VOXNEURO
UNLOCKING THE BRAIN

# Determining Cognitive Function after Brain Injury – from Coma to Concussion

*Kyle I. Ruiter, PhD*
*John F. Connolly, PhD*

• OBJECTIVE • QUANTITATIVE • COGNITIVE HEALTH ASSESSMENTS

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# ACKNOWLEDGEMENTS

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DISCLAIMER: The opinions expressed herein are those of the presenters and do not represent the official views of CIHR, NSERC, CFI, NIH, Heart & Stroke Foundation, March of Dimes Research Foundation, Scottish Rite Charitable Foundation, the Ontario Centres of Excellence, the Ontario Brain Institute, McMaster University, the Hamilton General Hospital, or VoxNeuro.

# TripAdvisor for this presentation

- Choice of measures and why
- Altered state of awareness, cognition, state of consciousness
- Value added of neurophysiological recordings
- Vegetative State / Coma / Concussion
- Progress in measuring & assessing consciousness
- Application of ERPs into clinical practice

# The question determines the technology

- One choice for brain structure – MRI
- Two choices for brain function – EEG/ERP & MEG/ERMF – concept of componentry (time, space, frequency)

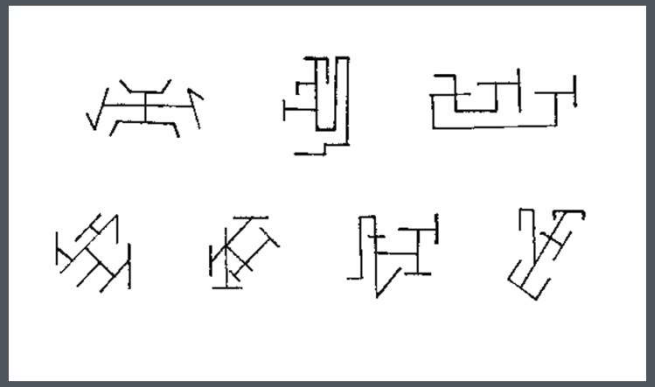
# Use of EEG/ERP in point-of-care assessment

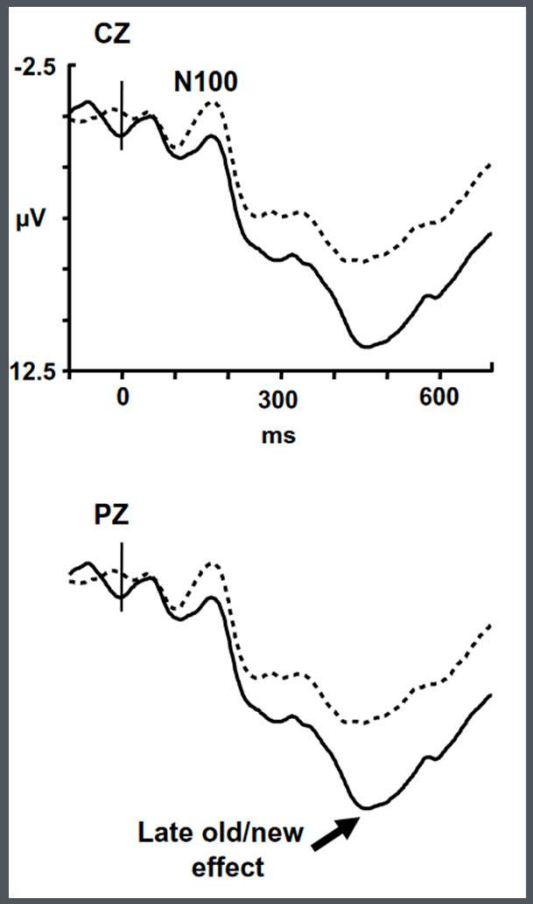
- Assessment and differentiation of  functional symptoms
- Assessment of change over time
- Assessment of responses to therapeutic intervention
- Measures that are objective, quantitative, replicable, and clinically relevant.
- Moving past problematic diagnostic issues to direct assessment of symptoms

# Adapted Neuropsychology: CVMT

[Trahan DE, Larrabee GJ. Continuous Visual Memory Test. Lutz, FL: Psychological Assessment Resources; 1988]

- Series of black-and-white shapes, some of which repeat 6 times.
- Participants indicate whether the shape is repeating or not.



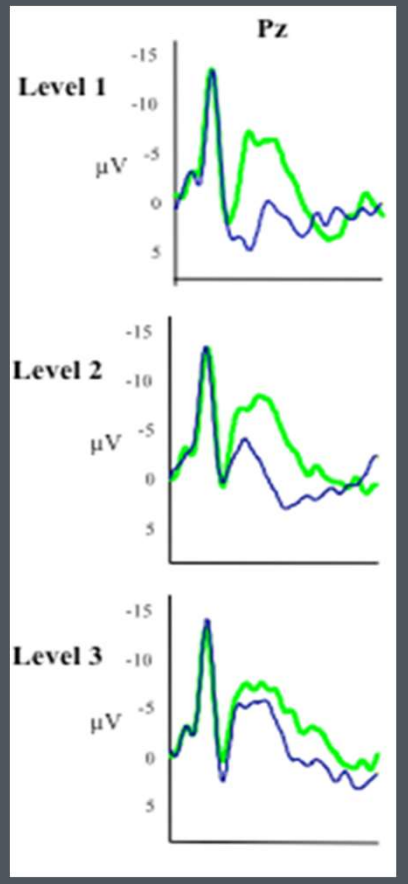


# Adapted Neuropsychology: PPVT

- Series of black-and-white pictures presented individually.
- 750 ms after picture onset, participant hears either a related or unrelated word relating to it.

Bus (Related - **BLUE**)

Cat (Unrelated - **GREEN**)



# EEG/ERP-adapted Neuropsychology

- The (Boston) Process Approach to Neuropsychological Assessment (Kaplan, 1988)

- It is more about the process than the outcome

# Are behavioural measures not sufficient?

# Diagnosis of vegetative state (UWS)

- Schnakers et al 2009:

  18 (41%)  of 44 patients diagnosed as VS based on the clinical consensus of the medical team were found to be in MCS following standardized assessment with the CRS-R.

