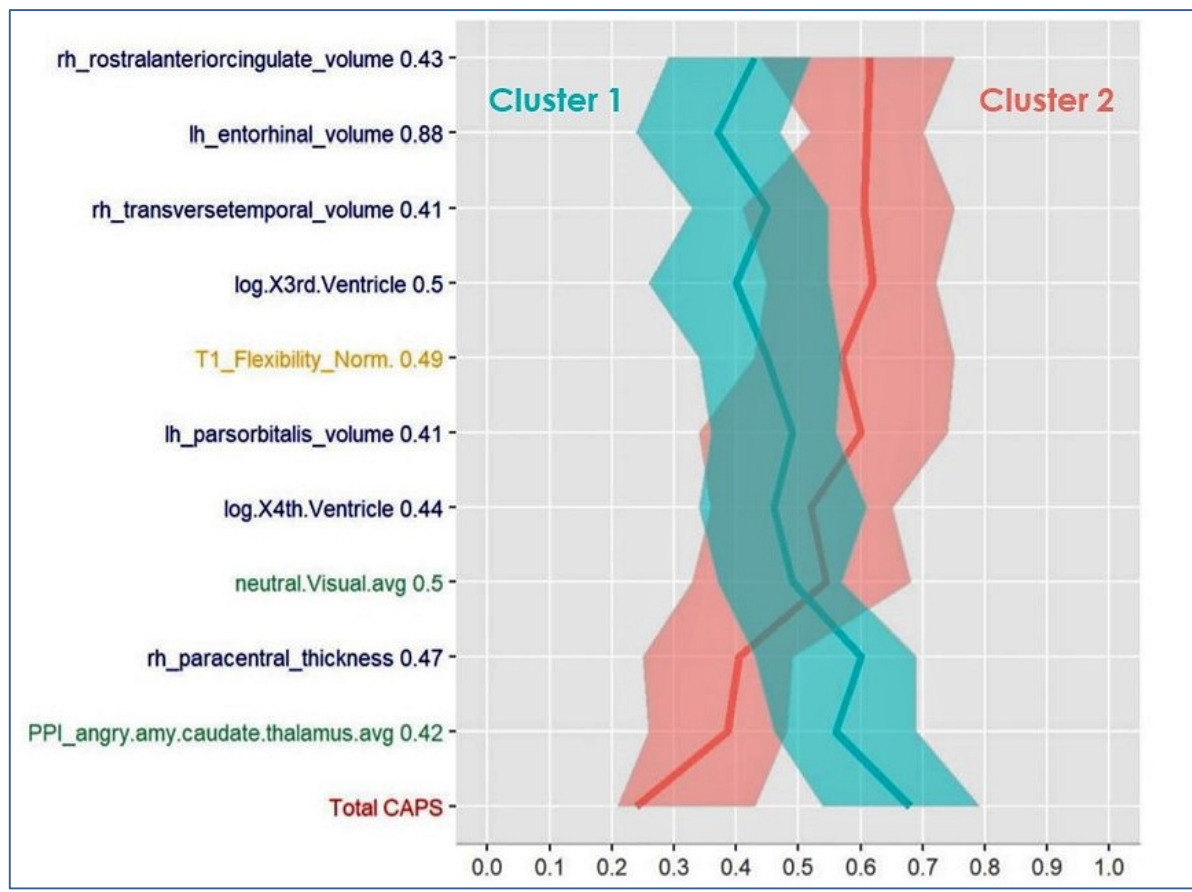


Reports on Disease Signatures via Sub-type Identification, on Development and Application of Methods, and Tools (D8.4.1 - SGA2)



Parallel Coordinates Plot of Potential Neurocognitive Biomarkers for Post-Traumatic Stress Disorder (PTSD) Severity in Recent Trauma Survivors

The Y-axis depicts the top ten most important potential biomarkers for each cluster, together with their mean decrease GINI measure (i.e. importance index). Biomarkers from cognitive domains are coloured in yellow, biomarkers from structural brain measurements are coloured in dark blue, and biomarkers from functional brain measurements are coloured in green. Average CAPS-4 total score is presented for both “Low-Symptomatic” Cluster (cluster 1, turquoise) and “High-Symptomatic” Cluster (cluster 1, red). The bold line of each cluster represents the median of each variable for this cluster, whereas the scattered “cloud” around it represents the 95% confidence interval (CI).

