





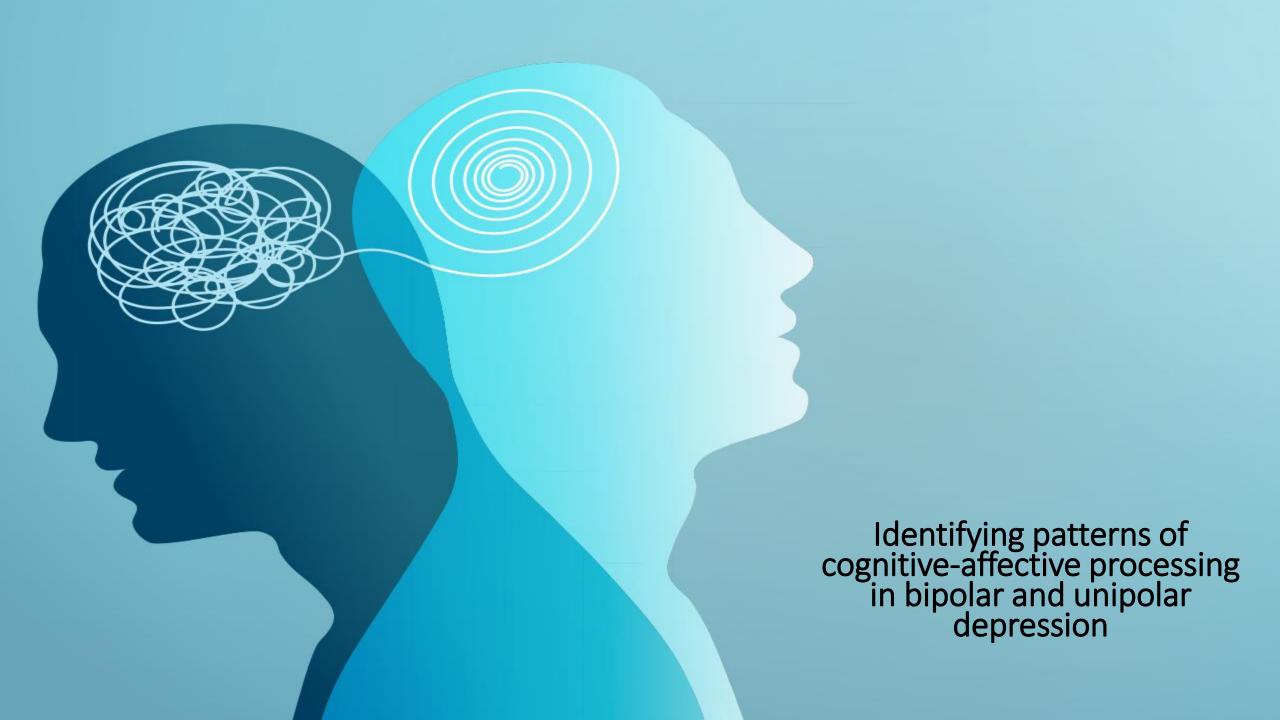
Cognitive Neuroscience in Clinical Context: Insight from 3 studies

Medha Amarnath Nair, MA | PhD Student in Clinical Neuropsychology @ SFU 11 February 2025

Agenda

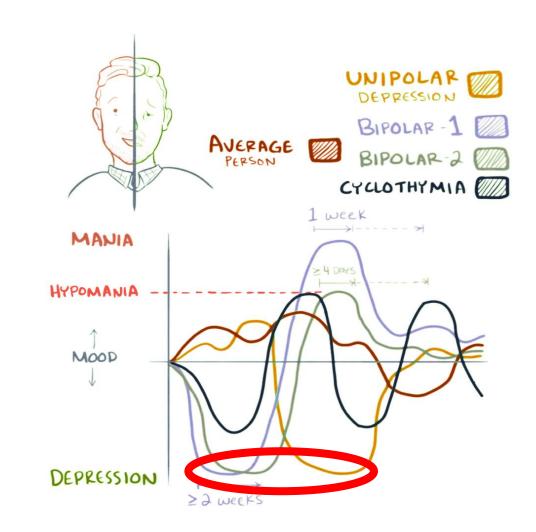
- Cognitive-affective processes in Major Depressive and Bipolar Spectrum Disorders
- 2. Examining biased attentional processes post-concussion
- 3. The role of cognitive neuroscience in clinical neuropsychology





Differentiating Unipolar and Bipolar Depression

- Clinically, it is difficult to differentiate BSDs from MDD during a major depressive episode
- BSDs can require different pharmacological treatment approaches than MDD
- Objective, behavioural markers can help with differential diagnosis



Why might behavioural markers help?

• Clinical features exist, but rely primarily on self-report





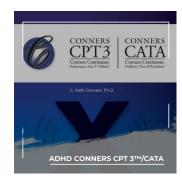






fear-related symptoms, anxious temperament

• Behavioural tasks measuring cognitive-affective processes have been used to aid in the classification of other mental health conditions



continuous performance tests



facial emotion recognition tasks

Which cognitive-affective processes and why?

Reward Sensitivity

Differences in the tendency to **detect** and **derive** pleasure

- Anticipatory reward sensitivity
- Consummatory reward sensitivity

Patterns of differential neural activation in MDD vs.

BSD (Caseras et al., 2013; Chase et al., 2013; Satterthwaite et al., 2015; Wakatsuki et al., 2022)



Which cognitive-affective processes and why?

Facial Emotion Judgment

Ability to detect and differentiate facial emotional expressions



- General deficits in categorization and differential of all emotions in MDD and BD (Kohler et al., 2011)
- MDD: better at identifying facial expressions vs. BSD (Ruihua et al., 2021)
- BSD: require more intense expressions (Scahefer et al., 2010)

Which cognitive-affective processes and why?

Self-referential processing

- Cognitions about the self
 - Positive

Overall limitation of the existent research: there are few direct comparisons between aspects of cognitive-affective processing in people with MDD and BSDs, and even fewer amongst those who are currently acutely depressed.

No direct comparison yet

The Current Study

1. Aim: Investigate if and how reward sensitivity, facial emotion judgment, and self-referential processing differ between acutely depressed people with MDD and BSD, as well as healthy controls.

