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Original Article

# Exploring the correlation between dental procedures and trigemino-cardiac reflex

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**Abstract** *Background* /purpose: The trigemino-cardiac reflex (TCR) is a brainstem reflex characterized by sudden reductions in heart rate (HR) and mean arterial blood pressure (MABP) following trigeminal nerve stimulation. Although well-documented in other surgical fields, its role during dental procedures remains unclear. This study examined the association between routine dental interventions and TCR using an experimental animal model.

*Materials and methods:* This study presented a comprehensive analysis of physiological monitoring data obtained during a series of animal experimental surgeries conducted by our research team between 2016 and 2023. Changes in HR and MABP during routine dental procedures were evaluated using two male Beagle dogs and six Lee-Sung miniature swine.

*Results:* No significant changes in HR or MABP were observed during the scaling procedures. In contrast, root canal treatments showed the highest TCR incidence, with simultaneous HR and MABP decreases exceeding 15 % in 9.6 % of cases and 20 % in 5.6 % of cases. Tooth extraction triggered TCR in 2.7 % of 36 cases, while implant placement did not result in simultaneous HR and MABP reductions, but notable HR fluctuations were observed.

*Conclusion:* This study indicates that discomfort experienced during dental scaling is unlikely to induce TCR, whereas root canal treatment, involving both physical and chemical stimulation, appears more likely to trigger its occurrence. Tooth extraction may similarly provoke TCR through mechanical stimulation. Although implant placement does not result in a simultaneous reduction in HR and MABP exceeding 15 % in this study, significant HR fluctuations greater than 20 % were observed, potentially representing early signs of TCR.

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## Introduction

The trigeminal nerve is the largest cranial nerve of the face, composed of the ophthalmic division (V1), the maxillary division (V2), and the mandibular division (V3). V1 contains 26,000 myelinated fibers, V2 has 50,000 fibers, and V3 has up to 78,000 fibers.[1] These branches primarily control the sensation in the face, oral cavity, and nasal cavity, as well as the motor function of the masticatory muscles. Smaller branches further subdivide from these main branches, transmitting sensory information from the face to the brain. The trigemino-cardiac reflex (TCR) describes the arrhythmias that occur after the trigeminal nerve is stimulated, resulting in a rapid brainstem reflex. This includes cardiac arrest, arterial hypotension, apnea, and increased gastric motility. These reflex phenomena can cause a drop in blood pressure, leading to hypotension and bradycardia, which in severe cases can result in syncope or even death.[2] In 1870, Kratschmer et al. first described the TCR after manipulating the nasal mucosa of cats and rabbits, observing sudden cardiac arrhythmias, including cardiac arrest, arterial hypotension, apnea, and excessive gastric activity.[3] The more rigorous definition of the TCR is a sudden decrease in heart rate (HR) and mean arterial blood pressure (MABP) by more than 20 % from the baseline.[4] However, more inclusive criteria define TCR as any cardiac reflex triggered by stimulation of any part of the trigeminal nerve or when HR changes by more than 10 %.[2,5,6] Adopting such a broader definition may help encompass a wider range of hemodynamic responses, thereby providing a more comprehensive understanding of TCR, its clinical significance, and its safety implications.

Most of the literature on TCR comes from neurosurgery, anesthesiology,[7] and ophthalmology.[8] However, dental treatments closely related to the V2 and V3 branches of the trigeminal nerve have only been sparsely studied in relation to TCR.[9] Therefore, this study used Beagle dogs and Lee-Sung miniature swine models to investigate the relationship between common dental procedures such as scaling, root canal treatment, tooth extraction, or implant placement and TCR.

## Materials and methods

This study conducted a comprehensive analysis of physiological monitoring data collected during a series of animal experimental surgeries performed by our research team between 2016 and 2023. The dataset comprised two 12-month-old male Beagle dogs, and six Lee-Sung miniature swine (three males and three females) aged between 12 and 18 months. All procedures were carried out under general anesthesia.

A total of 72 tooth positions underwent dental scaling, 52 received root canal treatment, and 47 were involved in both tooth extraction and subsequent dental implantation. To ensure animal welfare and procedural consistency, licensed dentists and veterinarians collaboratively performed all surgical interventions.

Each experimental session adhered to a standardized dental protocol, encompassing sequential dental scaling procedures, root canal therapy, material sealing, tooth extraction, and dental implantation. Throughout the surgical process, continuous physiological parameters were recorded using an A-line monitoring system, enabling real-time assessment of vital signs and overall physiological stability.

