Congrès

INTERVENTION PRÉCOCE ET PRÉVENTION DES PSYCHOSES

Connaissances actuelles et orientations futures

Conference

EARLY INTERVENTION IN PSYCHOSIS

Current knowledge and future directions

Neurocognition and Neuroimaging Correlates of Persistent Negative Symptoms

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McGill

PEPP MONTRÉAL

NEGATIVE SYMPTOMS

Anhedonia

Loss of Pleasure

Asociality

Decreased Social Drive

Avolition

Lack of Motivation

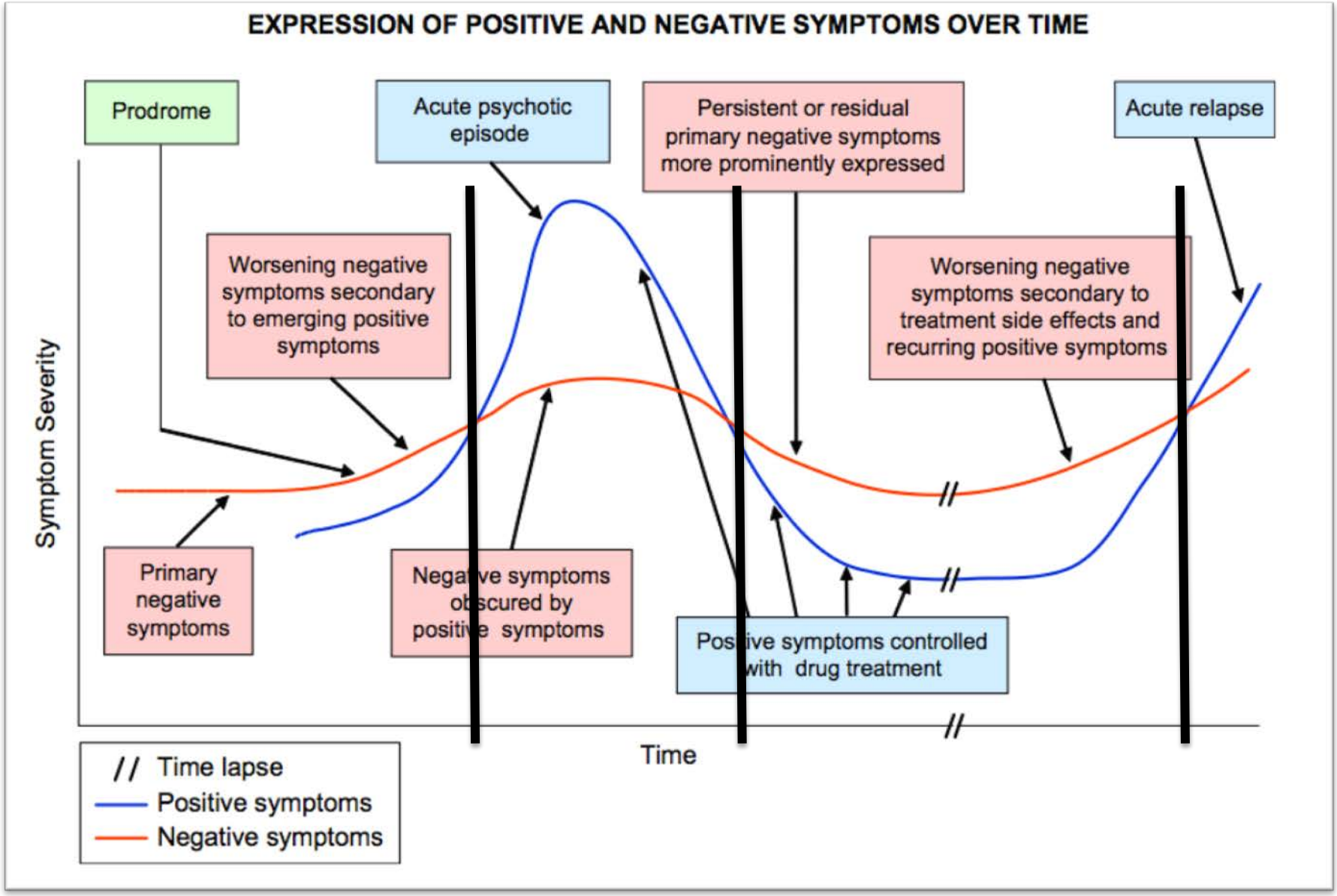
Blunted Affect

Emotional Unresponsiveness

Alogia

Impoverished Speech

Kirkpatrick et al. 2006



Moller 2007 – *Eur Psychiatry*

WHAT IS THE IMPACT OF PERSISTENT NEGATIVE SYMPTOMS?