2. Hypotheses:

- 1. Reward sensitivity: MDD < BSD < CTL
- 2. Facial emotion recognition: MDD > BSD
- 3. Self-referential processing: MDD = BSD > CTL



Methods

Participants:

MDD* n = 72BSD n = 26CTL n = 27

Inclusion Criteria:

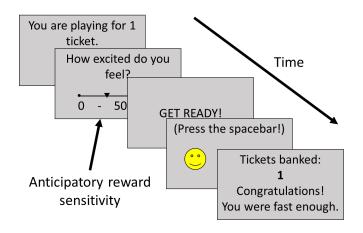
- 18 70 years of age
- Pts.: Primary DSM-5 diagnosis of MDD, BDII or OS-BD with current MDE based on MINI
- CTL: no current or past psychiatric disorder
- No psychotropic medications

Exclusion Criteria:

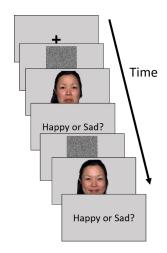
- Meeting criteria for SUD
- No proficiency in English
- Have a neurological disorder

All participants completed the MINI, MADRS, YMRS, and 3 behavioural tasks:

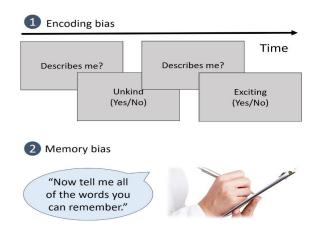
Monetary Incentive Delay Task



Facial Emotion Labelling Task

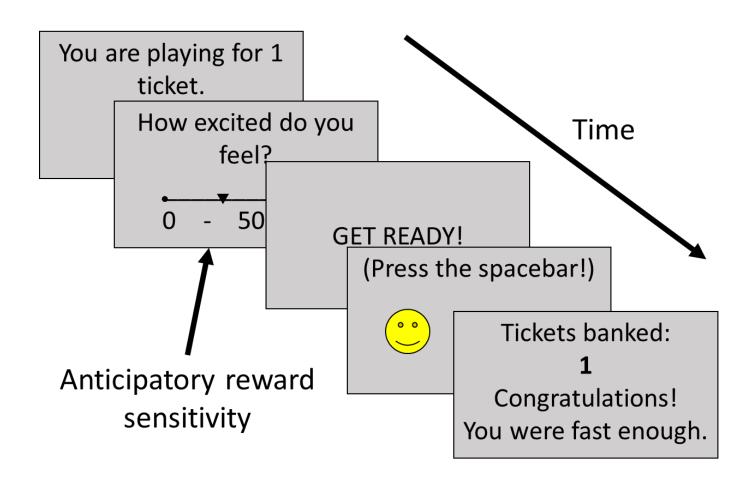


Self-referential Encoding and Memory Task

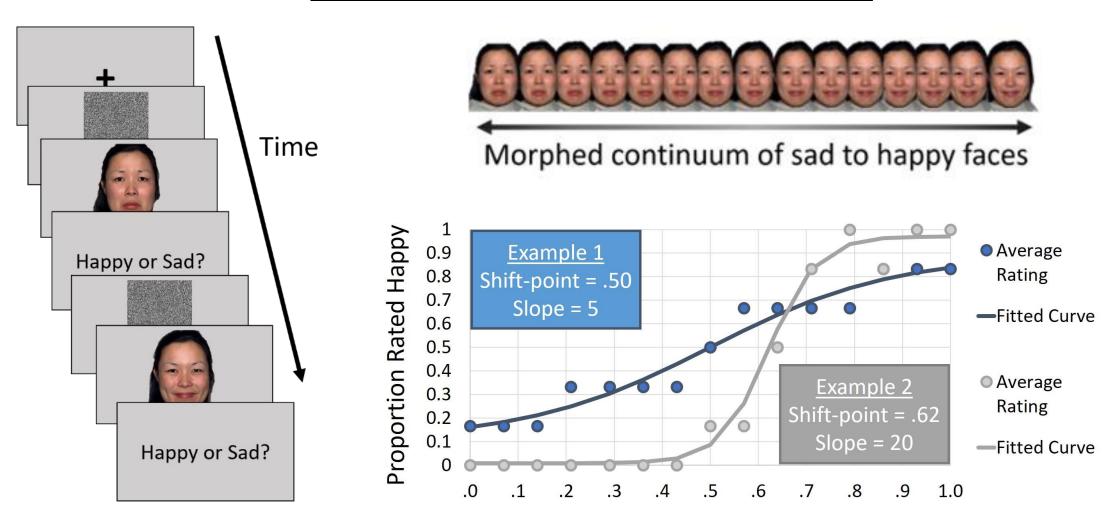


^{*}participants were recruited from 2 sources

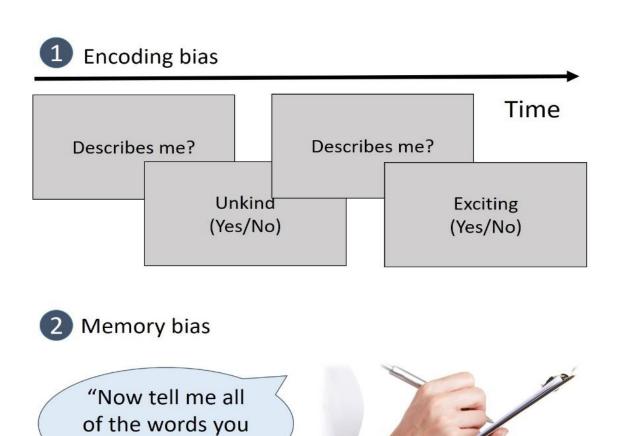
Monetary Incentive Delay Task



Facial Emotion Labelling Task

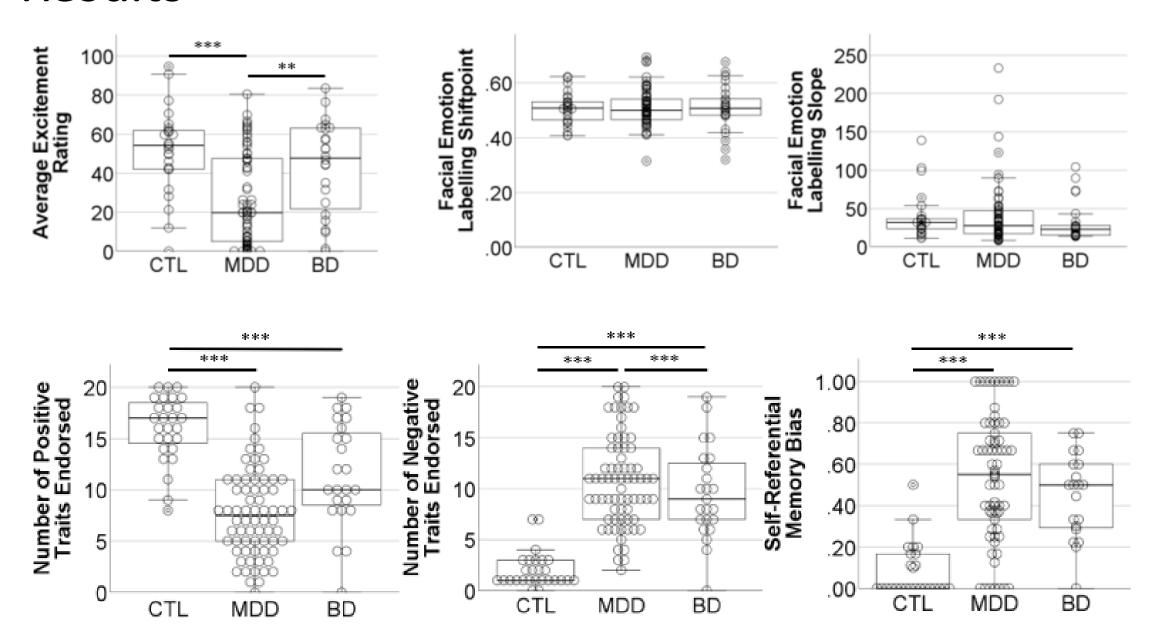


Self-Referential Processing Task



can remember."

