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## Original article

# Impact of clear aligner therapy on tooth pain and jaw muscle tenderness

## Johnny Tran\*, DDS, MClD, FRCD(C)

Division of Graduate Orthodontics, Schulich School of Medicine and Dentistry, The University of Western Ontario, London, ON, Canada.

## Tiantong Lou\*, DDS, MSc, FRCD(C)

Faculty of Dentistry, Orthodontics, University of Toronto, Toronto, ON, Canada.

#### Bianca Nebiolo, DDS

Department of Orthodontics, Dental School, University of Turin, Turin, Italy.

**Tommaso Castroflorio**, DDS, PhD, Dip. Ortho, Assistant Professor Department of Orthodontics, Dental School, University of Turin, Turin, Italy.

## Ali Tassi, DDS, MClD, FRCD(C), Assistant Professor

Division of Graduate Orthodontics, Schulich School of Medicine and Dentistry, The University of Western Ontario, London, ON, Canada.

**Iacopo Cioffi**, DDS, PhD, Dip. Ortho, FRCD(C), Assistant Professor Faculty of Dentistry, Orthodontics, University of Toronto, Toronto, ON, Canada. University of Toronto, Centre for The Study of Pain, Toronto, ON, Canada. Mount Sinai Hospital, Department of Dentistry, Toronto, ON, Canada.

## Corresponding author:

Dr. Iacopo Cioffi University of Toronto, Faculty of Dentistry, University of Toronto 123 Edward Street, rm 501c, M5G 1E2 Toronto, Ontario, Canada +1 416-864-8107 iacopo.cioffi@dentistry.utoronto.ca

<sup>\*</sup> equal contribution

#### **ABSTRACT**

**Introduction:** This multi-site prospective clinical study aimed to investigate tooth pain and jaw muscle tenderness in patients undergoing clear aligner therapy (CAT) and explored whether psychological traits affected these outcomes.

**Methods:** Twenty-seven healthy adults (mean age= $35.3\pm17.6$  years) about to undergo orthodontic treatment with Invisalign© were recruited from three university-based clinics. Patients completed a set of psychological questionnaires at the beginning of the study. Prior to and during CAT, patients were asked to report, utilizing 100mm visual analog scales, their tooth pain, jaw muscle tenderness, and stress three times per day over four weeks (week 1 = baseline; week  $2 = dummy \ aligner$ ; week  $3 = first \ active \ aligner$ ; week  $4 = second \ active \ aligner$ ). Pressure pain thresholds (PPTs) were measured at the masseter and temporalis at baseline and after four weeks. Mixed effect models were used to evaluate the outcome measures over time.

**Results:** CAT determined tooth pain, which was significantly greater with the passive  $(8.5\pm14.7\text{mm})$  than the first and second active aligners  $(6.4\pm9.8 \text{ mm} \text{ and } 4.3\pm7.3 \text{ mm}; \text{ p}<0.001)$ . Mild jaw muscle tenderness was produced by both the first active  $(4.10\pm7.7 \text{ mm})$ , second active  $(5.1\pm11.2 \text{ mm})$  and dummy aligners  $(6.2\pm13.6 \text{ mm}; \text{ all p}<0.05)$  with the first active aligner resulting in less muscle tenderness than the dummy aligner (p<0.001). PPTs did not change significantly after 4 weeks. Tooth pain and jaw muscle tenderness were affected by participants' stress, while jaw muscle tenderness was also affected by oral behaviors.

Conclusions: CAT triggers mild tooth pain and jaw muscle tenderness of limited clinical significance.