- This result replicates others who found signs of awareness in 37% to 43% of patients diagnosed as VS (Childs et al., 1993; Andrews et al., 1996).

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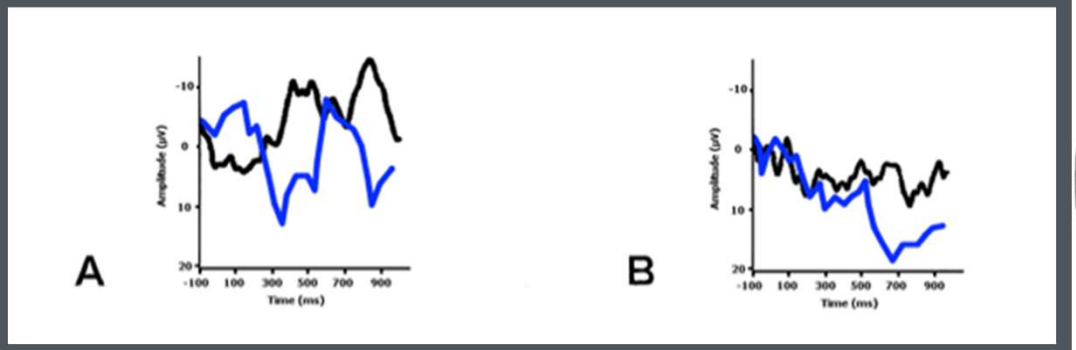
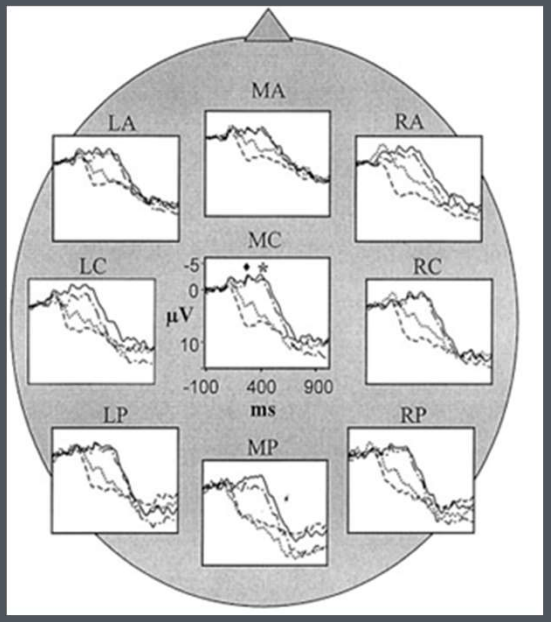
# Traumatic brain injury – vegetative state

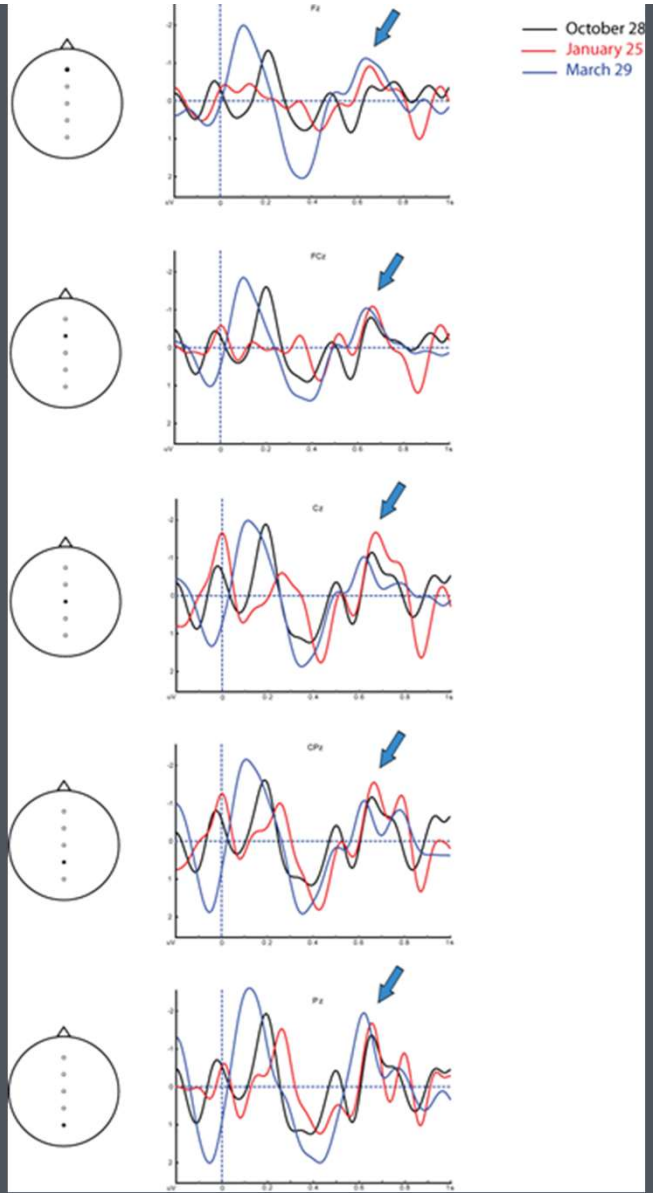
- Young male, average pre-morbid functioning
- Stabbed in head, left frontal entry, right posterior extent
- Little/no behavior, assessment problem
- Poor prognosis: VS

