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**AAO Foundation Final Report Form
(a/o 1/3/2018)**

In an attempt to make things a little easier for the reviewer who will read this report, please consider these two questions before this is sent for review:

- Is this an example of your very best work, in that it provides sufficient explanation and justification, and is something otherwise worthy of publication? (We do publish the Final Report on our website, so this does need to be complete and polished.)*
- Does this Final Report provide the level of detail, etc. that you would expect, if you were the reviewer?*

Please prepare a report that addresses the following:

Type of Award: Orthodontic Faculty Development Fellowship Award

Name(s) of Principal Investigator(s): IACOPO CIOFFI

Institution: University of Toronoto, Faculty of Dentistry

Title of Project: PHYSIOLOGICAL AND PSYCHOLOGICAL FACTORS AFFECTING THE PAIN RESPONSE DURING ORTHODONTIC TREATMENT AND THE INDIVIDUAL ADAPTATION TO CHANGES IN DENTAL OCCLUSION

Period of AAOF Support 07-01-2017 to 12-30-2018

Amount of Funding 19,600

Summary/Abstract.

Pain is frequently reported by patients during orthodontic treatment, and it has been considered one of the main causes discontinuing care or terminating treatment early. The reasons for which some patients adapt fairly well to temporary changes in the dental occlusion and others do not and may develop pain and temporomandibular disorders like symptoms have been minimally investigated so far.

In this project, we investigated:

1. Whether and how trait anxiety and oral behaviors, such as daytime tooth clenching, affect the individual adaptation to experimental changes in the dental occlusion and tooth pain, and
2. The physiologic modifications occurring in the central nervous system as a consequence of experimental orthodontic tooth movement

We screened a cohort of 255 University Students using a Web-survey and recruited forty-five healthy volunteers based on their trait anxiety-levels (low, intermediate, and high). Orthodontic separators were positioned between their mandibular molars to induce experimental tooth movement and pain, and kept in place for 5 days. Somatosensory changes at trigeminal and extra trigeminal locations were measured using quantitative sensory testing. Diaries were used to monitor tooth pain, and frequency of wake-time tooth clenching.

A cohort of adult 18 individuals was submitted to MRI scanning at baseline and after five days. Resting-state fMRI scans were analysed with seed-based functional connectivity of a key node of the salience network (aMCC).

Experimental orthodontic tooth movement and pain determined significant changes in the pressure pain thresholds (PPT) of the masticatory muscles (superficial masseter and anterior temporalis) and the thenar eminence (extra trigeminal location).

At the masseter, the changes in somatosensory function were dependent on trait anxiety levels ($P=0.011$). PPTs decreased significantly in the high-anxiety group ($P=0.001$), while increased in both the intermediate and low anxiety group (all $P<0.05$). No effect of sex on PPT changes was found at this location ($P=0.703$).

At the temporalis, the changes in PPTs were not affected by anxiety ($P=0.248$) but only by sex, and increased in male individuals ($P=0.021$).

At the thenar eminence, the changes in PPTs were affected by the interaction sex*anxiety ($P=0.029$). PPTs decreased in HA females and increased in HA males, being the difference greater in males than females ($P=0.001$).

At days 3-4-5, subjects with high anxiety had less tooth pain than the other groups (all $P<0.05$) and, from day 4, they had less tooth clenching episodes ($P=0.005$). The aMCC showed reduced functional connectivity to the bilateral posterior parietal cortices and the dorsolateral prefrontal cortex (both $p<0.05$) – nodes of the executive control network at five days post-insertion, compared to baseline.

Orthodontic pain induced by experimental tooth movement determines significant somatosensory changes and favors greater sensitivity to painful stimuli, by sensitizing the trigeminal and extra trigeminal systems. These changes are dependent on the levels of anxiety.