Results



Terpstra et al., 2024 (in review at Journal of Affective Disorders)

Results

Reward Sensitivity



• Individuals with MDD had sig. lower anticipatory reward sensitivity than BSD participants (p = .006, d = .73) and control participants (p < .001, d = 1.14)

• Participants with BSD did not differ from controls in anticipatory reward sensitivity (p = .454,)

Facial Emotion Recognition



• MDD/BSD/CTL groups did not have significant differences in labelling faces as sad vs. happy or sensitivity to the changes in expressed emotions

Self-Referential Processing



- Individuals with MDD endorsed sig. fewer positive traits than the BSD (p = .002, d = .80) and CTL groups (p < .001, d = 2.01)
- Individuals with BSD endorsed sig. fewer positive traits compared to CTLs (p < .001, d = 1.11)
- MDD and BSD did not differ sig. for number of negative traits (p = .535) or negative self-referential memory bias (p = .311)

Conclusions and Implications





Defining cognitive-affective processing subgroups in major depressive and bipolar spectrum disorders

We know that...

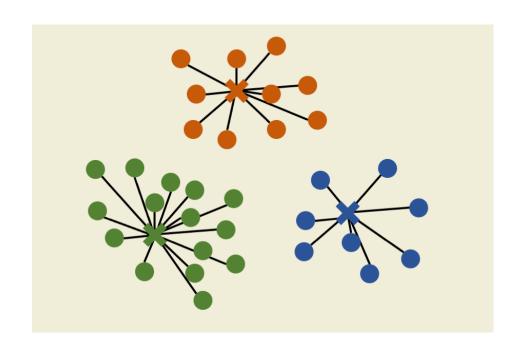
- Differences in cognitive-affective processes exist among currently-depressed individuals with MDD vs. BSD.
- **As a group**, individuals with BSD ascribe more positive traits to themselves compared to those with MDD and CTLs and have greater anticipatory reward sensitivity compared to people with MDD.
- But, how much heterogeneity might there be?



Why might there be heterogeneity?

- Previous research that has explored clusters of cognitive-affective processing across the mood spectrum include participants who are not acutely depressed
 - Among those studies, they looked primarily at facial recognition tasks

The Current Study



Aim: To identify data-driven subgroups based on cognitive-affective processing amongst acutely depressed individuals with MDD and BSD

Methods

Participants:

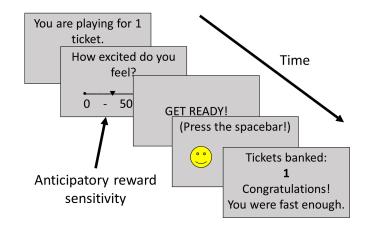
MDD* n = 65 BSD n = 19 CTL n = 25

Inclusion Criteria:

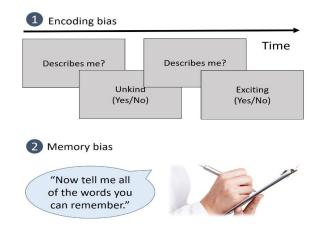
- 18 70 years of age
- Pts.: Primary DSM-5 diagnosis of MDD, BDII or OS-BD with current MDE based on MINI
- CTL: no current or past psychiatric disorder
- No psychotropic medications

- Meeting criteria for SUD
- No proficiency in English
- Have a neurological disorder

Monetary Incentive Delay Task



Self-referential Encoding and Memory Task

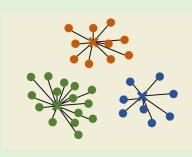


Exclusion Criteria:

^{*}participants were recruited from 2 sources

Analyses

k-means clustering



1. Identify clusters/sub-groups

one-way ANVOA



2. Assess cluster differences in task performance as well as clinical (MADRS score) and demographic variables

chi-square



3. Assess proportion of diagnoses across clusters

Results – Identifying Clusters

k = 2 clusters was the optimal solution (as per gap statistic).



On visual inspection, those in **Cluster 1** had:

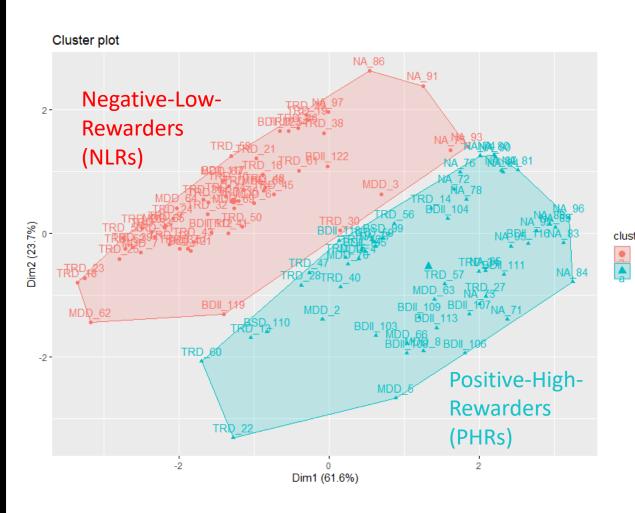
- Lower reward anticipation
- Higher negative encoding
- Lower positive encoding
- More negative memory bias

Those in Cluster 2 had:

- Higher reward anticipation
- Lower negative encoding
- Higher positive encoding
- Less negative memory bias

We proceeded to test the significance of these differences →

Results – Assessing Cluster Differences



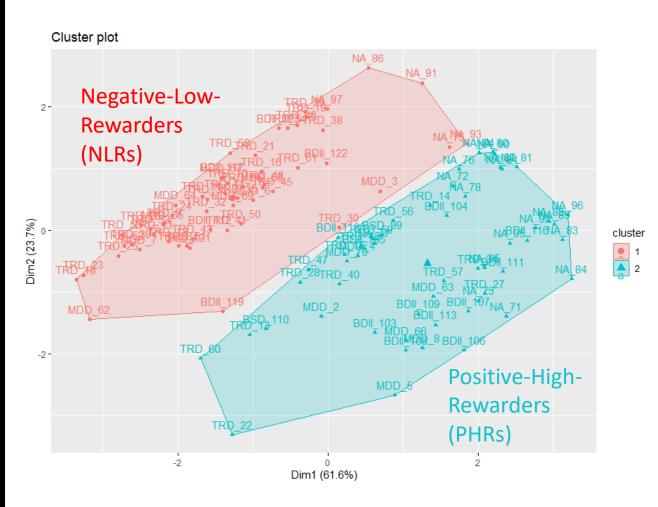
	n	MDD	BDII/BSD	HC (n,	Age (M)	Gender	MADRS (M)	Reward	Positive	Negative	Memory
		(n. %	(n, % grp)	96)		(%		Anticipation	Encoding	Encoding	Bias (M)
		grp)				male)		(M)	(M)	(M)	
Group	56	45	6 (11)	5 (9)	39.82	34	27.36	12.28	7.63	10.34	.52
1		(80)									
Group	53	20	13 (25)	20 (37)	36.26	37	18.15	57.45	12.89	7.21	.30
2		(37)									

Significance testing revealed:

- Group 1 had significantly <u>lower</u> anticipatory reward sensitivity (F = 413.470, p < .001) and positive self-referential encoding (F = 35.291, p < .001) as well as significantly <u>higher</u> negative self-referential coding (F = 9.950, p < .002) and negative memory bias (F = 14.134, p < .001), compared to Group 2.
- Accordingly, we named:
 - Group 1: "Negative-Low-Rewarders" (NLRs)
 - Group 2: "Positive-High-Rewarders" (PHRs)

As well, MADRS score amongst patients did not differ significantly in both groups.