# BRAIN SIGNS OF Comprehension



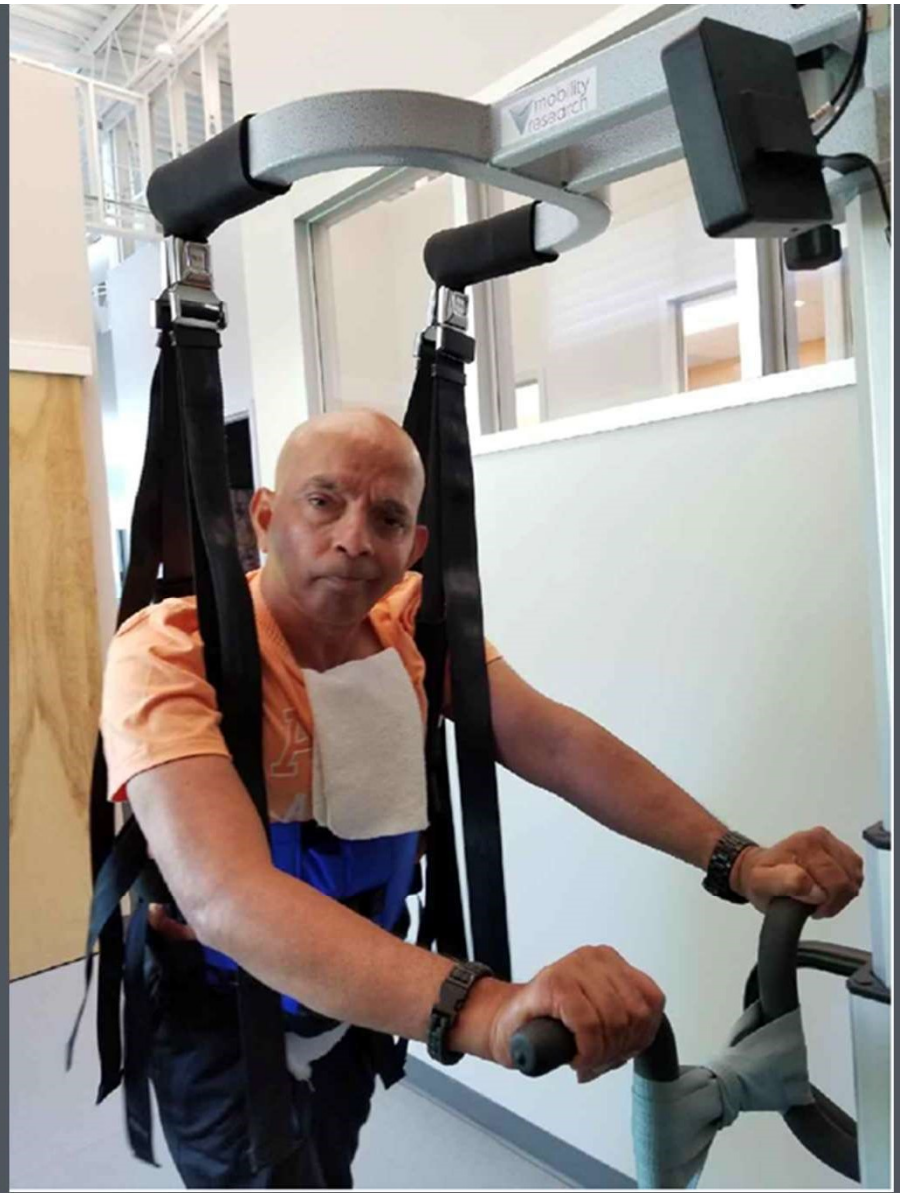




- The pigs wallowed in the mud.
- The scared cat ran up the cloud [tree].




# BRAIN SIGNS OF Comprehension

- 46 year-old male at the time of testing.
- Traumatic brain injury: car-bicycle collision 4 months earlier.
- Coma with later diagnosis of “vegetative state.”