#### INTRODUCTION

Fear of pain is a significant reason why patients decline orthodontic treatment.<sup>1-3</sup> In one survey, patients rated pain as the greatest dislike in regard to their experience with orthodontic treatment, and ranked fourth among major fears and apprehensions.<sup>4</sup> Orthodontic pain—nociceptive and inflammatory tooth pain associated with orthodontic tooth movement<sup>5</sup>—can negatively impact patients' compliance,<sup>6-8</sup> lead to an increased frequency of missed appointments,<sup>9</sup> as well as compromising the overall treatment results and patient satisfaction.<sup>5,7,8,10</sup> In some cases, the impact of pain in patients' daily lives could be a significant factor for the termination of orthodontic treatment.<sup>1,11,12</sup> Therefore, practitioners should focus on improving the pain experience during treatment, in order to potentially improve patient compliance, treatment time, and ensure an overall better orthodontic experience.<sup>13</sup>

Previous studies have demonstrated that patients' perception of pain and discomfort varies between fixed and removable appliances. <sup>14</sup> In general, fixed appliances produce higher levels of discomfort, pressure and pain compared to functional appliances and removable appliances. <sup>7,15-17</sup> Orthodontic pain associated with clear aligner therapy (CAT) has been investigated in only a limited number of studies. CAT appears to follow an analogous pattern of pain progression compared to fixed orthodontic appliances in terms of peaking at 24 hours and trending towards baseline levels after 7 days. <sup>14,18-20</sup> The results of the available studies are generally in agreement with each other, showing that fixed appliances tend to cause more pain and discomfort than CAT. Deformation of the aligners trays has been reported as the primary cause of this pain and discomfort. <sup>19</sup>

The two main factors that influenceinfluencing the adaptation of the masticatory muscles' -adaptation of mastication to orthodontic treatment are orthodontic pain and occlusal changes occurring during treatment. It has been reported that patients undergoing orthodontic treatment with fixed edgewise appliances adapt by avoiding tooth contact in an effort to reduce tooth pain related to orthodontic treatment. Also, occlusal interferences generated during treatment could trigger an avoidance behavior. In fact, it has been reported that the electromyographic activity of the muscles of mastication can decrease during fixed appliance treatment. However, there is some clinical evidence for a different adaptation mechanism for the muscles of mastication masticatory muscles of in patients who undergo CAT patients. Indeed, patients undergoing CAT have been reported to increase the frequency of wake-time tooth clenching episodes, and produce wear facets on their aligner trays. It is possible that repetitive clenching on aligners trays would be an acquired behavior acting as a conditioning stimulus to reduce the perception of the orthodontic nociceptive stimuli in a conditioned pain modulation paradigm. In fact, it has been proposed that the amount of pain experienced by patients undergoing orthodontic treatment with fixed appliances could be reduced by having them clench on plastic wafers after appliance activation. The repetitive behavior could induce a

temporary displacement of the teeth and promote blood flow through the compressed areas of the periodontal ligament, thus preventing accumulation of pro-algesic mediators<sup>5</sup> in the periodontal ligament space, and promoting pain relief.<sup>28,29</sup> One potential drawback is that repetitive and sustained wake-time tooth clenching has been reported to trigger masticatory muscle tenderness and temporomandibular disorders (TMD).<sup>30,31</sup> Therefore, it is possible that patients undergoing CAT may have transient TMD as a result of repetitive clenching on their trays in order to relieve orthodontic pain. Yet, the effects of CAT on the muscles of mastication have been minimally investigated, and whether CAT could contribute to the onset of TMD symptoms is not currently known.

The magnitude of orthodontic pain varies considerably across individuals. Pain perception is influenced by factors such as somatosensory amplification—an estimate of an individuals' somatic awareness—stress, anxiety, depression, and pain catastrophizing. Patients with prolonged pain during orthodontic treatment exhibit higher levels of anxiety than do individuals with pain of short duration. In addition, experimentally-induced orthodontic pain is greater in individuals with higher levels of trait anxiety and somatosensory amplification. Of note, anxiety and somatosensory amplification have also been associated with increased frequencies of oral waking-state parafunctional behaviors, including tooth clenching.

The primary aim of this study was to determine the short-term effects of CAT on orthodontic tooth pain and jaw muscle tenderness. Further, we explored whether levels of stress, trait anxiety, somatosensory amplification, depression, and pain catastrophizing influence perceived orthodontic pain and jaw muscle tenderness during CAT. We hypothesize that 1) CAT produces mild to moderate tooth pain and transient jaw muscle tenderness, and 2) the individual pain response to CAT correlates with indices of stress and anxiety, somatosensory amplification, depression, and catastrophizing.

