

Developing Methods to Achieve Large-Scale Neuroimaging of Trauma Survivors: Lessons from the AURORA Study

McGill L^{1,2}, Hill MA^{1,2}, Marginean V^{1,2}, Stevens J³, Lebois L⁴, Van Rooij, S³, Harnett N⁴, Jovanovic, T⁵, Murty V⁶, Price R^{1,2}, Stanek J^{1,2}, Mintz A^{1,2}, An X^{1,2}, McLean SA^{1,2,7}, Ressler K⁴

¹Institute for Trauma Recovery; ²Department of Anesthesiology, University of North Carolina, Chapel Hill, NC; ³Emory University School of Medicine, Atlanta, GA; ⁴McLean Hospital, Harvard Medical School, Boston, MA; ⁵Wayne State University, Department of Psychiatry & Behavioral Neuroscience, Detroit, MI; ⁶Temple University, Department of Psychology, Philadelphia, PA; ⁷Department of Emergency Medicine, University of North Carolina, Chapel Hill, NC

Introduction

- Adverse posttraumatic neuropsychiatric sequelae (APNS), including posttraumatic stress, post-concussion syndrome, depression, and regional widespread pain, are common among civilian trauma survivors and military veterans.¹⁻⁴
- Large-scale prospective neuroimaging of trauma survivors is needed to better understand structural and functional changes during the development of APNS.
- Sharing experiences and methods across studies improves data collection success within the field and best serves patients.

Methods

- AURORA is enrolling trauma survivors at 28 emergency departments across the U.S. (target n = 5,000)
- A subset of participants undergo “deep phenotyping” sessions 2 weeks and 6 months after trauma at 4 neuroimaging sites (target n of 800 at each timepoint). These deep phenotyping sessions include blood sample collection, psychophysical assessment (startle response, pain sensitivity), MRI-based evaluations (structural scanning, diffusion tensor imaging (DTI), resting state, specific fMRI tasks), and a neurocognitive assessment (6-month time point only).
- Participants are contacted via phone, email, and text to gauge interest. Before scanning, extensive MRI safety screening is performed to assess participant eligibility.
- Study experiences and procedural improvements to date are summarized here.

Table 1. Study cohort characteristics for eligible individuals enrolled at DP feeder sites (n=479) 09/25/17 – 05/07/19 (study ongoing)

Characteristics	Frequency
Age (mean, SD)	35 (14)
Female (%)	64%
Race (%)	
White	37%
Black or African American	42%
Other	21%
Income (%)	
0-35K	60%
35K-75K	23%
75K+	18%
Education (%)	
No high school	10%
High school diploma/GED	27%
Some college/Associates	40%
Bachelors or Postgraduate Degree	23%
Trauma Type (%)	
Motor Vehicle Collision	77%
Physical Assault	11%
Other	12%

Table 2. AURORA deep phenotyping session components.

Domain	Task	Time(min)	Total Time(min)
Blood Collection	Phlebotomy	15	30
	Plasma processing	15	
Psychophysical	Prep	25	90
	Dark enhanced startle	10	
	Acquisition	20	
	Dot probe	15	
	Extinction	20	
Neurosensory	Cold pressor	10	60
	Cuff algometry	20	
	Temporal summation (CNS sensitization)	10	
	Pressure pain threshold	10	
	Condition pain modulation	10	
Functional MRI	Resting state	8	32
	Fearful faces task	5	
	Response inhibition task (go/no go)	10	
	Monetary incentives delay (reward task)	9	
Structural MRI	T1 structural (anatomical)	7	7
DTI	Diffusion tensor imaging	10	10
NCA	Neurocognitive assessment (6 month only)	50	50