Results – Assessing Proportions

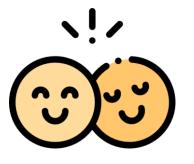




More MDD participants were **NLRs** vs. PHRs (χ^2 =9.615, p=.002)



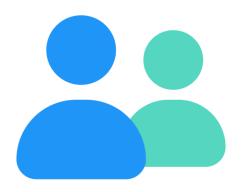
There was **no significant difference** in **BSD** participants who were NLRs vs. PHRs $(\chi^2=2.579, p=.108)$

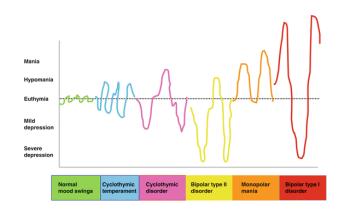


More HC participants were PHRs vs. NLRs $(\chi^2=9.000,p=.003)$

Conclusions and Implications

NLRs and PHRs represent distinct cognitiveaffective processing subgroups.

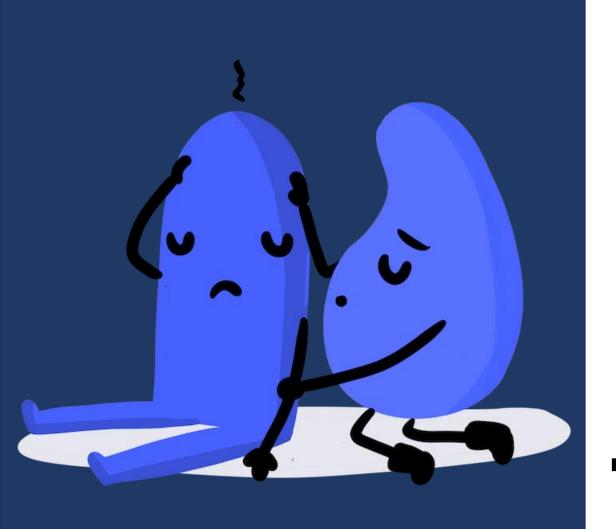




There is heterogeneity in cognitive-affective processes across the mood spectrum

Some patients (MDD, BSD) cluster together with most healthy controls.

Personalized treatment approaches are important.



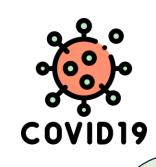
Investigating Attentional Biases and the Fear-Avoidance Model in Adults with Persistent Post-Concussion Symptoms

A little thought experiment to start....

Think back to March 2020, when it all went down

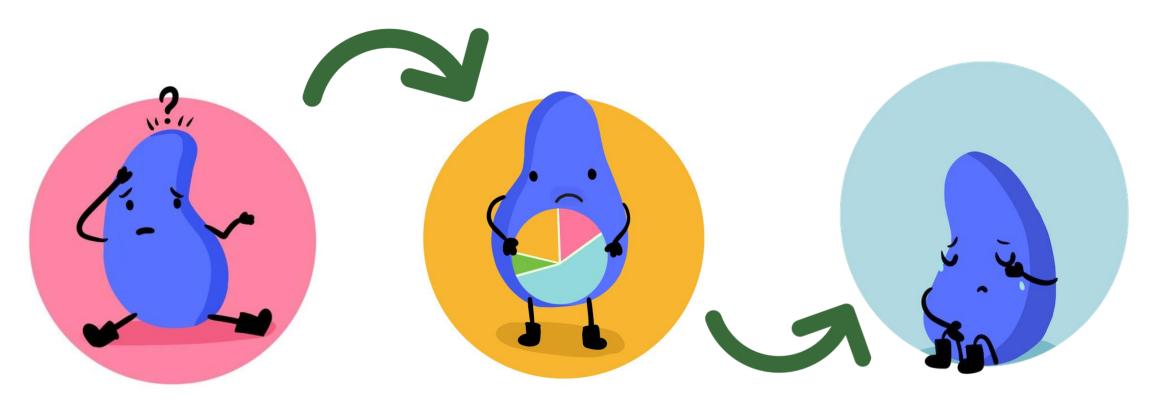
Oh no!!! I just sneezed.

That was the second time today. Is it COVID-19? Or is it a cold? Or maybe it's just allergies??? BUT WHAT IF IT'S COVID?????



That person couldn't stop coughing on the bus. AND THAT PERSON IN THE GROCERY STORE!!! Maybe I got it from them. I'M ONLY GOING TO GET GROCERIES DELIVERED FROM NOW ON!!!

Concussion & Persistent Post-Concussion Symptoms (PPCS)



Worldwide, more than 30 million individuals sustain a concussion each year

18-31% of those who sustain a concussion experience persisting symptoms (PPCS), lasting months to even years

PPCS has a significant impact on overall wellbeing and quality of life

Why do some people develop PPCS, but others don't?

Injury-Related
Characteristics (e.g.,
GCS score, duration of
PTA, LOC, significant
imaging findings, etc.)



Psychosocial Factors
(e.g., preinjury
mental health
concerns, anxiety
sensitivity, low social

support, etc.)



