MACHINE LEARNING IN PREDICTING AND MONITORING MENTAL HEALTH AND HUMAN PERFORMANCE

Katharina Schultebraucks, PhD
Director of Computational Medicine and Artificial Intelligence
Assistant Professor in Behavioral and Cognitive Sciences
Disclosure

No financial or professional conflict of interest.

I am Director of Computational Medicine and Artificial Intelligence and Assistant Professor in Behavioral and Cognitive Sciences at Columbia University, Department of Emergency Medicine.

I only receive salary from Columbia University.
About 70% of the population experience a potentially traumatic event at some point in their lives.

Shalev, Liberzon, & Marmar (2017) NEJM
Functioning & Posttraumatic Stress

Responses are Biologically Hardwired to Aid in Adaptation to Threat and Harm
Genetics and epigenetics
Proteomics
Transcriptomics
Metabolomics
Neuroendocrine functions
Immunology
Psychophysiological arousal
Social environment and biography

NYU/Bellevue Stress and Resilience Study
• Every year in the US there are \(~30\text{ million}\) discharges from the emergency room after a potentially traumatic event.

• 10-20\% develop symptoms of posttraumatic stress after the discharge from emergency room.
STUDIES IN CROP VARIATION.
II. THE MANURIAL RESPONSE OF DIFFERENT POTATO VARIETIES.

By R. A. FISHER, M.A. AND W. A. MACKENZIE, B.Sc.
Rothamsted Experimental Station, Harpenden.
(With Two Charts.)

I. Introductory.

It is not infrequently assumed that varieties of cultivated plants differ not only in their suitability to different climatic and soil conditions, but in their response to different manures. Since the experimental error of field experiments is often underestimated, this supposition affords a means of explaining discrepancies between the results of manurial ex-

\[ \frac{\mu_1}{\mu_2} \]

\[ \mu_1 = \mu_2 = \mu_3 \]

\[ H_0: \text{Mean values are different} \]

\[ P(\text{Observation} \mid H_0) \text{ with } \alpha = .05 \]
Interestingly most of those risk factors we discussed earlier are routinely collected in the ED using electronic medical records.
Currently there are no accurate methods to predict psychiatric risk in the immediate aftermath after a traumatic event.
Development and implementation of a validated prediction model for PTSD risk could:

- Improve the likelihood of success of early interventions for posttraumatic stress
- Avoid potential overtreatment and unfavorable effects from blanket interventions.

Previous studies have shown that early interventions are more likely to succeed if targeted at those who are at higher risk of PTSD.
• Potential early interventions may require identification of patients at risk and application directly within the ED:
  - Clinically useful to be able to predict PTSD risk as early as possible
  - Using available ED data
• Develop a prediction model that is:
  - Accurate, but also scalable and cost-effective
  - Low additional burden to routine ED procedures.
1. Data collection of potential predictor variables in two Level 1 trauma centers:
   1) Grady Memorial Hospital, Atlanta
   2) Bellevue Hospital, NYC

2. Model development sample: 12 months follow-up

3. Deep Super Learner Risk score for longitudinal symptom development

4. Independent external validation sample: 12 months follow-up
## Results

<table>
<thead>
<tr>
<th></th>
<th>Precision</th>
<th>Recall</th>
<th>F1-score</th>
<th>ROC-AUC</th>
<th>Positive events/Total events</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Model development</strong></td>
<td>.86</td>
<td>.84</td>
<td>.84</td>
<td>.84</td>
<td>27/164</td>
</tr>
<tr>
<td><strong>Internal validation</strong></td>
<td>.83</td>
<td>.64</td>
<td>.69</td>
<td>.7</td>
<td>14/89</td>
</tr>
<tr>
<td><strong>External validation</strong></td>
<td>.86</td>
<td>.85</td>
<td>.85</td>
<td>.83</td>
<td>38/93</td>
</tr>
</tbody>
</table>
Variable importance using SHAP (SHapley Additive exPlanations) – Model development sample
Variable importance using SHAP (SHapley Additive exPlanations) – External validation set

![Variable importance chart]

- Chloride
- Neutrophils
- ISRC item 26
- ISRC
- Hematocrit
- Blood glucose
- Lymphocytes
- PDEQ
- Creatinine
- Systolic blood pressure
- Anion gap
- Age
- Blood urea nitrogen
- Diastolic blood pressure
- ISRC item 6
- Monocytes
- Carbon dioxide
- Mean corpuscular volume
- ISRC item 7
- ISRC item 27

mean([SHAP value]) (average impact on model output magnitude)
Most important features

- Peripheral immune markers: neutrophils, lymphocyte, monocytes
- Acute stress disorder symptoms and peritraumatic dissociation
- Physiological marker of stress response
- Metabolic markers: blood glucose, carbon dioxide, chloride, anion gap

