Changes in perception of risk and valuation of monetary rewards with transition from acute to chronic back pain

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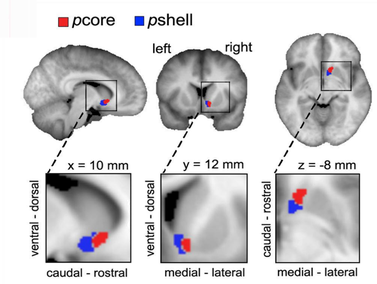
INTRODUCTION

- Recent observations show the involvement of nucleus accumbens (NAc) - a mesolimbic region mediating reward-valuation, decision-making, and motivation – in chronic pain conditions.
- Since nociceptive input provides motivational and value-based information, we are interested in exploring the link between pain and reward perception, specifically during the transition from an acute to a chronic pain state.
- In a separate analysis, we found that two functionally and anatomically distinct subdivisions of the NAc - core and shell (**Figure 1**)– displayed different temporal activation patterns in response to an acute painful stimulus, and these patterns differed between healthy individuals and those in chronic pain at stimulus offset.
- Here, we compare performance scores and NAc activity for a monetary gambling task – ***behavioral loss aversion*** – among healthy individuals and individuals with either subacute or chronic back pain to see if there are differences, and if so, to investigate if these differences mimic those seen during acute pain.

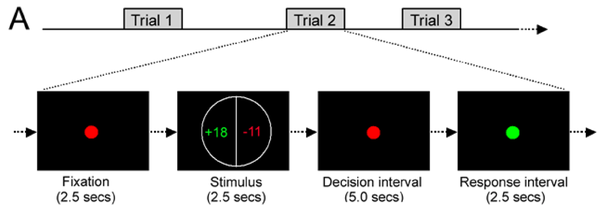
METHODS

- 21 Healthy Controls (HCs), 56 individuals with Subacute Back Pain (SBPs), and 14 individuals with Chronic Back Pain (CBPs) successfully completed the task. Of these subjects, 15 HCs, 26 SBPs, and 10 CBPs had scanning data that was usable.
- All patients were diagnosed by a clinician using IASP criteria: CBPs had back pain >1 year, CBPs and SBPs had no other pain comorbidities, and HCs had no history of back pain.
- The task was performed over the course of two event-related fMRI scans of identical length and the resulting behavioral performances were calculated according to previous reports by Tom et al (2009) (**Figures 2 and 3**).
- We extracted the time-series from the NAc core and shell using previously-made ROI masks, which were created by clustering DTI tractography output from a different scanning session (**Figure 4)**. Time series were then z-scored, low-pass filtered, and averaged according to each trial's response (which divided them into accepted versus rejected decisions).

1 DTI-Based Clustering of NAc into Core and Shell Subdivisions (poster 108.12/DDD41)

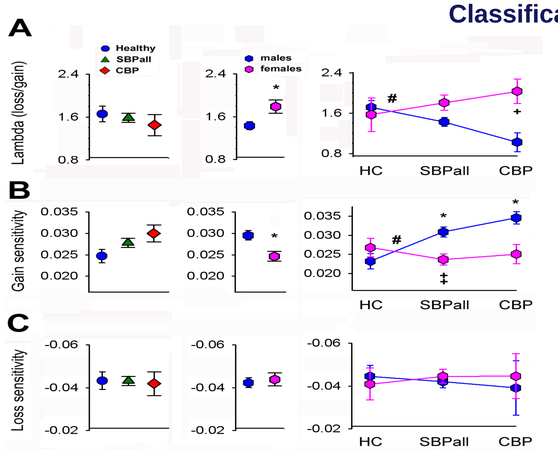


2 Behavioral Loss Aversion: Task Design



A. The task was performed during an fMRI scan. For each trial, subjects were shown a display depicting an amount of potential gain (green) and potential loss (red), and after a decision period, had to accept or reject the gamble with a computer mouse. Gains ranged between $10 and $38 (increments of 4) and losses between $5 and $19 (increments of 2). There were 64 trials total divided over two scans. Regression coefficients for each person's loss and gain sensitivity were computed from these trials, and the log of the ratio of loss/gain sensitivity equaled their individual level of loss aversion (lambda). Lambda scores were averaged across groups.

3 Behavioral Results: Loss Aversion Performance Scores Differ According to Pain Classification and Gender



Behavioral loss aversion components were compared among pain cohorts (**panel 1**), between males and females (**panel 2**), and as an interaction between pain group and gender (**panel 3**).