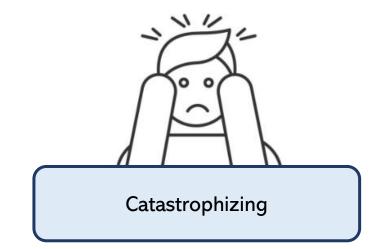






Disuse; Deconditioning; Depressive Symptoms

The Fear-Avoidance Model of Concussion





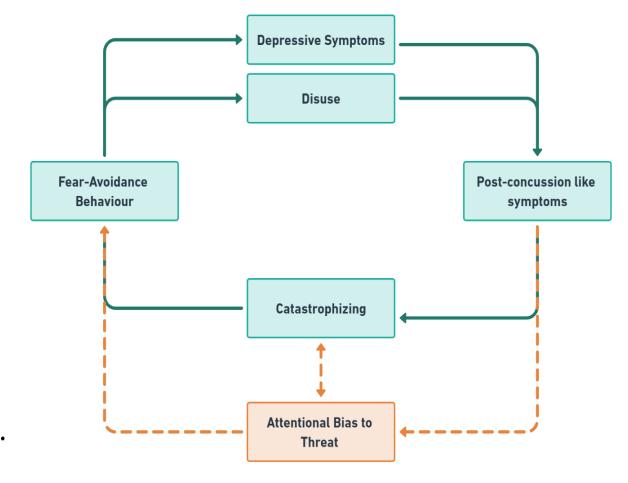


Post-concussion like symptoms

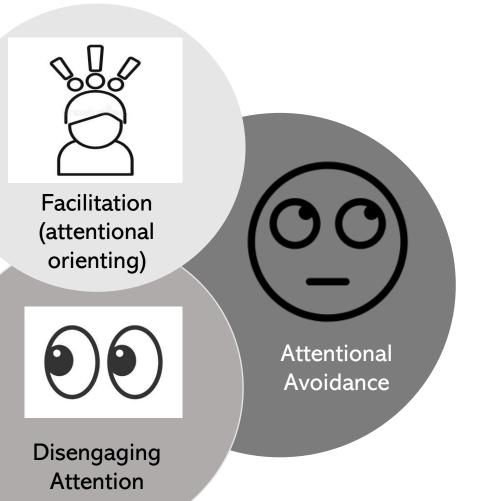


Is there a role of attentional bias?

- Attentional bias could be one cognitive process which underlies the maladaptive thought patterns and behaviours in the FAM
- In the FAM of chronic pain, associations between FAM constructs and attentional biases have been identified.
- No studies have yet explored the connection between attentional biases and FAM constructs in PPCS.



What are attentional biases, anyways?





The potential for the role of attentional bias...

relationships between attentional bias and:



Symptom Severity



Pain Catastrophizing



Fear-Avoidance Behaviour

Measuring Attentional Biases

There are several experimental tasks which can measure attentional biases...

emotional stroop tasks



spatial cueing tasks

dot probe tasks visual search tasks

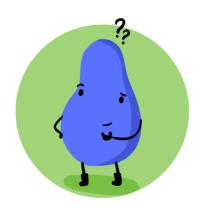


... each of which can measure different types of attentional biases and have varying levels of robustness and reliability.

Aims



To establish whether or not attentional biases exist in PPCS





To investigate if attentional biases, in terms of difficulty disengaging from pain-related stimuli, exist in individuals with PPCS, using an attentional blink task



To investigate if attentional biases, in terms of preferential looking towards symptom-relevant stimuli, exist in individuals with PPCS, using a mouse-movement task which simulates eye-tracking, Mouseview.js.

Hypotheses



Participants with PPCS will show greater difficulty disengaging attention pain faces versus neutral faces, compared to those who have recovered from their concussion.

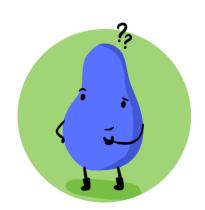


Participants with PPCS will demonstrate longer dwell time on symptom relevant images (i.e., images expressing general threat and illness threat), compared to those who have recovered from their concussion.

Aims



To describe correlations between attentional biases and fear-avoidance model constructs (i.e., fear-avoidance behaviour, pain-catastrophizing, and increased post-concussion symptoms).





To describe correlations between attentional biases as measured on the attentional blink task (in terms of difficulty disengaging from pain-related stimuli), and fear-avoidance model constructs.



To describe correlations between attentional biases as measured on the gaze-time task (in terms of preferential looking towards symptom-relevant stimuli), and fear-avoidance model constructs.

Hypotheses



Participants who demonstrate greater attentional biases in difficulty disengaging attention from pain-related stimuli will also report greater severity of the fear-avoidance model constructs (i.e., symptom severity, pain-catastrophizing, and fear-avoidance behaviour).



Participants who spend more time fixating attention on symptomrelevant stimuli will also report greater severity of the fear-avoidance model constructs (i.e., symptom severity, pain-catastrophizing, and fearavoidance behaviour).

Participants

- Two groups:
 - Persistent Post-Concussion
 Symptoms (PPCS) group
 - Recovered group
- Recruited through undergraduate research recruitment pool at Simon Fraser University (SFU)

Inclusion Criteria PPCS Group:

- Aged between 18-50 years
- Sustained a self-reported concussion at least one month ago
- RPQ score with 2 or more symptoms with moderate severity or higher

Recovered Group:

- Aged between 18-50 years
- Sustained a self-reported concussion at least one month ago
- RPQ score with 1 or fewer symptoms with moderate severity or higher



Exclusion Criteria

- Have a severe or unstable physical health condition (e.g., non-concussion related chronic pain)
- Not fluent in English
- No access to a computer with Internet connection for the duration of the study

Attentional Bias Experimental Tasks

Target 1: Pain or Neutral Face Lag 3 Target 2: Bird, Flower, or Furniture





order counterbalanced

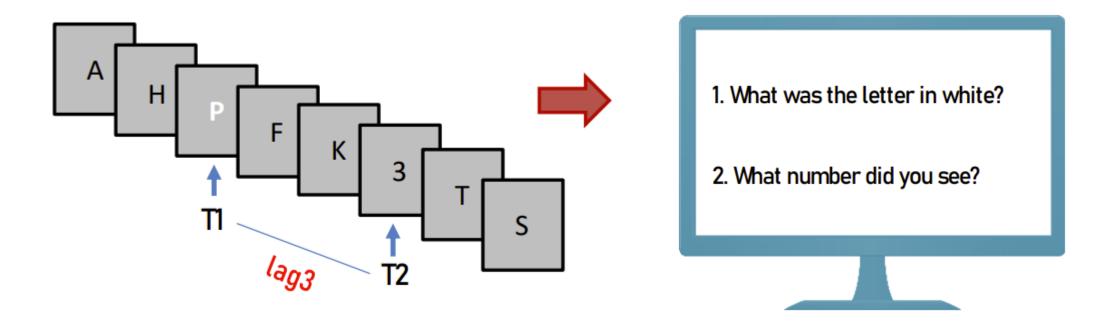
Attentional Blink Task

Dwell/Gaze-Time Task

Questionnaires

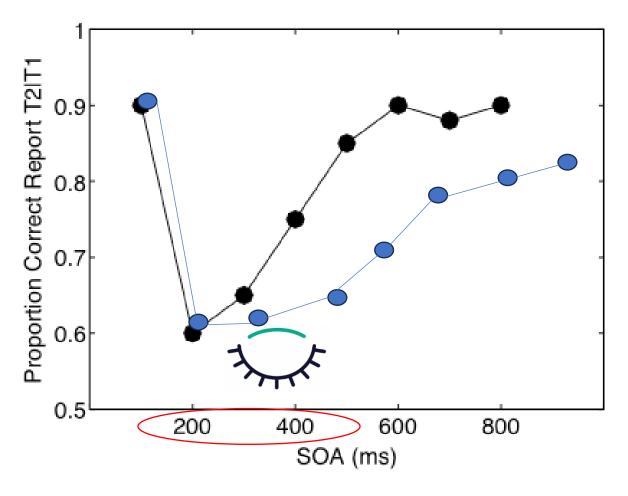
- Rivermead Post-Concussion
 Symptom Questionnaire (RPQ)
- Pain-Catastrophizing Scale (PCS)
- Fear-Avoidance Behaviour after Traumatic Brain Injury (FAB-TBI)
- Generalized Anxiety Disorder 7 (GAD-7)
- Patient Health Questionnaire 9 (PHQ – 9)