1. Contribute to poor functional and clinical outcome outcome (Ho et al. 1998; Bodnar et al. 2008)

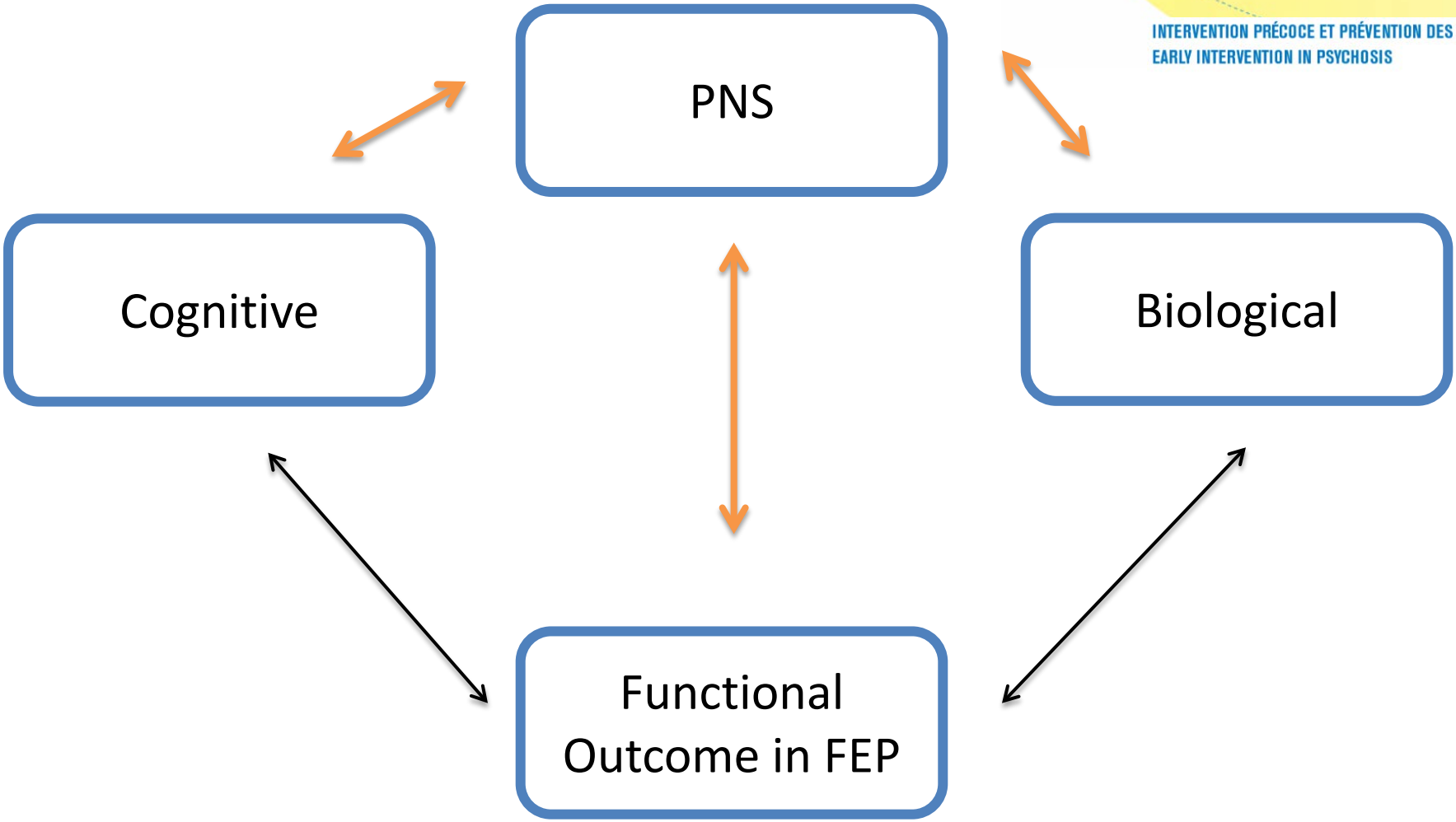
2. Related to elevated levels of treatment discontinuation (Galderisi et al. 2012)

3. Associated with cognitive deficits (O'Leary 2000)

WHY STUDY PNS IN FEP?

