and conducts research and research training on the normal and disordered processes of hearing, balance, taste, smell, voice, speech, and language and provides health information, based upon scientific discovery, to the public.

About the National Institutes of Health (NIH): NIH, the nation's medical research agency, includes 27 Institutes and Centers and is a component of the U.S. Department of Health and Human Services. NIH is the primary federal agency conducting and supporting basic, clinical, and translational medical research, and is investigating the causes, treatments, and cures for both common and rare diseases. For more information about NIH and its programs, visit http://www.nih.gov.

About the Foundation for the NIH (FNIH): Established by the United States Congress to support the mission of the NIH—improving health through scientific discovery in the search for cures—the Foundation for the NIH is a leader in identifying and addressing complex scientific and health issues. The foundation is a not-for-profit, 501(c)(3) charitable organization that raises private-sector funds for a broad portfolio of unique programs that complement and enhance NIH priorities and activities. For additional information about the Foundation for the NIH, please visit www.fnih.org.

Jason, Cailin (NIH/NINDS) [C]

From: Lauren Musiol <lmusiol@gymr.com>
Sent: Monday, December 21, 2015 9:29 AM
To: McMakin, Barbara (NIH/NINDS) [E]
Cc: Hieu Nguyen; Emr, Marian (NIH/NINDS) [E]
Subject: PRESS: For Approval: Local CTE Grant Release

Barbara – Thank you for your feedback. We will add the grant number in and then I will send you a final copy for your records.

Best,
Lauren

From: McMakin, Barbara (NIH/NINDS) [E] [mailto:mcmakinbi@ninds.nih.gov]
Sent: Monday, December 21, 2015 9:28 AM
To: Lauren Musiol
Cc: Hieu Nguyen; Emr, Marian (NIH/NINDS) [E]
Subject: RE: For Approval: Local CTE Grant Release

Hi Lauren,

Thank you for sharing your draft with us. We sent it to our program director for review and he said it looks good. The only request we have is for you to add the grant number (1U01NS093334-01) somewhere in the release (a footnote will do).

Best,
Barbara

From: Lauren Musiol [mailto:lmusiol@gymr.com]
Sent: Friday, December 18, 2015 11:13 AM
To: McMakin, Barbara (NIH/NINDS) [E]; Emr, Marian (NIH/NINDS) [E]
Cc: Hieu Nguyen
Subject: For Approval: Local CTE Grant Release

Hi Barbara and Marian – My name is Lauren Musiol and I work with the Banner Alzheimer's Institute on media and communications support. As you know, BAI and Mayo Clinic are part of the group receiving the grant from NIH/NINDS to fund CTE research.

Boston University will be putting out a release announcing the grant next week and has been working with you on approval of that.

We would like to do some media outreach in Arizona and have created a release that highlights BAI and Mayo Clinic's role more specifically. We based this local market release off of the national one that Boston University will be issuing.

Could you please review and let us know if you are OK with the release?

We will plan to distribute following the national release.

Please let me know if you have any questions.

Thanks!
Lauren Musiol

Lauren Musiol, Managing Supervisor
lmusiol@gymr.com | [illegible]

GYMR Public Relations / [illegible]
[illegible] / www.gymr.com / @gymrpr

Jason, Cailin (NIH/NINDS) [C]

From: Mott, Meghan (NIH/NINDS) [E]
Sent: Monday, December 21, 2015 10:39 AM
To: Emr, Marian (NIH/NINDS) [E]; Walker, Paula (NIH/NINDS) [E]
Cc: Koroshetz, Walter (NIH/NINDS) [E]
Subject: RE: Background for today's ESPN interview

Thanks for this, Marian. See you soon!

From: Emr, Marian (NIH/NINDS) [E]
Sent: Monday, December 21, 2015 10:38 AM
To: Mott, Meghan (NIH/NINDS) [E]; Walker, Paula (NIH/NINDS) [E]
Cc: Koroshetz, Walter (NIH/NINDS) [E]
Subject: Background for today's ESPN interview
Importance: High

Meghan and Paula: Walter is scheduled to speak with Steve Fainaru of ESPN on Monday at noon. We will take the call in his conference room (31/8A-52) so that John Burklow and I can sit in, as requested by Dr. Collins. Attached are some draft talking points approved by Bldg One. Also attached is some background information about the recently awarded grant, a copy of the BU release, and the paper published last week highlighting the results of the NIH-run (SIRP- funded) consensus meeting on the pathological diagnosis of CTE. In the event that Steve asks what the NFL is currently funding, I've included a copy of our 2013 press release.

By the way, Walter will remember that Fainaru wrote a story in March 2014 (**Union, NFL split over research funds**) which included some rather provocative quotes.
Marian

Marian Emr

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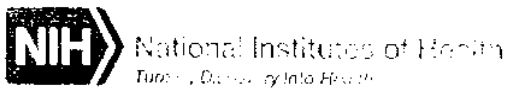

Talking Points: CTE Media Interview

Chronic Traumatic Encephalopathy: Detection, Diagnostic, Course, and Risk Factors

To be funded by the National Institute of Neurological Disorders and Stroke
U01NS093334

Principal Investigators
Robert A. Stern, Ph.D. (Contact PI)
Jeffrey Cummings, M.D.
Eric Reiman, M.D.
Martha Shenton, Ph.D.

Summary: December 1, 2015

Chronic traumatic encephalopathy (CTE) is a neurodegenerative disease characterized by a distinct deposition of an abnormal form of the tau protein in a pattern that is unique from other diseases, including Alzheimer's disease (AD). CTE has been found most often in professional contact sport athletes (e.g., boxing, football) who have been subjected to repetitive blows to the head resulting in concussive and subconcussive trauma. Neuropathologically-confirmed CTE has been reported in individuals as young as 17 and in athletes who only played sports through high school or college. It also has been found in non-athletes who experienced repetitive head impacts, including epileptics, victims of physical abuse, and military service members. In contrast to what may be inferred by the extensive media attention on CTE, the science of CTE remains in its infancy; critical questions remain, such as whether or not it is a common disease.

Although the neuropathological features of CTE have become further clarified in recent years, the clinical presentation of CTE is still not well characterized, even though there have been case reports in the literature of "dementia pugilistica" in boxers since the early 1900's. Clinical diagnostic criteria have only recently been published and lack validation. Neuroimaging and fluid biomarkers developed for the diagnosis of other neurodegenerative diseases have only been used in preliminary studies. There is thus an urgent need to develop accurate methods for detecting and diagnosing CTE during life so that effective interventions for prevention and treatment can be developed. Moreover, though a history of repetitive head impacts is a necessary risk factor for CTE, it alone is not sufficient. There is a need to understand what specific aspects of the head impact exposure places an individual at increased risk for CTE and to examine potential genetic modifiers of that risk.

To address these needs, NINDS is funding a multidisciplinary, multicenter, longitudinal study of former athletes with high exposure to repetitive head impacts (120 former NFL players with and without symptoms) or medium exposure to repetitive head impact (60 former college football players with and without symptoms) and a control group of 60 asymptomatic same-age men without any history of repetitive head impact exposure or traumatic brain injury. The aims of the 7-year project are: (1) to collect and analyze neuroimaging and fluid biomarkers for the detection of CTE during life, including the use of a novel PET tracer to measure the amount of abnormal brain tau; (2) to characterize the clinical presentation of CTE; (3) to examine the progression of CTE over a three year period; (4) to refine and validate diagnostic criteria for the clinical diagnosis of CTE; (5) to investigate genetic and head impact exposure risk factors for CTE; and (6) to share project data with researchers across the country and abroad in order to expedite growth in our understanding and treatment of this disease.

CTE U01 Investigator Team

CTE is a neurodegenerative disease. Although the necessary risk factor for the development of this tauopathy is a history of repetitive head impacts, CTE itself should not be confused with traumatic brain injury or considered the cumulative effect of multiple concussions. It therefore cannot be studied with the same approaches and tools used to study brain trauma. Rather, to study the clinical presentation, diagnostic criteria, biomarkers, and risk factors of CTE requires expertise across many disciplines, including neurology, neuropsychology, psychiatry, neuroimaging, molecular medicine, neuropathology, exposure science, genetics, biostatistics, bioinformatics, engineering, and others. The success of this project will be facilitated by the multiple resources available across several sites. One of the primary resources is the superb group of co-investigators, consultants, and advisors working collaboratively on this study. A primary goal of this research program is to break down typical academic "silos" in order to conduct the best science in the most efficient manner. The proposed project brings together a network of scientists and resources across major academic institutions and industry leaders, including:

- Boston University School of Medicine and School of Public Health
- Brigham and Women's Hospital, Harvard Medical School
- Cleveland Clinic Lou Ruvo Center for Brain Health
- Mayo Clinic Arizona and Banner Alzheimer's Institute
- NYU Langone Medical Center and New York University School of Medicine
- VA Puget Sound and University of Washington
- Molecular NeuroImaging
- Neuroinformatics Research Group and Central Neuroimaging Data Archive (CNDA) at Washington University School of Medicine

The groups of investigators for this project are leaders in most of the major collaborative studies of Alzheimer's disease, as well as TBI, PTSD, Sports-Related Concussion, Frontotemporal Lobar Degeneration, and Parkinson's disease. In addition, many of the principle investigators and co-investigators already have extensive experience in the study of CTE, including NIH-funded projects that have led to important preliminary data to help guide the development of this proposal and, ultimately, to expedite the initiation of the proposed work as well as the speed at which critical questions will be answered.

This project will be overseen by an Executive Committee made up of the four Project PIs (Drs. Cummings, Reiman, Shenton, and Stern), the four Clinic Site PIs (Drs. Adler, Balcer, Bernick, and Stern), the Chair of the Advisory Board (Dr. Knopman), six Team Leaders (see below), the Project Coordinator, and Dr. McKee (to assure harmonization with the findings and procedures of her NINDS-funded CTE neuropathology U01 project). The Executive Committee will meet monthly through web-conference. Each major component of the project will be overseen by multidisciplinary and multi-institutional study teams. Each team is comprised of sub-teams focusing on specific aspects of the team's activities. The teams will interact closely with one another, through informal discussions, through monthly Executive Committee meetings, and through annual Investigator Meetings that will involve all investigators across all sites. The Data Team, in particular, will work closely with all other teams, throughout the entire project, assuring that all aspects of study design, variable definitions, data collection methods, database design and entry, and data analysis, are consistent across the entire breadth of the study and throughout the duration of the project. The following pages provides a list of the project leadership.