#### MATERIALS AND METHODS

## **Participants**

Subjects, 17 years or older, treatment planned to undergo CAT—with Invisalign©, were recruited from the graduate orthodontic clinics at the University of Western Ontario (London, ON, Canada), University of Toronto (Toronto, ON, Canada), and University of Turin (Italy). Ethics approval was obtained from the corresponding Research Ethics Boards at each Institution and informed consent was acquired from each subject prior to entering the study. Each potential participant completed an initial screening questionnaire using the TMD-Pain screener.<sup>43</sup> As well, each patient underwent a preliminary TMD examination by a single-examiner at each center according to the DC/TMD protocol.<sup>44</sup> Exclusion criteria consisted of current

symptoms of TMD<sup>44</sup> or orofacial pain, current use of muscle relaxants or other medications affecting masticatory muscle activity, presence of any systemic disorders affecting motor behaviors and pain perception, and daily use of any analgesics.

A total of 27 subjects were recruited (mean age = 35.3±17.6 years) from the three research units (Fig. 1). All patients were treated with Invisalign-© clear aligners (Align Technology, San Jose, CA, USA) elear aligners, (Align Technology, San Jose, CA, USA), made of the latest generation of multi-layer thermoplastic polyurethane-based material, SmartTrack. Using the ClinCheck Pro software (Align Technology, San Jose, CA, USA), the first stage of aligners for all patients consisted of upper and lower aligners programmed with no active tooth movements (passive aligners). Active tooth movements were programmed for the subsequent stages at the standard rate recommended by the ClinCheck Pro algorithms. All participants had class I or moderate class II malocclusion with mild to moderate crowding or spacing in the upper and lower dental arches.

## **Questionnaires**

At the beginning of the study, subjects were asked to complete sets of psychological assessment questionnaires including the State Trait Anxiety Inventory<sup>45</sup> (STAI, trait anxiety: score range 20-80), the Oral Behavior Checklist<sup>40</sup> (OBC, score range: 0-84), the Somatosensory Amplification Scale<sup>46</sup> (SSAS, range: 0-40), the Pain Catastrophizing Scale<sup>47</sup> (PCS, range 0-52), and the Beck Depression Inventory<sup>48</sup> (BDI, range: 0-63). The use of these questionnaires allowed for determining the effect of these psychological traits, as well as pre-existing parafunctional oral behaviors, on differences in individual pain perception.

## Study design

The study design is depicted in Figure 2. All subjects commencing treatment with CAT were monitored over 4 weeks for tooth pain, masticatory muscle tenderness, and daily stress using the provided custom-made diaries. Specifically, data was collected prior to the start of CAT, with no aligners (week 1 = baseline stage), for one week wearing a passive aligner (week 2 = dummy stage), for one week wearing their first active aligner (week 3 = active1 stage), and finally for one week wearing their second active aligner (week 4 = active2 stage). There were no dropouts during the experimental period and all subjects fully completed the longitudinal monitoring of pain and jaw muscle tenderness across the four conditions.

## Pressure pain thresholds (PPTs)

PPTs—the minimum pressure that is perceived as painful—were measured at baseline and at the end of week 4 with an electronic algometer (Wagner Inc., Greenwich, CT, USA) equipped with a rubber tip of 1

cm<sup>2</sup> surface area. The PPT data served as an objective measurement of participants' jaw muscle tenderness and to determine if CAT resulted in trigeminal and extra-trigeminal somatosensory changes.

PPTs were taken at three locations on both right and left sides, the superficial masseter, anterior temporalis, and thenar eminence of the right hand. For the superficial masseter, the site was located midway between the origin and insertion, 1 cm posterior to its anterior boundary. For the anterior temporalis muscle, the site was located on the line from the top edge of the eyebrow to the highest point of the pinna of the ear, 2 cm posterior to the anterior margin of the muscle as determined by palpating the muscle during voluntary contraction. For the thenar muscle, measurements were made on the skin of the palmar side of the hand, on the thenar prominence. PPTs at the thenar muscles were measured with hands supinated flat on a tabletop. The latter measurement was collected to assess whether participants had significant changes at extratrigeminal locations, which could have been determined by other conditions, unrelated to CAT.