1. Avoid confounds due to illness chronicity
   - Antipsychotic medications
   - Sedentary lifestyle
   - Institutionalization

2. Identify them earlier and provide appropriate treatment


PNS
Cognitive
Biological
Functional
Outcome in FEP

PERSISTENT NEGATIVE SYMPTOMS?

1. Include both ***primary*** and ***secondary*** negative symptoms

2. Identified using any validated negative symptoms scale (i.e. SANS, PANSS)

3. Estimated prevalence in FEP: 15-40%

Buchanan 2007; Malla et al. 2004

CRITERIA FOR PNS

Hovington et al. 2012; Buchanan 2007; Malla et al. 2004

Score ≥ 3 on SANS on a ***min of 1 global item of the SANS***

Have moderate NS at "initial baseline" (month 3)

Min. depressive + extrapyramidal symptoms

At least moderate severity of NS

Min. positive symptoms

PNS

Maintain moderate NS for min of 6 months

PREVALENCE OF PNS IN FEP

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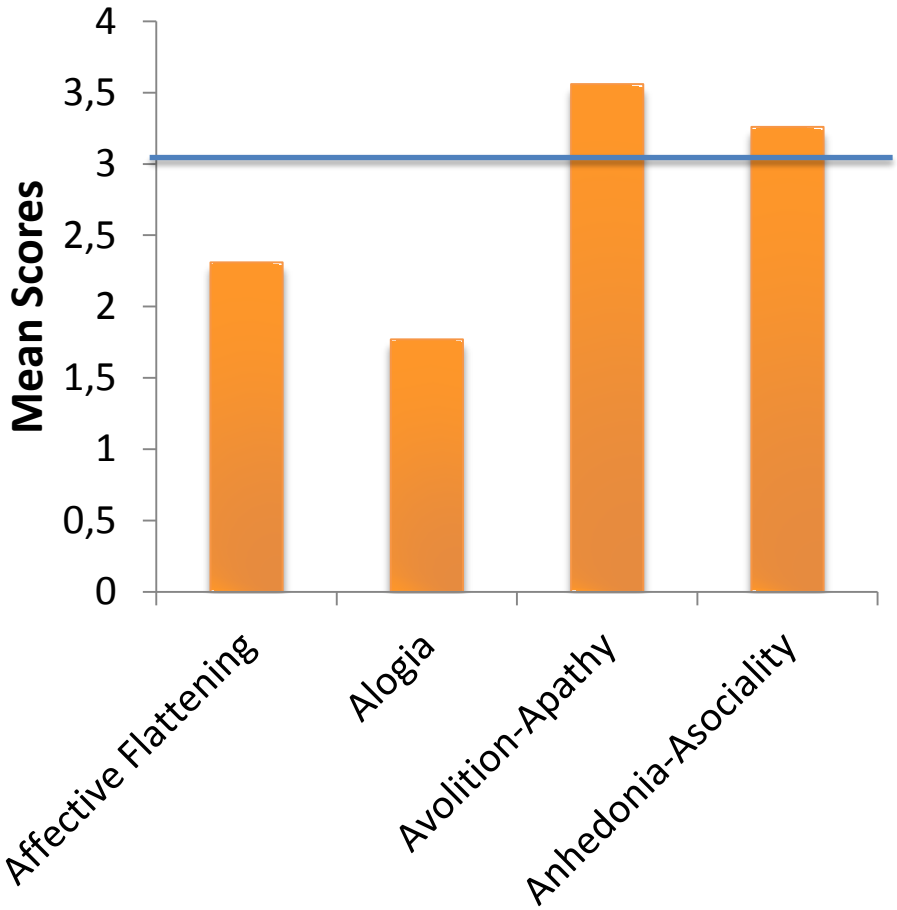
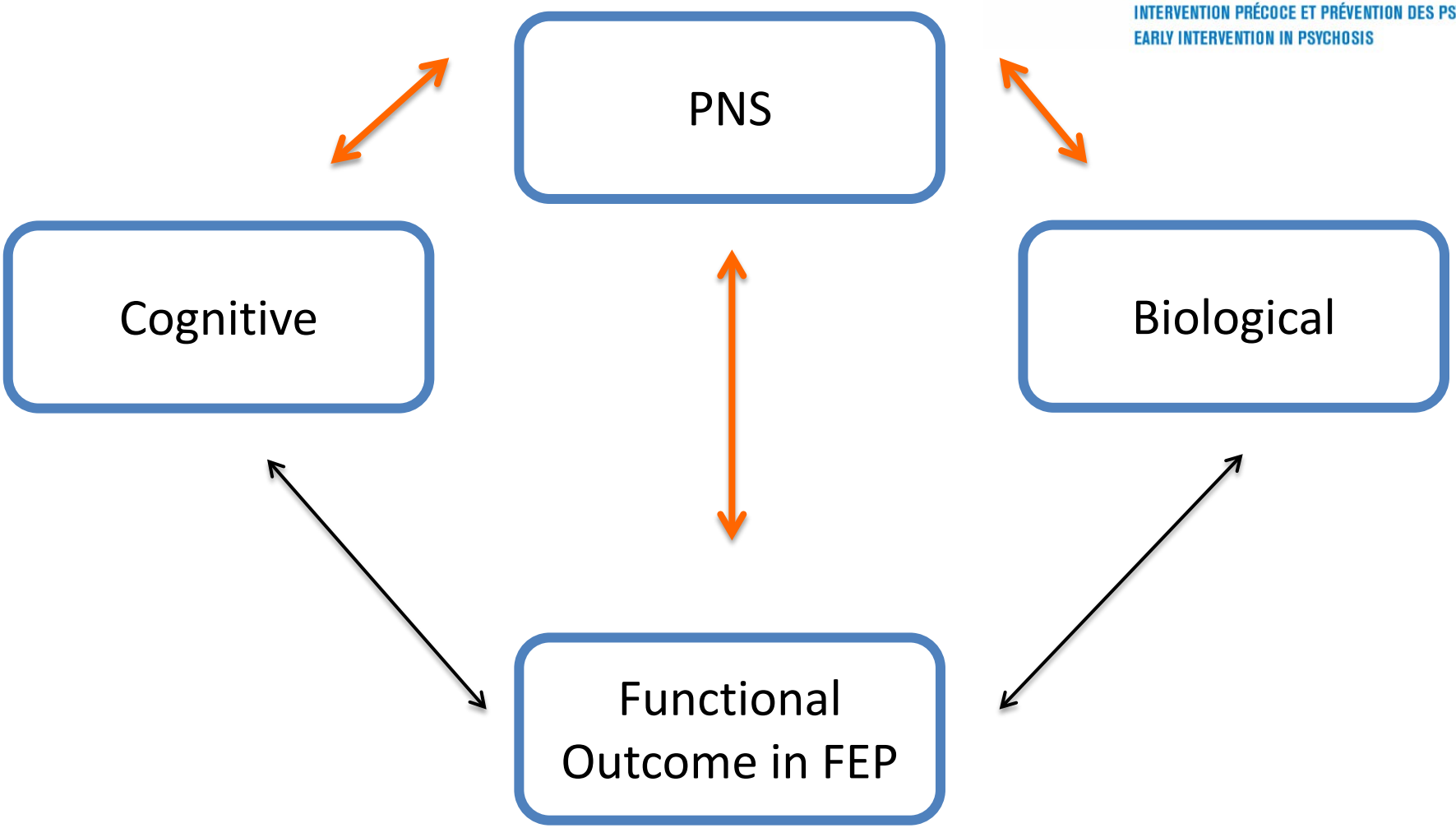
Prevalence of PNS in FEP: 27%