### Animal model

Beagle dogs (Biovet farms, Pingtung, Taiwan) were initially employed as animal models because they had already been established as a suitable model for experimental endodontics and had been widely utilized for this purpose. Their teeth are sufficiently large, making root canal treatment easier, and their premolars are preferred due to their similarity to human molars.[10–12] However, due to ethical considerations and the rising costs, our team transitioned to using miniature swine as the animal model. We adopted Lee-Sung miniature swine (National Taiwan University experimental farm, Taipei, Taiwan) for continued dental-related research. The selection of miniature swine was based on their anatomical and physiological similarities to humans, making them widely used as biomedical research animal models in various fields,[13–15] including dental and oral studies.[15–17] All experimental procedures complied with the conditions set by the Institutional Animal Care and Use Committee of National Taiwan University (Approval numbers: 20160244; 20190097; 20190476).

### Anesthesia drugs and dosage regimen in animal experiments

The drugs used in this experiment included Atropine (YAI YU, Hsinchu County, Taiwan), Zoletil® 50 (Virbac, Carros, France), Attane (Panion & BF Biotech, Taipei, Taiwan), Xylestesin-A® (3M ESPE, Seefeld, Germany), Melicam (Synmosa, Taipei, Taiwan), Cephaloridine (U-Liang, Hsinchu County, Taiwan), Flunixin (China Chemical & Pharmaceutical, Taipei, Taiwan), Carprofen (China Chemical & Pharmaceutical), Oxytetracycline (China Chemical & Pharmaceutical), Amoxicillin (China Chemical & Pharmaceutical), and KCl (Taiwan Biotech, Taoyuan, Taiwan). Table 1 summarizes the types of drugs, dosages, and administration routes used during the animal experiments. To ensure animal welfare, all drugs were administered by licensed dentists and veterinarians.

**Table 1** Anesthesia drugs and dosage regimen.

| Category | Beagle dogs | Lee-Sung miniature swine |
|---|---|---|
| Preoperative medication | Atropine: 0.02—0.05 mg/kg, IM | Atropine: 0.04 mg/kg, IM<br>Xylazine: 2—4 mg/kg, IM |
| Anesthesia induction | Zoletil® 50: 6—10 mg/kg, IM | Zoletil® 50: 6—10 mg/kg, IM |
| Inhalation anesthesia | Attane: 22—44 mL/kg/min, administered via a vaporizer | Attane: 22—44 mL/kg/min, administered via a vaporizer |
| Local anesthesia | Xylestesin-A 1.8 mL (with epinephrine 1:100,000), Injected at the surgical site | Not specified |
| Postoperative analgesia/anti-inflammatory | Meloxicam: Initial dose 0.2 mg/kg, then 0.1 mg/kg every 24 h for 3 days, PO | Flunixin: 2.2 mg/kg, IM (Days 1—3)<br>Carprofen: 2.0—4.0 mg/kg, PO (from day 3) |
| Antibiotics (Infection control) | Cephaloridine: 25 mg/kg, IM | Oxytetracycline: 0.15 mg/kg, IM (Days 1—3)<br>Amoxicillin: 10 mg/kg,PO (from day 3) |
| Muthanized | KCl: 2 mmol/kg, IV | KCl: 2 mmol/kg, IV |
| Drug administration | All medications administered by licensed veterinarians | All medications administered by licensed veterinarians |

Abbreviations: IM, Intramuscular injection; PO, By mouth; IV, Intravenous injection.

## Surgical procedures

(1) To ensure the safety of the experimental animals during surgery, anesthesia specialists used Mindray's portable ultrasound system M6Vet (Mindray, Shenzhen, China) for arterial catheter placement, followed by continuous physiological monitoring with the B20i monitor (General Electric, Boston, MA, USA).
(2) Prior to surgery, oral cleaning was performed on the experimental animals to ensure oral hygiene.
(3) Based on the experimental requirements, the selected surgical target teeth included the second, third, and fourth premolars (P2, P3, P4) and the first molar (M1) in the right maxilla and right mandible. Root canal treatment was performed, with continuous monitoring and recording of physiological indicators throughout the procedure.
(4) After inducing general anesthesia, tooth extraction surgery was carried out, with real-time monitoring of systolic and diastolic blood pressure and heart rate throughout the procedure.
(5) Six weeks after tooth extraction, artificial dental implants were placed, with continuous physiological monitoring to ensure the smooth progress of the surgery.
(6) At the end of the experiment, the animals were euthanized under deep anesthesia, followed by humane euthanasia through intravenous injection of potassium chloride (KCl, 10—20 mL).

