Principal Investigator	John Dolan
Co-Investigator	N/A
Secondary Investigators	Brian Schmidt
Award Type	Orthodontic Faculty Development Fellowship Award
Project Title	Dolognawmeter Assay for Rats: Validation of a Behavioral Index of Orofacial Nociception
Project Year	2014 (with extension)
Institution	New York University, College of Dentistry
Summary/Abstract (250 word maximum)	I designed and fabricated 6 dolognawmeters scaled for rats. Gnaw task rigor was titrated with different polyvinyl dowel diameters for the first (7mm) and second (11mm) gnawing tasks. Outcome variable was defined as time required by the rat to gnaw (sever) the second in the series of 2 dowels that block escape from the confinement tube. Sprague Dawley rats (6 female) were trained each day over 7 days in dolognawmeters. Gnaw-time for each animal rapidly decreased in all rats and plateaued by training trial 7 (as previously observed in mice). Gnawing activity was then timed once a day for 3 days. Mean gnaw-time for each respective rat for these 3 trials was calculated and employed as the baseline gnaw-time. A TMJ inflammatory pain model was generated under 1-5% isoflurane. A 30-gauge needle was walked to the edge of the zygomatic arch and into the superior joint space. Fifty µl of Complete Freund's Adjuvant was injected into right and left TMJ. Gnawing function was then quantified in the dolognawmeter at post-injection (P.I.) day 1, 3, 4 and 5. Gnaw-times were significantly greater for all six rats (relative to respective baselines) at P.I. day 1 and 3. By P.I. day 5, half of the rats still exhibited elevated gnaw-times. Trials will be continued to P.I. day 28. In future work I will validate the rat dolognawmeter as a pain/nociceptive assay; I will demonstrate analgesic reversal of dysfunction in inflammatory orofacial models and also in an oral squamous cell carcinoma model.
Were the original specific aims of the proposal realized	Aims 1 and 2 have been completed. The original aims included: **1. Redesign the dolognawmeter to accommodate rats.** **2. Quantify (with the dolognawmeter) attenuated gnawing secondary to respective TMJ inflammation and masseter inflammation models in rats.** **3. Demonstrate analgesic reversal of gnawing attenuation to validate the dolognawmeter outcome variable (gnaw-time) as a behavioral index of nociception in the two rat models** Aim 3 must still be completed; validation trials demonstrating

	analgesic reversal of gnawing dysfunction simply require gnawing trials with several new groups/models of rats. The initial phase of the project is complete and has been very successful. The device design was refined, 6 devices were fabricated, dowel diameter was established through trial and error to titrate the difficulty of the gnawing task, baseline gnaw-times were generated for each of six rats, TMJ inflammation model was generated, gnawing/incising dysfunction was quantified in the prototype devices following creation of the pain/nociception model. I found that rat behavior is similar to mouse behavior in the dolognawmeter. Following injection of the inflammatory agent, gnaw-times were significantly greater than baseline. Several days after injection the rats regained function (gnaw-times revert back to baseline).
Were the results published? If not, are there plans to publish? If not, Why not?	Results will not be published yet. I will proceed with the ongoing validation of the device (to demonstrate gnawing dysfunction as an index of orofacial pain/nociception). The dolognawmeter scaled for rats will be published once the results of device validation are completed. Validation will include demonstration of analgesic reversal of dysfunction in inflammatory orofacial pain models (masseter and TMJ) and also in an oral squamous cell carcinoma model.
Have the results of this proposal been presented? If so, when and where? If not, are there plans to do so? If no, why not?	I will complete the work needed to validate the device before the results are presented. Ultimately the results will be used to support a grant proposal. Once this is accomplished the results will be presented at a national meeting.
To what extent have you used, or how do you intend to use, AAOF funding to further your career?	AAOF funding allowed me to dedicate additional time to develop a new device for quantifying oral function in rats. This device will be useful to a variety of investigators interested in chewing function, TMD, occlusion, and the effect of diet on function. As a result of my preliminary work on the dolognawmeter scaled for rats, I have nearly completed validation of the device as an automated assay for quantification of oral dysfunction to index orofacial pain/nociception. I will now proceed with a sham control group and inflammation/analgesic groups. In future work I will characterize and modulate gnawing function in a rat model of TMD as well as in mouse models of TMJ osteoarthritis (biglycan and fibromodulin double deficient mice first generated by Dr. Marian Young at the NIH). Oral function in these models will be quantified with my previously developed dolognawmeters for mice and with the dolognawmeters scaled for rats that were developed in the current AAOF supported project.

Educational, Teaching and Clinical Objectives: Successes and Failures

My academic program has changed significantly from the time I submitted my AAOF proposal entitled "Dolognawmeter Assay for Rats: Validation of a Behavioral Index of Orofacial Nociception". I remain as full time faculty at NYU but my academic appointment is now in the Department of Oral and Maxillofacial Surgery and I am no longer on a tenure track. I previously intended to establish an independently funded orofacial pain program. In retrospect that was a naïve goal. Going forward, all of my research will be carried out as part of collaborative work with Dr. Brian Schmidt. The majority of my time is dedicated to clinical research at NYU Bluestone Center for Clinical Research (BCCR) and to work in the basic science laboratory that I share with Dr. Schmidt. All of my basic science work relates to orofacial pain. One day a week I continue my work as clinical attending faculty in the NYU orthodontic residency program.

Educational Plan: Over the last couple years I gained immense benefit from mentorship opportunities in clinical and basic research. I have worked with a wide variety of talented and experienced clinicians and scientists while fulfilling my obligations at BCCR. I continue to collaborate with Dr. Kulkarni's neuroscience lab at NIH and I now also collaborate with the neuroscience lab of Dr. Feng Tao at Texas A and M University; I consult and provide dolognawmeters for both of these labs.

The machinist that I work with became seriously ill while I was undertaking my AAOF related research project; he was unable to deliver on design and fabrication of my new devices. Subsequently I did the design and fabrication work. The data that I acquired for the project was obtained with six prototypes that I fabricated in our small laboratory shop. I had intended to acquire a CAD/CAM (computer aided design/manufacturing) experience by attending a course at NYU but the course could not be accommodated in my work schedule. In due time I will attend a CAD/CAM course as this will streamline prototype development in several of my projects. Ultimately I intend to provide rat scaled dolognawmeters to collaborators in Toronto at the Centre for the Study of Pain. This collaboration will be postponed until the rat devices are fabricated on a more commercial scale.

Teaching Skills Plan: I have curtailed time spent on formal teaching skills courses. I did not attend the Compass Program as I had expected. I am now trying to limit my time away from NYU; time away is difficult to accommodate while we are undertaking long-term behavioral experiments with rodents (over weeks and months). The trajectory of my work now primarily entails clinical research in BCCR, basic science work in our lab, mentoring dental students and residents that conduct work in our lab, and consulting with other labs who seek to utilize my behavioral assays. I recently took on mentorship responsibilities related to the research project of a first year orthodontic resident in my lab.

Clinical Skills: Over the last two years I have increased the amount of time that I dedicate to clinical orthodontics. Accordingly, I have improved my clinical acumen. I work in private practice most Fridays and I occasionally work on the weekend. I am assembling cases from private practice to gain ABO certification. NYU encourages faculty to perform clinical work one day a week. I think that this is an important institutional policy; faculty maintain and refine their clinical skills and the policy probably helps retain a few faculty members. I continue work as an attending faculty member one day a week in the NYU orthodontic residency clinic. I also undertake research responsibilities in the operating room for extended clinical and translational work that Dr. Schmidt and I have conducted over many years.