Patients with PNS had poorer functional outcome (at month 12) compared to patients without PNS



Hovington et al. 2012


PNS
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PNS AND MEMORY

Patients with more severe NS = ↓ neurocognitive performance

(Bora et al. 2009; McDowd et al. 2011; Puig et al. 2008)

1. Avolition correlated with verbal memory impairments

(Brebion et al. 2000)

2. Alogia correlated with poorer working memory and verbal fluency

(Berenbaum et al. 2008)

LONGITUDINAL RELATIONSHIP

- Most studies provide evidence for relative stability of cognition over time in FEP
  (Becker 2010;Bowie 2005)

- Others have shown that improvements in negative symptoms are paralleled with cognitive improvements (Censits 1997; Schuepbach 2002)

1) Investigate memory ability in FEP patients with PNS
2) Assess the trajectory of memory in relation to PNS over a 12 month period

METHODS

HOVINGTON ET AL. 2012

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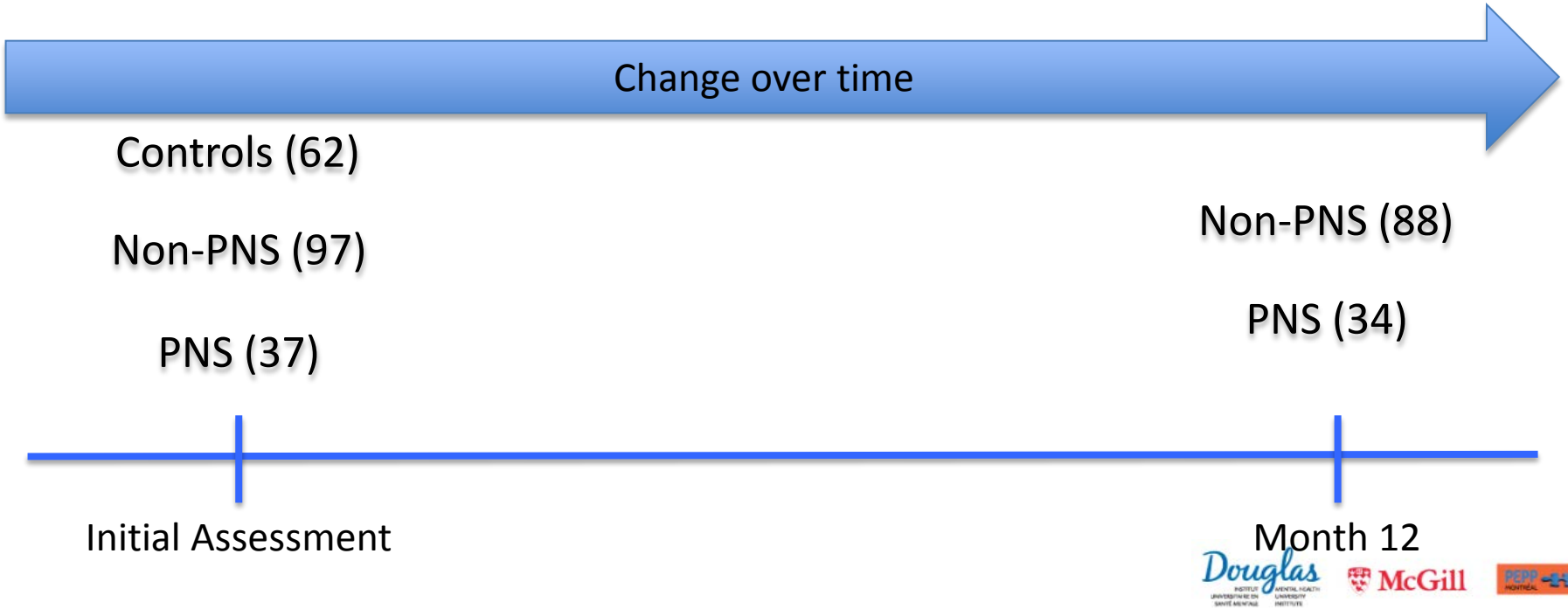
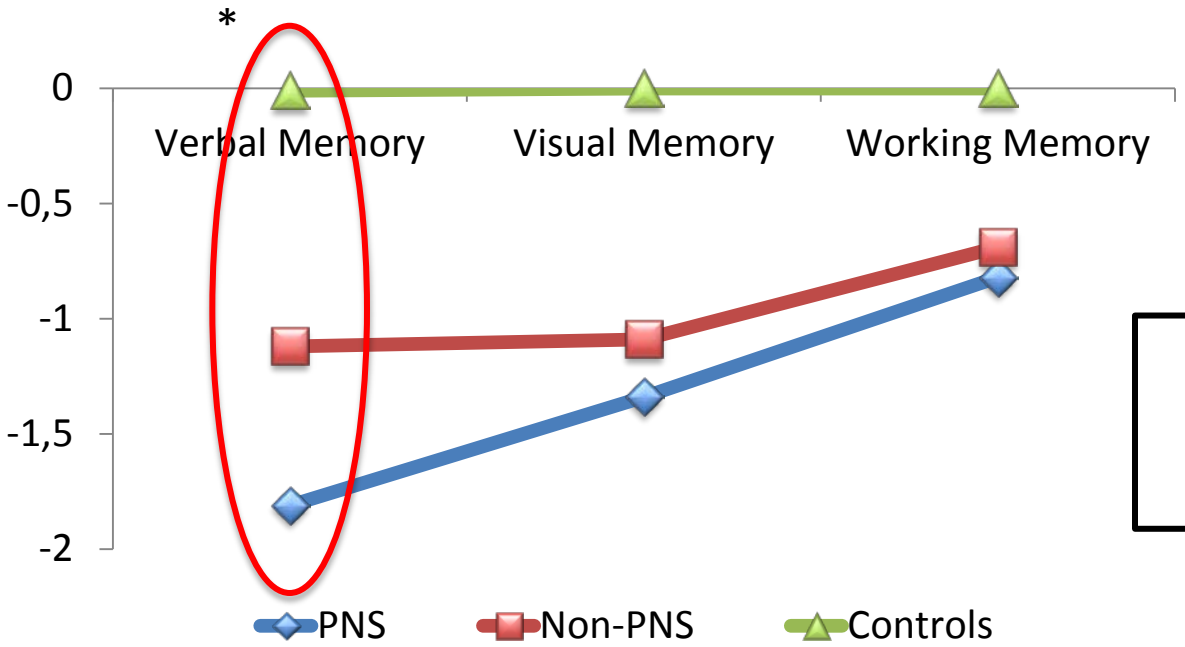
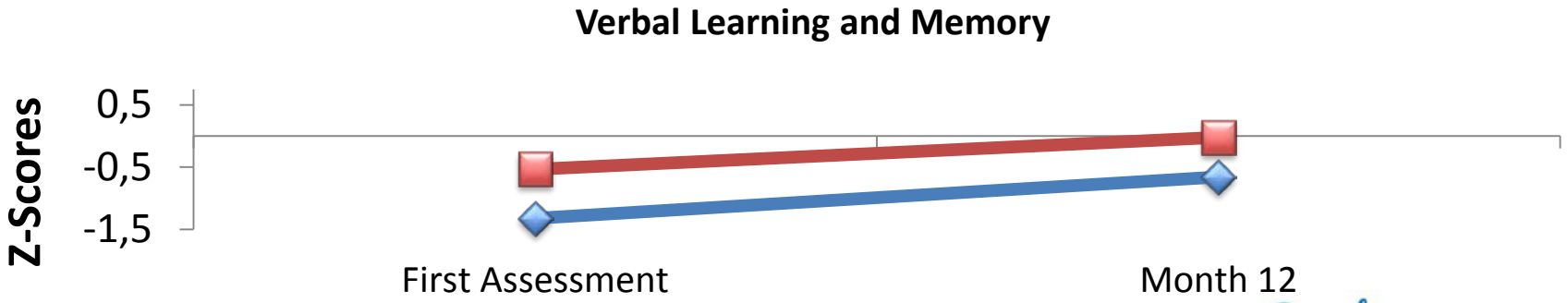
Visual Memory:	Logical Memory (WMS-III)
Verbal Memory:	Visual Reproduction (WMS-III)
Working Memory:	Spatial and Digit Span (WAIS-III)