- Carbon dioxide has been shown to be associated with acute panicogenic and anxiogenic effects and panic attacks
- Chloride and anion gap are critical measures of the body’s pH (acid-base) status, and as with CO2, are associated with acidosis, which is associated with panic attack and fear in numerous studies. Whether or not chloride levels are mediated by potential blood and/or NaCl infusion warrants further investigation.
- Recent work from our group has identified nausea as a predictor variable for later PTSD development, which wasn’t included in these analyses, however nausea is also associated with altered chloride, anion gap, and CO2 status
prediction of longitudinal PTSD symptom trajectories:
multiclass AUC = 0.89

Prediction of clinician-rated PTSD (CAPS) at 12 months:
AUC = 0.83
Summary

• Data collected in emergency rooms contain highly predictive information for PTSD.

• The algorithm can be implemented in medical emergency systems.

• The algorithm can be continuously updated and improved, using data from every patient who is discharged from the emergency room.

• Targeted prevention strategies can be implemented earlier, using the algorithm to inform clinical decision-making.
The clinical phenotype of PTSD is heterogeneous

How many different possibilities exist to fulfill the diagnosis of PTSD according to DSM-5?

\[ \sum \binom{n}{k} \text{ mit } \binom{n}{k} = \frac{n!}{k!(n-k)!} \]

\[ \prod_{n=i} \left[ \sum \binom{n}{k} \right] \quad \text{31 x 3 x 57 x 120 = ?} \]

636,120 Ways to Have Posttraumatic Stress Disorder

Isaac R. Galatzer-Levy and Richard A. Bryant

1 New York University School of Medicine and 2 University of New South Wales, Kensington, New South Wales, Australia
How can we get other measures of clinical functioning?

- more reliable
- more efficient
- more patient-relevant
- more comprehensive
- much easier available
Behavior is indicative of clinical functioning

Individual with Major Depressive Disorder

- Lowered gaze
- Lack of eye contact
- Facial expressivity
- Slow movement
- Verbal valence
- Speech content

Behavior allows interviewer to assess clinical state
\[ Y = \beta_0 + \beta_1 X_1 + \beta_2 X_2 \ldots + \beta_n X_n \]
What is a phenotype?

the set of observable characteristics of an individual resulting from the interaction of its genotype with the environment

A clinical description

Phenotype is what you see - the visible or observable expression of the results of genes, combined with the environmental influence on an organism's appearance or behavior. For example:

It is the expression of gene information which is observable with the senses (like the sound of a bird's chirping or the color of a cat's hair)
Behavioral & Physiological Phenotypes

- Biologically conserved
- Ecologically valid
- Transdiagnostic
- Quantifiable
Digital Phenotyping


Digital Phenotyping
Physiologically Enhanced Qualitative Interview
Facial features

Emotional expressivity
- Happiness
- Sadness
- Anger
- Fear
- Contempt
- Disgust
- Surprise
- Composite

Facial expressivity has been shown to be relevant in distinguishing clinical populations

Number of peer-reviewed journal articles that mention facial expressivity alongside clinical states

Depression  Schizophrenia  Cancer  Parkinson's  Alzheimer's  Heart Disease

0  5000  10000  15000  20000  0  5000  10000  15000  20000  0  5000  10000  15000  20000  0  5000  10000  15000  20000
Voice features

Verbal features
- Expressivity
- Pitch
- Harmonic noise ratio
- Guttural noise excitation
- Normalized amplitude quotient
- Formant variability

Speech features
- Content valence
- Speech intent
- Speech rate
- Speech repetition

Verbal and speech features have been shown to be relevant in distinguishing clinical populations

Number of peer-reviewed journal articles that mention speech alongside clinical states:
- Depression
- Schizophrenia
- Cancer
- Parkinson’s
- Alzheimer’s
- Heart Disease
Measuring movement

- General body movement
- Tremor analysis using
  - Body movement
  - Movement of facial musculature
- Variations in speech

Scientific literature studying movement extends beyond movement disorders
Behavioral indicators of health

Eye-tracking

- Gaze during countdown
- Gaze when image is revealed

Gaze Tracking

Gaze DOF Orientation

Time (frames)
Predictive model development

Feature extraction for unstructured raw audio and video material via Transfer Learning by using a pre-trained neural net to detect features of facial expression, voice prosody, natural language processing and movement.

Preprocessing
- One-hot encoding of categorical variables
- Normalization of numerical variables to range [0,1]
- Variables with near-zero variance were removed
- Missing variables were imputed using knn imputation

Training set (75%)
Repeated k-fold cross-validation
- Resampled data of the training set used to tune the neural net
- Resampled data of the training set used to evaluated the tuning parameters

Hold-out test set (25%)
Evaluation of the final model performance.