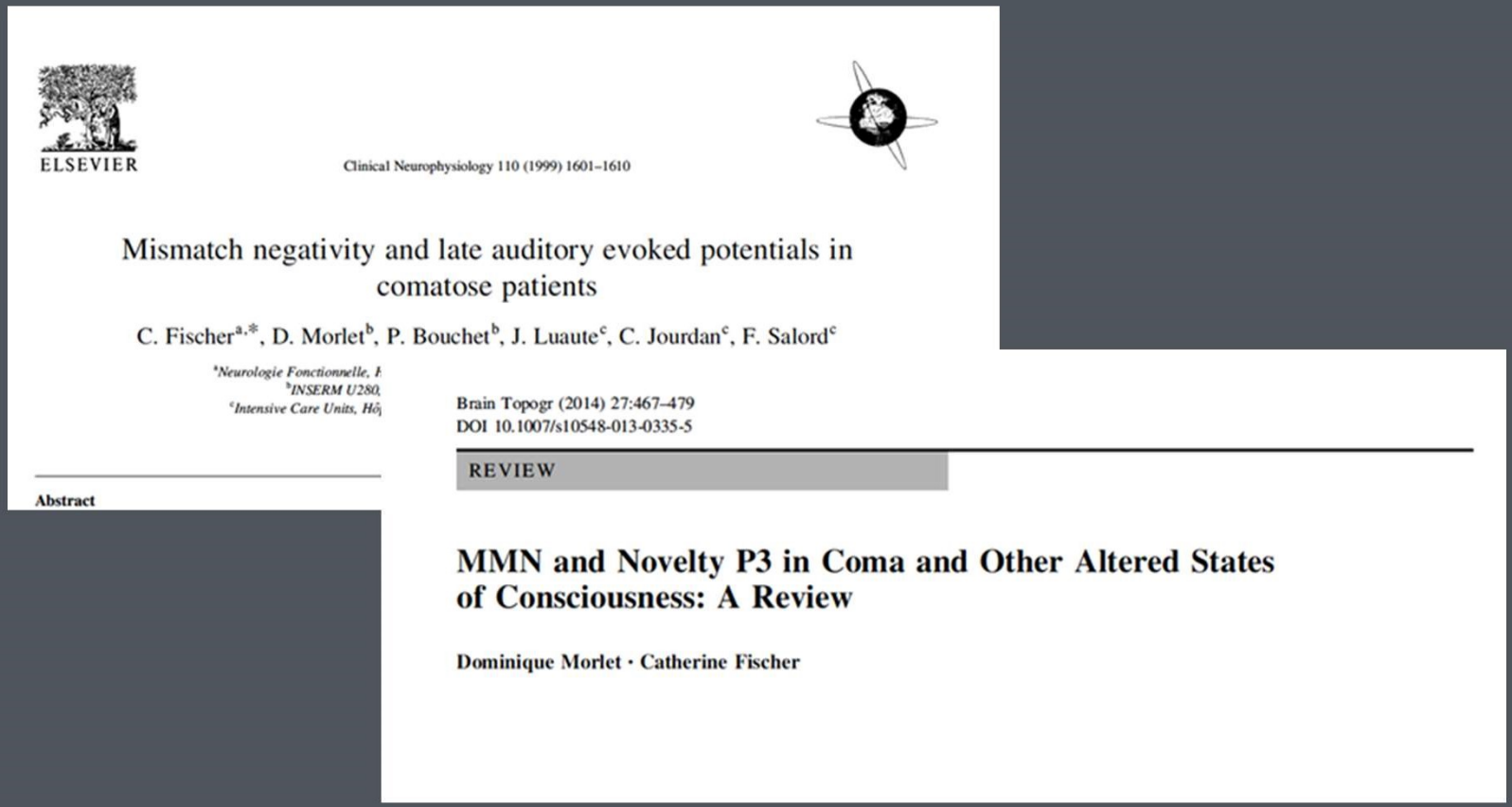


Continued improvement over 10 years.

Speech (singing) began 2 months after 2 test

Learning to walk in 2018.

# Mismatch Negativity in Coma



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Clinical Neurophysiology 110 (1999) 1601–1610

Mismatch negativity and late auditory evoked potentials in comatose patients

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Abstract

Brain Topogr (2014) 27:467–479
DOI 10.1007/s10548-013-0335-5

REVIEW

MMN and Novelty P3 in Coma and Other Altered States of Consciousness: A Review

Dominique Morlet · Catherine Fischer

# Mismatch Negativity in Coma



## A Machine Learning Framework for Automatic and Continuous MMN Detection With Preliminary Results for Coma Outcome Prediction

Narges Armanfard, Majid Komeili, James P. Reilly, and John F. Connolly

*Abstract*—Mismatch negativity (MMN) is a component of the event-related potential (ERP) that is elicited through an odd-ball paradigm. The existence of the MMN in a coma patient has a good correlation with coma emergence; however, this component can be difficult to detect. Previously, MMN detection was based on visual inspection of the averaged ERPs by a skilled clinician, a process that is expensive and not always feasible in practice. In this paper, we propose a practical machine learning (ML) based approach for de- approach that may prove useful in future, unrelated studies where ML methods are used.

*Index Terms*—Mismatch negativity detection, coma outcome prediction, machine learning, automatic detection of ERP components.

### I. Introduction

COMA is a state of prolonged unconsciousness that has a

# Mismatch Negativity in Coma

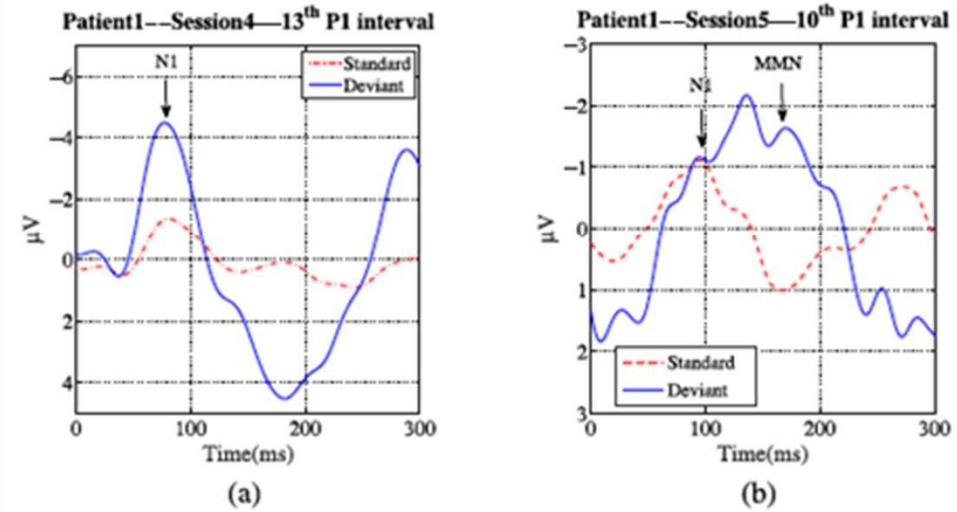
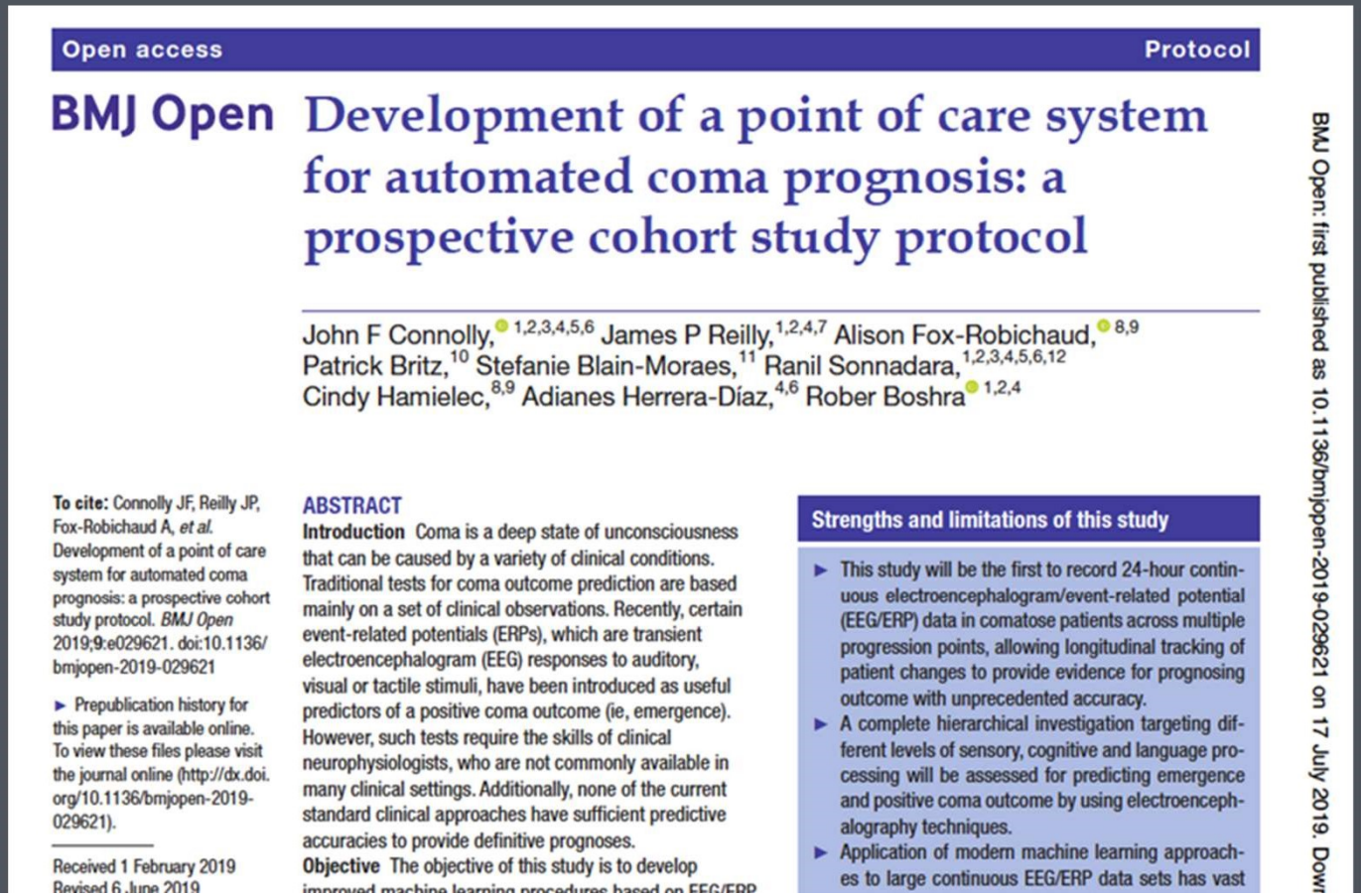



