Glutamate as a Salivary Biomarker for Acute Pain: A Study in Healthy Volunteers After Undergoing the Cold Pressor Task

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Introduction

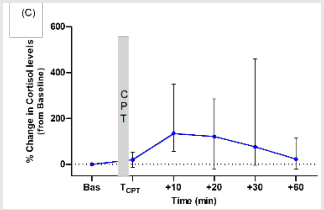
- Acute pain measurement is difficult in unconscious patients or those with cognitive disability. Reliable, non-invasive methods of detecting nociception to guide treatment would benefit this group[1].
- Salivary cortisol rises after exposure to acute pain. Glutamate is associated with nociceptive pathways and its salivary concentration has been found to be higher in people with chronic pain[2].
- We explored change in the salivary cortisol and glutamate after acute pain induced by the cold pressor task (CPT) in healthy pain-free volunteers.
- Approved by the University College London Research Ethics Committee (15021/001). Participants provided with written information and gave written informed consent.
- Funded by the Wellcome Trust [ISSF3/H17RCO/NG16].

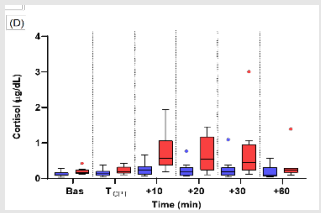
Results

Cortisol

Median baseline: 0.14 µg/dL (IQR 0.1) Increased to median of 0.34 µg/dL (IQR 0.4) at t= +10' (p=0.007).

Levels at t= +10' were significantly higher than those at t= +60' (p=0.02), but no significant difference compared with t= +20' and t= +30', indicating a peak 10-30 minutes after the CPT.





Participants:

Eighteen participants (median age 25 years, range 21-40 years, male to female ratio 1:1)

None of the participants reported any pain prior to starting the CPT

All tolerated submersion for 5 minutes except one person who removed their arm from the ice bath at t= +1.33'.

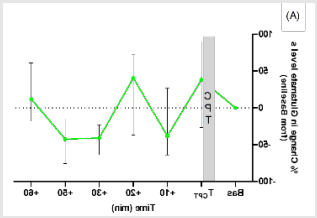
Median pain intensity after CPT: 6.25 (IQR 2 ,range 3-6, mode 6).

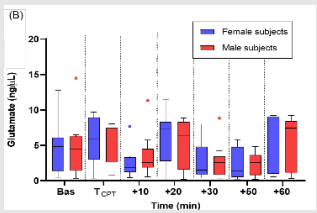
Dropouts - None

Glutamate

Median baseline: 4.90 ng/µL (IQR 4.7) Increased to median of 5.66 ng/µL (IQR 4.6) immediately after CPT and fluctuated thereafter.

None of these changes were significant except at t= +50' when the levels dropped below baseline to 2.08 ng/µL (IQR 3.3) (p=0.014).





Materials & Methods

Cold Pain Induction:

- Submersion of forearm and hand into an ice bath (0-5°C)
- Maximum of 5 minutes immersion with full control over when to start and end the experiment
- Maximum pain intensity score recorded on 0-10 numerical rating scale (NRS).

Saliva Sampling & Assays:

- Whole saliva samples collected by passive drool, before & immediately after CPT then, every 10 minutes for an hour
- Samples frozen at -20°C until assayed
- Enzyme-linked immunospecific assay (ELISA) was used for cortisol measurement in the samples.
- Colorimetric assay was used for glutamate

Pain Intensity Measurement:

Self-reported on a 0-10 numerical rating scale(NRS)

Statistical Methods:

- D'Agostino Pearson test for distribution normality
- Comparison of biomolecule levels - Friedman test & Dunn's comparisons test

Conclusions

The changes in salivary cortisol concentration are in line with previous studies of cortisol change after CPT which valides the study methodology[3].

This is the first study of salivary glutamate reported in the literature after acute pain induction. No statistically significant change in salivary glutamate concentration has been found, however it is possible that a peak in glutamate concentration occurred in the first 10 minutes after CPT and was missed because the sampling intervals (of 10') were designed in accordance with the known time scales of change in salivary cortisol.

References

[1] Herr K, et al. Pain Assessment in the Patient Unable to Self-Report: Clinical Practice Recommendations in Support of the ASPMN 2019 Position Statement. Pain Manag Nurs. [2] Nam JH, et al. Salivary glutamate is elevated in individuals with chronic migraine. Cephalalgia. 2018;38(8):1485-1492. [3] Larra MF, et al. Enhanced stress response by a bilateral feet compared to a unilateral hand Cold Pressor Test. Stress. 2015;18(5):589-596.