For all sites, the algometer was positioned perpendicular to the skin surface at the selected sites and pressure applied at an increasing rate of 20 kPa/sec.<sup>49</sup> The PPT was determined as the point at which the pressure stimulus changed from a sensation of pressure into a sensation of pain. The patient indicated this by raising one hand to signal the examiner to release the pressure, which froze the current pressure value on the digital display, and this peak pressure value was subsequently recorded. Measurements were repeated for a total of 4 trials at each muscle, with 1-min intervals between trials. The order of muscle site measurements was randomized across patients. A single examiner at each center was trained and calibrated -to perform the PPT measurements.

#### Calibration of operators

The operators were trained in pressure algometry by an expert researcher (IC) with more than 15 years of experience. Using a visual feedback (Medoc, Algomed, Israel), they were trained to apply pressure at an increasing rate of 20 KPa/sec. The operators repeated the training for a few days. The intra-operator reliability in applying pressure at an increasing rate of 20 KPa/sec with the algometer was measured during a session prior to the start of data collection. During this session, the operators were asked to use their algometers (the ones assigned by each research unit, and previously calibrated by the vendor) and apply pressure at about 20 KPa/sec, against a vertical flat surface, without using the visual feedback, and stop after pre-determined time intervals. Inter-rater reliability was computed thereafter (see statistical analysis paragraph).

## Longitudinal behavioral assessment

A diary was provided to each patient to evaluate and record their tooth pain and jaw muscle tenderness at four time points (8:00, 12:00, 16:00, 20:00) during each day of the four conditions (baseline, dummy stage, active1, and active2). The diary included the following questions, with corresponding 100 mm Visual Analogue Scales (VAS) and anchors:

- TOOTH PAIN (VAS = 0-100 mm). "How severe is your tooth pain?"
   Anchors: no pain, pain as bad as could be.
- JAW MUSCLE TENDERNESS (VAS = 0-100 mm). "Do you feel your jaw muscles are tense? "Anchors: no tenderness, discomfort as bad as could be.

Participants' stress was rated at the end of each day using a separate single VAS:

PERCEIVED STRESS (VAS = 0-100 mm). "How bad is your stress today?"
 Anchors: "no stress", "stress as bad as could be".

Patients were instructed to take note of any intake of analgesics. Participants returned their diary after the end of the fourth experimental week. At this point, they each underwent another TMD examination.

#### Statistical analysis

Normality of data was tested using the Kolmogorov-Smirnov test. Correlations between tooth pain, masticatory muscle tenderness, and VAS stress, STAI, SSAS, PCS and BDI scores were tested using the Spearman's test. Since daily VAS stress correlated with pain and muscle tenderness, it was incorporated in the mixed models (see below) as a covariate.

The effect of the condition (baseline, dummy, active1, and active2) on VAS tooth pain and VAS muscle tenderness were assessed over time by using generalized linear mixed effect models. Data from the four timepoints (8:00, 12:00, 16:00, 20:00) were aggregated for each day. Two models were used, one for tooth pain and one for jaw muscle tenderness. In each model, day, sex, and condition (baseline, dummy, active1, and active2) were used as fixed factors, and VAS stress as covariate. Interactions between the model's variables were tested and retained in the model when statistically significant.

PPT data were aggregated by computing the mean of the trials obtained at each location, after having discarded the first trial, as done previously.<sup>39,49</sup> Differences between right and left sides of PPTs at the masseter, temporalis and thenar eminence were tested using T-test. Since there were no differences between

sides (all p>0.05), the data was pooled for each muscle location. Inter-rater reliability in PPT assessments was measured by computing intra-class correlation to estimate the inter-rater reliability between the researches using the data collected during the calibration sessions. ANCOVA was used to test whether PPTs at different muscle locations changed after 4 weeks. Sex was included in the model as a fixed factor

An a priori power analysis was conducted using G\*Power (Heinrich-Heine-Universität Düsseldorf, Germany).<sup>50</sup> The analysis showed that a total sample of 24 participants was required to achieve a power of 0.80 using a medium to large effect size (d=0.4) and an alpha of 0.05. Statistical significance was set at p<0.05. SPSS software ver. 24.0 (IBM, Armonk, NY, USA) was used for statistical analysis.

