

Using Parameter Estimation for Mathematical Model Predicting Pediatric SCD Pain

Quindel Jones^a, Angela Reynolds PhD^{a, b}, Cecelia Valrie PhD^b, Reginald McGee PhD^c, Rebecca A Segal PhD^a

^a Department of Mathematics, VCU, ^b Psychology Department, VCU, ^c Department of Mathematics, Holy Cross

Abstract

Sickle Cell Disease (SCD) is a family of genetic blood disorders that affects over 20 million people worldwide, whose prevalent complication is pain. Pain crises in SCD are strongly linked to mortality & morbidity and increased medical costs. The study in Valrie et al. 2019 revealed a correlation between sleep and pain using actigraphy and patient reported sleep quality and pain in 88 pediatric SCD patients. Our mathematical model builds on the modeling idea of Clifton et al [2017] predictive model which used disease predictors and e-diary data from adult SCD patients. Our model modifications reflect that sickle cell pain in childhood presents differently, without chronic pain, and that poor sleep quality is correlated with increased SCD pain. Our initial model captures some components of the patient data but indicates further model refinement is needed. We plan to refine the model using cumulating data effects, adding patient data factors, and/or incorporating additional model components. Our hope is to develop a warning system for upcoming pain events for pediatric SCD patients.

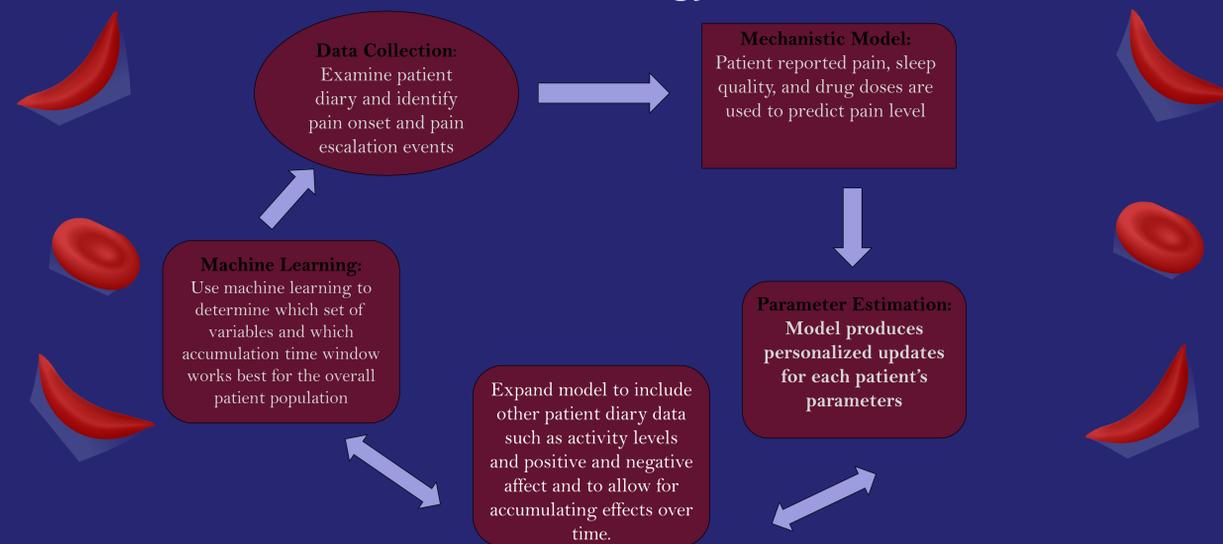
Background

- ❖ Context: During childhood, SCD often presents as severe, acute pain episodes characterized by unanticipated pain periods ranging from hours to weeks, usually occurring a few times a year
- ❖ Motivation: Accurate mathematical models to predict SCD pain in pediatric patients would allow for the development of earlier, more timely interventions for preventing, reducing, and managing pain
- ❖ Previous Model: Clifton et al. proposed a hybrid statistical and mechanistic model for predicting SCD pain severity in adults that assumes a chronic background level of pain

Data Breakdown

- ❖ Dr. Valrie (NIH K01 HL103155) conducted a prospective study of 88 pediatric SCD patients aged 8 to 17 years using twice daily electronic surveys (e-diaries) for up to 4 weeks with concurrent sleep actigraphy for 2 weeks.
- ❖ This resulted in 4473 total e-diary assessments completed across the sample.

