Higher HbA1c Is Associated With Impaired Pain Inhibition, An Effect Buffered by Cultural Connectedness: Preliminary Results From The Oklahoma Study of Native American Pain Risk III (OK-SNAP III)

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INTRODUCTION

- Native Americans (NAs) experience disproportionate rates of chronic pain and diabetes than other U.S. racial/ethnic communities.
- There is an absence of studies investigating the mechanistic link between chronic pain and diabetes for NA individuals.
- Glucose dysmetabolism has been shown to increase chronic pain risk in non-NA samples.
- Additionally, our laboratory has found that impaired descending inhibition of spinal nociception (i.e., CPM-NFR), but not self-report assessment of pain (i.e., CPM-Pain) partially explains the NA chronic pain inequity.
- Greater NA cultural connectedness is associated with better physical and mental health outcomes for NA individuals.
- However, it is unknown if cultural connectedness buffers against glucose dysmetabolism and chronic pain risk factors.

OBJECTIVE

- To investigate whether NA cultural connectedness moderates a relationship between glucose dysmetabolism and CPM-NFR or CPM-Pain.

PARTICIPANT CHARACTERISTICS

- Participants were 101 healthy, chronic pain-free NAs from the Oklahoma Study of Native American Pain Risk III (OK-SNAP III).
- Exclusion criteria for OK-SNAP III were: (1) <18 years old, (2) self-reported history of cardiovascular, neuroendocrine, musculoskeletal, and/or neurological disorders, (3) current chronic or acute pain, (4) current substance dependence, (5) medication use that could interfere with pain testing (e.g., analgesics, anti-depressants, anti-anxiety, stimulants), (6) current psychotic symptoms, (7) serious cognitive impairment (<20 on the Montreal Cognitive Assessment), (8) abnormal nerve conduction result (e.g., amplitude ≤4 or conduction velocity ≤40), indicating possible neuropathy, and (9) an inability to speak or read English.
  - Average Age = 30.61 years (SD = 10.98)
  - Female (61%), Male (39%)

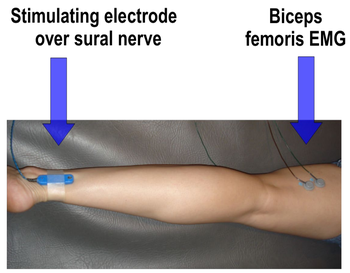
MATERIALS & METHODS

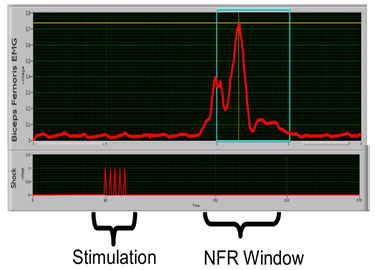
- Participants who met inclusion criteria and completed measures of glucose dysmetabolism (i.e., HbA1c), NA cultural connectedness, and descending inhibition of spinal nociception were included in the current study.
- Procedures were approved by the University of Oklahoma Health Sciences, Cherokee Nation, and Indian Health Service Oklahoma City Area Office institutional review boards (IRBs).
- Participants provided written informed consent and could withdraw from the study at any point.

- **HbA1c**
  - HbA1c is a marker of glucose dysmetabolism.
  - Participants HbA1c levels were assessed from a finger stick and point-of-care device.
  - Higher HbA1c levels indicate greater glucose dysmetabolism.

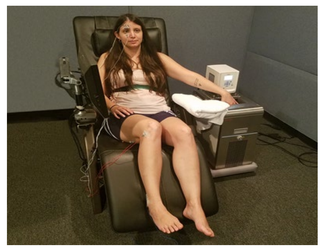
- **NA Cultural Connectedness**
  - Facets of NA cultural connectedness were assessed from four validated scales:
    - The American Indian Enculturation Scale measured the degree of NA enculturation (e.g., engagement in traditional practices) for participants.
    - The Cultural Connectedness Scale measured the level of integration within NA culture for participants. It includes identity, traditions, and spirituality subscales.
    - The NA Spirituality Scale measured the frequency participants engaged with NA spiritual beliefs and behaviors.
    - The Vancouver Index of Acculturation – Heritage Subscale measured participants orientation with NA culture.
  - Higher scores on each measure indicate greater NA cultural connectedness.

- **Descending Inhibition of Spinal Nociception**
  - Assessed from conditioned pain modulation of the nociceptive flexion reflex (CPM-NFR) and self-report pain ratings (CPM-Pain).
  - NFR is a spinally-mediated protective withdrawal reflex elicited by Aδ fiber activation.





- CPM was assessed from painful electric stimulations delivered to the ankle during which participants placed their hands in 26˚C warm water (baseline stimulus) and in painful 10˚C cold water (conditioning stimulus). CPM was calculated by subtracting baseline and conditioning scores.



Phase	Conditioned Pain Modulation (CPM)
Baseline	9 stimulations Warm water [26 °C]
Conditioning	9 stimulations Cold water [10 °C]

DATA ANALYSIS

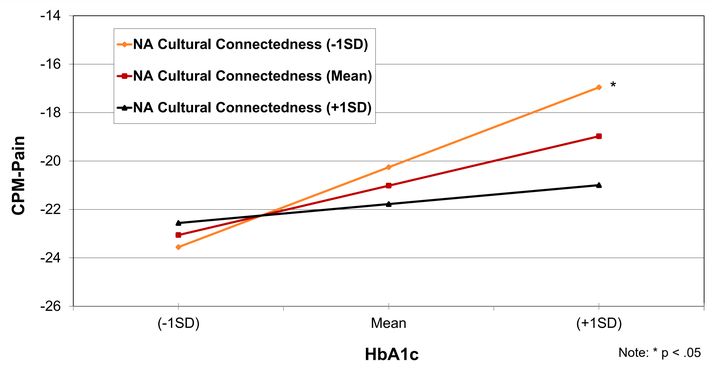
- A principal component analysis was used to create a single NA cultural connectedness latent variable that explained 64% of the variance in the four NA cultural connectedness scales.
- PROCESS was used to conduct two moderated regression analyses.
- All variables that contributed to the moderated regression analyses were mean centered.
- **Models: Criterion=** CPM-NFR or CPM-Pain. **Predictor=** HbA1c. **Moderator=** Latent NA cultural connectedness variable. **Control Variables**: Age, sex assigned at birth, income, and BMI.

RESULTS

Models:

- Results indicated a significant interaction between HbA1c and NA cultural connectedness when predicting CPM-Pain (Fig 1; $\Delta R^2 = 0.045$, $p=0.026$). A significant relationship between HbA1c and CPM-Pain was found in those reporting low NA cultural connectedness (B=12.21, $p=0.003$), indicating HbA1c is associated with impaired pain inhibition. By contrast, HbA1c and CPM-Pain were unrelated in those reporting high NA cultural connectedness (B=2.89, $p=0.32$).

Fig 1. NA Cultural Connectedness Moderates the Relationship between HbA1c and CPM-Pain



- Results indicated HbA1c was not associated with CPM-NFR (B=0.012, $p=0.94$), nor did NA cultural connectedness moderate this relationship ($\Delta R^2 = 0.018$, $p=0.21$).

CONCLUSIONS & FUTURE DIRECTIONS

- These findings suggest even non-clinical levels of glucose dysmetabolism may impair pain inhibition to promote chronic pain risk in NAs.
- However, a stronger connection to NA culture may buffer against this effect.
- Future research should investigate if NA cultural connectedness buffers against other chronic pain risk factors.

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