Fig. 4. Sub-session average signals corresponding to standard and deviant stimuli, at channel Fz, of patient 1 at P1 intervals (a) 13 of Session 4, and (b) 10 of Session 5.

# Mismatch Negativity in Coma



Open access Protocol

BMJ Open

## Development of a point of care system for automated coma prognosis: a prospective cohort study protocol

John F Connolly,[1,2,3,4,5,6] James P Reilly,[1,2,4,7] Alison Fox-Robichaud,[8,9] Patrick Britz,[10] Stefanie Blain-Moraes,[11] Ranil Sonnadara,[1,2,3,4,5,6,12] Cindy Hamielec,[8,9] Adianes Herrera-Díaz,[4,6] Rober Boshra[1,2,4]

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**ABSTRACT**

**Introduction** Coma is a deep state of unconsciousness that can be caused by a variety of clinical conditions. Traditional tests for coma outcome prediction are based mainly on a set of clinical observations. Recently, certain event-related potentials (ERPs), which are transient electroencephalogram (EEG) responses to auditory, visual or tactile stimuli, have been introduced as useful predictors of a positive coma outcome (ie, emergence). However, such tests require the skills of clinical neurophysiologists, who are not commonly available in many clinical settings. Additionally, none of the current standard clinical approaches have sufficient predictive accuracies to provide definitive prognoses.

**Objective** The objective of this study is to develop improved machine learning procedures based on EEG/ERP

**Strengths and limitations of this study**

- ► This study will be the first to record 24-hour continuous electroencephalogram/event-related potential (EEG/ERP) data in comatose patients across multiple progression points, allowing longitudinal tracking of patient changes to provide evidence for prognosing outcome with unprecedented accuracy.
- ► A complete hierarchical investigation targeting different levels of sensory, cognitive and language processing will be assessed for predicting emergence and positive coma outcome by using electroencephalography techniques.
- ► Application of modern machine learning approaches to large continuous EEG/ERP data sets has vast

# Other applications

- Spastic Quadriplegic Cerebral Palsy
- Stroke
- Autism (Non-Verbal)
- General Cognitive Health

# EEG in Concussion

- Preliminary work done in resting state, showing transient effects
- ERP work followed, showing effects primarily in the N2 and the P3