#### **Results**

The average tooth pain (VAS data) experienced by participants during the 4 weeks and tooth pain trajectories during each day are reported in Figures 3 and 4. Results from the mixed effect model are reported in table 1. Tooth pain was significantly affected by sex, and by the interactions day\*stress (p<0.001) and day\*condition (p<0.001). During the dummy condition, participants had greater tooth pain compared to the baseline (p<0.001). Overall, the dummy aligner produced significantly more tooth pain than the active aligners (active1 and active2, all p<0.001). There was also a significant decrease in tooth pain transitioning from the dummy aligner to active1 (p<0.001) and from active1 to active2 (p<0.001). Significant difference in mean tooth pain were detected between males (mean  $\pm$ SEM = 3.2 $\pm$ 0.8 mm) and females (11.2 $\pm$ 1.6 mm; p<0.001). For the majority of days, the dummy and active aligners produced more tooth pain than at baseline (all p<0.05), and during the first four days, the dummy aligner produced more pain than the active aligners (all p<0.05). The highest tooth pain (VAS=16 mm) occurred on day 2 of the dummy aligner stage and decreased significantly from day 2 to day 7 (all p<0.05). No significant differences were evident across days within the active1 condition (all p>0.05). Tooth pain was significantly less at day 7 than day 1 during active2 (p<0.05).

The average jaw muscle tenderness (VAS data) experienced by the participants during the 4 weeks and jaw muscle tenderness trajectories during each day are reported in Figures 5 and 6. Results from the mixed effect model are reported in table 2. Jaw muscle tenderness was significantly affected by the interactions day\*stress (p<0.001) and day\*condition (p<0.001). Sex did not affect jaw muscle tenderness (p=0.361). Compared to baseline, both the dummy aligner (p<0.001) and active2 (p<0.001) determined an increase in jaw muscle tenderness. Active1 resulted in significantly less muscle tenderness than the dummy aligner (p<0.001). Active2 resulted in a significant increase in mean muscle tenderness compared to Active1 (p<0.001). At baseline, and during active1 and active2, there were no significant differences across the days

(p>0.05). During the dummy condition, jaw muscle tenderness decreased significantly from day 1 to day 6 (all p<0.05). During active2, muscle tenderness decreased significantly from day 1 to day 6 (all p<0.05).

The inter-rater reliability for PPT measurements between the operators was high (ICC 0.966 [95%CI: 0.938-0.981]; p<0.001). PPTs at all muscle locations did not change significantly from baseline to week 4 (p=0.639) after having corrected for sex (data not shown). Females had lower PPTs at all locations than males (all p<0.001). None of the patients developed TMD according to the DC/TMD after 4 weeks.

Jaw muscle tenderness was moderately correlated with self-reported wake-time oral parafunctions (OBC; r=0.409; p=0.042; Table 3). A significant correlation was found between trait anxiety and tooth pain (r=0.473; p=0.008) and jaw muscle tenderness (r=0.343; p=0.047). Tooth pain and jaw muscle tenderness did not correlate with PCS, BDI, and SSAS (all p>0.05; Table 3).

#### **DISCUSSION**

This study sought to determine the short-term effects of CAT on tooth pain and jaw muscle tenderness, and explored whether levels of stress, trait anxiety, somatosensory amplification, depression and pain catastrophizing influence perceived pain and jaw muscle tenderness during CAT. It was found that CAT is associated with mild tooth pain and jaw muscle tenderness of limited clinical significance over 4 weeks. A mild increase in tooth pain was evident from baseline to the dummy (i.e. passive aligner) condition. The passive aligner stage produced the greatest tooth pain. Thereafter, when active tooth movements were programmed into the aligners (active1 and active2 stages), tooth pain decreased, being lower in the second than the first active aligner. Therefore, it was likely that the fitting of the aligner rather than the active tooth movement that was perceived painful by the subjects. SThey subjects also reported mild jaw muscle tenderness during the first few weeks of treatment, which was greater with the passive aligner and the second active aligner.