Principal Investigators

Robert A. Stern, Ph.D. (Contact PI)
Professor of Neurology, Neurosurgery, and Anatomy and Neurobiology
Director, Clinical Core, Boston University Alzheimer's Disease and CTE Center (BU AD&CTEC)
Boston University School of Medicine

Jeffrey Cummings, M.D.
Director, Cleveland Clinic Lou Ruvo Center for Brain Health
Cleveland Clinic Lou Ruvo Center for Brain Health

Eric Reiman, M.D.
Executive Director, Banner Alzheimer's Institute
CEO, Banner Research
Banner Sun Health Research Institute

Martha Shenton, Ph.D.
Professor, Department of Psychiatry and Radiology, Harvard Medical School
Senior Scientist, Brigham and Women's Hospital

Advisory Board

David Knopman, M.D., Advisory Board Chair
Professor of Neurology
Mayo Clinic

Unconfirmed: Col. Dallas Hack, M.D.
Previously: Brain Health Research Program Coordinator
U.S. Army Medical Research and Material Command

Brian Hainline, M.D.
Chief Medical Officer, National Collegiate Athletic Association

Mike Haynes
Special Advisor to the Commissioner, National Football League
National Spokesperson, American Urological Association Foundation

Thomas McAllister, M.D.
Chair, Department of Psychiatry
Albert Eugene Stern Professor of Clinical Psychiatry
Indiana University School of Medicine

Bruce Miller, M.D.
A.W. & Mary Margaret Clausen Distinguished Professor in Neurology
Director, Memory and Aging Center Joint Appointment in Psychiatry
University of California, San Francisco

Arthur Toga, M.D.
Provost Professor
Director of the Institute for Nueroimaging and Informations (INI)
Director of the Laboratory of Neuro Imaging
University of Southern California

Michael Weiner, M.D.
Professor of Medicine, Radiology, Psychiatry and Neurology
University of California San Francisco

Performance Site Principal Investigators

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NIH/NINDS Grant Awarded to Develop Methods for Diagnosing Chronic Traumatic Encephalopathy (CTE) During Life

(Boston)—Researchers from Boston University, the Cleveland Clinic, Banner Alzheimer's Institute and Brigham and Women's Hospital in Boston, have been awarded a $16 million grant from the National Institutes of Health/National Institute of Neurological Disorders and Stroke (NIH/NINDS). This seven-year, multi-center grant will be used to create methods for detecting and diagnosing chronic traumatic encephalopathy (CTE) during life as well as examining risk factors for CTE.

CTE is a degenerative brain disease characterized by changes in behavior, mood and cognition, including the development of dementia. Currently it can only be diagnosed post-mortem through examination of an abnormal form of tau protein. CTE has been found most often in professional contact sport athletes (e.g., boxers, football players) who have been subjected to repetitive blows to the head resulting in symptomatic concussive and asymptomatic subconcussive trauma. Neuropathologically-confirmed CTE has been reported in individuals as young as 17 and in athletes who only played sports through high school or college. It also has been found in non-athletes who experienced repetitive head impacts, including military service members.

According to the researchers, although the neuropathological features of CTE have become further clarified in recent years, the clinical presentation of CTE is still not well characterized and there remains no method to diagnose it before death. "There are so many critical unanswered questions about CTE. We are optimistic that this project will lead to many of these answers, by developing accurate methods of detecting and diagnosing CTE during life, and by examining genetic and other risk factors for this disease," explained lead principal investigator, Robert Stern, PhD, professor of neurology, neurosurgery, and anatomy & neurobiology at Boston University School of Medicine, where he is Clinical Core director of the Boston University Alzheimer's Disease and CTE Center.

Through this grant, NINDS is funding a longitudinal study of former NFL players, former college football players, and a control group of individuals without any history of contact sports or brain injury. Participants will be examined at one of four centers across the country, including Boston University School of Medicine; Cleveland Clinic Lou Ruvo Center for Brain Health in Las Vegas; Mayo Clinic in Scottsdale, Ariz; and New York University Langone Medical Center, New York City.

Participants in the study will undergo extensive clinical examinations, as well as state-of-the art PET scans, advanced MRI scans, experimental blood tests and other potential methods of detecting changes in the brain associated with CTE. Researchers also will refine and validate specific criteria for clinical diagnosis of the disease and will investigate genetic and head impact exposure risk factors for CTE in order to begin to determine why some people are more prone to get CTE than others. Project data will be shared with researchers across the country and abroad to facilitate a more complete understanding of this disease, ultimately leading to successful methods of preventing and treating CTE.

The other principal investigators are Jeffrey Cummings, MD, ScD, (director, Cleveland Clinic Lou Ruvo Center for Brain Health in Las Vegas and Cleveland; the Camille and Larry Ruvo Chair of the Neurological Institute of Cleveland Clinic; and professor of medicine, Cleveland Clinic Lerner College of Medicine at Case Western Reserve University); Eric Reiman, MD (executive director of the Banner Alzheimer's Institute, Phoenix) and Martha Shenton, PhD (director, Psychiatry Neuroimaging Laboratory and senior scientist, Brigham and Women's Hospital; professor of psychiatry and radiology, Harvard Medical School). The project involves a group of approximately 50 investigators, representing 17 research institutions.

"There is an urgent need to clarify the clinical and biological consequences of repetitive head impacts in athletics and to use this information to find the best ways to treat and prevent those consequences," said Reiman. "It is both a great privilege and responsibility to help in that endeavor."

"This research is an exciting and important opportunity to acquire new information about the potential devastating consequences of repetitive head impact including CTE," said Shenton. "We hope that by gaining this knowledge, new avenues of treatment will emerge for those who experience debilitating symptoms from repetitive brain trauma."

"We currently have no method to diagnosis CTE during life and it is crucial to take the next steps to better understand this disease," said Cummings. "This grant will allow us to take what we know about CTE and move to the next level of research, with the end goal of diagnosing these athletes at early stages of the illness when treatments may help prevent the progression of the disease."

Editors Note:
The exact amount of this grant is $15,859,906.

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CONSENSUS PAPER

The first NINDS/NIBIB consensus meeting to define neuropathological criteria for the diagnosis of chronic traumatic encephalopathy

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Abstract Chronic traumatic encephalopathy (CTE) is a neurodegeneration characterized by the abnormal accumulation of hyperphosphorylated tau protein within the brain. Like many other neurodegenerative conditions, at present, CTE can only be definitively diagnosed by post-mortem examination of brain tissue. As the first part of a series of consensus panels funded by the NINDS/NIBIB to define the neuropathological criteria for CTE, preliminary neuropathological criteria were used by 7 neuropathologists to blindly evaluate 25 cases of various tauopathies, including CTE, Alzheimer's disease, progressive supranuclear palsy, argyrophilic grain disease, corticobasal degeneration, primary age-related tauopathy, and parkinsonism dementia complex of Guam. The results demonstrated that there was good agreement among the neuropathologists who reviewed the cases (Cohen's kappa, 0.67) and even better agreement between reviewers and the diagnosis of CTE (Cohen's kappa, 0.78). Based on these results, the panel defined the pathognomonic lesion of CTE as an accumulation of abnormal hyperphosphorylated tau (p-tau) in neurons and astroglia distributed around small blood vessels at the depths of cortical sulci and in an irregular pattern. The group also defined supportive but non-specific p-tau-immunoreactive features of CTE as: pretangles and NFTs affecting superficial layers (layers II–III) of cerebral cortex;

The members representing TBI/CTE group are listed in the Appendix.

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pretangles, NFTs or extracellular tangles in CA2 and pretangles and proximal dendritic swellings in CA4 of the hippocampus; neuronal and astrocytic aggregates in subcortical nuclei; thorn-shaped astrocytes at the glial limitans of the subpial and periventricular regions; and large grain-like and dot-like structures. Supportive non-p-tau pathologies include TDP-43 immunoreactive neuronal cytoplasmic inclusions and dot-like structures in the hippocampus, anteromedial temporal cortex and amygdala. The panel also recommended a minimum blocking and staining scheme for pathological evaluation and made recommendations for future study. This study provides the first step towards the development of validated neuropathological criteria for CTE and will pave the way towards future clinical and mechanistic studies.

Keywords Chronic traumatic encephalopathy · Traumatic brain injury · Tauopathy · Brain trauma · Neurodegenerative disorders

Introduction

In 1928, the pathologist and medical examiner, Harrison Stanford Martland, introduced the term 'punch-drunk' to describe the clinical features of a distinct neuropsychiatric syndrome that affected boxers [26]; a condition that later came to be known as 'dementia pugilistica' [33]. Case reports and small series describing the neuropathologic features of the condition appeared in the 1950s and 1960s [3, 6, 16, 27, 35, 41]. Although the histological techniques varied, the most common pathological findings were cerebral atrophy, neuronal loss, gliosis and argyrophilic neurofibrillary tangles. In the seminal 1973 monograph on the clinicopathological features of dementia pugilistica in 15 former male boxers, Corsellis, Bruton, and Freeman-Browne described cerebral atrophy, enlargement of the lateral and third ventricles, thinning of the corpus callosum, cavum septum pellucidum with fenestrations, cerebellar scarring, and argyrophilic neurofibrillary degeneration using cresyl violet and Von Braunmühl's silver stains [5]. Subsequent re-examination of Corsellis' original series of boxers and additional cases using beta-amyloid (Aβ) immunohistochemistry determined that 95 % of CTE cases showed widespread diffuse Aβ deposits [43, 46].

Over the following decades, it was recognized that the condition affected men and women with a broad range of exposure to brain trauma, including physical abuse [42], head-banging [13, 18], poorly controlled epilepsy, "dwarf-throwing" [48], and rugby[1] [13]. Eventually, the term "chronic traumatic encephalopathy" or "CTE", introduced by Critchley in 1949 [8], became the preferred designation for the condition.

Coincident with the use of more refined methodology, the early pathology of CTE was reported in several young subjects [13, 14, 18]. Hof reported a single case of repetitive head-banging in a young autistic patient with numerous perivascular clusters of thioflavin and Gallyas-positive neurofibrillary tangles (NFTs) and neurites at the depths of the cerebral sulci and in the superficial layers of the inferior temporal, entorhinal and perirhinal cortices in the absence of Aβ plaques [18]. Hof and colleagues also quantitatively demonstrated the preferential distribution of the NFTs in superficial layers II and III in CTE, a laminar predilection characteristic of two other environmentally acquired tauopathies, post-encephalitic parkinsonism and Guamanian parkinsonism dementia complex (GPDC), but not found in Alzheimer's disease (AD) [19]. Geddes and colleagues further described argyrophilic, hyperphosphorylated tau (p-tau) immunopositive neocortical NFTs and neuropil threads strikingly arranged in groups around small cortical blood vessels, in addition to diffuse granular cytoplasmic immunopositivity in some neurons [13]. Geddes also noted that the topography of the p-tau pathology principally involved the depths of sulci and that there was no Aß deposition in the 5 young cases that formed the basis of their manuscript [13].