SHAP explanations

[Diagram showing the flow of data processing, from data collection to model tuning and evaluation.]
Tell me about what brought you to the hospital

Tell me about your experience in the hospital

Tell me about the past month

4 Min Each
NN Classification Results based on Interview
Figure 3. Receiver operating characteristic (ROC) curve of the internal test set for predicting (a) PCL-5 cut-off ≥ 33 (AUC = .90), (b) CES-D cut-off ≥ 23 (AUC = .86), (c) PTS symptom trajectories (non-remitting AUC = .86) and (d) depressive symptom trajectories (non-remitting AUC = .80).
Digital Signals of Cognitive Functioning

Inhibition

- AUD_INTENSITY_MEAN
- COM_NEG_EXP_MEAN
- V57_TEMP
- GAZE_ANGLE
- COM_ANGER_EXP_MEAN
- COM_DISGUST_EXP_MAX
- COM_SAD_EXP_MEAN
- COM_CONSTRAINT_EXP_MEAN
- AUD_INT_MEAN
- COM_FEAR_EXP_MEAN
- COM_DISGUST_EXP_MEAN
- EYE_MV_RIGHT
- DISGUST_COUNT_PERC
- EYE_MV_LEFT
- HEAD_MOTION_AVG_PER_FRAME
- COM_POS_EXP_MEAN
- COM_SAD_MEAN
- PUPIL_SIZE_RATIO
- COM_NET_EXP_MEAN
- FEAR_COUNT_PERC
- COM_EXP_STD
- NEG_EMOITION_COUNT_PERC
- COM_NET_EXP_STD
- COM_POS_EXP_MAX
- COM_NEG_EXP_MAX
- AUD_INTENSITY_STD
- COM_HAPPY_EXP_MAX
- HEAD_ROTATION_MAX
- COM_SURPRISE_EXP_MEAN
- COM_SURPRISE_EXP_STD
- COM_NET_EXP_MAX
- PUPIL_SIZE_LEFT
- AUD_INTENSITY_MAX
- COM_HAPPY_EXP_MAX
- PUPIL_DIAMETER_RIGHT
- ANGER_COUNT_PERC
- PUPIL_DIAMETER_LEFT
- COM_HAPPY_EXP_STD
- COM_ANGER_EXP_STD
- HEAD_ROTATION_DPITCH
- COM_NEG_EXP_STD
- COM_CONSTRAINT_PERC
- SURPRISE_COUNT_PERC
- HAPPY_COUNT_PERC
- HEAD_ROTATION_DPULL
- COM_DISGUST_EXP_STD
- COM_POS_EXP_STD
- COM_HAPPY_EXP_MEAN
- PUPIL_SIZE_RIGHT
- SAD_COUNT_PERC
How can we scale-up the clinical utility of this technology?

Creating a Learning Health System through Rapid-Cycle, Randomized Testing

Leora I. Horwitz, M.D., M.H.S., Masha Kuznetsova, M.P.H., and Simon A. Jones, Ph.D.

Welcome to VA Telehealth Services

VA Telehealth Services is changing the way Veterans access VA quality care. From your home, the clinic or the hospital, telehealth technologies make it easier for you to connect with your care team and share important health information.

At Home
Meet with VA providers virtually and send important health data from the comfort of your home or mobile device.

In the Clinic
Connect with VA health specialists around the country from a VA clinic near you.

In the Hospital
Telehealth technologies in hospitals help VA providers around the campus, region or country collaborate to improve your care.

Mobile Devices and Health
Ida Sim, M.D., Ph.D.
At what point in time can we implement it?
Stakeholder engagement is crucial to success
Thank you very much for your attention!

Isaac R. Galatzer-Levy & Arieh Y. Shalev: Department of Psychiatry, New York University School of Medicine, New York, New York

George Bonanno: Teachers College, Columbia University, New York, New York

Tanja Jovanovic, Vasiliki Michopoulos & Jennifer Stevens: Department of Psychiatry and Behavioral Sciences, Emory University School of Medicine, Atlanta, Georgia; Yerkes National Primate Research Center, Atlanta, Georgia

Kerry Ressler: Harvard McLean Hospital, Boston, Massachusetts, United States of America; Department of Psychiatry and Behavioral Sciences, Emory University School of Medicine, Atlanta, Georgia

Miranda Olff, Mirjam van Zuiden: Department of Psychiatry, Amsterdam University Medical Centers, location Amsterdam Medical Center, University of Amsterdam, Amsterdam Public Health Research Institute/Amsterdam Neuroscience Research Institute, Amsterdam, the Netherlands

Marit Sijbrandij: Faculty of Behavioural and Movement Sciences, Vrije Universiteit Amsterdam