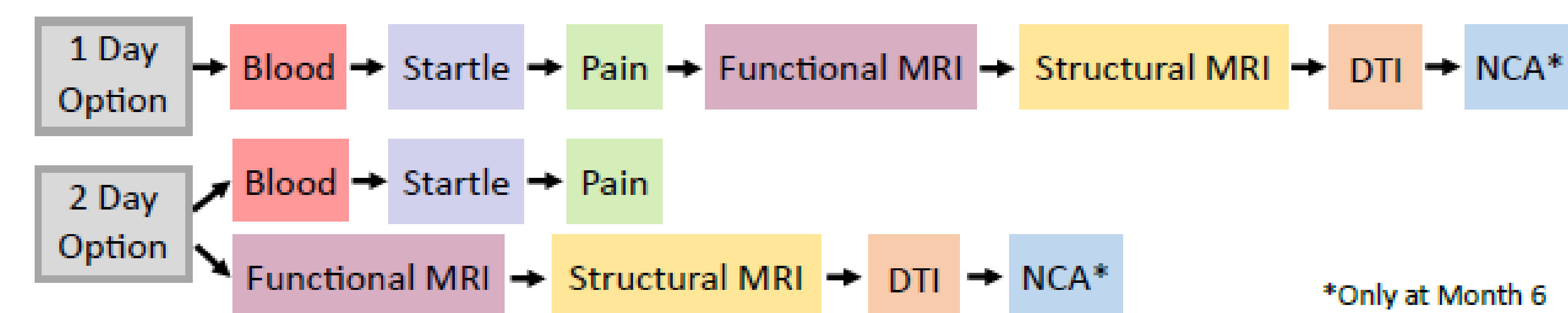


Figure 1. AURORA Study deep phenotyping assessment protocol.

Selected study participants complete protocol assessments two weeks and six months after trauma.

Table 3. Challenges and procedural improvements.

Challenge	Countermeasure	Results
Participant difficulty getting to sessions	Added Uber/Lyft ride option for those otherwise unable	31% of completed sessions have required Uber/Lyft
Scheduling participants within the 2-week window (20 days)	Increase contact protocol to one contact attempt (call, text, or email) per day	Average time from first contact to scheduling reduced to 3 days
Participants no-showing for scheduled sessions, or difficulty with follow-up after session	Participant adherence prediction model implemented	Session completion rate increased 13%
Low success rate for blood collection	Using a national mobile phlebotomy company at two sites	Percent of blood samples missing is 6% lower since implementation (3/28/19)

Results

- Many methodologic changes made to improve data collection (Table 3).
- Improved communication between each neuroimaging site and participants has reduced the time from first contact to scheduling from 5 days to 3 days (p=0.062).
- A prediction model has been implemented to disqualify participants that have a high likelihood of not adhering to the study protocol. Completion rate across all sites increased by 13% post prediction model (39% to 52%, p=0.001). The percentage of participants who were successfully contacted and agreed to be scheduled increased by 8% (75% to 83%, p=0.010).

Conclusions

- Large-scale prospective neuroimaging of trauma survivors is feasible.
- Optimizing methods to recruit trauma survivors for neuroimaging is critical to obtaining high quality data.

References

- Kessler RC. *Posttraumatic stress disorder: the burden to the individual and to society*. J Clin Psychiatry 2000;61:4-12.
- Kessler RC, Sonnega A, Bromet EJ, Hughes M, Nelson CB. *Posttraumatic stress disorder in the National Comorbidity Survey*. Arch Gen Psychiatry 1995;52:1048-60.
- Roberts AL, Gilman SE, Breslau J, Breslau N, Koenen KC. *Race/ethnic differences in exposure to traumatic events, development of post-traumatic stress disorder, and treatment-seeking for post-traumatic stress disorder in the United States*. Psychol Med 2011;41:71-83.
- Boscarino JA. *Posttraumatic Stress Disorder and Mortality Among U.S. Army Veterans 30 Years After Military Service*. Ann Epidemiol 2006;16:248-56.

Funding

This project was supported by NIMH U01MH110925 and the US Army Medical Research and Materiel Command.

The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.