Methodology



Mechanistic Model Equation

$$\frac{dP}{dt} = -(k_0 + k_1 D_1 + k_2 D_2 + k_3 D_3)P + \beta_0 * \delta S_b \times (100 - S_q)$$

Parameter	Definition
k_0	Pain relaxation rate without drugs
D_i	amount of standard drug i doses ($i = 1, 2, 3$)
k_i	Effect of drug i on pain relaxation rate
β_0	Strength of pain/sleep interaction
S_b	Bad sleep times: sleep quality below fixed threshold
S_q	Patient input sleep quality

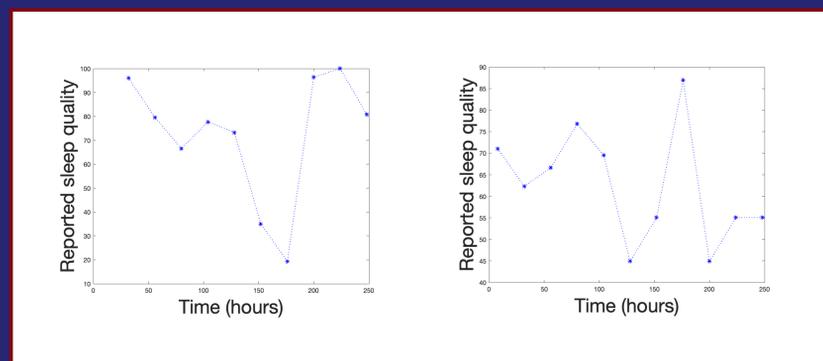


Figure 1: Pediatric patient reported sleep quality (in blue) over 10 days (240 hours). The patient on the left is patient A10, whose pain pattern is classified as pain onset, and the right is patient A46, whose pain pattern is classified as extended pain.

Results

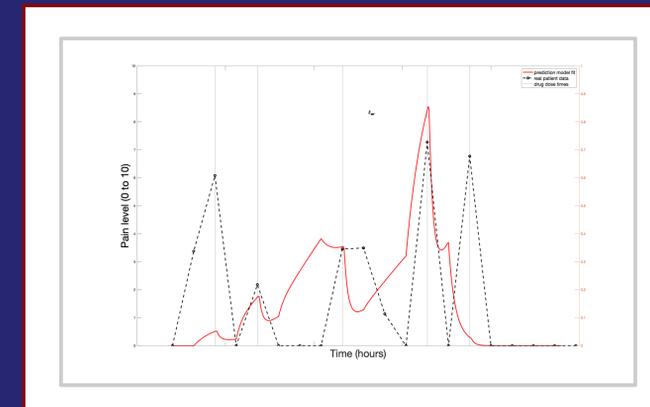


Figure 2: Pediatric patient pain episode model prediction (in red) compared to the patient's reported pain (black dashes) and reported drug dose times (vertical lines) over 10 days (240 hours). This is patient A10, whose pain pattern is classified as pain onset.

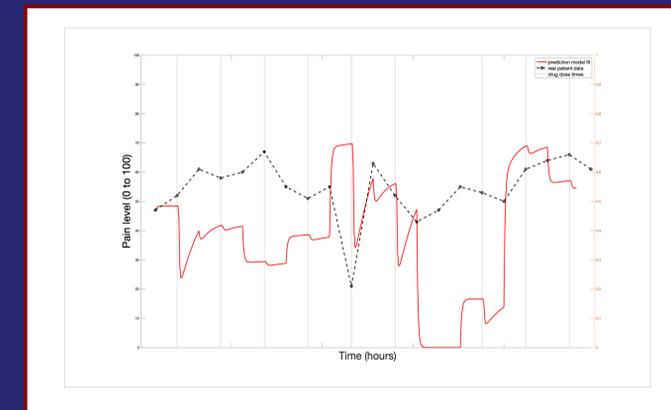


Figure 3: Pediatric patient pain episode model prediction (in red) compared to the patient's reported pain (black dashes) and reported drug dose times (vertical lines) over 10 days (240 hours). This is patient A46, whose pain pattern is classified as extended pain.

Future Work

Next steps:

- ❖ Looking at the cumulative effects of sleep on pain prediction accuracy
- ❖ Utilizing other patient data components within the model parameters
- ❖ Incorporating machine learning to optimize data compartment selection (e.g. grouping actigraphy \pm sleep \pm negative and positive affects \pm etc.)

References

- ❖ Cecelia Valrie, Rebecca Kilpatrick, Kristen Alston, Krystal Trout, Rupa Redding-Lallinger, India Sisler, and Beng Fuh. Investigating the sleep-pain relationship in youth with sickle cell utilizing mhealth technology. Journal of pediatric psychology, 44:323–332, 04 2019.
- ❖ Sara M. Clifton, Chaeryon Kang, Jingyi Jessica Li, Qi Long, Nirmish Shah, and Daniel M. Abrams. Hybrid statistical and mechanistic mathematical model guides mobile health intervention for chronic pain. Journal of Computational Biology, 24(7):675–688, 2017.