## Definition of the trigeminal cardiac reflex recommended

This study examined two different definitions of the trigemino-cardiac reflex. The first was a stricter definition proposed by Schaller and his team, which characterized the reflex as a decrease of more than 20 % in heart rate (HR) and mean arterial blood pressure (MABP) from the baseline values.[4] The second definition considered the reflex as a decrease of more than 15 % in HR and MABP from the baseline values. The mean arterial blood pressure was calculated as 1/3 systolic blood pressure +2/3 diastolic blood pressure.[18]

## Results

A total of 72 dental scaling procedures were performed in this study. Analysis of physiological monitoring data revealed no significant alterations in HR or MABP throughout these procedures. Specifically, there were no instances recorded in which simultaneous reductions of HR and MABP exceeded either 15 % or 20 % from the baseline values.

A total of 52 root canal treatments were performed in this study. During the procedures, a simultaneous decrease of more than 15 % in HR and MABP occurred in 5 cases (incidence rate: 9.6 %), specifically in two left mandibular P3s, one right mandibular P4, one right maxillary P4, and one left maxillary P4. A more than 20 % simultaneous decrease occurred in 3 cases (incidence rate: 5.6 %), including two left mandibular P3s and one right maxillary P4.

Tooth extraction is one of the common dental treatments, during which actions such as tapping, twisting, or pulling the tooth are performed. In this study, a total of 36 tooth extractions were conducted. A simultaneous decrease of more than 15 % in HR and MABP occurred in 1 case (incidence rate: 2.7 %), specifically in the right mandibular P2. There were no instances in which HR and MABP decreased by more than 20 %.

Dental implantation is a type of dental surgery that involves drilling into the alveolar bone to place the implant. This process may physically stimulate the maxillary or mandibular nerves and potentially trigger the TCR. In this study, a total of 36 dental implant procedures were performed. No instances were observed during which both HR and MABP simultaneously decreased by more than 15 % or 20 %.

## Discussion

The TCR refers to a reflex response triggered by physical or chemical stimulation of the trigeminal ganglion, the trigeminal brainstem center, or the peripheral branches of

**Table 2** Hemodynamic changes during the root canal treatment procedure for the right maxillary fourth premolar.

| Time (s) | Surgical procedure | DBP (mmHg) | SBP (mmHg) | MABP (mmHg) | HR (bpm) |
|---|---|---|---|---|---|
| 0 | Opening chamber | 94 | 113 | 100.3 | 125 |
| 45 | Opening chamber | 93 | 112 | 99.3 | 126 |
| 60 | Opening finished | 92 | 112 | 98.6 | 125 |
| 75 | Rinsing | 83 | 110 | 92 | 65 (48 %↓) |
| 90 | Rinsing finished | 83 | 111 | 92.3 | 67 |
| 105 | Removing pulp tissue | 78 | 110 | 88.6 | 65 |
| 120 | Removing pulp tissue | 76 | 110 | 87.3 | 70 |
| 135 | Cleaning and shaping | 79 | 111 | 89.6 | 71 |
| 375 | Rinsing | 71 | 104 | 82 | 75 |
| 390 | Root canal filling | 74 | 99 | 82.3 | 140 |
| 405 | Root canal filling | 72 | 98 | 80.6 (20 %↓) | 76 (39 %↓) |
| 585 | Perform emergency treatment | 67 | 98 | 77.3 (23 %↓) | 69 (44 %↓) |
| 645 | Monitoring | 86 | 102 | 91.3 | 120 |
| 705 | Monitoring | 87 | 103 | 92.3 | 118 |

Abbreviations: DBP, Diastolic blood pressure; SBP, Systolic blood pressure; MABP, Mean arterial blood pressure; HR, Heart rate.

the trigeminal nerve.[2] Common dental procedures involving physical stimulation include tooth extraction, implant placement, and root canal therapy (including pulp chamber access, pulpectomy, and canal enlargement). In contrast, the use of sodium hypochlorite (NaOCl) or ethylenediaminetetraacetic acid (EDTA) for irrigation during root canal treatment constitutes chemical stimulation. Therefore, it can be inferred that routine dental procedures carry a potential risk of inducing TCR. This is further supported by previous literature reporting occasional episodes of syncope in patients during dental treatment.[19,20]

According to the physiological monitoring results, the discomfort or soreness experienced during dental scaling is unlikely to trigger the TCR, as no simultaneous decrease in HR and MABP exceeding 15 % or 20 % was observed during the dental scaling procedures. These findings further support that the unpleasant sensations during dental scaling have a minimal role in eliciting the TCR.

In contrast, root canal treatment involves both physical and chemical stimuli to the dental pulp, such as pulp extirpation (physical stimulus) and NaOCl irrigation (chemical stimulus). These stimuli may trigger the TCR,[21] which is why the likelihood of TCR occurrence was highest during root canal treatment in this study.