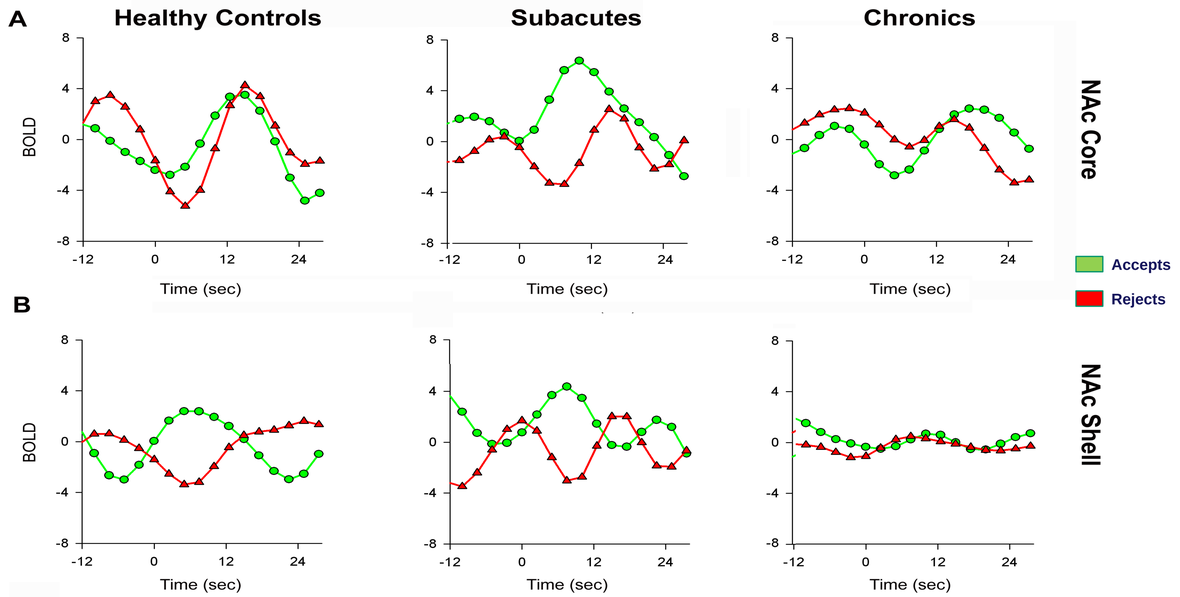
A. After correcting for age and gender, no difference in average lambda was found when looking at pain classification alone. There was a significant gender effect ($F_{84,2}$=6.84, p=0.01) & a significant interaction between pain chronicity & gender ($F_{84,2}$=3.34, p=0.04).

B. Gain sensitivity scores were compared: there were no differences between pain groups, but there were significant differences with regard to gender ($F_{89,1}$=5.77, p=0.02) and pain interacting with gender ($F_{89,2}$ =4.72, p=0.01). Post-hoc comparisons revealed significant differences between SBP males and HC males (p=0.02), CBP males and HC males (p=0.01), and SBP males and SBP females (p=0.003).

C. No differences in loss sensitivity scores were seen for any comparisons.

[*p<0.05 for between group comparisons; +p<0.05 for within group comparisons; #p<0.05 for interactions].

4 NAc Core and Shell Appear to Encode Different Aspects of the Task, A Property Which Disappears in Chronic Back Pain



Group averaged time courses of BOLD responses for the NAc core (**A**) and the NAc shell (**B**). For all three groups, the core showed similarly increased responses for both accepted (green) and rejected (red) choices, although the amplitude was less for CBPs. This suggests that it may be responding to the ***salience*** of a given decision. In contrast, the shell showed differential increased responses for accepts and decreased responses for rejections for both HCs and SBPs, suggesting that it may be encoding the ***value*** of a decision. These differential responses were not present in CBPs, and the overall response of the shell was greatly decreased, indicating a potential dysfunction within the reward circuitry.

CONCLUSIONS

- Our findings suggest that individuals with back pain are less loss-averse and more gain-sensitive, which may impact their decision-making and reward processing on a daily basis. This difference preferentially affects males and becomes more apparent as pain persists.
- The healthy NAc core and shell process the behavioral loss aversion task differently, with the core responding in the same way no matter the outcome, and the shell responding differentially to accepted vs rejected decisions. This was also true of the SBP core and shell. This result is interesting, given that the opposite pattern was found during an acute painful stimulus (see introduction).
- The CBP core responds similarly to its healthy counterpart except at a lower amplitude. The CBP shell, however, barely responds and does not display the differential pattern seen in the other cohorts. Since shell may encode value of monetary decisions, perhaps this difference could explain why CBPs show differences in their gain sensitivity during the task.
- Future work will continue to investigate these differences in the hope that we elucidate more of the changes that occur during the transition to chronic pain.

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