The temporal profile of tooth pain measured in this study follows the same pattern of conventional fixed appliances, being the greatest during the first 24-48 hours and the lowest after 5 days. However, in contrast to fixed buccal and lingual appliances, that have been found to produce up to 50 mm<sup>14,19,20</sup> and 60 mm of tooth pain on VAS,<sup>18</sup> the peaks of pain in the current study were around 20 mm. This maximum reported tooth pain is similar to that reported by White et al in 2017,<sup>20</sup> who utilized the newest generation multilayer thermoplastic material SmartTrack, as done in the present study. In an earlier study, using the Exceed-30 material, tooth pain was reported to be greater with aligners than fixed appliances. <sup>18</sup> Therefore, it seems that the change of the aligner material could have contributed to improve patient pain experience with Invisalign.

Jaw muscle tenderness resulting from CAT has been minimally investigated. Brien<sup>23</sup> demonstrated that CAT with Invisalign produces transient symptoms of TMD in the form of muscle tenderness within the first two weeks of treatment and subsides to baseline levels over time. This finding was not consistent with the current results. Indeed, in the present study, jaw muscle tenderness did not subside to baseline levels after 4 weeks. However, muscle tenderness was mild and likely of limited clinical significance as no patients developed TMD, and pressure pain thresholds did not significantly change after 4 weeks. Yet, it might be questioned what the effects of CAT in patients with TMD, or a previous history of, could be different. Indeed, as CAT results in a mild increase in muscle tenderness, it may exacerbate TMD symptoms, although further studies are needed to address this hypothesis. Similar to conventional orthodontic treatment, it is advisable to stop active treatment in patients reporting TMD symptoms during CAT, and manage symptoms prior to continue treatment.<sup>51</sup>

It has been reported that orthodontic pain reduces the electromyographic activity of the masseter. <sup>22,52</sup> Also, jaw muscle tenderness is infrequently reported by patients commencing orthodontic treatment with edgewise fixed appliances. Conversely, CAT determined mild jaw muscle tenderness in the current sample. Hence, patients' jaw muscle adaptation to CAT may differ from that to fixed orthodontic appliances. It is possible that patients with CAT may engage in parafunctional tooth clenching to alleviate the perception of tooth pain. This repetitive behavior could induce a temporary displacement of the teeth and promote blood flow through the compressed areas of the periodontal ligament, thus preventing accumulation of pro-algesic mediators in the periodontal ligament space and promoting pain relief. Of interest, jaw muscle tenderness had a moderate correlation with OBC scores (waking-state oral parafunctional behaviors), supporting the hypothesis that muscle tenderness may be related to increased oral behaviors. 40,53 However, further investigations which could monitor the activity of the jaw muscles during CAT are needed to address this hypothesis. Similarly, it is also possible that the increase in jaw muscle tenderness is the result of an increase in muscle hyperactivity related to the introduction of occlusal interferences, <sup>30,54,55</sup> rather than to tooth pain. However, experimental studies have demonstrated that the application of occlusal interferences leads to an avoidance behavior and reduction of masseter muscle activity in the short term.<sup>21</sup> Also, occlusal interferences produced by 2-week treatment with aligners are clinically negligible. Therefore, the latter proposed mechanism is not supported by the available evidence and the current research method.

