Acute Post-operative Pain can be Predicted by the Conditioned Pain Modulation (CPM) and Pain Catastrophizing Scale (PCS)

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AIM OF INVESTIGATION

- Incidence and severity of chronic post-operative pain may be predicted by conditioned pain modulation (CPM) examined before surgeries.[1)] It is however not known if CPM is predictive for the intensity of acute post-operative pain.
- The aim of the study was to investigate the relationship between pre-operative CPM effect and acute post-operative pain after orthognathic surgery.

METHODS

Subjects

- Forty-three patients scheduled for orthognathic surgery (13 men and 30 women, 24.0 [21.0-33.0] years, (median [interquartile range]) participated and had the CPM and PCS (Fig. 1) assessed prior to the surgery.

Pressure pain threshold: Test stimulus (TS) (Fig. 2)

- Pressure pain threshold (PPT) was measured as test stimulus (TS) using the electronic pressure algometer applied to the dominant forearm before and at the end of the conditioning stimulus (CS).

Cold-heat pulse stimulation: Conditioning stimulus (CS) (Figs. 2,3)

- Tonic cold-heat pulse stimulation (pulse duration of 40 seconds, min to max temp; -10 to 47 ℃) was applied to the contralateral forearm by the thermal stimulator with pain intensity of 70 on a visual analogue scale (VAS 0-100) as CS.

CPM evaluation (Fig. 2)

- The application of CS was started 2 min before TS measurement until the end of the measurement (for 5 min).
- CPM effect was defined as {(PPT during CS)/ (PPT at baseline)-1} x 100 (%).

Post-operative pain management protocol (Fig. 4)

- All patients received a routine acute post-operative pain management protocol, consisting of acetaminophen 3000 mg per day (every 8 hours). Patients were offered additional analgesia upon request.

Analyses

- The pain area under the post-operative VAS curve (VASAUC) was measured after surgery.
- The relationships between CPM effect, PCS, and VASAUC were analyzed with multiple regression analysis.

Fig. 1 PCS assessments (Japanese version)

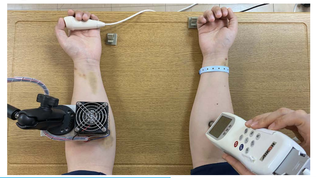
1 *	I worry all the time about whether the pain will end.
2	I feel I can't go on.
3	It's terrible and I think it's never going to get any better
4	It's awful and I feel that it overwhelms me.
5	I feel I can't stand it anymore.
6	I become afraid that the pain will get worse.
7	I keep thinking of other painful events.
8	I anxiously want the pain to go away
9	I can't seem to keep it out of my mind
10	I keep thinking about how much it hurts.
11	I keep thinking about how badly I want the pain to stop.
12	There's nothing I can do to reduce the intensity of the pain.
13	I wonder whether something serious may happen.

0 - not at all
1 - to a slight degree
2 – to a moderate degree
3 - to a great degree
4 - all the time

PCS total scoer:52
rumination:1 8 9 10 11, Max. score:20
helplessness:2 3 4 5 12, Max. score:20
magnification:6 7 13, Max. score:12

*: 1 is classified as helplessness in English version

Fig. 2 CPM evaluation



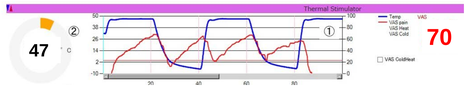
CS was applied by thermal stimulator with a Peltier element probe (16 cm²) for 5 min.
PPT was measured by the electronic pressure algometer (AIKOH Engineering, Japan) before and during CS.

Conditioning stimulus (CS) (cold-heat pulse stimulation) to non-dominant forearm

Test stimulus (TS) (PPT) to dominant forearm

$$\text{CPM effect} = \left\{ \frac{(\text{PPT during CS})}{(\text{PPT at baseline})} - 1 \right\} \times 100\ (\%)$$

Fig.3 An example of cold-heat pulse stimulation



Blue line is an example of cold-heat pulse stimulation and red line is an example of VAS values for cold-heat pulse stimulation.