Omalu and colleagues were the first to report CTE in a professional American football player [38, 39] and a professional wrestler [37]. Recent neuropathological studies have identified CTE in athletes who played soccer, baseball, ice hockey and rugby, as well as in military personnel exposed to explosive blast [15, 29, 31, 32, 36, 45]. P-tau pathology, with some features of CTE, has also been

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[1] Although often referred to as a *soccer* player, the young subject with CTE described by Geddes et al. 1999 as the "keen amateur footballer who frequently "headed" the ball while playing" [13], was an amateur *rugby* player (personal communication, T. Revesz).

described following exposure to single moderate or severe traumatic brain injury, together with Aβ plaques [20, 44].

In 2013, McKee and colleagues described a spectrum of p-tau pathology in 68 male subjects with a history of exposure to repetitive brain trauma with neuropathological evidence of CTE, ranging in age from 17 to 98 years (mean 59.5 years). In young subjects with the mildest forms of CTE, focal perivascular epicenters of NFTs and astrocytic tangles (ATs) were found clustered at the depths of the cortical sulci; in subjects with severe disease, a profound tauopathy involved widespread brain regions [32]. Other abnormalities encountered in advanced disease included abnormal deposits of phosphorylated TAR DNA-binding protein of 43 kDa (TDP-43) protein that occasionally co-localized with p-tau, varying degrees of Aβ pathology, axonal dystrophy and neuroinflammation [30, 32]. Based on these findings, preliminary criteria for the neuropathological diagnosis of CTE were proposed, as follows:

1. Perivascular foci of p-tau immunoreactive NFTs and ATs in the neocortex
2. Irregular distribution of p-tau immunoreactive NFTs and ATs at the depths of cerebral sulci
3. NFTs in the cerebral cortex located preferentially in the superficial layers (often most pronounced in temporal cortex)
4. Supportive, non-diagnostic features: Clusters of subpial ATs in the cerebral cortex, most pronounced at the sulcal depths.

In March 2013, the National Institutes of Health (NIH), supported by the Foundation for NIH's Sports Health Research Program with funding from the National Football League (NFL), launched a major effort to define the neuropathological characteristics of CTE. Two projects were initiated on the neuropathology of CTE and the delayed effects of traumatic brain injury. One of the initial objectives was to convene a consensus meeting to define the neuropathological criteria for the diagnosis of CTE. The primary objective for the first meeting was to determine whether CTE was a distinctive tauopathy that could be reliably distinguished from other tauopathies using the preliminary criteria. The study design was modeled after previous successful NIH-sponsored consensus conferences for other tauopathies, specifically progressive supranuclear palsy (PSP) and corticobasal degeneration (CBD) [10, 17, 25].

Materials and methods

Individuals not directly involved in the pathological evaluation (ACM, VEA, KFB, JFC) selected 25 cases of the various tauopathies. The selected cases were considered to be representative of the disease and of at least moderate disease severity. The cases included 10 recently acquired cases of suspected CTE that were donated as part of the NINDs-funded traumatic brain injury (TBI) brain bank at Boston University School of Medicine (BUSM), including 7 cases with Aβ plaques and 3 cases without Aß plaques. Five cases of AD, Braak stage V-VI, 2 cases of PSP and 2 cases of CBD were selected from the Alzheimer's Disease Center (ADC) brain bank at BUSM. Two cases of GPDC and 2 cases of argyrophilic grain disease (AGD) were selected from the Alzheimer's Disease Research Center (ADRC) brain bank at Mayo Clinic-Jacksonville, and 2 cases of primary age-related tauopathy (PART) were selected from the ADRC brain bank at Columbia University. Paraffin-embedded tissue blocks from 12 brain regions from each case were sent to the TBI Brain Bank at BUSM for uniform processing, staining and immunohistochemistry (IHC) (Table 1); 2 of the selected cases were missing the superior temporal block. Sections were stained with Luxol fast blue counterstained with hematoxylin and eosin (LHE) and Bielschowsky silver impregnation; IHC was performed using anti-Aβ42 (Aß 1-42, EMD Millipore, 1:2000, pretreated with 88 % formic acid for 2 min; or Aβ-4G8, Bio Legend, 1:100,000, pretreated with formic acid); anti-p-tau (AT8, Thermo Fisher Scientific/

Table 1 Brain regions evaluated in the case review

Brain region	Stains/IHC				
	LHE	AT8	Aβ42	TDP43	BIEL
Superior frontal (BA 8, 9)	X	X			
Dorsolateral superior frontal (BA 45, 46)	X	X	X		
Caudate nucleus, nucleus accumbens, putamen	X	X			
Temporal pole (BA 38)	X	X			
Superior temporal gyrus (BA 20, 21,22)	X	X		X	
Amygdala, with entorhinal cortex (BA 28)	X	X			
Hippocampus and lateral geniculate nucleus	X	X	X	X	X
Thalamus and mammillary body	X	X			
Cerebellum with dentate nucleus	X	X			

Digitized images of the following microscopic slides were provided to the evaluating neuropathologists on 25 cases of tauopathies including AD, AGD, CBD, CTE, GPDC, PART and PSP. The slides were all uniformly processed by a single laboratory

Aβ Beta-amyloid, *AD* Alzheimer's disease, *AGD* Argyrophilic grain disease, *BA* Brodmann area, *BIEL* Bielschowsky's silver method, *CTE* Chronic traumatic encephalopathy, *GPDC* Guamanian Parkinson's dementia complex, *LHE* Luxol fast blue, counterstained with hematoxylin and eosin, *PART* Primary age-related tauopathy, *PSP* Progressive supranuclear palsy

Pierce, 1:2000, pretreated with formic acid) and anti-p-TDP-43 (Anti-TDP-43, phospho, 1:2000, pretreated with formic acid) for a total of 27 slides per case (25 slides in 2 cases). An individual blinded to the origin and identity of the cases (KFB) scanned the 671 glass pathology slides into digital images at the Mayo Clinic Jacksonville using an Aperio scanner (Leica Biosystems, Buffalo Grove, IL). The digitized images were organized into folders labeled with only the case number (#1-25), brain region, stain and IHC and provided to the evaluating neuropathologists on portable hard drives as well as on an online slide-hosting website (Leica Biosystems-Aperio). No clinical or demographic information was provided to the evaluating neuropathologists—including no information regarding the subjects' age, gender, clinical symptoms, diagnosis or athletic exposure. No information was supplied regarding the gross neuropathological features of the brains. The neuropathologists were given a tauopathy criteria guide that provided the provisional criteria for CTE [32] as well as published criteria for the other tauopathies (See supplementary material for full tauopathy criteria guide) [4, 7, 11, 21, 25, 34, 40, 47]. Although the neuropathologists knew that the selected cases represented presumptive CTE, AD, PSP, CBD, AGD, PART, and GPDC, they did not know how many cases representing each diagnosis were to be evaluated.

Seven neuropathologists with experience in neurodegenerative diseases, including the tauopathies, participated in the evaluation of the digitized images (NJC, DWD, RDF, CDK, DPP, TDS, JPV). The neuropathologists evaluated the cases independently, at their own pace, and completed an evaluation form that included the pathological diagnosis and a 4-scale level of certainty (1, unsure; 2, possible; 3, probable; 4, definite). After the initial evaluations were sent to BUSM for analysis, the evaluator was provided the gross neuropathological findings and clinical summaries for each case, and asked to reevaluate the diagnosis and provide a second level of conviction. The results of all evaluations were analyzed prior to the face-to-face meeting held on February 25–26, 2015.

Statistical analysis

To evaluate the agreement among the neuropathologists who reviewed the cases, two sets of Cohen's kappa statistics were calculated. The first kappa coefficient measured the agreement among the overall neuropathological diagnoses; the second kappa coefficient measured the agreement among neuropathologists regarding the specific diagnosis of CTE. The overall kappa coefficient combines the neuropathologist-level estimates of kappa into an overall estimate of the common agreement. Kappa values of 0.81–1.0 indicate very good agreement, kappa values of 0.61–0.80 show good agreement, while kappa values of 0.41–0.60 indicate moderate agreement [12]. All statistical analyses were done using SAS 9.4 (SAS Institute Inc., Cary, North Carolina, USA) software.

At the face-to-face consensus meeting, a larger panel that included ACM[2], WS,[2] IL, WAG and members of the NINDs TBI/CTE group reviewed the results of the neuropathological evaluations, digitized images and glass pathology slides and discussed the cases as a group. Discussions led to refinements in the neuropathological criteria for CTE, as well as "best practice" recommendations for neuropathologists examining brains for evidence of CTE.

Results

There was good agreement regarding the overall neuropathological diagnosis of all 25 cases (Cohen's kappa, 0.67), and even better agreement regarding the specific diagnosis of CTE (Cohen's kappa, 0.78), using the proposed criteria. In evaluating the 10 cases submitted with the presumptive diagnosis of CTE (Supplementary Table 1), 64 of the 70 reviewers responses (91.4 %) indicated CTE as the diagnosis. There was a significant decrease of errors that paralleled the sequence of cases evaluated. The log of the expected errors significantly decreased by 0.43 for each case of CTE reviewed (p value = 0.024). There were common additions to the CTE diagnosis, including "Changes of Alzheimer's disease" (ADC) and AD in the cases with Aß plaques (cases #4–10). Other co-morbid diagnoses included hippocampal sclerosis (HS), AGD and PART. In the 15 other tauopathy cases (cases submitted for review with diagnoses other than CTE) (Supplementary Table 2), the reviewers generally agreed with the submission diagnoses of AD (97.1 % of responses), CBD (92.8 %), and PART (78.5 %); however, there were frequent discrepancies in cases with the presumptive diagnoses of PSP, AGD and GPDC (Supplementary Table 2). The evaluators reported a significantly increased degree of certainty (t test = 4.36, p value <0.001) in the diagnosis of CTE from an overall mean of 3.1 in a 4-point scale of conviction (1, unsure; 2, possible; 3, probable; 4, definite) to a mean of 3.7 after the gross neuropathological features and clinical features of the cases were provided to the evaluator. Three initial diagnoses of non-CTE were changed to CTE and 9 diagnoses of co-morbid CTE in non-CTE cases were changed to no CTE after revealing the clinical and gross neuropathological features.

[2] Neuropathologist present at the face-to-face panel discussion, but did not participate in the slide evaluations.

Diagnostic neuropathological features of CTE

The group defined a neuropathological lesion specific to CTE that distinguished the disorder from other tauopathies. The pathognomonic lesion of CTE consists of p-tau aggregates in neurons, astrocytes, and cell processes around small vessels in an irregular pattern at the depths of the cortical sulci (Figs. 1, 2; Table 2). The group also noted that the distinctively irregular spatial pattern of p-tau in CTE was often visible with low-power inspection (Fig. 1). Although other abnormalities in p-tau were also found, especially in the more severely affected brains, the pathognomonic lesion was distinct and not found in the other degenerative tauopathies (Fig. 2). In addition, the group observed frequent evidence of other pathologies in CTE, including TDP-43-immunoreactive neuronal cytoplasmic inclusions, Aβ plaques and amyloid angiopathy, and hippocampal neurofibrillary degeneration, including extracellular tangles best seen with silver stains.