CAT did not affect PPTs of the superficial masseter and anterior temporalis. This is contrary to what was found in previous studies<sup>56,57</sup> where orthodontic interventions resulted in significant somatosensory changes in trigeminal locations. These PPT findings confirm that jaw muscle tenderness produced by CAT is only mild, of limited clinical significance, and did not produce peripheral sensitization in the short-term. A significant effect of sex on PPTs was found, with females having lower mean PPTs than males. Sex

differences in clinical and experimental pain conditions have been previously described<sup>58</sup> with females generally having higher pain sensitivity than males.<sup>59</sup>

It is well-known that orthodontic pain can be affected by multiple factors including psychological traits such as somatosensory amplification, trait anxiety and stress. 36,37,39 Stress and anxiety had a considerable effect on tooth pain perception and jaw muscle tenderness, as it was a significant predictors in the statistical models. Therefore, the apprehension and stress involved with starting orthodontic treatment with a new appliance, 4,39 could contribute to explaining the greater pain experienced with aligners. Yet, we did not find correlations between other psychological variables and tooth pain and jaw muscle tenderness. It has been previously established that experimentally-induced orthodontic pain is greater in individuals with higher somatosensory amplification. Therefore, it is possible that this variable may have less impact on orthodontic pain and jaw muscle tenderness when the latter are of very limited magnitude.

This study has some limitations. First, it included adults of different ages. Although the effect of age on orthodontic pain is controversial, <sup>60</sup> the biologic response to orthodontic forces is age dependent. <sup>61</sup> Therefore, for this study, we preliminarily tested whether age correlated with orthodontic pain and jaw muscle tenderness. Since age was not significantly correlated with pain and jaw muscle tenderness in the current sample, we did not include it as a potential confounder in our analysis. Second, occlusal characteristics, such as crowding, were not considered in the models as potential confounders. A previous study showed no relationship between crowding and orthodontic pain. <sup>62</sup> Also, differences in crowding across participants likely did not affect the results, because the Invisalign technique produces controlled and very limited tooth movements in two weeks. Third, in this study we used paper-based diaries, which could have increased the chances of recall bias. The use of mobile apps for collecting data in real time could have minimized recall bias, and, in turn, maximized the ecological validity of our data. <sup>63</sup> Also, randomization in sequence of dummy and active aligners was not performed. Yet, this allowed us to determine that tooth pain was mostly determined by the fitting of the aligner rather than the active tooth movement. Finally, we evaluated the effects of CAT on jaw muscles only in the short-term (i.e. 4 weeks) and we cannot draw conclusions on long term effects.

#### **CONCLUSIONS**

Clear aligner therapy produces mild tooth pain and jaw muscle tenderness of limited clinical significance. Stress plays a significant role in orthodontic pain perception and jaw muscle tenderness experienced during clear aligner therapy and individuals with more frequent oral behaviors experience greater jaw muscle tenderness during treatment. It is advisable to carefully screen patients for temporomandibular disorders

and oral behaviors prior to commence any orthodontic treatment, even if planned with treatment with clear aligners CAT.

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Figure 1. Study design.

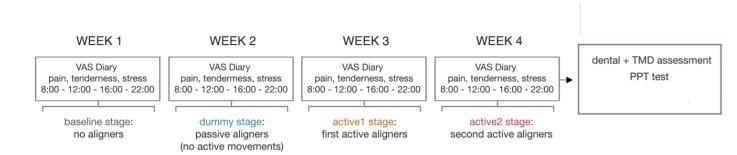
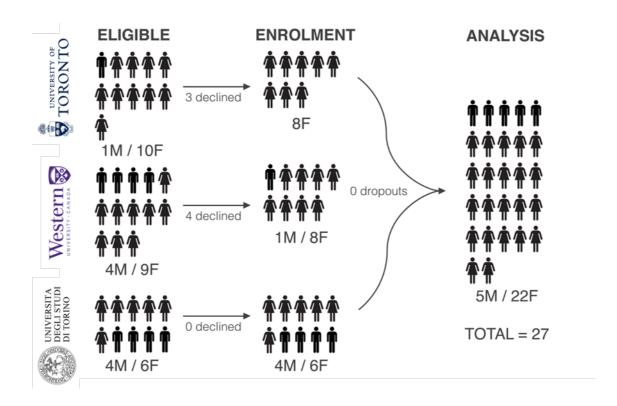


Figure 2. Recruitment of participants.



**Figure 3.** Estimated marginal means of tooth pain ( $\pm$  SEM) for each condition. \*All pairwise comparisons were statistically significant at P<0.001.