Individuals with high anxiety demonstrate a fear-avoidance behavior while exposed to experimental tooth movement and tooth pain, which contributes to decrease the intensity of pain. Indeed, they reduce the frequency of clenching episodes in response to the painful stimulus, which may reduce the mechanical stimulation of periodontal ligament. Orthodontic pain induced by experimental tooth movement reduce the connectivity between the salience network and the executive control network, suggesting that the participants disengaged from pain.

Response to the following questions:

1. Were the original, specific aims of the proposal realized?
All the objectives of the investigation were achieved.
2. Were the results published?
 - a. If so, cite reference/s for publication/s including titles, dates, author or co-authors, journal, issue and page numbers
YES, see list aattached
 - b. Was AAOF support acknowledged?
YES
 - c. If not, are there plans to publish? If not, why not?
N/A
3. Have the results of this proposal been presented?
 - a. If so, list titles, author or co-authors of these presentation/s, year and locations
YES, see list above
 - b. Was AAOF support acknowledged?
YES
 - c. If not, are there plans to do so? If not, why not?
N/A
4. To what extent have you used, or how do you intend to use, AAOF funding to further your career?

The data generated with this research allowed to apply for major grant agencies including NIH and CIHR (Canadian Institutes of Health Research)

The funding generated the following publications:

Presentation at conferences:

1. Rofaeel M, Chow J, **Cioffi I**. Influence Of Anxiety Severity On Electromyographic Characteristics of Tooth Clenching (2019). International Association for Dental Research IADR General Session, Vancouver, Canada, CA, US. **Submitted**
2. Spano VE, Chow J, Imbriglio TV, **Cioffi I**. Effects Of Anxiety And Oral Behaviors On Somatosensory Function (2019). International Association for Dental Research IADR General Session, Vancouver, Canada, CA, US. **Submitted**
3. Ayoub L, **Cioffi I**, Moayedi M. Persistent orofacial pain drives salience network plasticity in the human brain (2018). International Association for The Study of Pain congress. Boston, MA, US. **Poster presentation.**
4. Chow J, **Cioffi I**. Impact of Anxiety on the Sensory and Motor Response to Tonic Painful Stimuli Induced by Experimental Orthodontic Tooth Movement (2018). International Association for The Study of Pain congress. Boston, MA, US. **Poster presentation.**
5. Chow JC, Cong F, Marwah V, Gong SG, Suri S, **Cioffi I** (2017). Tooth Clenching is More Frequent In Individuals With Increased Somatosensory Amplification. International Association for Dental Research IADR General Session, San Francisco, CA, US. **Oral presentation.**

Manuscripts:

1. Chow J, **Cioffi I**. Effects of trait anxiety, somatosensory amplification, and facial pain on self-reported oral behaviors. *Clinical Oral Investigations*. 2018, *in press*; doi: 10.1007/s00784-018-2600-1
2. Chow J, **Cioffi I**. Pain and orthodontic patient compliance: A clinical perspective. *Seminars in Orthodontics*. 2018; 24: 242-247.
3. **Cioffi I**. Orthodontic pain: an overlooked issue? *Seminars in Orthodontics*. 2018; 24: 207-208.

MSc Thesis (Orthodontics, University of Toronto):

Chow, Jeffrey Chi-Fai. Effects of Anxiety and Daytime Clenching on Orthodontic Pain Perception (2018).

Advisor. Iacopo Cioffi

Recognition of expertise

My expertise is widely recognized in both orofacial pain/neuroscience and orthodontics. I was appointed as Communication Officer of two IADR (International Association for Dental Research) networks (Neuroscience and the International Network for Orofacial pain & Related disorders Methodology - INFORM). This position allows me to be continuously in contact with leading scientists and research agencies in pain/neuroscience. I have organized a topical symposium about novel biomarkers of orofacial pain with leading scientists in pain (Peter Svensson, University of Aarhus, Denmark – Luda Diatchenko, McGill University, Montreal – Massieh Moayedi, University of Toronto) at the International Association for The Study of Pain Conference in Boston (IASP). Acceptance of topical symposia at IASP is limited only to cutting-edge research and is highly competitive. Also, I was invited to give a lecture at the American Academy of Orofacial Pain conference in Chicago (2018). In 2018, ten abstracts authored by students working in my lab were accepted for presentation at major national and international conferences, including IADR, IASP and the Canadian Association of Orthodontists. I was a reviewer of the abstracts submitted to the IADR conferences in London, UK (2018), and Vancouver (2019) for the pain/neuroscience area.