The hemodynamic changes observed during the root canal treatment procedure on the right maxillary fourth premolar are presented in Table 2. It can be seen that initially, during rinsing with NaOCl, there was a sudden drop in HR of up to 48 %, while MABP remained relatively stable. This aligns with the criterion for a TCR warning sign,[21] which is defined as a drop of more than 20 % in either HR or MABP. Although the HR showed signs of spontaneous recovery afterward, a significant drop occurred again at 405 s into the surgery, with MABP decreasing by 20 % and HR by 39 %. At this juncture, the experimental procedure was transiently suspended. However, spontaneous recovery of physiological parameters was not observed. Consequently, emergency veterinary intervention was initiated at 585 s. The trial was terminated upon stabilization of the animal's physiological indicators, representing a characteristic instance of TCR occurrence.

As shown in Table 3, pulp stimulation elicited a transient 15.4 % decrease in HR, while MABP remained stable. HR subsequently returned to the baseline levels. Upon

**Table 3** Hemodynamic changes during the root canal treatment procedure for the maxillary left fourth premolar.

| Time (s) | Surgical procedure | DBP (mmHg) | SBP (mmHg) | MABP (mmHg) | HR (bpm) |
|---|---|---|---|---|---|
| 0 | Open | 65 | 118 | 82.7 | 110 |
| 6 | Dentin | 63 | 116 | 80.7 | 108 |
| 35 | Pulp stimulation | 63 | 114 | 80.0 | 94 |
| 43 | Pulp stimulation | 63 | 114 | 80.0 | 93 (15.4 %↓) |
| 63 | Supplemental anesthesia | 61 | 113 | 78.3 | 94 |
| 214 | Removing pulp tissue | 60 | 113 | 77.7 | 109 |
| 275 | Rinsing | 60 | 112 | 77.3 | 132 |
| 324 | Rinsing | 59 | 111 | 76.3 | 89 |
| 735 | Material placement | 52 | 105 | 69.7 (15.9 %↓) | 82 (25.4 %↓) |
| 855 | Sealing | 53 | 106 | 70.7 | 83 |
| 883 | Completion | 59 | 110 | 76.0 | 110 |

Abbreviations: DBP, Diastolic blood pressure; SBP, Systolic blood pressure; MABP, Mean arterial blood pressure; HR, Heart rate.

**Table 4** Hemodynamic changes during the extraction of the mandibular right first premolar.

| Time (s) | Surgical Procedure | DBP (mmHg) | SBP (mmHg) | MABP (mmHg) | HR (bpm) |
|---|---|---|---|---|---|
| 0 | Extraction | 56 | 90 | 67.3 | 76 |
| 30 | Extraction | 55 | 88 | 66.0 | 75 |
| 60 | Extraction | 54 | 87 | 65.0 | 74 |
| 90 | Extraction | 55 | 87 | 65.7 | 73 |
| 120 | Extraction | 54 | 87 | 65.0 | 71 |
| 150 | Extraction | 53 | 86 | 64.0 | 69 |
| 180 | Extraction | 51 | 83 | 61.7 | 67 |
| 210 | Extraction | 50 | 82 | 60.7 | 66 |
| 240 | Extraction | 49 | 80 | 59.3 | 66 |
| 270 | Extraction | 49 | 80 | 59.3 | 65 |
| 300 | Extraction | 48 | 78 | 58.0 | 64 |
| 330 | Extraction complete | 47 | 76 | 56.7 (15.8 %↓) | 63 (17.1 %↓) |
| 333 | Observation | 47 | 76 | 56.7 | 63 |
| 535 | Stabilized | 49 | 80 | 59.3 | 79 |

Abbreviations: DBP, Diastolic blood pressure; SBP, Systolic blood pressure; MABP, Mean arterial blood pressure; HR, Heart rate.

placement of the experimental material (chemical stimulus), HR decreased by 25.4 % and MABP by 15.9 %, meeting the definition criteria of the TCR, defined as a simultaneous reduction of more than 15 % in both parameters. Notably, in contrast to instances involving a ≥20 % concurrent decline, the physiological parameters, in this case, exhibited spontaneous recovery to the baseline.

During tooth extraction surgery, the incidence of TCR was defined as 0 % when both HR and MABP decreased simultaneously by 20 % and 2.7 % when both decreased by 15 %, which was lower than the 4.5 % reported in earlier studies.[9] This discrepancy may be attributed to the fact that most extracted teeth in the present study were already non-vital. Nevertheless, even in teeth with extirpated pulps, physical stimulation during extraction may still induce the TCR.