The Attentional Blink Task



- RSVP stream = Rapid Serial Visual Presentation stream
- Target 1 (T1): Letter in white that participant needs to identify
- Target 2 (T2): Number that participant needs to identify
- **Distractors**: Letters between targets
- Lag: Distance between targets

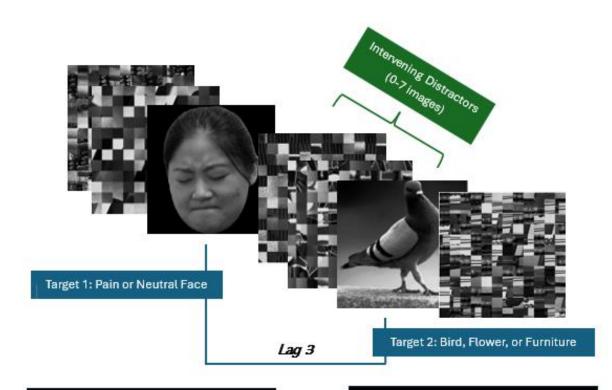
The Attentional Blink Task (cont'd.)



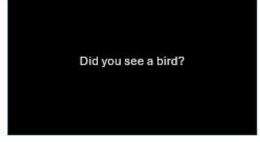
"Greater difficulty disengaging"

The Attentional Blink Task

- RSVP stream = Rapid Serial Visual Presentation stream
- Target 1 (T1): First picture that participant needs to identify
 - Pain or Neutral Face
- Target 2 (T2): Second picture that participant needs to identify
 - Bird, Flower or Furniture
- **Distractors**: Images between targets
 - Scrambled images of objects
- Lag: distance between images
 - Lag 3 and 7 examined



Was the face pain or neutral?



Gaze-Time Task (mouseview.js)

- Simulates eye-tracking tasks with mouse movement
- Side-by-side images with overlay
 - Neutral-Neutral
 - General Threat Neutral
 - Concussion Threat Neutral
- Gaze Time = time spent viewing each image (amount of time mouse within image coordinates)

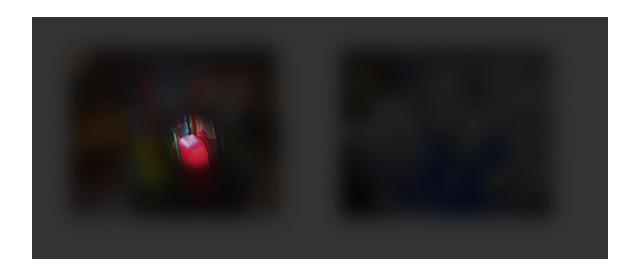


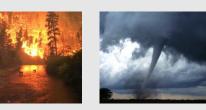
Image Examples







Neutral



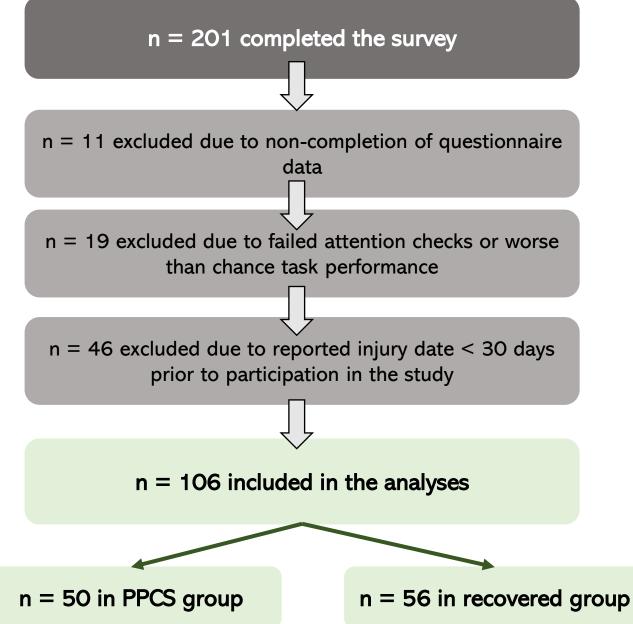
General Threat





Concussion-Threat

Participant Flow



Sample Characteristics

Selected Demographic and Injury Characteristic Descriptive Statistics

	Total Sample	PPCS Group	Recovered Group
Age [M, (SD)]	19.5 (2.1)	19.5 (2.2)	19.6 (2.1)
Gender (n, % women)	72 (67.9)	39 (78.0)	34 (60.7)
Time Since Injury [months - M, (SD)]	23.7 (31.5)	25.3 (35.7)	22.2 (29.1)
Mechanism of Injury, n (%)			
Sports and Recreation	72 (67.29)	36 (72.0)	36 (64.2)
MVA	14 (13.2)	5 (10.0)	9 (16.1)
Fall	13 (12.2)	4 (8.0)	9 (16.1)
Workplace Injury	2 (1.9)	1 (2.0)	1 (1.8)
Other	5 (4.7)	4 (8.0)	1 (1.8)















Our sample was relatively young...

...and predominantly female...

...consisting mostly of people who had concussions a long time ago...

...mainly resulting from sports.

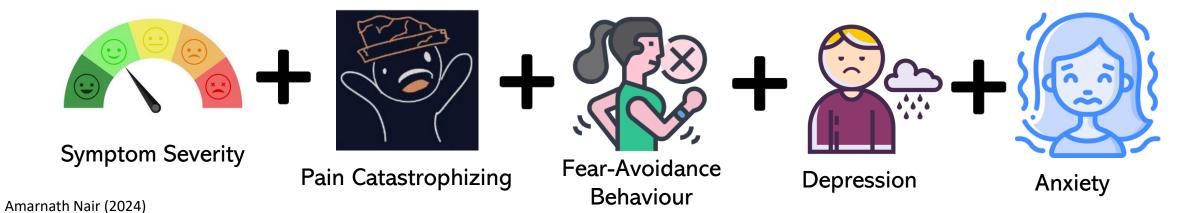
Amarnath Nair (2024)

Questionnaires

Questionnaire and Task Performance Descriptive Statistics

	Scale Range	Total Sample	PPCS Group	Recovered Group
Symptom Severity (RPQ) [M, (SD)]	0-52	17.2 (13.3)	27.0 (11.6)	8.5 (7.2)
Pain Catastrophizing Scale (PCS) [M, (SD)]	0-52	13.8 (12.3)	18.6 (13.3)	9.5 (9.6)
Fear-Avoidance Behaviour after Traumatic Brain Injury (FAB-TBI) [M, (SD)]	0-64	17.2 (6.0)	19.5 (5.1)	15.2 (6.1)
Depression (PHQ-9) [M, (SD)]	0-27	8.2 (5.2)	10.6 (5.0)	6.0 (4.5)
Anxiety (GAD-7) [M, (SD)]	0-21	7.5 (4.9)	9.4 (5.1)	5.8 (4.2)