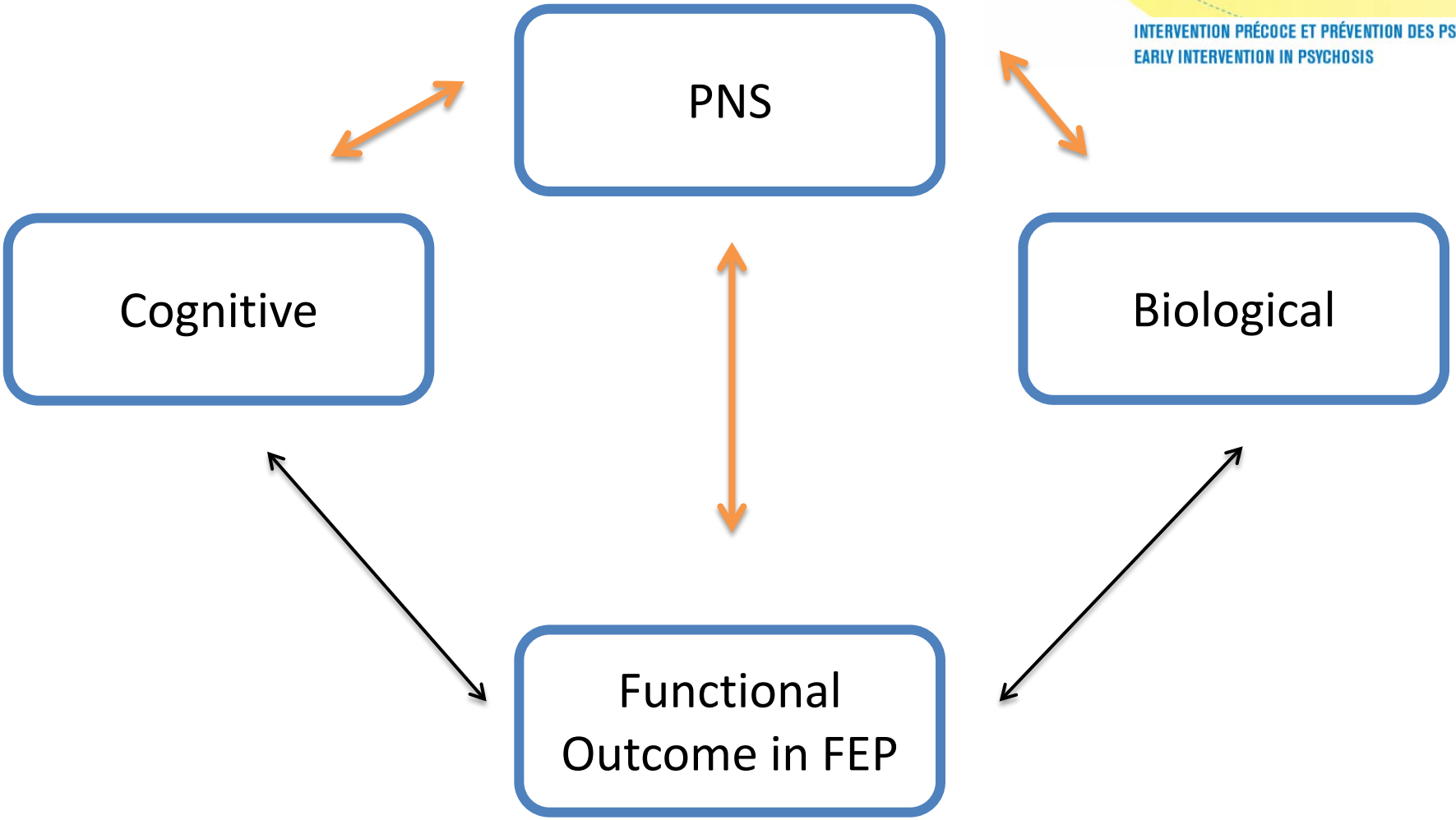
RESULTS: MEMORY AND PNS



Greater levels of Alogia in PNS was correlated with poorer verbal memory



*p<0.001