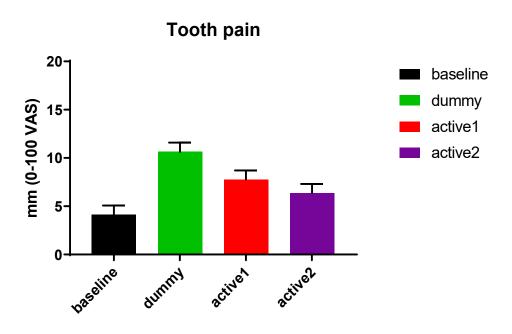
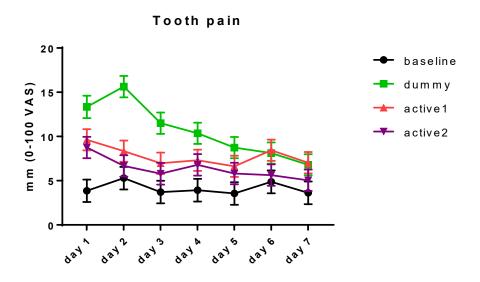
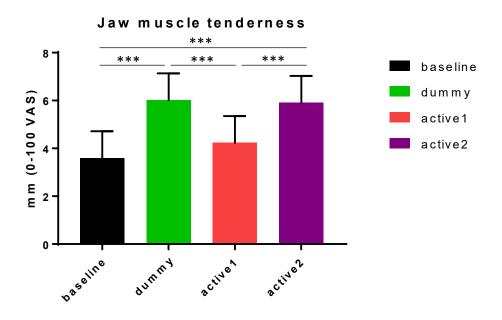


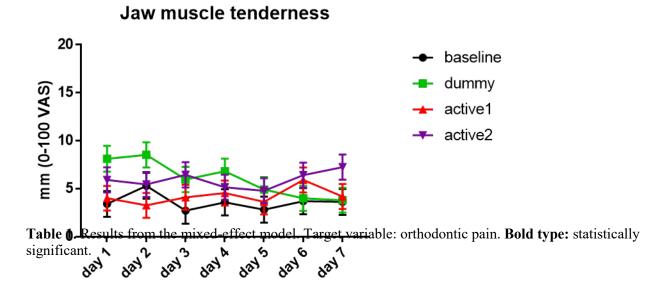
Figure 4. Tooth pain trajectories (means±SEM) over 7 days for each condition.



**Figure 5.** Estimated marginal means of jaw muscle tenderness ( $\pm$  SEM) for each condition. \*\*\* Pairwise comparisons statistically significant at p<0.001.



**Figure 6.** Jaw muscle tenderness trajectories (means±SEM) over 7 days for each condition. All pairwise (between conditions) comparisons within each day were not statistically significant (all p>0.05



Independent variable	F	p-value
Sex	19.176	<0.001
Day	4.872	< 0.001
Condition	68.293	<0.001
Stress	210.945	< 0.001
Day*Stress	10.576	<0.001
Day*condition	2.982	< 0.001

**Table 2.** Results from the mixed-effect model. Target variable: jaw muscle tenderness. **Bold type:** statistically significant.

Independent variable	F	p-value
Sex	0.833	0.361
Day	2.403	0.026
Condition	16.772	< 0.001
Stress	380.471	<0.001
Day*stress	23.877	< 0.001
Day*condition	2.914	< 0.001

**Table 3.** Correlations between longitudinal VAS data and depression (BDI), pain catastrophizing (PCS), oral behavior checklist (OBC) scores, somatosensory Amplification (SSA), and trait anxiety. \* Statistically significant.

		Correlation coefficients	
	Median [IQR]	Tooth pain (VAS)	Jaw muscle tenderness (VAS)
BDI	2	-0.370	-0.305
	[7]	(p=0.075)	(p=0.148)
PCS	7	-0.042	-0.237
	[16]	(p=0.840)	(p=0.254)
OBC	25	0.150	0.409
	[16]	(p=0.476)	(p=0.042)*
SSAS	15	-0.367	-0.155
	[9]	(p=0.071)	(p=0.460)
Trait	37	0.473	0.343
anxiety	[22]	(p=0.008) *	(p=0.047)*