Overall, both our PPCS group and our recovered group demonstrated low levels of fear-avoidance model constructs, including:



Task Performance

Task Performance Descriptive Statistics

	Total Sample	PPCS Group	Recovered Group
Attentional Blink Task - Lag 3 Accuracy [M %, (SD)]			
Pain Faces	64.1 (16.2)	63.6 (15.2)	64.6 (17.1)
Neutral Faces	68.5 (13.4)	68.2 (14.0)	68.7 (12.9)
Attentional Blink Task - Lag 7 Accuracy [M %, (SD)]			
Pain Faces	64.1 (16.2)	63.6 (15.2)	64.6 (17.1)
Neutral Faces	68.5 (13.4)	68.2 (14.0)	68.7 (12.9)
Gaze Time Task - Gaze Time (ms) [M, (SD)]			
Neutral	3172.9 (682.9)	3314.2 (672.9)	3046.8 (672.7)
Concussion Threat	3724.2 (977.7)	3821.5 (955.9)	3637.4 (997.3)
General Threat	3748.3 (980.2)	3814.8 (992.7)	3688.9 (973.)

Group Differences in Attentional Blink Task Performance

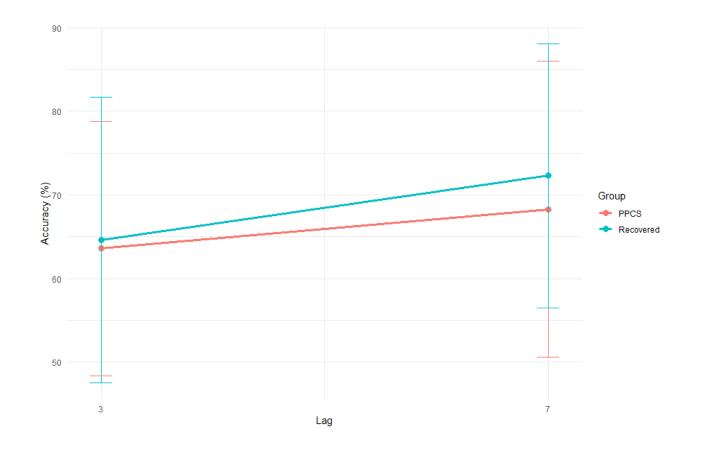
Neutral Faces

- Significant main effect of lag (F = 20.270, p = <.001, $\eta_p^2 = .159$) on accuracy of detecting the T2 image when the image at T1 was a neutral face
- No main effect of group (F = .239, p = .626, $\eta_p^2 = .002$).
- There was no group x lag interaction (F = .458, p = .500, η_p^2 = .004)

As expected, we saw the attentional blink phenomenon in both the PPCS group and recovered group for neutral faces.

And, as expected, we did not see that there was any differences in attentional blink between the two groups for neutral faces.





We did not see differences between the PPCS and recovered group in difficulty disengaging attention from neutral faces.

Group Differences in Attentional Blink Task Performance

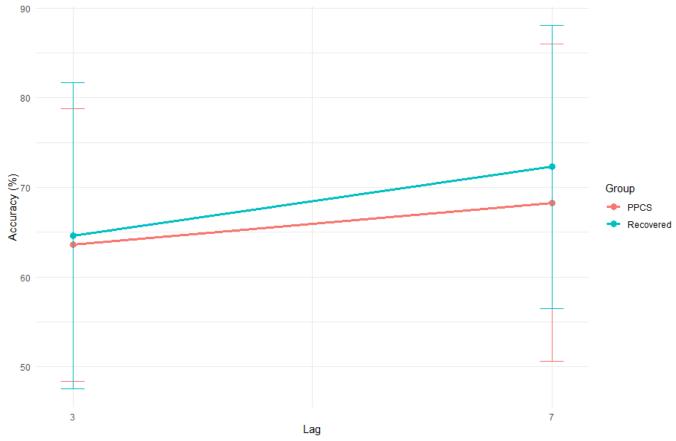
Pain Faces

- Significant main effect of lag (F = 22.580, p = <.001, $\eta_p^2 = .174$) on accuracy of detecting the T2 image when the image at T1 was a pain face
- No main effect of group (F = .741, p = .391, $\eta_p^2 = .007$).
- There was no group x lag interaction (F = 1.091, p = .299, η_p^2 = .010)

As expected, we saw the attentional blink phenomenon in both the PPCS group and recovered group for pain faces.

However, against what we were expecting, we did not see that there was any differences in attentional blink between the two groups for pain faces.





We did not see differences between the PPCS and recovered group in difficulty disengaging attention from pain faces.

Correlations between Experimental Task Performance and Fear-Avoidance Model Constructs

- In the full sample, a weak positive correlation between anxiety and time spent viewing concussion images was identified (r = .23, p = .019).
- No correlations between attentional biases to pain stimuli on the attentional blink task (i.e., quantified by Pain-Neutral Difference Score: lag 7 pain accuracy – lag 7 neutral accuracy) and fearavoidance model constructs were identified.





Greater anxiety was associated with more time spent viewing concussion-threat images.

Sensitivity Analysis



We saw that a small number of people (n = 4) in our Recovered group had a high amount of fear-avoidance behaviour...



...and a substantial subset in our PPCS group (n = 36) had fear-avoidance behaviour below the 50th percentile...



...so we re-ran our analyses, grouping by fear-avoidance behaviour instead of symptom persistence.

FAB-TBI Cutoff: 22.5

High Avoidance: n = 34

Low Avoidance: n = 72

Sensitivity Analyses – What did we find?

Like in the primary analyses,

Attentional Blink Task

- There was no significant group x lag interaction for the neutral images (F = .341, p = .561, η_p^2 = .003)
- There was no significant group x lag interaction for the pain images (F = 1.649, p = .202, η_p^2 = .016)

Gaze-Time Task

• There was no significant group x image type interaction (F = 1.616, p = .204, $\eta_p^2 = .030$)

Ultimately, the sensitivity analysis did not reveal that grouping participants by fear-avoidance behaviour instead of symptom persistence impacted our results in any way.

So, what does it all mean?

Individuals with PPCS in our sample didn't demonstrate attentional biases towards symptom relevant stimuli.

BUT THIS WASN'T WHAT WE WERE EXPECTING, SO WHY?

The attentional blink task may not be sensitive enough to detect the group differences.

The concussion images we chose may not adequately threatening enough.



Our sample consisted of participants who were 1) quite removed from their injury, and 2) did not endorse high levels of FAM constructs

Pain faces may not have been a full representation of symptom relevant stimuli in the attentional blink task.

There may be more complex attentional engagement and avoidance processes at play.