PNS
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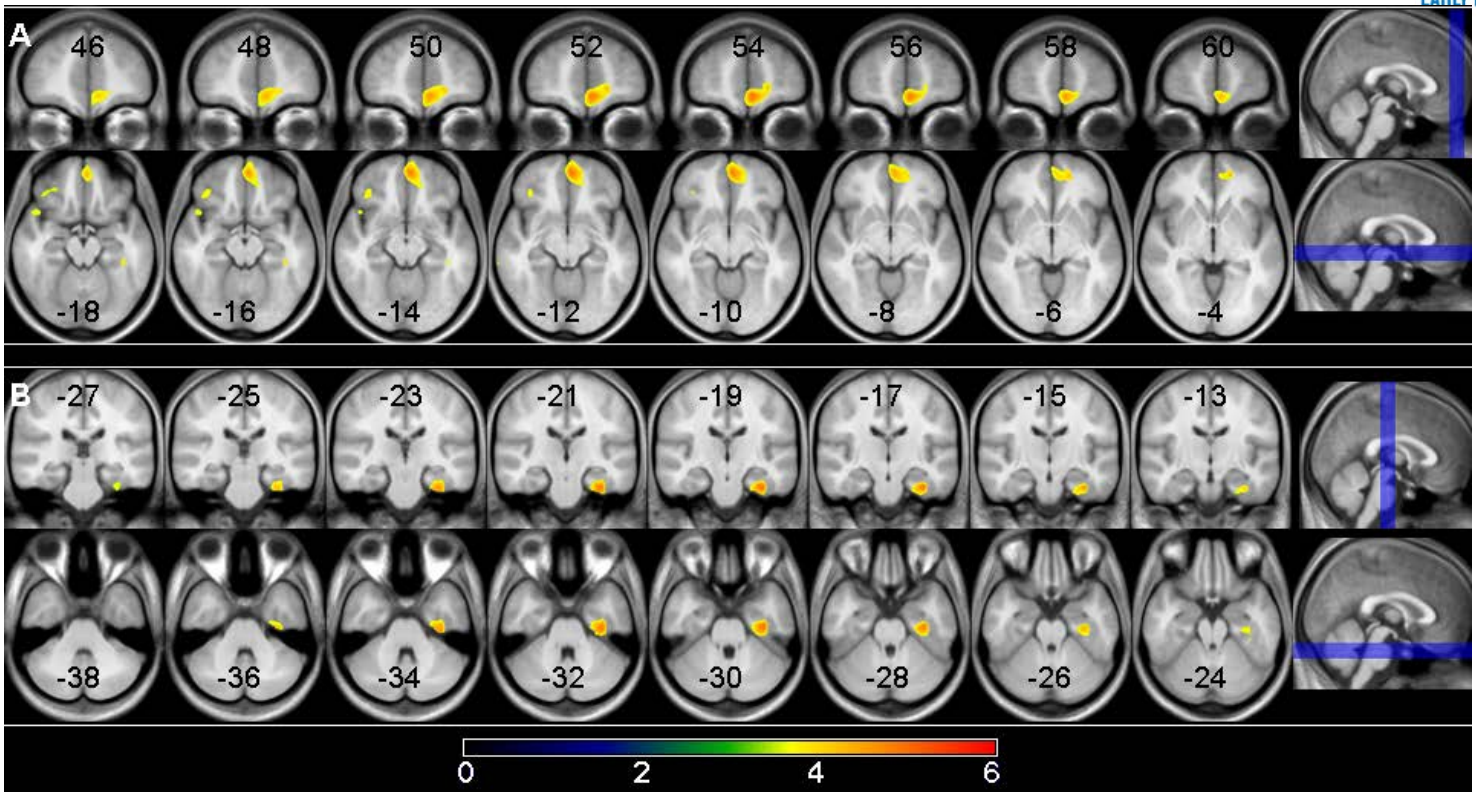
GREY MATTER VOLUME IN FEP PATIENTS WITH PNS