My expertise in orthodontics is confirmed by the huge amount of reviews I perform for the major orthodontic journals (American Journal of Orthodontics and Dentofacial Orthopaedics, The Angle Orthodontist, European Journal of Orthodontics). I am also an Affiliate Member of the Angle Society - East component. Enter this society is extremely challenging. The Angle Society welcomes very talented researchers or clinicians, and those who have significantly contributed to the orthodontic specialty. The Angle East has only five members in Canada. Every year, the Angle Scientific Committee evaluates the members' research contribution by reviewing their original papers. Each year, some papers are selected to be presented at the annual conference.

In 2016, I was invited by the Italian Academy of Orthodontics to give a lecture at their annual scientific meeting. In 2017, I was invited to be the Guest Editor of a special issue of Seminars in Orthodontics about orthodontic pain, which was published in June 2018. I was also invited in the Editorial Board of The Journal of Aligner Orthodontics.

Education and clinical skills

I graduated in Orthodontics at the University of Naples Federico II, Italy. Currently I hold a dental academic license which allows me to examine patients at the University of Toronto and Mount Sinai Hospital, Department of Dentistry. In order to get a specialty license in Canada, In 2018 I applied for the Dental Specialty Assessment and Training Program (DSATP) in Orthodontics at University of Toronto. During this academic year (from June 2018 to July 2019) I will treat approximately 20 orthodontic patients and audit lectures relevant to the discipline.

The DSATP program, which takes approximately 30% of my time, is designed to clinically assess applicants to determine whether they have the knowledge, skill and judgement equivalent to the standards set to graduate a student from a CDAC (The Commission on Dental Accreditation of Canada) or CODA (Commission on Dental Accreditation) accredited dental specialty program. Upon successful completion of the DSATP, I will be eligible to apply to write the National Dental Specialty Examination (NDSE) administered by the Royal College of Dentists of Canada. Upon successful completion of this examination, I will be eligible for licensure by one of the Dental Regulatory Authorities. The NDSE exam is scheduled in June 2019.

I will also present my clinical cases at the next Angle East meeting in Toronto (April 2019) to get full Angle membership. The Angle East is dedicated to educating orthodontists to achieve and maintain a high level of professionalism in their field and to facilitate the sharing of knowledge and experience. Enter the Angle East is extremely challenging. Only a few people, who have

recognized clinical and/or research skills, are invited to be members.

Teaching responsibilities

Since 2015, I have been involved in teaching to both D.D.S and M.Sc. students at the Faculty of Dentistry, the University of Toronto. I have also been involved in the Interfaculty pain curriculum (IPC) of the University of Toronto Centre for the Study of Pain (UTCSP).

List of courses taught

Doctor of Dental Surgery (D.D.S) program

DEN222 – Orthodontics. I teach “*Etiology of malocclusion*” and I am a seminar instructor in the course DEN222/Orthodontics. The DEN222 course is offered every year, and involves about one-hundred students (second year D.D.S). The course is given in the second term. The students audit one hour frontal lecture (9.00 -10.00 am), and then the seminars, in small groups of twelve (from 10.00 am to 12.00 pm). I have participated in the courses given in the academic years 2015-16, 2016-17, and 2017-18. During the seminars, I mainly taught cephalometric and model analyses. Also, under my guidance, students were able to formulate a proper diagnosis and to elaborate on possible treatment plans. I was also in charge to score the cephalometric analysis and the model competency tests. At the end of the course, students were assigned clinical cases. The goal of the assignment was to perform accurate cephalometric and model analyses, and to formulate a correct diagnostic statement supported by clinical and cephalometric findings. Finally, each student was invited to give a presentation about the assigned clinical case which I had to grade.