Supportive neuropathological features of CTE

The group defined supportive pathological features for CTE. These features were commonly found in the CTE cases in addition to the required criteria, but were not considered diagnostic in isolation (Table 2).

Exclusions to the sole diagnosis of CTE

The presence of changes compatible with the diagnosis of another neurodegenerative disease excludes CTE as a

Fig. 1 Low magnification inspection of p-tau-stained slides often revealed the irregular spatial pattern of CTE pathology. AT8-stained slides of cerebral cortex in 3 cases of CTE showing irregular patches of p-tau pathology most dense at the depths of the sulci

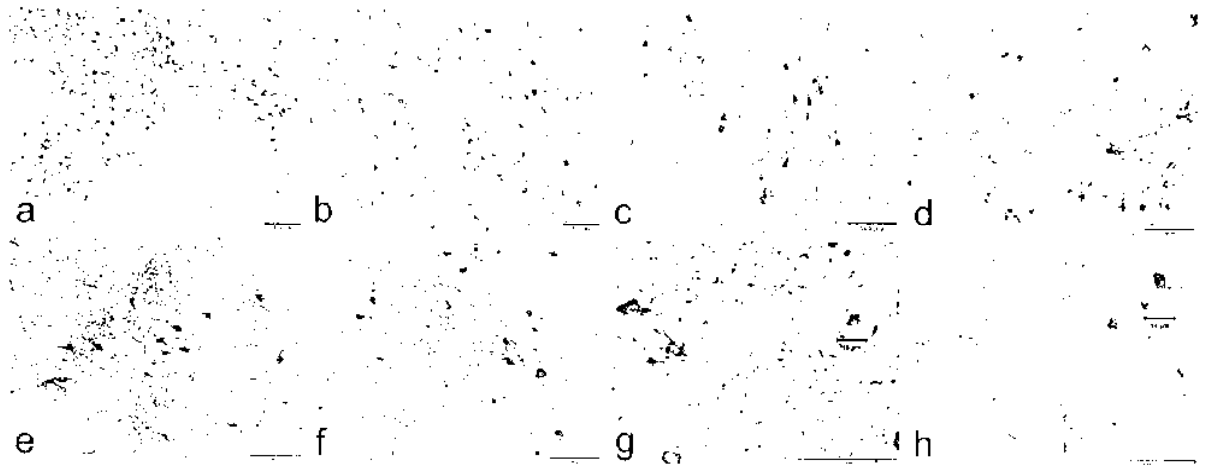

Fig. 2 The microscopic features of the pathognomonic lesion of CTE. The pathognomonic feature of CTE is a perivascular accumulation of p-tau aggregates in neurons, astrocytes and cell processes in an irregular spatial pattern in the cerebral cortex and found preferentially at the depths of the sulci. **a** A large perivascular p-tau lesion is found at the sulcal depths in a subject with CTE. **b**–**f** Multiple perivascular foci are often found in the cortex in CTE. **g** The p-tau aggregates in CTE include strikingly rounded structures in the neuropil that often are most dense in the areas surrounding the vessel. **h** The rounded p-tau immunoreactive cell processes are more densely distributed than those found in argyrophilic grain disease. All sections immunostained for AT8, *bars* indicate 100 μm, except in **g** and **h** where the *small bars* indicate 10 μm

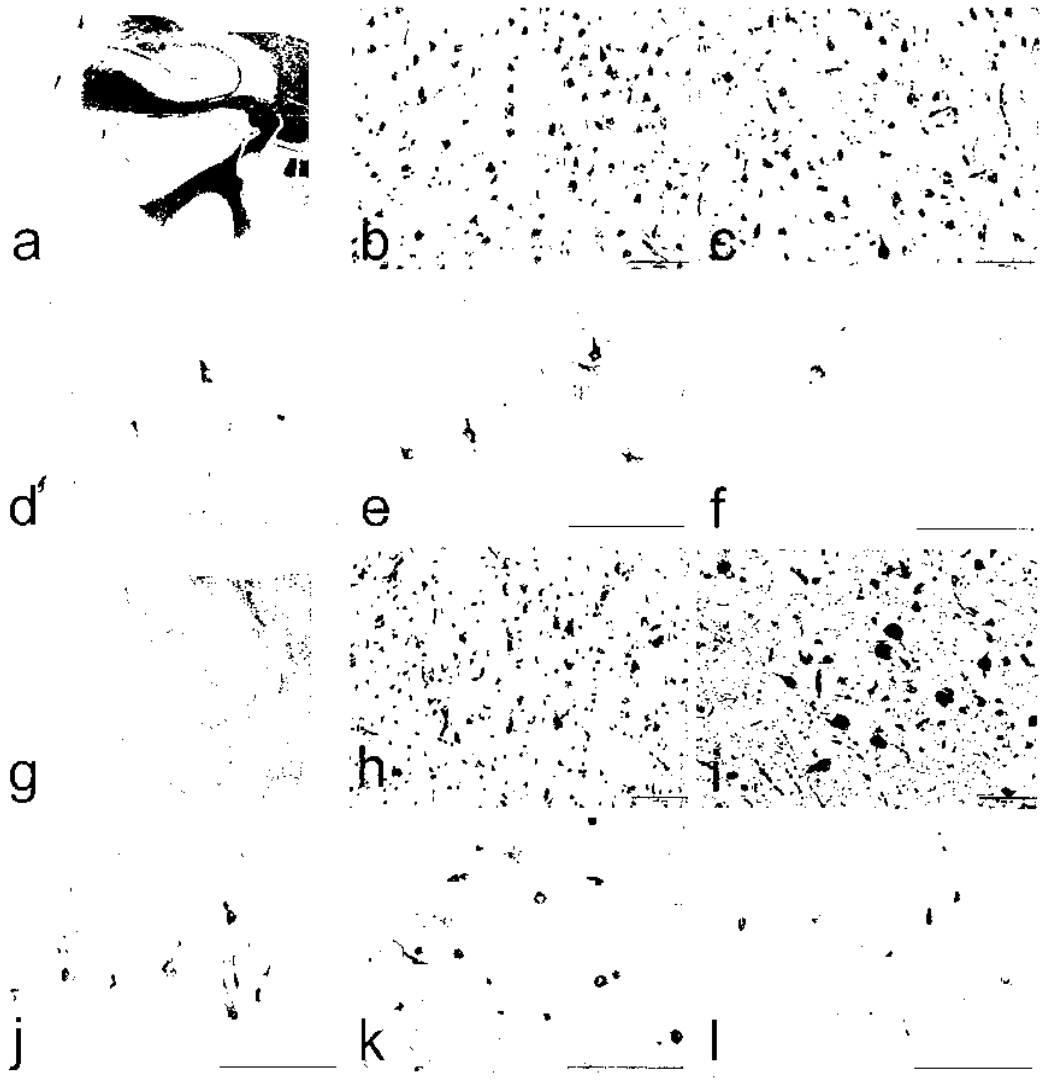

Fig. 3 Hippocampal pathology in CTE. Examples of hippocampal pathology in 2 cases of CTE of moderate severity. In example 1 (**a**–**f**), there is **a** mild hippocampal atrophy, **b** mild neuronal loss in CA1, **c** sparse NFTs in CA1, Bielschowsky silver stain, **d** sparse NFTs in CA1, AT8 immunostain, **e** moderate numbers of diffusely immunopositive AT8 stained neurons in CA4, and **f** occasional AT8 immunopositive NFTs in the dentate gyrus. In example 2 (**g**–**l**), there is **g** more severe hippocampal atrophy, **h** clear neuronal loss in CA1, **i** moderate density of NFTs in CA1, Bielschowsky silver stain, **j** moderate density of NFTs in CA1, AT8 immunostain, **k** high numbers of AT8-stained neurons and NFTs in CA4, and **l** moderate numbers of AT8 immunopositive NFTs in the dentate gyrus. *Bars* indicate 100 μm

single diagnosis, and indicates the presence of co-morbid pathology. These features include CA1-predominant neurofibrillary degeneration in the hippocampus in association with Aβ plaques consistent with AD [34]; prominent cerebellar dentate nucleus cell loss, coiled bodies in oligodendroglia, and tufted astrocytes as seen in PSP [25]; severe involvement of the striatum and pallidum with extensive astrocytic plaques in cortical and subcortical structures as seen in CBD [21] or globular astrocytic inclusions of globular glial tauopathy [1].

Discussion

The consensus panel of neuropathologists found that the p-tau pathology of CTE is clearly distinct from other tauopathies. The panel concluded that there is a pathognomonic lesion of CTE that consists of an accumulation of abnormal tau in neurons and astroglia distributed around small blood vessels at the depths of sulci in the cortex in an irregular spatial pattern. Other supportive features of CTE include abnormal p-tau immunoreactive pretangles

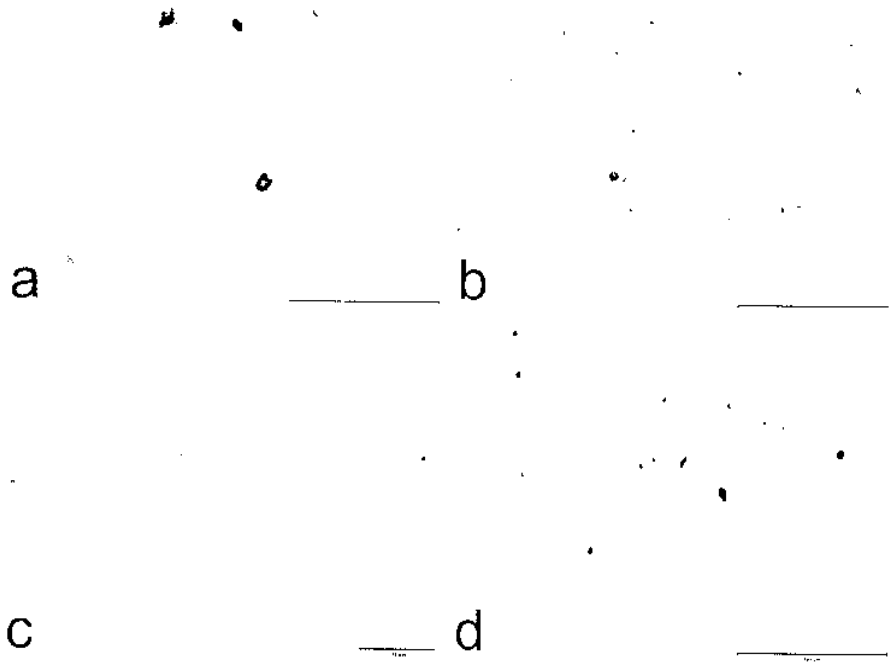

Fig. 4 pTDP-43 pathology in CTE. **a** pTDP-43 neuronal inclusions in the amygdala. **b** p-TDP-43 inclusions and dot-like neurites in CA1. **c** p-TDP-43 dot-like neurites in entorhinal cortex. **d** pTDP-43 inclusions and dot-like neurites in the dentate granule cell layer. All sections immunostained for p-TDP-43, bars indicate 100 μm

