

Improvements in Heart Rate Variability Following ACT for Chronic Pain

Taryn M. Allen, Ph.D.¹, Stephanie Reda, BS.², Mary Anne Toledo-Tamula, M.A.¹, Kari Struempf, Ph.D.¹, and Staci Martin, Ph.D.²

¹Clinical Research Directorate, Frederick National Laboratory for Cancer Research
²Pediatric Oncology Branch, National Cancer Institute, Bethesda, MD 20892



Background

- Neurofibromatosis type 1 (NF1) is an autosomal dominant genetic condition associated with chronic pain due to plexiform neurofibromas (i.e., a type peripheral nerve sheath tumor), scoliosis, and migraines.
- Due to the challenges of treating pain in NF1 (Wolters et al., 2015), there is a need to examine the impact of complementary interventions such as acceptance and commitment therapy (ACT) for this population.
- Alongside patient-reported outcomes such as pain intensity and pain interference, there is increasing interest in better understanding the potential physiological benefits of ACT among individuals with chronic pain.
- Heart rate variability (HRV) is a measure of autonomic functioning that reflects the time elapsed between heart beats, and is impacted by chronic pain.
- Specifically, lower levels of HRV are associated with increased pain, diminished emotional regulation and less psychological flexibility (Appelhans, 2006).

Objective

- The current analysis examined HRV before and after an 8-week multimodal (in person and online) trial of ACT for individuals with NF1 and chronic pain
- Hypothesis:** There will be an increase (i.e., improvement) in HRV following the ACT intervention

Methods

- Adults and older adolescents (ages 16 to 59 years old) with NF1 and chronic pain (lasting >3 months) were enrolled in an 8-week waitlist-controlled trial of ACT.
- The intervention utilized four hours of in-person ACT training, which took place over 2 consecutive days, followed by weekly emails and biweekly video chat sessions for 8 weeks.
- Questionnaires regarding pain, psychological flexibility, and acceptance were administered to all participants pre- and post-intervention
- Participants also underwent a 5-minute resting electrocardiogram (ECG) at each time point to obtain a measure of high-frequency HRV (HF-HRV).
- For the current analysis, a within-subjects design was used and data was pooled among all participants to include pre- and post-intervention time points. HRV was non-normal and a log transformation was applied.
- Preliminary correlations examined the relationship between HRV, pain, and psychological processes (i.e., flexibility and acceptance) in the current sample.
- A one-way repeated-measures analysis of covariance examined the difference in HRV before and after the ACT trial.
- In addition, bootstrapping was used to test the indirect effect of HRV on pain interference, mediated by pain inflexibility at follow-up.

Measures

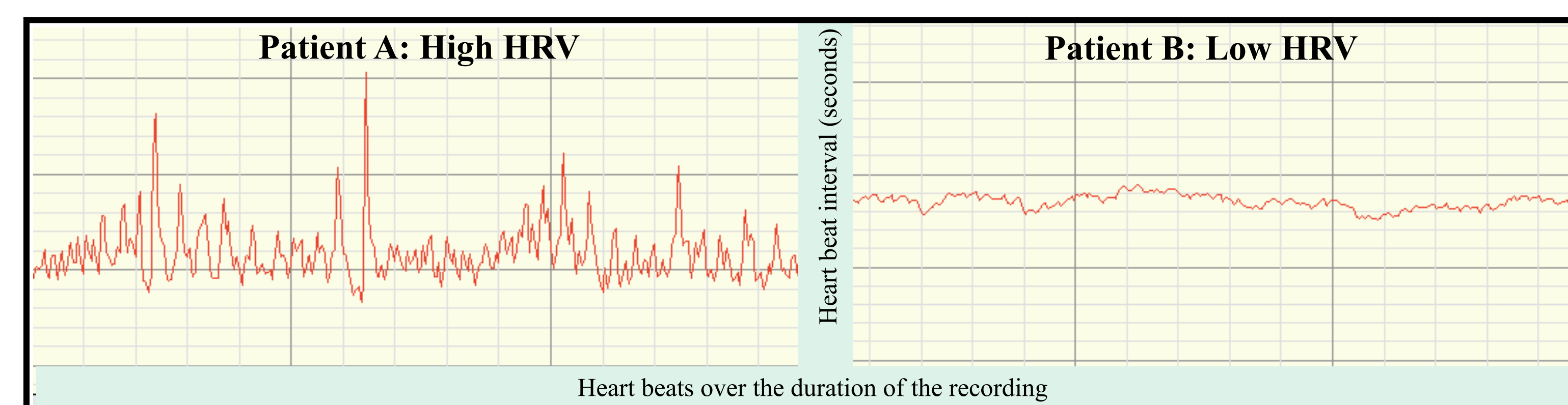
- Numeric Rating Scale-11 (NRS-11):** A 0 to 10 scale assessing worst tumor pain in the last week (Wolters et al., 2013)
- PROMIS Pain Interference Scale:** Assesses how pain interferes with daily life in the past week (Amtmann et al., 2010)
- Psychological Inflexibility in Pain Scale (PIPS):** Assesses the extent to which a person avoids activities or exhibits inflexible thoughts about pain (Wicksell et al., 2010)
- Chronic Pain Acceptance Questionnaire (CPAQ):** Assesses psychological acceptance of pain (McCracken et al., 2004)
- Heart rate variability (HRV):** Spectral analyses of ECGs yielded a measure of high frequency HRV

