**Final report**

**-Biostats and Big data 2-**

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1. **Abstract**

Cognitive pain differs from person to person which makes it difficult to measure objective levels. Biomarkers that represent pain sensation to patients have been studied and it has been suggested that nociceptive procedure goes through two routes; one is from sensory organs to deep brain areas at which decoding this sensation occurs and the other is ‘self-regulatory’ network assuming that our self-regulation may reconstruct physical pain autonomously through pain-related regulation process. Therefore, in this report, under the condition that multiple levels if heat stimulations were given to the subjects during functional magnetic resonance imaging (fMRI) imaging, we studied change of pain ratings collected by subjects’ response and neurologic pain signature (NPS), which represents pain response predicted from multivariate pattern-based brain marker so that we can consider as objective values according to three different levels of cognitive self-regulation; “down”, “passive, and “up.

1. **Introduction**

According to study 1[[1]](#endnote-1), pain is a multidimensional experience that combines sensory, cognitive, and evaluative process from peripheral stimulation to self-regulation in central nervous system. The study reported that the pain intensity of thermal stimulus is mediated by neurologic pain signature (NPS) while the effects of cognitive regulation on pain are not. The research question derived from study 1 is here: whether the self-regulation of subjects affects pain experience at the primary representation of stimuli in the brain or neural pathways that is differentiated from any pain-related pathways. There are two measures for scoring nociceptive effect; pain intensity and NPS response which are dependent on heat intensity delivered by Neurosensory Analyzer on the forearm and self-regulation (“Up” indicates subjects were asked to imagine the thermal stimulations are more painful as lava from a volcano and pay attention to the burning sensations. While “down” indicates that asked to imagine the thermal sensation as a warm blanket on a cold day.)

In the similar way, in study 2[[2]](#endnote-2), we collected three scores from subjects; pain intensity rating, pain unpleasantness rating, and skin conductance response (SCR). We can see the new dependent variable called pain unpleasantness, which is about how unpleasant the stimulus is. In this case, there could be strong but, pleasant stimuli, but in general, pain is unpleasant at the stimulus gets stronger. Since painful sensation leads to changes in autonomic nervous systems such as increasement of blood pressure, heart rate, skin conductance and pupil dilation derived by activation of sympathetic neurons and withdrawal of parasympathetic neuron, we used SCR measurements as physiological pain markers to eliminate subjectivity involved in measuring pain rating.

With data from these two studies, we will see the effect of self-regulation at nociceptive process and whether sex and age affect these results at what extent.

1. **Results**
   1. **Demographics of subjects**

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| --- | --- |
| **Study1** | **Study2** |
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|  |  |

In case of study 1, the number of subjects were totally 33 with no missing value. The number of female subjects were two times larger than that of male subjects. Most subjects were 20’s to early 30’s with some older subjects who were late 40’s to early 50’s.

In case of study 2, the number of subjects were totally 41 with no missing value. The number of female and male subjects were almost same this time. Age of most subjects were distributed between 20 and 25 with some older subjects between 30’s and 40’s.

* 1. **Multiple regression of self–regulate and pain rating**

*study 1*

⚫ **NPS/Rating**

|  |  |
| --- | --- |
| **NPS** | **Ratings** |
|  |  |
|  |  |
|  |  |

⚫ **Sex**

|  |  |
| --- | --- |
| **NPS** | **Ratings** |
|  |  |
|  |  |

⚫ **Age**

|  |
| --- |
| **NPS** |
|  |
| **Ratings** |
|  |

*study 2*

⚫ **Rating/Unpleasantness**

|  |  |
| --- | --- |
| **Rating** | **Unpleasantness** |
|  |  |
|  |  |
|  |  |

⚫ **Heat Level (lv1 ~ lv6)**

|  |  |
| --- | --- |
| **Rating** | **Unpleasantness** |
|  |  |
|  |  |
|  |  |

**⚫ SCR - ANS**

|  |  |
| --- | --- |
| **Cognitive Regulation** | **Heat Level** |
|  |  |
|  |  |
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1. **Discussion**

In study 1, pain ratings recorded by asking subjects so that necessarily include subjective nuisance variable, seem to be affected by self-regulation. However, results from NPS which represents physiological response seem to be not affected by self-regulation, because heat intensity appears parallel regardless of cognitive regulation. It implies that both nociceptive input and self-regulation strongly influenced pain. However, the NPS mediated the only the effects of nociceptive input. Therefore, present study shows that nociceptive and cognitive manipulations of pain influence two distinct, separable neural pathways, which operate together to construct the pain experience.

No significant difference of results from NPS and pain ratings between sex as well as NPS response among ages of subjects. But in case of pain rating, older subjects (from late 40’s to early 50’s) have reported lower ratings. Though the number of older subjects were relatively small than overall subjects, it can provide a clue that tactile sensation becomes dull as becoming old.

In study 2, pain ratings were reported lower in ‘down’ self-regulation than others while the difference of rating between ‘up’ and ‘passive’ condition was hardly observed. Unpleasantness have shown to increase as the subjects were asked to self-regulate themselves in much more painful situation. SCR were similar to the pain ratings, it was hard to observe the difference between ‘up’ and ‘passive’ conditions. In the pain intensity, pain unpleasantness, and SCR, both Heat intensity and Cognitive Regulation produced statistically significant results. In the pain intensity there are no effects of interaction when heat level is 1, 2, and 3, but it seems to some have effect when 4, 5, and 6. However, in the pain unpleasantness, the interaction effect was not significant. In the ANS, there are no interaction effects when heat level is 1, 2, and 3, but it seems to have some effect extent when it is 4, 5, and 6, but the effect is small.

In conclusion, the pain is influenced by both noxious input and cognitive self-regulation, but they are mediated by two distinct brain systems. The effects of noxious stimulus intensity were mediated by the NPS. Conversely, the effects of self-regulation were mediated by the NAc-vmPFC[[3]](#endnote-3) pathway, which did not respond to changes in noxious stimulus intensity. Cognitive self-regulation is far from controlling pain that we feel physiologically, however at least, it can induce a sort of decision bias so that we may feel ‘less painful’ than what our body actually feels.

1. **Reference**

1. Woo et al. (2015), Distinct Brain Systems Mediate the Effects of Nociceptive Input and Self-Regulation on Pain, https://doi.org/10.1371/journal.pbio.1002036 [↑](#endnote-ref-1)
2. Matthewson et al. (2019), Cognitive self-regulation influences pain-related physiology, doi: 10.1097/j.pain.0000000000001621 [↑](#endnote-ref-2)
3. # [Liane Schmidt](https://pubmed.ncbi.nlm.nih.gov/?term=Schmidt+L&cauthor_id=29866743) et al. (2018), Neuroanatomy of the vmPFC and dlPFC Predicts Individual Differences in Cognitive Regulation During Dietary Self-Control Across Regulation Strategies, doi: 10.1523/JNEUROSCI.3402-17

   [↑](#endnote-ref-3)