Table 2 Preliminary NINDS criteria for the pathological diagnosis of CTE

Required for diagnosis of CTE	
1. The pathognomonic lesion consists of p-tau aggregates in neurons, astrocytes, and cell processes around small vessels in an irregular pattern at the depths of the cortical sulci	
Supportive neuropathological features of CTE	
p-Tau-related pathologies:	
1. Abnormal p-tau immunoreactive pretangles and NFTs preferentially affecting superficial layers (layers II–III), in contrast to layers III and V as in AD	
2. In the hippocampus, pretangles, NFTs or extracellular tangles preferentially affecting CA2 and pretangles and prominent proximal dendritic swellings in CA4. These regional p-tau pathologies differ from the preferential involvement of CA1 and subiculum found in AD (Fig. 3)	
3. Abnormal p-tau immunoreactive neuronal and astrocytic aggregates in subcortical nuclei, including the mammillary bodies and other hypothalamic nuclei, amygdala, nucleus accumbens, thalamus, midbrain tegmentum, and isodendritic core (nucleus basalis of Meynert, raphe nuclei, substantia nigra and locus coeruleus)	
4. p-Tau immunoreactive thorny astrocytes at the glial limitans most commonly found in the subpial and periventricular regions	
5. p-Tau immunoreactive large grain-like and dot-like structures (in addition to some threadlike neurites) (Fig. 2h)	
Non-p-tau-related pathologies:	
1. Macroscopic features: disproportionate dilatation of the third ventricle, septal abnormalities, mammillary body atrophy, and contusions or other signs of previous traumatic injury	
2. TDP-43 immunoreactive neuronal cytoplasmic inclusions and dot-like structures in the hippocampus, anteromedial temporal cortex and amygdala (Fig. 4)	
Age-related p-tau astrogliopathy that may be present; non-diagnostic and non-supportive [22]	
1.	Patches of thorn-shaped astrocytes in subcortical white matter
2.	Subependymal, periventricular, and perivascular thorn-shaped astrocytes in the mediobasal regions
3.	Thorn-shaped astrocytes in amygdala or hippocampus [22]

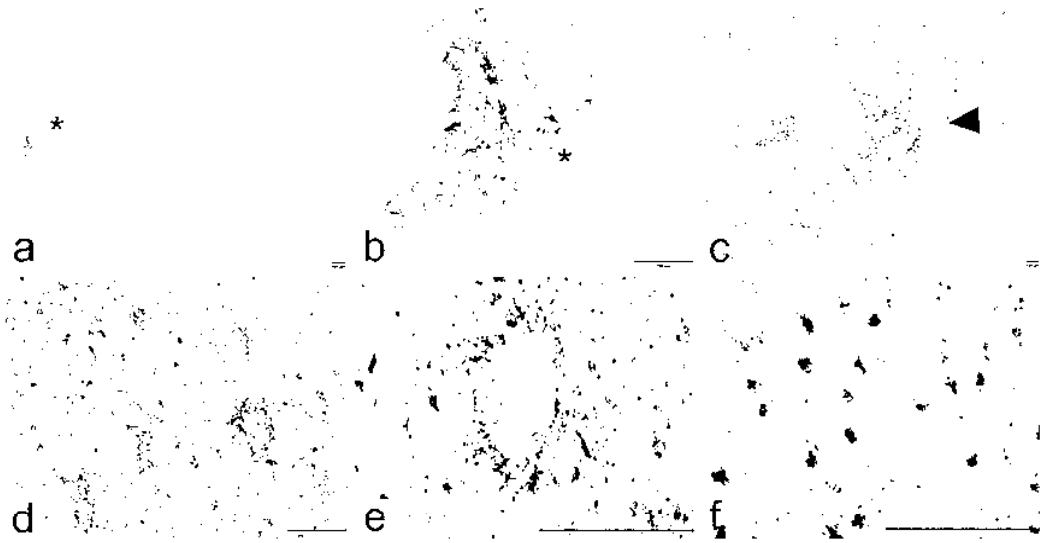

Fig. 5 Age-related p-tau astrogliopathy that may be present. **a** and **b**. Subpial p-tau immunopositive astrocytes may be found at the glial limitans in the sulcal depths but are non-specific and non-diagnostic for CTE (*asterisks*). **c** However, p-tau immunopositive subpial astrocytes accompanied by perivascular foci of p-tau positive neurons and astrocytes (*arrowhead*) at the depths of the sulci are diagnostic for CTE. **d** and **e** p-Tau immunopositive astrocytes surrounding small venules in the deep white matter of the temporal lobe are not diagnostic for CTE and are often found in association with aging [22]. **f** p-Tau positive astrocytes may also be found in the crests of the white matter of the frontal and temporal lobes with aging and other conditions that are not diagnostic for CTE [22]. All sections immunostained for AT8, *bars* indicate 100 μm

and NFTs preferentially affecting superficial layers (layers II–III), pretangles, NFTs or extracellular tangles primarily in CA2 and CA4 of the hippocampus, NFTs in subcortical nuclei, including the mammillary bodies and other hypothalamic nuclei, amygdala, nucleus accumbens, thalamus, midbrain tegmentum, isodendritic core (nucleus basalis of Meynert, raphe nuclei, substantia nigra and locus coeruleus), p-tau immunoreactive thorned astrocytes at the glial limitans in the subpial and periventricular regions, p-tau immunoreactive large grain-like and dot-like structures, and TDP-43 immunoreactive neuronal cytoplasmic inclusions and dot-like structures in the hippocampus, anteromedial temporal cortex and amygdala. While this was only the first meeting to address the neuropathological diagnosis of CTE, and more research is needed to determine the nature and degree of brain injury necessary to cause this neurodegeneration, the panel members also noted that the pathognomonic lesion of CTE has, thus far, only been found in individuals who were exposed to brain trauma, typically multiple episodes.

The panel also determined that the pathognomonic lesion of CTE is distinct from age-related tau astrogliopathy (ARTAG), a morphological spectrum of astroglial pathology detected by p-tau immunohistochemistry that may coexist in the same brain with other disorders and is of unclear etiology (Fig. 5). P-tau-immunoreactive astrocytes in ARTAG include thorn-shaped astrocytes in the subpial, subependymal, and perivascular regions of the white and gray matter (Kovacs, in press). Changes of ARTAG may be present in CTE, but in isolation, are non-specific and non-diagnostic.

Although 9 of the 10 subjects diagnosed with CTE in this study were former American football players and only one was a former professional boxer, previous data has shown that the pathological features of CTE associated with boxing (often referred to as "dementia pugilistica") are similar to the pathological features of CTE associated with football [28, 32]. Furthermore, the cortical areas most likely to show early focal CTE pathology in boxers are similar to American football players. While initial reports of boxers with CTE described cerebellar scarring, atrophy and loss of Purkinje cells [5], recent studies of pugilists find that cerebellar pathology is rare aside from p-tau NFTs and neurites in the dentate nucleus, Purkinje cells and roof of the 4th ventricle [28, 32].

Future directions

Using criteria from this consensus meeting, Bieniek and colleagues reviewed the clinical records and brains of 1721 cases donated to the Mayo Clinic Brain Bank over the past 18 years, and found CTE pathology in 32 % of contact sport athletes [2]. No cases of CTE were found in 162 control brains without a history of brain trauma or in 33

Table 3 Recommended brain regions to be sampled and evaluated

Region	CTE		
Middle frontal gyrus*	pTau[a]	pTDP-43	Aβ[c]
Superior and middle temporal gyri*	pTau[a]		
Inferior parietal lobule*	pTau[a]		Aβ[c]
Hippocampus and entorhinal cortex	pTau	pTDP-43[b]	Aβ[c]
Amygdala	pTau	pTDP-43[b]	
Thalamus	pTau		
Basal ganglia with basal nucleus of Meynert	pTau		
Midbrain including substantia nigra	pTau		
Pons including locus coeruleus	pTau		
Medulla including dorsal motor nucleus of vagus	pTau		
Cerebellar cortex and dentate nucleus	pTau		
Additional sections if high suspicion			
Superior frontal gyrus	pTau[d]		
Temporal pole	pTau[d]	pTDP-43	
Hypothalamus including mammillary body	pTau[d]		

In addition to the NIA-AA recommended regions for the evaluation of Alzheimer's disease (AD) neuropathologic change and Lewy body disease (LBD) [34], we recommend wider p-tau screening to capture CTE and other tauopathies. In addition, if there is a high index of suspicion of CTE, we recommend taking extra sections of frontal and temporal cortices, and hypothalamus including the mammillary body

Bilateral representative sections from each region are recommended if both cerebral hemispheres are available for microscopic analysis

* Most valuable for detecting CTE neuropathology

[a] AT8 or equivalent Tau (CP-13 or PHF-1) on all cortical sections, if positive: stain other areas and possibly sample additional areas[d]. We do not recommend thioflavin or silver stains for the detection of CTE lesions

[b] TDP-43: amygdala and hippocampus, if positive then temporal pole and frontal cortex

[c] Aβ: middle frontal gyrus, inferior parietal lobule and hippocampus and entorhinal cortex; if positive wider sampling is recommended

[d] If there is a high index of suspicion consider taking extra sections, specifically superior frontal gyrus, temporal pole, and hypothalamus including mammillary body

cases with a history of a single traumatic brain injury. Of the 21 with CTE pathology, 19 had participated in football or boxing, and many were multiple sport athletes including rugby, wrestling, basketball, and baseball. One athlete played only baseball, and another athlete only played basketball. Similarly, Ling and colleagues screened 268 cases of neurodegenerative disease and controls in the Queen Square Brain Bank for Neurological Disorders using the preliminary McKee criteria [32] and found changes of CTE in 11.9 % of neurodegenerative disorders and 12.8 % of elderly controls. Of the cases with changes of CTE, 93.8 % had a history of TBIs, 34 % had participated in high-risk sports including rugby, soccer, cricket, lacrosse, judo and squash, and 18.8 % were military veterans [24]. However, it is unclear if all the cases with CTE changes described by Ling and colleagues would have met strict criteria for CTE using these newly defined NINDS guidelines. Furthermore, the relationship between non-diagnostic, non-specific astrocytic p-tau pathology and a history of traumatic exposure remains to be determined (Kovacs, in press).