Results

Table 1. Demographic and Pain-Related Characteristics of the Sample (N=62)

	M ± SD	N(%)
Age	30.7 ± 11.51	
Gender		
Male		24 (38.7)
Female		38 (61.3)
Race		
Caucasian		46 (74.2)
African American		9 (14.5)
Other		7 (13.3)
NRS Pain Rating (0-10)	7.4 ± 1.6	
Pain Interference (T-score; M=50; SD=10)	61.6 ± 5.9	

Figure 1. Raw Tachograms Depicting High and Low Levels of HRV



- Spectral analysis provides a measure of parasympathetically-mediated HRV
- Fluctuations in vertical peaks over the duration of the recording suggests greater HRV

Table 2. Cross-sectional Correlations with HRV at Baseline (N=58)

	Pain Acceptance	Pain Inflexibility	Pain Interference	Pain Anxiety	Pain Intensity
HRV _{Log}	.30*	-.41**	-.31*	-.16	.16

*p<.05; **p<.01

- At baseline, lower HRV is associated with more *inflexibility* and pain interference
- Further, baseline HRV was also positively correlated with pain acceptance

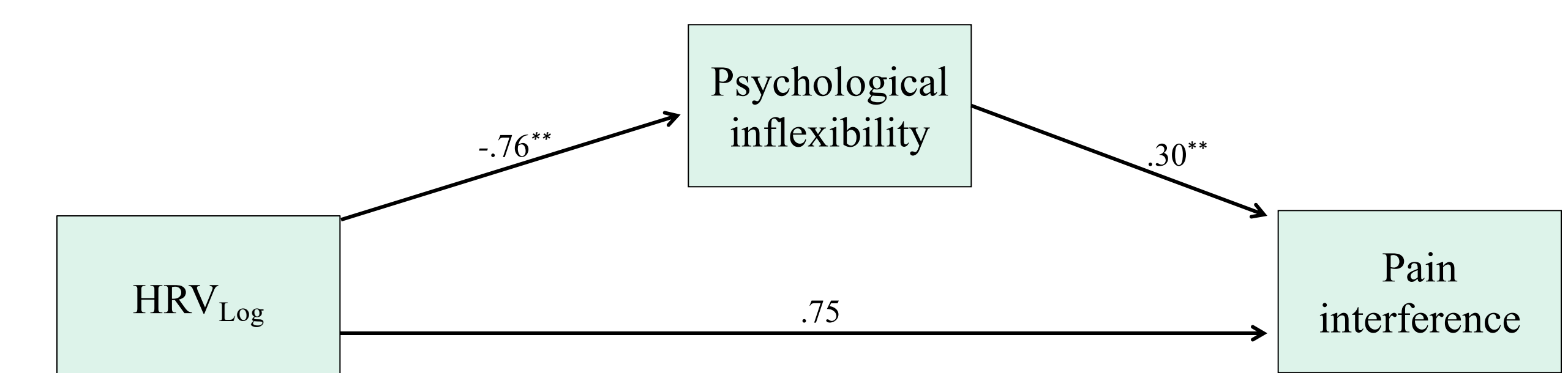
Table 3. Repeated Measures ANCOVA Evaluating Change in HRV Pre- and Post-ACT