121Y1 - Biological basis of oral health and disease. I teach “*Muscle and simple reflexes*” and “*Mastication, occlusion, and swallowing*”. The course is given to D.D.S 1 students in the second term.

Master of Science (M.Sc.) programs

Journal Review – M.Sc. Program in Orthodontics. Since 2015, I coordinate the Journal review presentations in the Graduate Program in Orthodontics together with Prof. Siew-Ging Gong. 1st and 2nd year Orthodontic residents are asked to review and discuss a paper of relevance to the orthodontic discipline, which is assigned by the coordinators for a total of twelve hours per year.

PDE9094Y - Clinical Case Conferences. Starting 2015, I have joined Prof. Siew-Ging Gong in the Clinical Case Conference course. This course is offered every year. The course aims to promote interspecialty collaboration in clinical case diagnosis and treatment. During each seminar, three M.Sc. students of three different specialty programs, are asked to present a multidisciplinary clinical case of relevance to their specialties. At the end of the course, to get credit, students are asked to write a clinical case report and submit it to the Ontario Dentist. In 2018, I was asked to lead the course (Prof. Gong on sabbatical leave).

DEN1060H - Oral physiology. Since 2016, I teach “*Psychological aspects of Orofacial Pain*”. The course is given to M.Sc. Students from the different clinical specialty programs. I have taught in the courses given in the academic years 2016-, 2017-18, and 2018-19.

Other courses

M.Sc. Program in Orthodontics – Scientific Methodology course. Although I am not formally

involved in the Scientific Methodology course (Coordinator: Dr. Siew-Ging Gong) of the Graduate Program in Orthodontics, I often attend the sessions to facilitate discussion and provide feedback about the research projects of the M.Sc. students involved in the program.

M.Sc. Program in Orthodontics – Lunch and Learn Series. Orthodontic residents often attend special lectures given by local and international speakers during lunchtime. In 2017, I invited Dr. Marino Musilli, who is a worldwide renowned expert in lingual orthodontics, to give a lecture to our orthodontic residents. The lecture was entitled “*Biomechanics-based Orthodontics: A Journey From Conventional To Custom-made Orthodontic Appliances*” and was given via Zoom to all orthodontic residents on June 14th 2017. Orthodontic residents do not receive training in lingual orthodontics. Therefore, it was a great opportunity for them to be exposed to a different method of treatment.

IPC- UTCSP. I also teach in the Interfaculty Pain Curriculum (IPC) of the University of Toronto Center for the Study of Pain (UTCSP). UTCSP-IPC is a comprehensive and unique 20-hour integrated, interdisciplinary, pain curriculum for pre-licensure health science students. The goal of the curriculum is to improve pain knowledge and understanding of interprofessional pain assessment and management processes. Every March, approximately 1000 students from Dentistry, Medicine, Nursing, Occupational Therapy, Pharmacy, Physical Therapy, and the Physician Assistant Program participate in the UTCSP-IPC. Using cases based on real patients, they complete comprehensive assessments of multiple factors that contribute to the pain experience, present comprehensive pain management plans justifying their choices, describe multiprofessional and interprofessional strategies for the planning, intervention, and monitoring of pain management outcomes and describe ethical, legal, social, and political issues that may impact on patients’ pain management.

In the academic years 2015-16 and 2017-18, I gave two hour lectures about “*Chronic Pain*” to the D.D.S students involved in the program (D.D.S3) during the Monday session. I also facilitated interprofessional small group discussions (twenty students – 8 hours) in the Wednesday and Thursday sessions. During the sessions, clinical cases are discussed with a multidisciplinary approach. Students are asked to prepare treatment plans which are reviewed together with the facilitators. Clinical cases are then assigned to students and evaluated by the IPC Committees.