Fig.5 An example of VASAUC

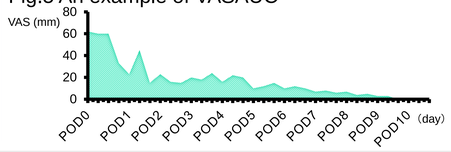


Fig. 4 Schematic illustration of the study protocol (after operative day)

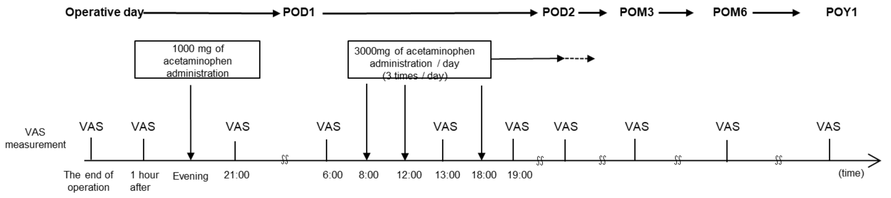


Table 1 CS Temp

Cold (℃)	-2.0	[-10.0 – 4.0]
Heat (℃)	47.0	[47.0 - 47.0]

(Median [interquartile range])

Table 2 CPM effect

	CPM≧0	CPM＜0
n	36	7

	n=43 (Total)	n=36 (positive CPM effect)
CPM effect(%)	13.1 [4.4 – 23.8]	16.3 [8.4 – 26.5]

(Median [interquartile range])

Table 4 VASAUC

	n=43 (Total)	n=36 (positive CPM effect)
VASAUC (day x mm)	188.0 [96.6 – 286.1]	184.7 [101.8 – 289.5]

(Median [interquartile range])

Table 3 PCS

	n=43 (Total)	n=36 (positive CPM effect)
PCS-total	21.0 [15.0 – 32.0]	20.5 [13.5 – 30.5]
PCS-rumination	12.0 [10.0 – 16.0]	11.0 [9.3 – 15.0]
PCS-magnification	4.0 [1.0 – 6.0]	3.0 [1.0 – 5.0]
PCS-helplessness	6.0 [2.0 – 10.0]	5.5 [2.0 – 10.0]

(Median [interquartile range])

Fig.6 Result of multiple regression analysis

1) VASAUC = (-4.11 x CPM effect) + (6.90 x PCS-total) + 161.77
(R=0.57, p=0.0005, CPM effect; p=0.008, PCS-total; p=0.002)
2) VASAUC = (-4.21 x CPM effect) + (10.76 x PCS-rumination) + 188.33
(R=0.46, p=0.008, CPM effect; p=0.012, PCS-rumination; p=0.036)
3) VASAUC = (-3.18 x **CPM effect**) + (29.02 x **PCS-magnification**) + 182.78
(**R=0.61**, p=0.0002, CPM effect; p=0.032, PCS-magnification; p=0.001)
4) VASAUC = (-4.39 x CPM effect) + (16.70 x PCS-helplessness) + 209.30
(R=0.56, p=0.0008, CPM effect; p=0.005, PCS-helplessness; p=0.003)

RESULTS

- Cold-heat pulse stimulation consisted of -2.0 [-10.0 - 4.0] ° C for cold stimulus and 47.0 [47.0 - 47.0] ° C for heat stimulus (median [interquartile range]) (Table 1).
- Positive CPM effect (≥ 0 %) was detected in 36 patients and negative CPM effect (< 0 %) was detected in 7 subjects (Table 2).
- PCS-total, PCS-rumination, PCS-magnification, and PCS-helplessness were 21.0 [15.0-32.0], 12.0 [10.0-16.0], 4.0 [1.0-6.0], 6.0 [2.0-10.0], respectively (Table 3).
- VASAUC was 188.0 [96.6-286.1] (mm x day) (Table 4).
- In the patients with positive CPM effect, multiple regression analysis showed (Fig. 6);

1) VASAUC = (-4.11 x CPM effect) + (6.90 x PCS-total) + 161.77 (R=0.57, p=0.0005, CPM effect; p=0.008, PCS-total; p=0.002)
2) VASAUC = (-4.21 x CPM effect) + (10.76 x PCS-rumination) + 188.33 (R=0.46, p=0.008, CPM effect; p=0.012, PCS-rumination; p=0.036)
3) VASAUC = (-3.18 x CPM effect) + (29.02 x PCS-magnification) + 182.78 (R=0.61, p=0.0002, CPM effect; p=0.032, PCS-magnification; p=0.001)
4) VASAUC = (-4.39 x CPM effect) + (16.70 x PCS-helplessness) + 209.30 (R=0.56, p=0.0008, CPM effect; p=0.005, PCS-helplessness; p=0.003)

CONCLUSIONS

- Acute post-operative pain of orthognathic surgery can be predicted by the pre-operative evaluation of CPM and PCS.
- Evaluation of CPM and PCS-magnification would be the most predictive biomarker for acute post-operative pain of orthognathic surgery.

REFERENCES
1) Steyaert A, Lavand'homme P: Prevention and treatment of chronic postsurgical pain : A narrative review. Drugs 2018;78:339-354.

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- The study was conducted in accordance with the Declaration of Helsinki, and approved by the Ethics Committee of Meikai University (A1624). This study was registered with the University Hospital Medical Information Network (UMIN) clinical trials registry (number UMIN 000026719).