	Sums of Square	df	F	p	ηp ²
Time	57401.98	1	8.11	<.01	.14
Time x Gender	31730.48	2	4.48	.039	.08
Error	353997.94	50	--	--	--

- When controlling for gender, there were significant improvements in HF-HRV pre to post ACT intervention ($F(2, 50)=4.48; p<.05$).

Results continued

Figure 2. Indirect Effect of HRV on Pain Interference (n=58)



- There is a significant indirect effect of HRV on pain interference, mediated by psychological inflexibility (Adj. $R^2=0.35, F(2, 54)=14.70, p<.001; -3.88 < CI < -.59$)

**p<.01

Discussion & Future Directions

- This is the first study to connect pain with psychophysiological processes in individuals with NF1 and chronic pain following a pain-related intervention.
- Cross-sectional analyses revealed significant associations between HRV and pain interference, pain acceptance and pain inflexibility.
- These correlations are consistent with previous research suggesting a link between HRV and pain, in addition to HRV and psychological self-regulatory processes such as acceptance and flexibility (Thayer & Lane, 2000).
- The current results suggest that treatment with ACT improves HRV in individuals with NF1 and chronic pain.
- In addition, HRV has an indirect effect on pain interference via psychological inflexibility.
- These data have implications for pain interventions. Specifically, pain processing and psychological flexibility have common neurobiological underpinnings involving prefrontal-limbic circuits. These same circuits impact HRV.
- Thus, interventions, such as ACT or mindfulness-based approaches, that influence the prefrontal-limbic circuits may have particular benefit for individuals with chronic pain.
- The current analyses were limited by a relatively small sample size with limited racial diversity, and a specific patient population of individuals with chronic pain (i.e., NF1).
- Further, we utilized a within-subjects design so it remains to be seen whether these findings would persist in the context of a controlled trial with sufficient power.
- Future research should continue to include biological markers of pain in an effort to better understand how behavioral interventions influence psychological experiences and physical wellbeing.

References

- Amtmann et al. (2010). The development of a PROMIS item bank to measure pain interference. *Pain, 150*(1), 173-182.
- Appelhans (2006). Heart rate variability as an index of regulated emotional responding. *Review of General Psychology, 10*, 229-240.
- McCracken et al., (2004). Acceptance of chronic pain: Component analysis and a revised assessment method. *Pain, 107*, 159-166.
- Thayer & Lane (2000). A model of neurovisceral integration in emotion regulation and dysregulation. *Journal of Affective Disorders*
- Wicksell et al., (2010). The Psychological Inflexibility in Pain Scale (PIPS) – Statistical properties and model fit of an instrument to assess change processes in pain related disability. *European Journal of Pain, 14*, 771-714.
- Wolters et al. (2015). Pain interference in youth with neurofibromatosis type 1 and plexiform neurofibromas and relation to disease severity, social-emotional functioning, and quality of life. *American Journal of Medical Genetics, 167A*(9), 2103-2113.
- Wolters et al., (2013). Patient-reported outcomes in neurofibromatosis and schwannomatosis clinical trials. *Neurology, 81*, S6-S14.

This work was supported by a grant from the Neurofibromatosis Therapeutics Acceleration Program (NTAP) and the Intramural Research Program of the NCI, NIH. This project also has been funded in whole or in part with federal funds from the NCI, NIH, under Contract No. HHSN261200800001E. 75N910D00024, Task Order No. 75N91019F00129. The content of this publication does not necessarily reflect the views or policies of the Department of Health and Human Services, nor does mention of trade names, commercial products, or organizations imply endorsement by the U.S. Government.