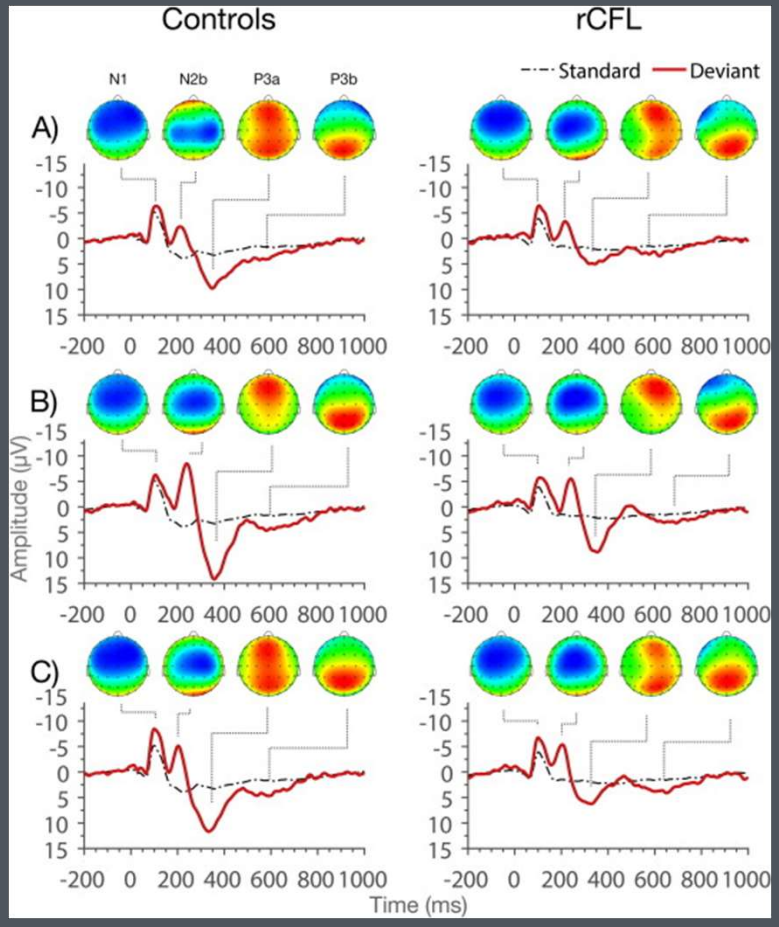
Gaetz et al., 2000; Gosselin et al., 2006; De Beaumont et al., 2007, 2009; Broglio et al., 2009

# What we know

- P3s are smaller and/or delayed in concussion beyond the acute stage
- Concussion effects are cumulative
- ERP effects don’t often correlate to symptoms
- N2s are “affected” after concussion

Gaetz et al., 2000; Gosselin et al., 2006; De Beaumont et al., 2007, 2009; Broglio et al., 2009

# Retired CFL players (Ruiter et al, 2019)

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## Disruption of function: Neurophysiological markers of cognitive deficits in retired football players

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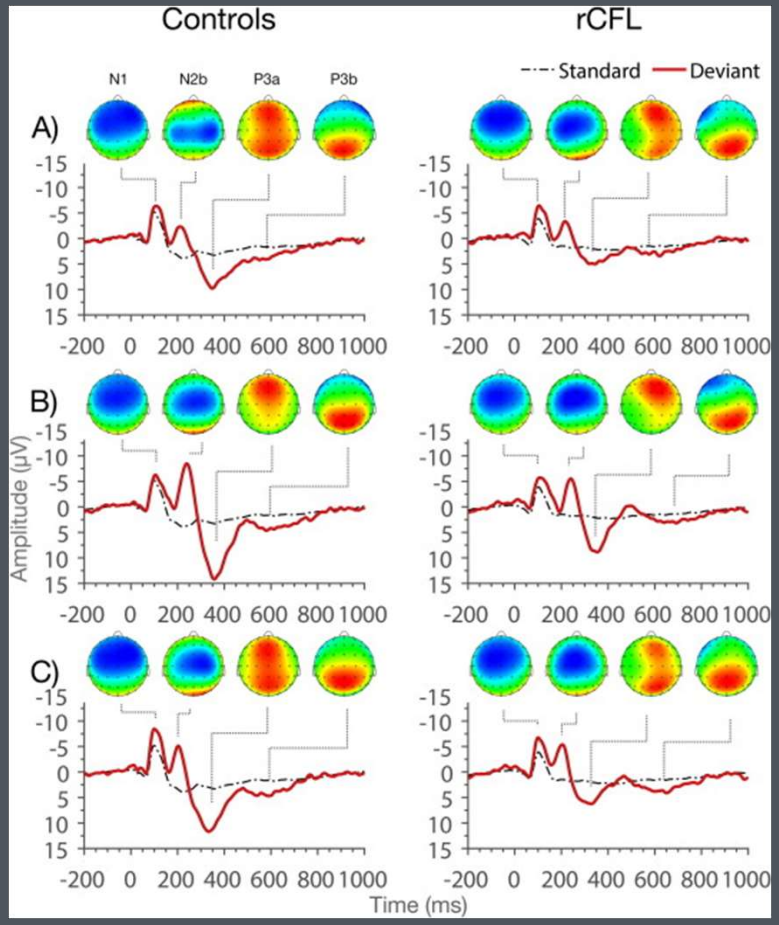
mTBI

HIGHLIGHTS

- For the first time, a deficit in a pre-attentive brain response has been linked to concussion.
- Former professional football players show significant deficits in Pain and Social Function.
- Former professional football players show elevated levels of depression and concussive symptoms.

ABSTRACT

# Retired CFL players (Boshra et al, 2019)






## From Group-Level Statistics to Single-Subject Prediction: Machine Learning Detection of Concussion in Retired Athletes

Rober Boshra, Kiret Dhindsa, Omar Boursalie, Kyle I. Ruiter, Ranil Sonnadara, Reza Samavi, Thomas E. Doyle, James P. Reilly, and John F. Connolly

*Abstract*—**There has been increased effort to understand the neurophysiological effects of concussion aimed to move diagnosis and identification beyond current subjective behavioral assessments that suffer from poor sensitivity. Recent evidence suggests that event-related potentials (ERPs) measured with electroencephalography (EEG) are persistent neurophysiological markers of past concussions. However, as such evidence is limited to group-level analyzes, the extent to which they enable concussion detection at the individual-level is unclear. One promising avenue of research is the use of machine learning to create quantitative predictive models that can detect prior concussions in individuals. In this paper, we translate the recent group-level findings from ERP studies of concussed individuals into a machine learning framework for performing single-subject prediction of past concussion. We found that a combination of statistics of single-subject ERPs and wavelet features yielded a classification accuracy of 81% with a sensitivity of 82% and a specificity of 80%, improving on current practice. Notably, the model was able to detect concussion effects in individuals who sustained their last injury as much as 30 years earlier. However, failure to detect past concussions in a subset of individuals suggests that the clear effects found in group-level analyses may not provide us with a full picture of the neurophysiological effects of concussion.**

*Index Terms*—**Event-related potentials, brain injury, electroencephalography, EEG, concussions, machine learning, explainable models.**