At the present time, CTE remains a diagnosis that can only be made definitively upon neuropathological examination of the brain. Because the pathological diagnosis requires p-tau immunohistochemistry and the lesions are irregularly distributed, the detection of CTE in autopsy cohorts may require additional sampling compared to routine practices. The consensus panel's minimum recommended sampling for CTE is found in Table 3. Sampling follows the protocol recommended by Alzheimer Disease Centers (National Institute on Aging-Alzheimer's Association (NIA-AA) [34]) with the further recommendation that all cortical sections be taken to include the region at the depths of the cortical sulci. This has been shown in pilot studies to detect 80 % of CTE cases; however, 20 % of CTE cases, all early stage, would be missed by this sampling scheme [9]. Of the NIA-AA sampling guidelines, the following blocks are most valuable for detecting CTE: sulcal depths of the superior and middle frontal gyrus, superior and middle temporal gyrus and inferior parietal gyrus (Fig. 6). Of note, the Bielschowsky silver stain does not always detect the diagnostically significant focal perivascular cortical tau lesions, and the panel recommended p-tau immunohistochemistry for the diagnosis of CTE using AT8 immunostaining or equivalent p-tau antibody (CP-13 or PHF-1). The question of how extensive the sampling must be to "rule out" CTE was discussed, but no data were available to make this determination.

These criteria are the beginning of the process to fully characterize the pathology of CTE, and this is only the first of a series of consensus conferences on the subject funded by the U01 NINDS research initiative. Many important questions were not addressed in this first consensus panel, including the degree of neuronal cell loss, gliosis, inflammation, and hemosiderin deposition, and the diagnosis of CTE in the presence of comorbid pathologies, including AD. Future directions will include further validation of the neuropathological criteria for CTE, including staging of the severity of p-tau pathology and characterization of early disease. More pathological characterization will also be necessary to delineate the involvement of the other subcortical regions, including amygdala, globus pallidus, subthalamic nucleus, accumbens, neostriatum, thalamus, midbrain, cerebellum, spinal cord and white matter. It will also be important to determine the differential hippocampal p-tau pathology in CTE compared to AD, whether the TDP-43 pathology is distinctive for CTE and the contribution of hippocampal sclerosis and TDP-43 deposition to the clinical and pathological features. Population isolates

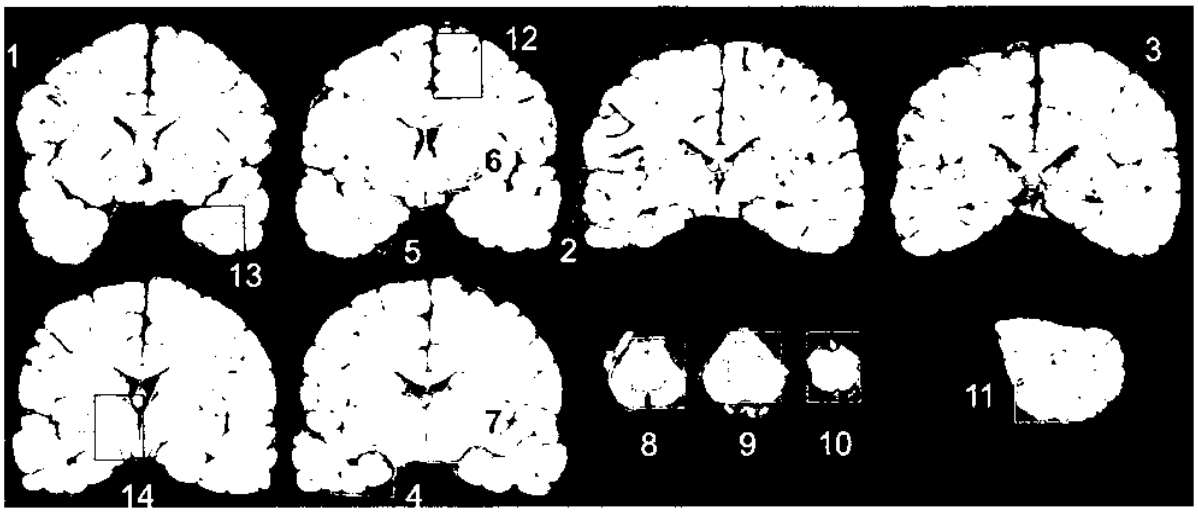

Fig. 6 Minimum recommended brain regions for evaluation for CTE. The following sections from the NIA-AA blocking scheme are recommended for p-tau immunostaining in evaluation for CTE (*blue rectangles*). In the cortical sections (blocks *1–5*, *12*, *13*), the depths of the cortical sulci should be included in the section. *1* Middle frontal gyrus, *2* superior and middle temporal gyri, *3* inferior parietal lobule, *4* hippocampus, *5* amygdala and entorhinal cortex, *6* basal ganglia at level of anterior commissure with basal nucleus of Meynert, *7* thalamus, *8* midbrain with substantia nigra, *9* pons with locus coeruleus, *10* medulla oblongata, *11* cerebellar cortex and dentate nucleus; additional sections if high suspicion of CTE (*red rectangles*): *12* superior frontal gyrus, *13* temporal pole, *14* hypothalamus and mammillary body

that develop unusual p-tau pathologies will need to be distinguished from CTE pathology in addition to Guam, such as the Kii peninsula of Japan [23]. In addition, the contributions of other proteinopathies, including β-amyloidosis (diffuse and dense core Aβ plaques and amyloid angiopathy) and alpha-synuclein will be important to determine. Similarly, the role of microvascular pathology, iron deposition, axonal injury, neuroinflammation and astrocytosis to the pathogenesis of CTE pathology needs resolution.

Future investigation will be needed to understand the relationship of the pathology to the clinical symptoms, genetics, neuroimaging and other biomarkers (including p-tau positron emission tomography (PET) imaging and cerebrospinal fluid (CSF) and blood biomarkers), metabolomics, proteomics, and epigenetics. It will also be important to determine whether specific "tau strains" are involved in the development of CTE. Furthermore, more information is needed regarding the frequency, severity, and nature of the traumatic exposures, length of survival after trauma, as well as factors such as the age at first and last exposure to trauma, and the effects of military compared to civilian brain trauma.

The limitations of the present study include the relatively small sample set, the use of digitized images, the selection of suspected CTE cases by a single source, the use of representative cases of moderate-to-late stage severity of CTE, and presence of some age-related co-morbidities. However, these limitations are offset by the fact that all evaluating neuropathologists were evaluating the exact same digital images, the cases were all uniformly prepared by a central laboratory, and the evaluation was performed blinded to all clinical or demographical data and gross neuropathological findings. Other limitations to the present study include the lack of data regarding TBI history in the non-CTE cases under evaluation. Future studies are being designed to specifically address the contribution of TBI at all levels of severity to neurodegenerative pathologies.

Conclusion

A consensus panel of 7 neuropathologists blinded to all clinical conditions and demographics evaluated the identical digitized images of 25 cases representing various tauopathies and concluded that the pathology of CTE is distinct from other tauopathies. In addition, the panel described the pathognomonic lesion of CTE as an accumulation of abnormal tau in neurons and astroglia distributed perivascularly at the depths of sulci in the isocortex in an irregular pattern. Future consensus meetings will address validation of the criteria among a wider group of neuropathologists using cases submitted from multiple sources. In addition, future meetings will address the identification of comorbid CTE when other neurodegenerative diseases and other diseases are present. Furthermore, additional research will be necessary to determine the contribution of p-tau and other pathologies to the development of clinical symptoms of CTE.

The incidence and prevalence of CTE remain unknown and will likely require methods of in vivo detection and diagnosis to make a clear determination. This first consensus conference on the pathological criteria for CTE represents the first step along the path to standardizing the neuropathology of CTE and paving the way for future determinations of specific clinical symptomatology and refinements in clinical diagnosis.

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Compliance with ethical standards

Conflict of interest ACM, NJC, DWD, RDF, CDK, IL, DPP, TDS, JPVS, WS, YT, JFC, KFB, KDO, VEA and WAG have no conflicts of interest to disclose.

Appendix: TBI/CTE group

Elissa Flannery, Daniel H. Daneshvar, Patrick T. Kiernan, Jesse Mez, Lauren Murphy, Todd M. Solomon, Debra Babcock, Patrick S. F. Bellgowan, and Walter J. Koroshetz.

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www.ninds.nih.gov

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NIH and NFL tackle concussion research

NIH announces research projects funded largely by donation from the NFL

The National Institutes of Health has selected eight projects to receive support to answer some of the most fundamental problems on traumatic brain injury, including understanding long-term effects of repeated head injuries and improving diagnosis of concussions.

Funding is provided by the Sports and Health Research Program, a partnership among the NIH, the National Football League, and the Foundation for the National Institutes of Health (FNIH). In 2012, the NFL donated $30 million to FNIH for research studies on injuries affecting athletes, with brain trauma being the primary area of focus.

Traumatic brain injury (TBI) is a major public health problem that affects all age groups and is the leading cause of death in young adults. Recently, concern has been raised about the potential long-term effects of repeated concussion, particularly in those most at risk: young athletes and those engaged in professions associated with frequent head injury, including men and women in the military. Current tests cannot reliably identify concussions, and there is no way to predict who will recover quickly, who will suffer long-term symptoms, and which few individuals will develop progressive brain degeneration, called chronic traumatic encephalopathy (CTE).

"We need to be able to predict which patterns of injury are rapidly reversible and which are not. This program will help researchers get closer to answering some of the important questions about concussion for our youth who play sports and their parents," said Story Landis, Ph.D., director of the National Institute of Neurological Disorders and Stroke (NINDS), part of NIH.

Two ($6 million each) are large, cooperative agreements focused on defining the scope of long-term changes that occur in the brain years after a head injury or after multiple concussions. The cooperative awards form a partnership between NINDS, the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD) and multiple academic medical centers.

NIH also will fund six pilot projects totaling just over $2 million that will last up to two years and are designed to provide support for the early stages of sports-related concussion projects. If the

early results are encouraging, they may become the basis of more comprehensive projects. The NIH institutes responsible for managing these grants are NINDS, NICHD, and the National Institute on Deafness and Other Communication Disorders (NIDCD).

The eight projects were selected by the NIH following a rigorous scientific review process.

The cooperative awards bring together two teams of independent scientists to study and compare the brains of donors who were at high or low risk for developing long-term effects of TBI. Ten neuropathologists from eight universities will coordinate to describe the chronic effects of head injury in tissue from hundreds of individuals in order to develop standards for diagnosis.

