Review of: "A Minimally Invasive Method for Observing Wind-Up of Flexion Reflex in Humans: Comparison of Electrical and Magnetic Stimulation"

Nathanial Eckert[1]

1 University of Indianapolis

Potential competing interests: The author(s) declared that no potential competing interests exist.

General Impressions:

This writeup serves as a commentary on the study entitled, “A Minimally Invasive Method for Observing Wind-Up of Flexion Reflex in Humans: Comparison of Electrical and Magnetic Stimulation.” This study focused on investigating different techniques associated with eliciting windup within the RIII reflex. The RIII reflex is suggested as a proxy for quantifying painful sensations such as windup and a correlate for the temporal summation of pain. The study provides a straight forward approach to investigating different methodologies (i.e., electrical vs magnetic stimulation) and protocols associated with eliciting the windup of the RIII reflex. The hope of which may provide a less painful way to for observing windup of the RIII reflex. Care should be taken by the reader to differentiate between the differences between the painful sensation terms of windup and temporal summation as the authors state, “…temporal summation of pain in humans is not considered identical to the wind-up of dorsal horn neurons or flexion reflexes in animal experiments. However…. we use the term “wind-up” in this study to denote progressive increases in reflex magnitude and pain.” This distinction is important as, in humans, the specific mechanisms (i.e., similarities and differences) of wind-up and the temporal summation of pain likely have yet to be fully elucidated and appreciated. The results of the study indicate that the wind-up of the RIII reflex can be seen similarly within all three types of stimulation (i.e., magnetic, bipolar electrical, monopolar electrical) and that pain sensations are lower for magnetic and monopolar electrical stimulation types when compared to bipolar electrical stimulation. These results demonstrate the possibility or warranting the use of magnetic stimulation or monopolar electrical stimulation for eliciting wind-up of the RIII reflex in an effort to keep overall pain sensations experienced by the subject down. This would allow for greater ease in conducting investigations using the RIII reflex on human subjects in an effort to better investigate pain physiology. Overall, the study is well done and thought out.

Points of Interest:

Introduction –

1. A causal link is made between the pain phenomena of wind-up and central sensitization however there are some shared mechanisms between the two. The authors suggest that by better understanding the wind-up of the RIII reflex we may gain a better understanding of pathological pain conditions.
2. The authors touch on the aspect of the differences seen within the potential mechanisms associated with the wind-up

of the RIII reflex and its differences seen between the animal and intact human literature. Specifically, statements are made in the introduction specifying wind-up in animals is seen through stimulation of peripheral C-fibers which is in contrast to humans where the results suggest the increase in the RIII reflex amplitude early on is indicative of A-fiber involvement due to the differences in conduction velocity of the A and C-fibers.

3. Once again, care needs to be taken by the reader as the authors chose to use the term wind-up as, generally, synonymous with temporal summation for the purposes of their study. Any attempt to correlate these findings with a methodology to investigate central sensitization requires further investigation._

Methods -

1. While not of major concern but rather a curiosity the authors chose to use the statistical software R for some calculations but then SPSS for others.

Results –

1. Pain scores were found to be significantly different across stimulation modalities however the wind-up effect on the RIII reflex were not. Meaning, all methodologies elicit the wind-up effect, perhaps some more effective than others. However, the pain experienced by the subjects was significantly different across modalities demonstrating the potential lowering the pain experienced by subjects during RIII reflex testing.
2. The study provides data to demonstrate optimal parameters for RIII reflex testing via the different modalities listed.

Discussion –

1. The biggest take home from the study is the demonstration that there are less painful modalities to elicit the RIII reflex. The importance of which resides in the ability to utilize the RIII reflex as a quantification tool, with some assumptions, of painful phenomena such as windup and temporal summation. This capability may provide for specific testing of pain physiology across a variety of settings but perhaps most importantly, issues concerning chronic or enhanced pain populations.
2. Perhaps of interest to some is the stimulation parameters effects demonstrated within the results. Specifically, the timing associated with some of the RIII reflex results is tied back to A-fiber input rather than purely C-fiber input. Further research into this may provide protocols for isolating activation of these fiber types from one another allowing for quantification of their influence, non-invasively in intact humans. This would allow for testing paradigms across various populations (e.g., aging, chronic pain, etc..) looking to see how the function of these fibers change and how they influence the pain experience.

Closing Remarks:

The study is well done and builds on the usefulness of the RIII reflex as a testing model by adding methodologies that reduce the pain experienced by subjects during testing. Additionally, it builds on the concept of using the RIII reflex as a quantification tool of pain phenomena such as windup and the temporal summation of pain. This may have implications in pain research focused on trying to better understanding issues such as chronic pain or enhanced pain in specific populations. Overall, the data helps substantiate and build upon a solid literature base on the RIII reflex but provides additional possibilities on eliciting the reflex.