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Description in GA:	Report on identification of disease signatures and application development is delivered.		
Abstract:	<p>We aimed to computationally derive potential biomarkers that could efficiently differentiate PTSD subtypes, based on an observational cohort study of recent trauma survivors. A three-staged semi-supervised method ("3C") was used to categorise trauma survivors based on current PTSD diagnostics, derive clusters of severe and mild PTSD based on features related to symptom load, and to classify participants' cluster membership using objective features (the code for implementing the method is available on the MIP). A total of 256 features were extracted from psychometrics, cognitive, structural and functional neuroimaging data, obtained from 101 adult civilians evaluated within a month of trauma exposure. Results revealed that entorhinal and rostral anterior cingulate cortices volumes (structural domain), the amygdala's functional connectivity with the insula and thalamus (functional domain), executive function and cognitive flexibility (cognitive domain) best differentiated between two PTSD severity clusters. Multi-domain biomarkers revealed by the 3C analytics offer objective classifiers of post-traumatic morbidity shortly following trauma, and also map onto previously documented neurobehavioural PTSD features, supporting the future use of standardised and objective measurements to more precisely identify psychopathology subgroups shortly after trauma.</p>		
Keywords:	Post-Traumatic Stress Disorder; Categorisation; Clustering; Classification; Computational Psychiatry; Early Potential Biomarkers; Precision Psychiatry		
Target Users/Readers:	Clinicians, neuroimaging community, neuroinformaticians, neuroscientific community, neuroscientists, researchers, scientific community, students		

# 1. Summary

Our deliverable is a pre-print, available on bioRxiv: the pre-print server for biology - <https://www.biorxiv.org/content/10.1101/721068v2.full>

New Results Comment on this paper

**Potential Neurocognitive Biomarkers for Post Traumatic Stress Disorder (PTSD) Severity in Recent Trauma Survivors**

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This pre-print has not been certified by peer-review. Because the process of peer-review can be lengthy, authors use the bioRxiv service to make their manuscripts available as “preprints” before completing peer review and consequent certification by a journal. This allows other scientists to see, discuss, and comment on the findings immediately. Readers should therefore be aware that articles on bioRxiv have not been finalised by authors, might contain errors, and report information that has not yet been accepted or endorsed in any way by the scientific or medical community.

This pre-print was submitted to the journal *Translational Psychiatry* (IF=5.182) on August 26th, 2019. It underwent an extensive peer-review of 5 different reviewers who provided comments and remarks regarding this work (Decision letter inviting major revision was sent to us on October 10th, 2019). We have now completed revising the manuscript and addressing all the relevant issues, and the revised article was re-submitted to the journal on December 29th, 2019, and was assigned to a new set of reviewers.

# 2. Significance

Trauma has an enormous impact on both individuals and society as a whole, and unfortunately more than 70% of adults worldwide experience a traumatic event at some time in their lives. According to the U.S. Department of Veterans Affairs, about 8 million adults in the USA suffer from Post-Traumatic Stress Disease (PTSD) during a given year, and 7 or 8 out of every 100 people (7-8% of the population) will have PTSD at some point in their lives. The core features of PTSD are the persistence of intense, distressing, and fearfully avoided reactions to reminders of the triggering event, alteration of mood and cognition, a pervasive sense of imminent threat, disturbed sleep, and hypervigilance. Although therapies for PTSD include psychological, pharmacologic, and other innovative interventions, these therapies only show partial success in a small portion of PTSD individuals.

This work utilised an innovative computational approach (termed “3C”), which successfully provided objective potential markers for PTSD diagnosis, instead of the commonly used clinical definition which relies only on subjective reports of symptoms. These markers include both cognitive skills and neural measures of brain structure and function, and they are all in line with previous neural and cognitive studies of PTSD. Our alternative approach offers identification of objective variables linked to PTSD severity subtypes (high and low PTSD), based on testing within a single session closely after exposure to trauma. It may further refine post-traumatic diagnostic subtypes and guide mechanism-driven interventions for PTSD, such as cognitive interventions or neuromodulation treatments, playing an important role in the treatment management of recent trauma survivors.