The project includes four teams that will correlate brain scans with changes in brain tissue, using a variety of techniques. This may open the possibility of using these advanced brain imaging techniques to diagnose chronic effects of TBI in living individuals. The investigators in the two projects will also help NIH develop a registry dedicated to enrolling individuals with a history of TBI who are interested in donating brain and spinal cord tissue for study after their death. The new NIH Neurobiobank (https://neurobiobank.nih.gov) will coordinate the tissue collection, data gathering, and also distribute biospecimens, along with relevant information to enable other scientists to access this valuable tissue.

The two cooperative agreements are:

• CTE and Post-traumatic Neurodegeneration: Neuropathology and Ex Vivo Imaging
Principal Investigator: Ann C. McKee, M.D., Boston University School of Medicine and U.S. Department of Veterans Affairs

At present, the diagnosis of CTE is made by examining the brain after death; however, the range of specific features that identify this disorder has not been established. One goal of Dr. McKee's project is to define a clear set of criteria for the various stages of CTE and to distinguish it from Alzheimer's, amyotrophic lateral sclerosis, and other neurodegenerative disorders in post-mortem brain tissue. Once these characteristics have been defined in brain tissue, the imaging teams at Washington University in St. Louis and Massachusetts General Hospital in Boston will correlate them with brain scans to identify features that might eventually be used to diagnose CTE in individuals during their lifetimes.

• Neuropathology of CTE and Delayed Effects of TBI: Toward In Vivo Diagnostics
Principal Investigator: Wayne Gordon, Ph.D., Mount Sinai Hospital, New York City

The goal of Dr. Gordon's project is to identify and describe the chronic effects of mild, moderate and severe TBIs and compare these with the features of CTE. Dr. Gordon and his colleagues at the University of Washington in Seattle will comprehensively evaluate brain tissue obtained from an ongoing study of thousands of people, the Adult Changes in Thought (ACT) study, funded by the National Institute of Aging. They also will examine brain tissue from donors who suffered severe TBI and were cared for in the TBI Model Systems program funded by the Department of Education's National Institute on Disability and Rehabilitation Research. In Dr. Gordon's project, neuroimaging teams at Massachusetts General Hospital, Oregon Health Sciences University in Portland, and the University of Washington will use a variety of sophisticated brain scanning

techniques in patients with a range of head injuries, as well as on post-mortem tissue, to identify potential markers that may eventually be used to diagnose the degenerative effects of TBI in people.

"The investigators will collaborate to develop diagnostic criteria for identifying the chronic features of the entire scope of brain trauma ranging from mild TBI to full-blown CTE, and then work to extend these criteria to living humans using some of the most advanced neuroimaging tools available," said Walter Koroshetz, M.D., deputy director of NINDS.

"Although the two cooperative agreements focus on different aspects of TBI, their combined results promise to answer critical questions about the chronic effects of single versus repetitive injuries on the brain, how repetitive TBI might lead to CTE, how commonly these changes occur in an adult population, and how CTE relates to neurodegenerative disorders like Alzheimer's disease," Dr. Landis said.

The pilot studies will focus on improving the diagnosis of concussion and identifying potential biomarkers that can be used to track a person's recovery. The six pilot grants are:

• Cortical GABA in Pediatric Sports Concussion
Principal Investigator: Jeffrey G. Ojemann, M.D., Seattle Children's Hospital

The brain contains numerous chemicals such as gamma-amino butyric acid (GABA), which is important for many brain functions, including cognition and movement, and may be altered by traumatic brain injury. Magnetic resonance (MR) spectroscopy is a scanning technique that can measure a variety of brain chemicals, including GABA. The goal of Dr. Ojemann's project is to use MR spectroscopy to monitor GABA levels in adolescents who have sports-related concussions and compare those levels to uninjured controls. The researchers also will conduct preliminary comparisons of GABA levels with existing cognitive measures such as memory tests and structural brain imaging. Diagnostic tools that can reliably detect when the brain is injured and when it has recovered following a concussion are essential for determining when it is safe to resume normal activities.

• Evaluation of Spot Light: A Concussion Injury Management App for Youth Sports
Principal Investigators: Lara McKenzie, Ph.D., Center for Injury Research and Policy, The Research Institute at Nationwide Children's Hospital, Columbus, Ohio and Dawn Comstock, Ph.D., Colorado School of Public Health, University of Colorado, Denver

Guidelines exist to help doctors diagnose and manage sports-related concussions, but guidelines are not fully supported by evidence-based research, are applied inconsistently, and those responsible for the care of injured athletes do not always fully communicate with each other. The goal of Drs. McKenzie and Comstock's project is to test the effectiveness of Spot Light, an easy-to-use mobile application (or app), developed by Inlightened, LLC. This app was designed to help doctors, coaches, athletic trainers and parents of young football players track the progress of a young athlete from the time of a concussion injury until they are cleared to return to play. The researchers want to know if the app will result in more concussions being reported, a greater number of referrals to doctors and better adherence to return-to-play guidelines. The goal is to improve diagnosis of concussions that are occurring among young athletes, and ensure that they are receiving appropriate care and are fully recovered before getting back on the field.

• Eye Movement Dynamics: A Rapid Objective Involuntary Measure of Concussion/Mild Traumatic Brain Injury
Principal Investigators: Nicholas Port, Ph.D. and Steven Hitzeman, O.D., Indiana University School of Optometry, Bloomington

People can choose where to look, but they do not have much control over some of the intricate eye muscle movements that are usually made without thinking. Studies have shown that eye movement problems are common in mild traumatic brain injury patients. Drs. Port and Hitzeman, in collaboration with team trainers and physicians at Indiana University and local high schools, plan to take advantage of the involuntary, reflex nature of eye movements. They will develop a portable eye tracking instrument that can be used to help diagnose concussions on the sidelines and to monitor injury progression in high school and college athletes. Drs. Port and Hitzeman will compare the eye tracking data to results from a commonly used cognitive test to determine if changes in eye movement can serve as a biomarker for sports-related mild traumatic brain injury. If successful, this study will help provide an objective and more reliable measure to detect traumatic brain injury than is currently available.

• Imaging and Biomarkers in Adolescents Cleared for Return to Play After Concussion
Principal Investigator: Harvey Levin, Ph.D., Baylor College of Medicine, Houston

Sports concussions may cause persistent long-term effects in young athletes -- in some cases, even after they have been allowed to return to play. Using a variety of neuroimaging techniques, Dr. Levin and his group will look at the effects of sports-related concussions on brain structure and function one month following injury in adolescents who have been cleared to play. In addition, this project will evaluate microRNAs (miRNAs) as potential biomarkers for concussions and recovery. These are small portions of RNA (a molecule that is similar to DNA, which contains our genetic code) that play a role in turning genes on or off. The researchers plan to measure levels of specific miRNAs and determine if they correspond with cognitive test results and neuroimaging data.

• Somatosensory Processing — Assessing Youth Sport-Related Concussion and Recovery
Principal Investigator: Stacy Jennifer Marcus Suskauer, M.D., Kennedy Krieger Institute, Baltimore

The somatosensory system provides information about our environment — for example, what an object feels like to the touch — and may be affected by brain injury. Dr. Suskauer and her colleagues will investigate whether somatosensory system information processing (SSIP) could be used as a biomarker for concussion and recovery in youth aged 13-17. For these experiments, the researchers will use a new portable device that delivers vibrations to fingertips. Perception of the vibrations reflects activity of sensory neurons in the brain, thereby providing a measure of SSIP. The researchers will also investigate whether changes in SSIP are related to differences in certain brain chemicals after head injury.

• Characterization of the Brain and Serum Metabolome in Mouse Models of Concussion
Principal Investigator: Michael J. Whalen, M.D., Massachusetts General Hospital, Boston

Metabolites are small molecules formed in the body as a result of the normal breakdown of proteins, drugs and other large molecules. The collection of all metabolites in the body is the metabolome. Studies have suggested that head injury may change levels of various brain byproducts, but this has

not been researched in a systematic way. Dr. Whalen and his group plan to use an experimental model of traumatic brain injury to conduct a detailed analysis of changes in the brain metabolome following concussion. The researchers will compare those differences with serum byproducts to determine if the changes can be revealed in blood samples. The results of this project may uncover metabolites that contribute to serious effects of traumatic brain injury and may help identify potential targets for detecting and treating concussions.

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The NINDS (http://www.ninds.nih.gov) is the nation's leading funder of research on the brain and nervous system. The NINDS mission is to reduce the burden of neurological disease – a burden borne by every age group, by every segment of society, by people all over the world.

The NICHD (http:www.nichd.nih.gov) sponsors research on development, before and after birth; maternal, child, and family health; reproductive biology and population issues; and medical rehabilitation.

The NIDCD (http://www.nided.nih.gov) supports and conducts research and research training on the normal and disordered processes of hearing, balance, taste, smell, voice, speech, and language and provides health information, based upon scientific discovery, to the public.

About the National Institutes of Health (NIH): NIH, the nation's medical research agency, includes 27 Institutes and Centers and is a component of the U.S. Department of Health and Human Services. NIH is the primary federal agency conducting and supporting basic, clinical, and translational medical research, and is investigating the causes, treatments, and cures for both common and rare diseases. For more information about NIH and its programs, visit http://www.nih.gov.

About the Foundation for the NIH (FNIH): Established by the United States Congress to support the mission of the NIH—improving health through scientific discovery in the search for cures—the Foundation for the NIH is a leader in identifying and addressing complex scientific and health issues. The foundation is a not-for-profit, 501(c)(3) charitable organization that raises private-sector funds for a broad portfolio of unique programs that complement and enhance NIH priorities and activities. For additional information about the Foundation for the NIH, please visit www.fnih.org.

Jason, Cailin (NIH/NINDS) [C]

From: McMakin, Barbara (NIH/NINDS) [E]
Sent: Tuesday, December 22, 2015 10:06 AM
To: Emr, Marian (NIH/NINDS) [E]
Subject: PRIORITY ACTION: CTE statement
Attachments: NIH Statement_CTE.docx

Categories: Press

Hi Marian,

Attached is a draft of our statement to the press.

Thanks,
Barbara

Barbara I. McMakin
Science Writer
Office of Communications and Public Liaison
National Institute of Neurological Disorders & Stroke
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31 Center Drive MSC 2540
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NIH Statement regarding CTE funding

(b) (5)

Jason, Cailin (NIH/NINDS) [C]

From: Myles, Renate (NIH/OD) [E]
Sent: Tuesday, December 22, 2015 10:12 AM
To: Emr, Marian (NIH/NINDS) [E]; McMakin, Barbara (NIH/NINDS) [E]
Cc: Burklow, John (NIH/OD) [E]; Jackson, Calvin (NIH/OD) [E]; Fine, Amanda (NIH/OD) [E]; Wojtowicz, Emma (NIH/OD) [E]
Subject: PRIORITY ACTION: Reports on ESPN Story

Categories: Press

Hi Marian and Barbara:

We're starting to get calls on the ESPN story. I understand Barbara is drafting a response, so we're going to send reporters your way. John gave ASPA a heads up, but please send up the requests with the proposed statement so we can clear it.