Course development

DEN1017S – Temporomandibular disorders. In July 2017, I was asked by Prof. Ernest Lam – Associate Dean - School of Graduate Studies – to lead the graduate course DEN1017S “*The diagnosis and treatment of temporomandibular disorders*”. The course is offered every two years and involves M.Sc. students from the different dental specialties. The course was previously led by Dr. Thuan Dao.

Course structure description. Temporomandibular disorders (TMD) are the most common form of chronic orofacial pain and the second most frequent musculoskeletal pain condition. The complex multifactorial etiology of TMD makes diagnosis and treatment challenging.

The course is structured in three components. In the first one, students learn the pathological mechanisms of TMD, and acute and chronic orofacial pain. In the second component, they learn how to diagnose and treat the most common TMD. In the third part of the course, the students are asked to give a lecture about a topic of interest to their specialty that is linked to TMD and pain. The course is 32 hours, of which 26 hours are lectures. Students’ presentations are scheduled in the last 6 hours of the course.

Student centered learning objectives. Students learn the pathological mechanisms of TMD after having consolidated knowledge about anatomy and physiology of the masticatory muscles and temporomandibular joints. After developing a solid understanding of the peripheral and central nociceptive pathways, students will be able to diagnose temporomandibular disorders using the most recent and evidence-based criteria including the Diagnostic Criteria for TMD (Shiffmann et al, 2014), and treat the most common forms of TMD.

Method of evaluation. The final mark is based on attendance and participation (10%), evaluation of a written essay (40%) and an oral presentation (50%)

Class participation and attendance. Attendance and participation accounts for 10% of the final mark.

Assignments: written essays on assigned topics. Topics are assigned in mid-January. Deadline for Submission is mid-April. In 2018, I assigned the following topics:

- *Imaging of the temporomandibular joints (2 students)*
- *Imaging of the masticatory muscles (2 students)*

- *Vertical dimension and temporomandibular disorders (2 students)*
- *Bruxism and oral implants (2 students)*

- *Bruxism and dental occlusion (2 students)*
- *Functional appliances and temporomandibular disorders (2 students)*
- *Orthognathic surgery and temporomandibular disorders (2 students)*
- *Orthodontic treatment and condylar resorption (2 students)*

University of Toronto, Faculty of Dentistry
 School of Graduate Studies
**THE DIAGNOSIS AND MANAGEMENT OF TEMPOROMANDIBULAR
 DISORDERS (TMD) 2018 - DEN 1017S**

Wednesdays 11:00 to 12:45 - 481 University Avenue, 4th floor, room 7

Course Director: Dr. Iacopo Cioffi, - iacopo.cioffi@dentistry.utoronto.ca - phone 416-864-8107

DATE	TOPIC	LECTURER
Jan. 3	Classification of Temporomandibular disorders (TMD)	Dr. I. Cioffi
Jan. 10	Etiology of TMD	Dr. I. Cioffi
Jan. 17	Neural mechanisms of orofacial pain: acute vs chronic TMD	Dr. I. Cioffi
Jan. 24	Psychiatry, relationship style, pain and dentistry	Dr. J. Hunter
Jan. 31	Clinical exam	Dr. I. Cioffi
Feb. 7	TMJ imaging	Dr. E. Lam
Feb. 14	Conservative management of TMD	Dr. I. Cioffi
Feb. 21	<i>Reading week</i>	
Feb. 28	Bruxism	Dr. D. Manfredini
March 7	Disc displacement and traumatic disorders	Dr. M. Goldberg
March 14	Differential Diagnosis	Dr. B.V. Freeman
March 21	Brain Imaging and Orofacial Pains	Dr. K. Davis
March 28	Surgical management of TMD	Dr. M. Caminiti
Apr. 4	Orthodontics, dental occlusion, and TMD	Dr. I. Cioffi
Apr. 11	Residents' presentations and critiques	Dr. I. Cioffi
Apr. 18	Residents' presentations and critiques	Dr. I. Cioffi
Apr. 25	Residents' presentations and critiques	Dr. I. Cioffi