Limitations



Experimental Tasks & Stimuli Used

- No pre-existing concussion threat image stimuli
- Robustness of emotional variation of attentional blink task



Participant Characteristics

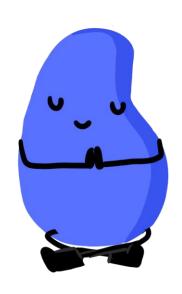
- Largely undergraduate sample
- Non-treatment-seeking
- Lower overall levels of fearavoidance model constructs
- Large variation in time since injury
- Mostly sports-related concussion



Power

 Significantly underpowered for correlational analyses performed

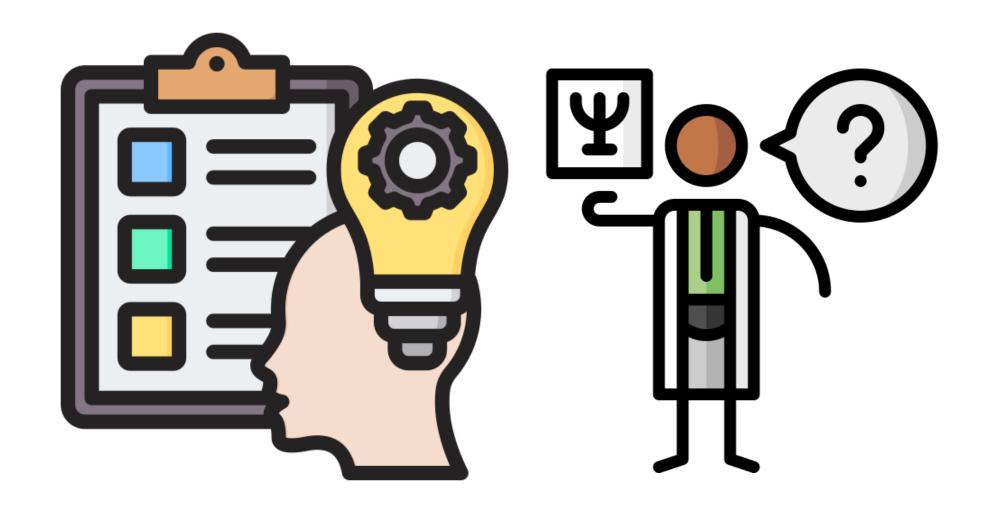
Implications and Possible Next Steps



Those with persisting symptoms but more removed from their concussion and experiencing lower fear-avoidance model constructs do not appear to demonstrate heightened attentional biases compared to those who have recovered fully from their concussion

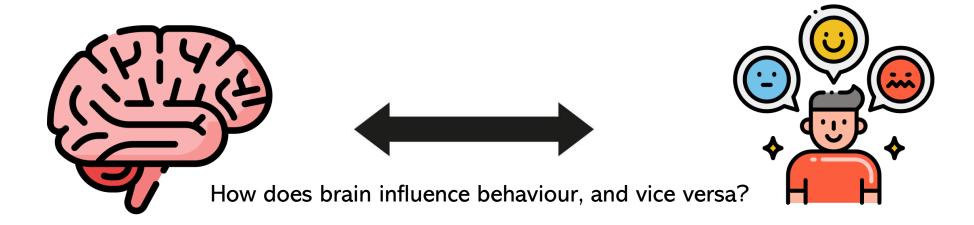


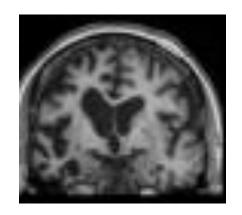
Assessing a more fearavoidant sample



A little aside on clinical neuropsychology....

What's Clinical Neuropsychology?









A Collection of Different Fields...



Behavioural Neurology

 Aspects of behaviour are hardwired into the nervous system



Neuropsychiatry

 There exist psychiatric manifestations of neurological disease



Neuropsychology

 We can use psychological tests to characterize the nature of neurological disease

...all with an emphasis on the relationship between brain and behaviour

"where an individual scientist falls on this spectrum is often an accident of training rather than a result of knowledge, skills, or interest"



Alfred Binet (1857-1911)



Ward C. Halstead (1908-1968)



Ralph M. Reitan (1922-2014)



Alexander R. Luria (1902-1977)



William Milberg

A brief history of clinical neuropsychology...and how cognitive neuroscience has come to play a growing role in our field

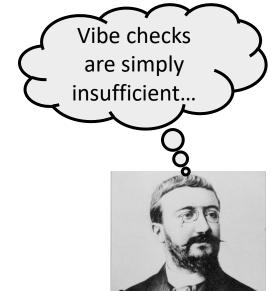
From the Early Days to Present Day...

- In the early days, things were more dichotomous:
 - Either your brain was "normal" or it was "abnormal", based on the clinician's clinical judgment
- Then came **Binet** who emphasized three things in testing & test development:









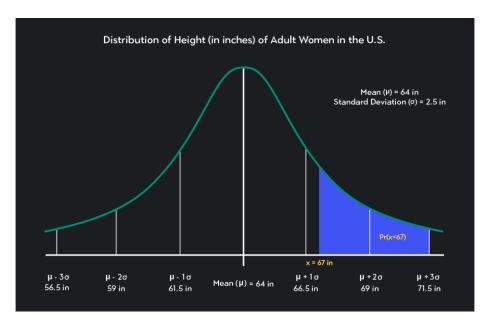
From the Early Days to Present Day...

 Halstead took this work further, emphasizing the use of a test battery with different categories of potential kinds of brain damage.



Reitan introduced the concept of norms





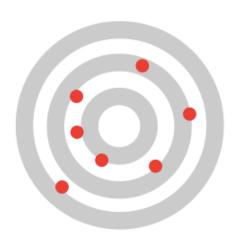
Then came along Luria...

- He emphasized sensitivity to individual differences (e.g., age, sex, handedness, patient's history/background, location of lesion)
- He also emphasized a more flexible or adaptable approach to testing
 - e.g., using the same battery of tests for everyone vs. performing a rapid general screen and then focusing on the most salient problems, adding in or removing certain tests as necessary
- There was criticism for more standardization towards this more clinical approach (e.g., standardizing the process which we record and observe qualitative observations, symptoms, etc.)
- There was also a push for understanding not just the final answer someone came to, but how they did it.
 - This approach is now also known as the **process approach** in neuropsychology

The Role of Cognitive Neuroscience in Clinical Neuropsychology

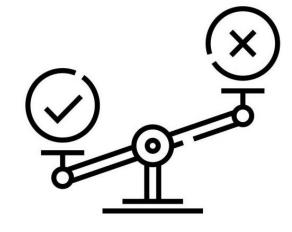
- The emphasis on standardization, norms, psychometric criteria etc. tells us a lot about how one individual might be different from the rest
- But it doesn't tell us much about the conceptual, fundamental, theoretical underpinnings of what we're measuring with our tests
- Cognitive Neuroscience elucidates the mechanisms and theories behind the clinical syndromes we assess for and treat in clinical neuropsychology
- We also often draw from tasks & paradigms developed in cognitive neuroscience research and use them in clinical research and practice

Barriers to the Implementation of New Cognitive Paradigms into Clinical Practice



psychometric properties

does it measure XYZ well? for who?



determining relative utility

does it measure XYZ better than an existing tool?



discriminant and predictive validity

Can it predict a person's prognosis?

Does it help us tell apart different disorders?



cooperation across fields

Who do we need to make it happen?