As shown in Table 4, during the tooth extraction procedure, HR decreased by 17.1 % and MABP by 15.8 %, meeting the criteria for the TCR, defined as a simultaneous decrease of more than 15 % in both parameters. It was also observed that, unlike cases involving a simultaneous 20 % decrease, the physiological indicators in this instance recovered autonomously to the baseline levels after the procedure was stopped.

No simultaneous decrease in HR and MABP exceeding 15 % or 20 % was observed during the dental implant placement. Nevertheless, it is noteworthy that although no simultaneous decrease in HR and MABP meeting the diagnostic criteria for the TCR was observed during the dental implant procedure, significant HR fluctuations were still recorded. According to the previous studies, the TCR can be classified into two types based on the triggering site: central TCR and peripheral TCR.[22] Peripheral TCR can be further subdivided according to the affected branches of the trigeminal nerve into the oculocardiac reflex (V1) and the maxillary and mandibular reflexes (V2, V3). The conduction pathways are shown in Fig. 1. All subtypes may cause bradycardia or a slowing of the HR. A decrease in MABP almost always accompanies the central TCR, while this is not necessarily the case for the peripheral type.[23] Since the dental procedures are categorized under the peripheral TCR, its occurrence may not be associated with a significant drop in MABP. Furthermore, according to recent literature on the TCR, an HR change of more than 20 % may indicate a prodromal sign of the TCR[21] and should not be overlooked.

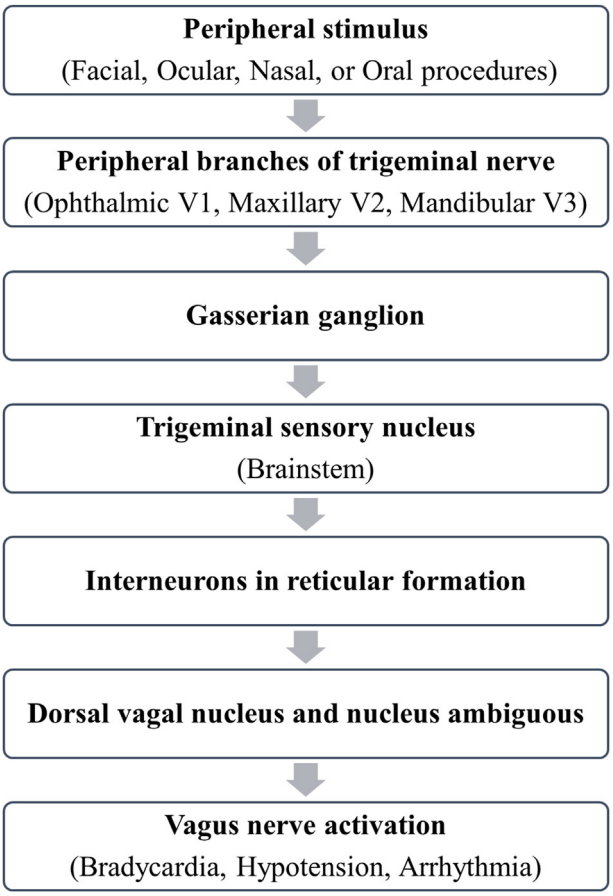


**Figure 1** Trigemino-cardiac reflex pathway.

This study demonstrates that discomfort or soreness during dental scaling is unlikely to induce the TCR, whereas

the physical and chemical stimuli involved in root canal treatment are more likely to trigger the TCR. Tooth extraction may also elicit the TCR due to mechanical stimulation. Although no simultaneous decrease in HR and MABP exceeding 15 % was observed during the implant placement, significant HR fluctuations exceeding 20 % were recorded, which may represent a prodromal sign of the TCR and should not be overlooked. These findings suggest that root canal treatment poses the highest risk for triggering the TCR among the dental procedures evaluated. Notably, three teeth exhibited simultaneous reductions in HR and MABP greater than 20 % during the root canal treatment. In two of these cases, physiological parameters did not return to the baseline after suspending the procedure, requiring emergency intervention to restore stability. Therefore, this study recommends that the clinical definition of the TCR should not be strictly limited to a simultaneous reduction in HR and MABP greater than 20 %, as such a threshold may expose patients to the excessive risk. Instead, enhanced physiological monitoring is advised when HR decreases by 15 %, and immediate suspension of the procedure is recommended if both HR and MABP simultaneously decrease by 15 %, resuming only once the patient has stabilized to ensure clinical safety.

## Declaration of competing interest

The authors have no conflicts of interest relevant to this article.

## Acknowledgments

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