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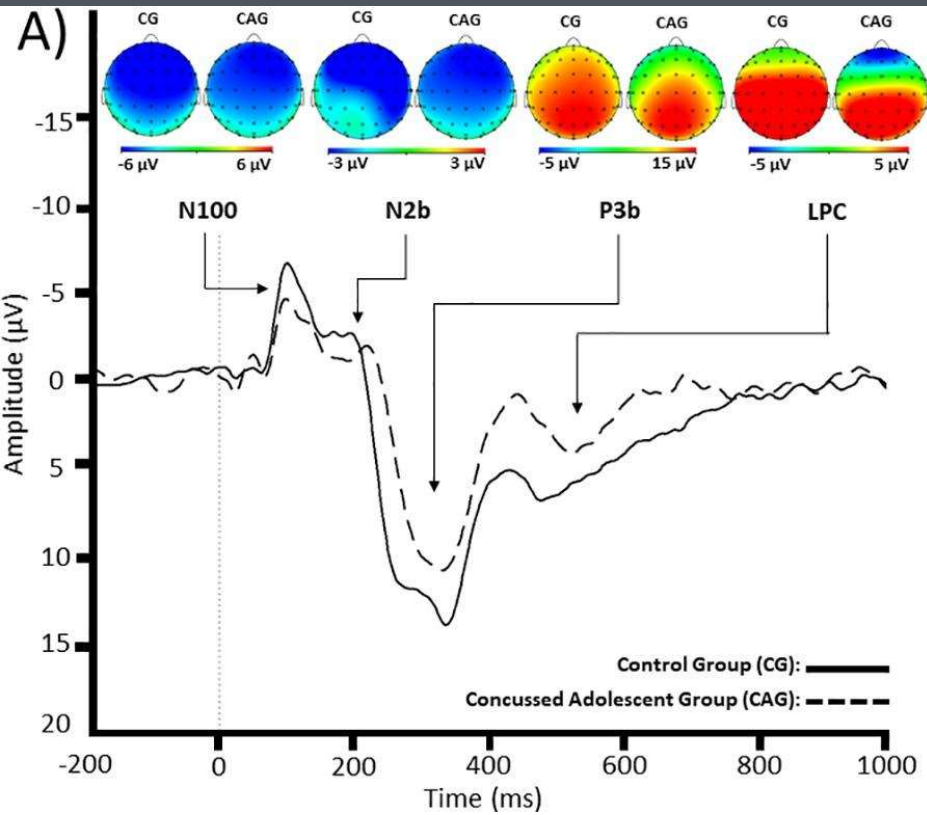
# Concussions in Adolescents (Ruiter et al, 2019)

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Brain Research

Volume 1746, 1 November 2020, 146998

Research report

## Neurophysiological markers of cognitive deficits and recovery in concussed adolescents

Kyle I. Ruiter [a, b], Rober Boshra [a, c, f], Carol DeMatteo [e], Michael Noseworthy [c], John F. Connolly [a, b, c, d, f]

Show more

https://doi.org/10.1016/j.brainres.2020.146998

# Research directions

- Progression and dynamics of injury
- Expand on ML tools for accurate individualized assessment
- Disentangling comorbidities
- Clinical interventions, PCS, and symptor resurgence

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OPEN

## Neurophysiological Correlates of Concussion: Deep Learning for Clinical Assessment

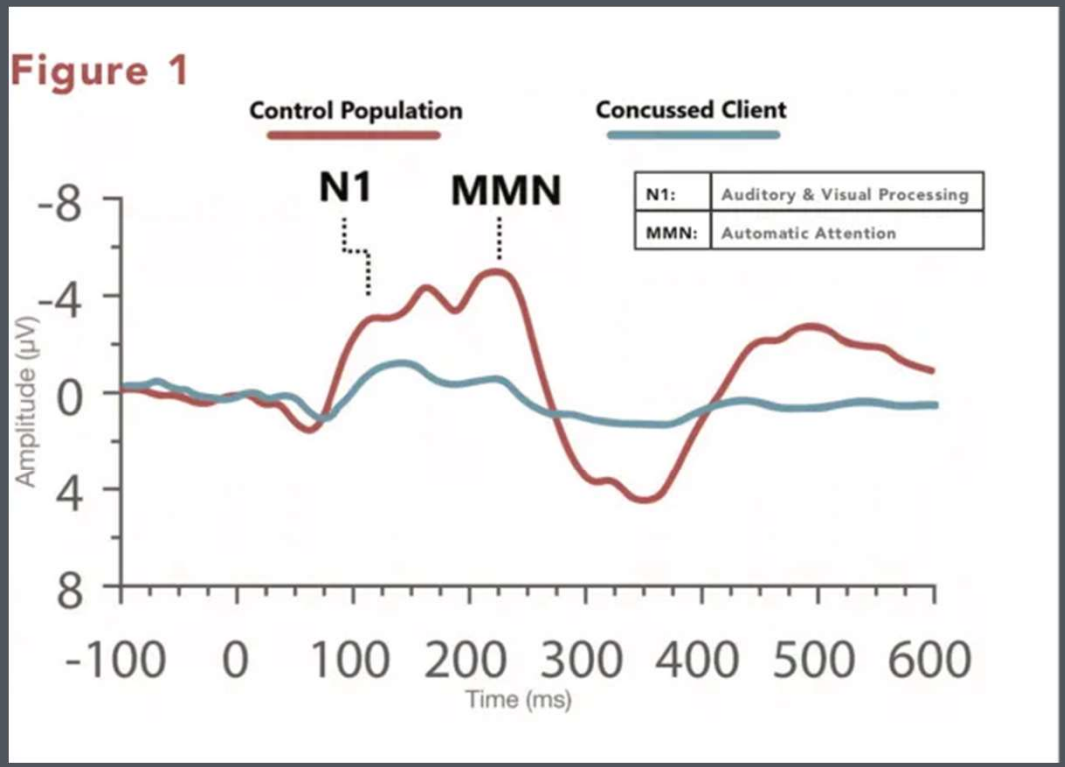
Rober Boshra[1,2,3*], Kyle I. Ruiter[1,4], Carol DeMatteo[5], James P. Reilly[1,2,3,6] & John F. Connolly[1,2,3,6,7*]