Thanks,
Renate

McMakin, Barbara (NIH/NINDS) [E]

From: Jason, Cailin (NIH/NINDS) [C]
Sent: Tuesday, December 22, 2015 10:27 AM
To: McMakin, Barbara (NIH/NINDS) [E]
Subject: FW: NFL-NIH
Attachments: NIH Statement_CTE ME edits.docx

Barbara,

Marian asked me to forward you this e-mail chain below. Also, a few other things:

1. Attached are Marian's revisions to your statement. Please make the changes and resend to her. She will then forward to John Burklow for approval, with a copy to Renate.
2. Look for a story that came out this morning from the NY Times
3. You can expect a call from a reporter at the Washington Post, Sarah Larimer

Thanks,
Cailin

From: McCarthy, Brian [mailto:Brian.McCarthy@NFL.com]
Sent: Tuesday, December 22, 2015 10:17 AM
To: Emr, Marian (NIH/NINDS) [E]
Subject: FW: NFL-NIH

From: Larimer, Sarah [mailto:Sarah.Larimer@washpost.com]
Sent: Tuesday, December 22, 2015 10:07 AM
To: McCarthy, Brian
Cc: Aiello, Greg
Subject: Re: NFL-NIH

Hey Brian,

Thanks so much for the quick reply. I really appreciate it. So just to clarify, funding from the NFL will be used in this project?

Thanks,

Sarah

From: McCarthy, Brian <Brian.McCarthy@NFL.com>
Sent: Tuesday, December 22, 2015 10:04 AM
To: Larimer, Sarah
Cc: Aiello, Greg
Subject: NFL-NIH

Aiello mentioned you asked about the ESPN story.

No it is not accurate. Have you spoken to someone at the NIH?

The NFL did not pull funding from the BU study. The NIH makes all funding decisions. The NFL has no "veto power" as part of its unrestricted $30 million grant to NIH.

In fact, the NFL in 2010 gave an unrestricted $1 million to Boston University for research into brain injuries. (AP story at the time:
http://www.nfl.com/news/story/09000d5d817a2623/article/nfl-gives-1-million-to-boston-university-for-study-of-brain-injuries[nfl.com])

The ESPN also references that BU received a $6 million grant from NIH that was from the NFL's donation to the NIH. From the ESPN story:

Dr. Ann McKee, a neuropathologist affiliated with Boston University and the U.S. Department of Veterans Affairs, recently received a $6 million grant that came through the NFL's 2012 donation to the NIH. McKee, like Stern, at times has criticized the league and has warned that the number of players with CTE is likely to be high.

#SB50
SuperBowl.com[nfl.com]
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NIH Statement regarding CTE funding

(b) (5)

McMakin, Barbara (NIH/NINDS) [E]

From: Myles, Renate (NIH/OD) [E]
Sent: Tuesday, December 22, 2015 11:44 AM
To: McMakin, Barbara (NIH/NINDS) [E]; ODOCPL Interviews (NIH/OD OCPL); OCPLPressTeam
Cc: Emr, Marian (NIH/NINDS) [E]; Burklow, John (NIH/OD) [E]
Subject: RE: Interview request: Chronic traumatic encephalopathy research grant
Attachments: NIH Statement_CTE 12.22.2015.docx

Hi Barbara:

See suggested edits, which Dr. Collins has reviewed. If you're okay with this, we'll send this up for clearance.

Thanks.
Renate

From: McMakin, Barbara (NIH/NINDS) [E]
Sent: Tuesday, December 22, 2015 11:06 AM
To: ODOCPL Interviews (NIH/OD OCPL); OCPLPressTeam
Cc: Emr, Marian (NIH/NINDS) [E]; Burklow, John (NIH/OD) [E]
Subject: Interview request: Chronic traumatic encephalopathy research grant

Attached is draft statement regarding CTE funding.

Best,
Barbara

Reporter: Sarah Larimer
Organization: Washington Post
Phone/Email: Sarah.Larimer@washpost.com
Subject: Chronic traumatic encephalopathy research grant
Deadline: ASAP
Spokesperson: **NIH Statement**
Expected place of publication (print, online, broadcast): online
Expected date of publication/airing: unknown
Expected prominence (e.g. front page, Sunday, evening/morning show, etc.): unknown

Key messages/talking points:

The reporter would like information clarifying the funding source of a $16 million CTE research grant.

Barbara L. McMakin
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NIH Statement regarding CTE funding:

The NIH is funding the CTE study led by Dr. Robert Stern at Boston University, in coordination with three other sites, which was announced this week. The NFL is currently funding eight ongoing studies in the area of traumatic brain injury: http://www.ninds.nih.gov/news_and_events/news_articles/pressrelease_nfl_tbi_12162013.htm We expect that the NFL will fund future studies to help improve player safety and health, on and off the field. Any questions about the donation from the NFL should be directed to the NFL.

Jason, Cailin (NIH/NINDS) [C]

From: Ober, Maria Pantages <mpober@bu.edu>
Sent: Tuesday, December 22, 2015 1:55 PM
To: Emr, Marian (NIH/NINDS) [E]
Subject: PRESS: U01
Attachments: CTE U01 award announcement.docx

Follow Up Flag: Follow up
Flag Status: Completed

Categories: Press

attached

www.bumc.bu.edu/busm

EMBARGOED FOR RELEASE UNTIL 9 a.m. Tuesday, Dec. 22, 2015
Contact: Gina DiGravio, 617-638-8480, ginad@bu.edu

NIH/NINDS Grant Awarded to Develop Methods for Diagnosing Chronic Traumatic Encephalopathy (CTE) During Life

(Boston)—Researchers from Boston University, the Cleveland Clinic, Banner Alzheimer's Institute and Brigham and Women's Hospital in Boston, have been awarded a $16 million* grant from the National Institutes of Health/National Institute of Neurological Disorders and Stroke (NIH/NINDS). This seven-year, multi-center grant will be used to create methods for detecting and diagnosing chronic traumatic encephalopathy (CTE) during life as well as examining risk factors for CTE.

CTE is a degenerative brain disease characterized by changes in behavior, mood and cognition, including the development of dementia. Currently it can only be diagnosed post-mortem through examination of an abnormal form of tau protein. CTE has been found most often in professional contact sport athletes (e.g., boxers, football players) who have been subjected to repetitive blows to the head resulting in symptomatic concussive and asymptomatic subconcussive trauma. Neuropathologically-confirmed CTE has been reported in individuals as young as 17 and in athletes who only played sports through high school or college. It also has been found in non-athletes who experienced repetitive head impacts, including military service members.

According to the researchers, although the neuropathological features of CTE have become further clarified in recent years, the clinical presentation of CTE is still not well characterized and there remains no method to diagnose it before death. "There are so many critical unanswered questions about CTE. We are optimistic that this project will lead to many of these answers, by developing accurate methods of detecting and diagnosing CTE during life, and by examining genetic and other risk factors for this disease," explained lead principal investigator, Robert Stern, PhD, professor of neurology, neurosurgery, and anatomy & neurobiology at Boston University School of Medicine, where he is Clinical Core director of the Boston University Alzheimer's Disease and CTE Center.

Through this grant, NINDS is funding a longitudinal study of former NFL players, former college football players and a control group of individuals without any history of contact sports or brain injury. Participants will be examined at one of four centers across the country, including Boston University School of Medicine; Cleveland Clinic Lou Ruvo Center for Brain Health in Las Vegas; Mayo Clinic in Scottsdale, Ariz.; and NYU Langone Medical Center, New York City.

Participants in the study will undergo extensive clinical examinations, as well as state-of-the art PET scans, advanced MRI scans, experimental blood tests and other potential methods of detecting changes in the brain associated with CTE. Researchers also will refine and validate specific criteria for clinical diagnosis of the disease and will investigate genetic and head impact exposure risk factors for CTE in order to begin to determine why some people are more prone to get CTE than others. Project data will be shared with researchers across the country and abroad to facilitate a more complete understanding of this disease, ultimately leading to successful methods of preventing and treating CTE.

The other principal investigators are Jeffrey Cummings, MD, ScD, (director, Cleveland Clinic Lou Ruvo Center for Brain Health in Las Vegas and Cleveland; the Camille and Larry Ruvo Chair of the Neurological Institute of Cleveland Clinic; and professor of medicine, Cleveland

Clinic Lerner College of Medicine at Case Western Reserve University); Eric Reiman, MD (executive director of the Banner Alzheimer's Institute, Phoenix) and Martha Shenton, PhD (director, Psychiatry Neuroimaging Laboratory and senior scientist, Brigham and Women's Hospital; professor of psychiatry and radiology, Harvard Medical School). The project involves a group of approximately 50 investigators, representing 17 research institutions.

"There is an urgent need to clarify the clinical and biological consequences of repetitive head impacts in athletics and to use this information to find the best ways to treat and prevent those consequences," said Reiman. "It is both a great privilege and responsibility to help in that endeavor."

"This research is an exciting and important opportunity to acquire new information about the potential devastating consequences of repetitive head impact including CTE," said Shenton. "We hope that by gaining this knowledge, new avenues of treatment will emerge for those who experience debilitating symptoms from repetitive brain trauma."

"We currently have no method to diagnosis CTE during life and it is crucial to take the next steps to better understand this disease," said Cummings. "This grant will allow us to take what we know about CTE and move to the next level of research, with the end goal of diagnosing these athletes at early stages of the illness when treatments may help prevent the progression of the disease."

***Editor's Note:** NIH/NINDS Grant No. U01NS093334; the exact amount of the award is $15,859,906.

Jason, Cailin (NIH/NINDS) [C]

From:	NINDS Press Team
Sent:	Tuesday, December 22, 2015 2:00 PM
To:	'belson@nytimes.com'
Subject:	PRESS: NIH Statement re CTE research
Attachments:	NIH Statement_12.22.2015.docx
Categories:	Press

Thank you for your inquiry. Attached is a statement from the NIH.

Marian Emr
Director, Office of Communications and Public Liaison/NINDS
NIH Building 31, Room 8A07
Phone: (301) 496-5924
marian.emr@nih.gov

NIH Statement regarding CTE funding:

The NIH is funding the CTE study led by Dr. Robert Stern at Boston University, in coordination with three other sites, which was announced this week. The NFL is currently funding eight ongoing studies in the area of traumatic brain injury: http://www.ninds.nih.gov/news_and_events/news_articles/pressrelease_nfl_tbi_12162013.htm We expect that the NFL will fund future studies to help improve player safety and health, on and off the field. Any questions about the donation from the NFL should be directed to the NFL.