Concussion has been shown to leave the afflicted with significant cognitive and neurobehavioural deficits. The persistence of these deficits and their link to neurophysiological indices of cognition, as measured by event-related potentials (ERP) using electroencephalography (EEG), remains restricted to population level analyses that limit their utility in the clinical setting. In the present paper, a convolutional neural network is extended to capitalize on characteristics specific to EEG/ERP data in order to assess for post-concussive effects. An aggregated measure of single-trial performance was able to classify accurately (85%) between 26 acutely to post-acutely concussed participants and 28 healthy controls in a stratified 10-fold cross-validation design. Additionally, the model was evaluated in a longitudinal subsample of the concussed group to indicate a dissociation between the progression of EEG/ERP and that of self-reported inventories. Concordant with a number of previous studies, symptomatology was found to be uncorrelated to EEG/ERP results as assessed with the proposed models. Our results form a first-step towards the clinical integration of neurophysiological results in concussion management and motivate a multi-site validation study for a concussion assessment tool in acute and post-acute cases.

Traumatic brain injury (TBI) impacts upwards of 2.8 million individuals annually in the united states alone[1]. Concussions (henceforth used synonymously with mild TBI; mTBI) form a considerable subset of that figure and are defined as closed-head injuries that leave the affected with functional and cognitive deficits[2,3]. The current understanding of underlying mechanisms in concussion remains lacking, with echoing concerns both in the identification and management of the condition[4]. An expansive body of work has targeted the multiple facets of concussion, offering different means of elucidating the cognitive deficits caused by concussion and its co-morbid sequelae[5]. Electrophysiology is one tool with promising applications in concussions. Specifically, event-related potentials (ERPs) as recorded by electroencephalography (EEG) have shown persistent changes in concussed individuals in the post-acute stage and decades after insult[6–10].

ERPs are non-invasively-recorded indices of cognitive function[11]. The P300, a positive-deflecting response

# Applying ERPs to Clinical Practice

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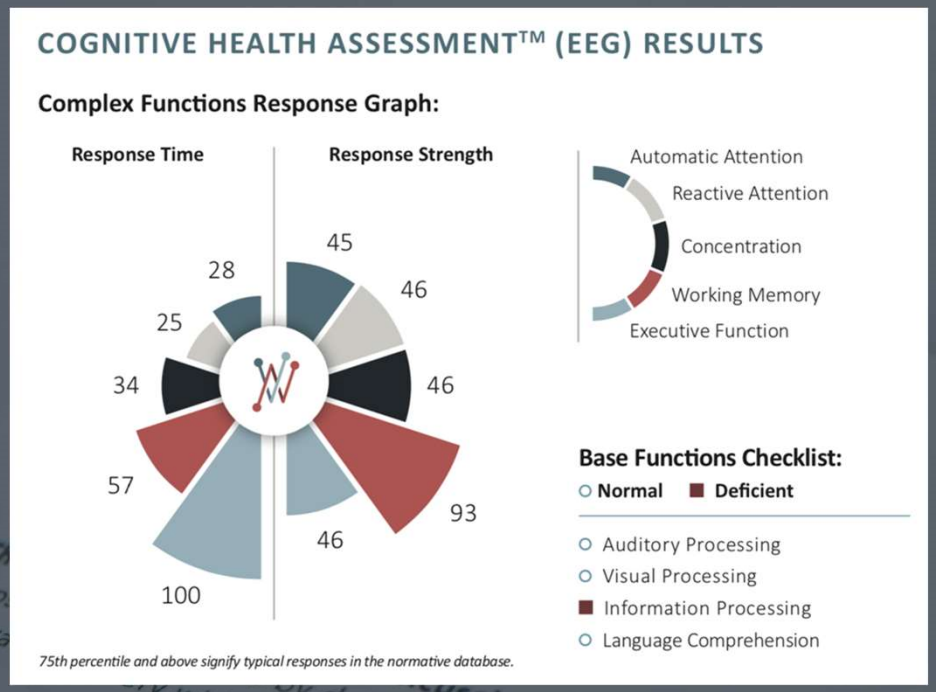
# THE REPORT: *FUNCTIONS GRAPH*




**Response Strength:** The amount of electrical activity

- Cognitive Function ability within a specific cognitive domain (e.g., Working Memory)

**Response Time:** When the response occurs

- Information processing

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# Informing Rehabilitation

- What rehabilitation methods should be used?
- Which methods are producing the best results?

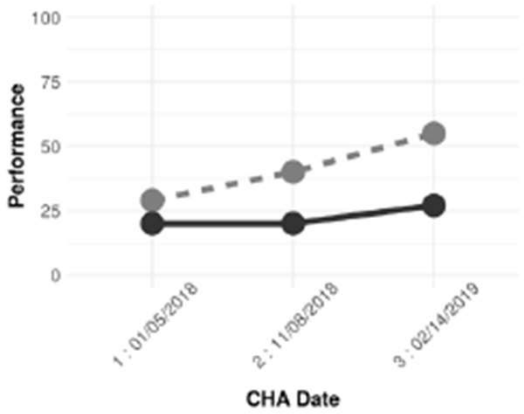
# THE REPORT:
## *FUNCTIONAL PROGRESS TRACKER*

### COMPLEX FUNCTIONS CHECKLIST:

**Compared to the previous assessment's results, the patient's complex functional performance indicated the following changes in neural responses:**

Response latency
Response Strength

**Automatic Attention**




| | | | |
|---|---|---|---|
| Response Time | ☐ Remained consistent | ☑ Improved | ☐ Declined |
| Response Strength | ☐ Remained consistent | ☑ Improved | ☐ Declined |

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Thank you
QUESTIONS?
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