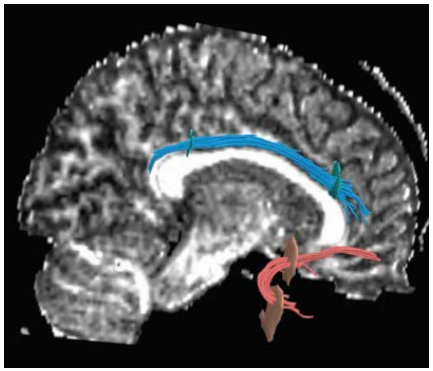
A) Right medial frontal gyrus: decreased gray matter in PNS

p<0.05, FWE-corrected

B) Right parahippocampal gyrus: decreased gray matter in PNS

Benoit et al. 2012

WHITE MATTER INTEGRITY AND NEGATIVE SYMPTOMS



Cingulum Bundle

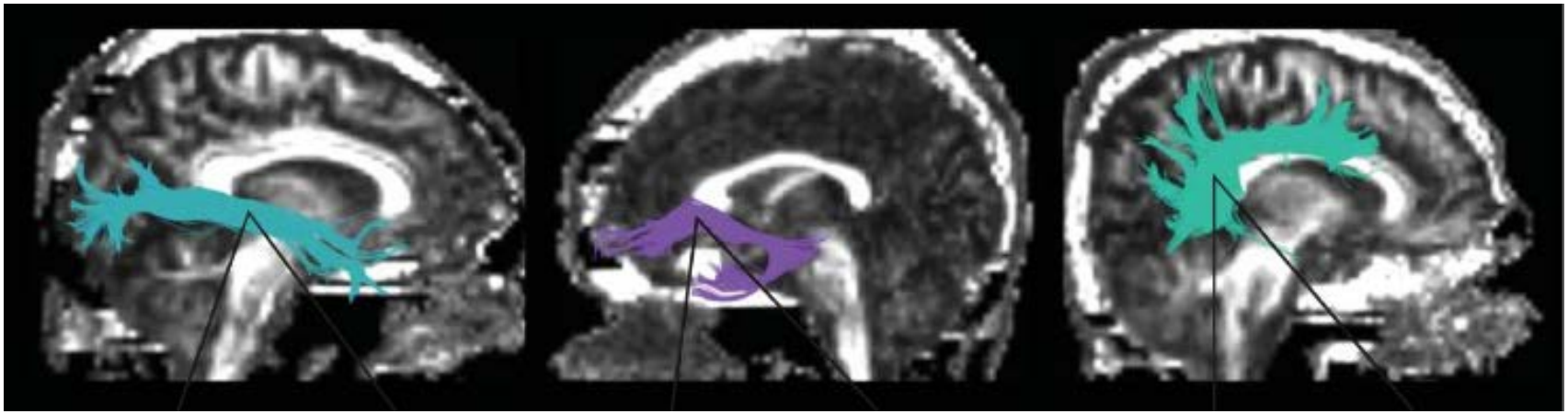
Nestor et al. 2008

Fractional anisotropy was lower in schizophrenia patients with more severe and enduring negative symptoms

Inferior Longitudinal Fasciculus

Uncinate Fasciculus

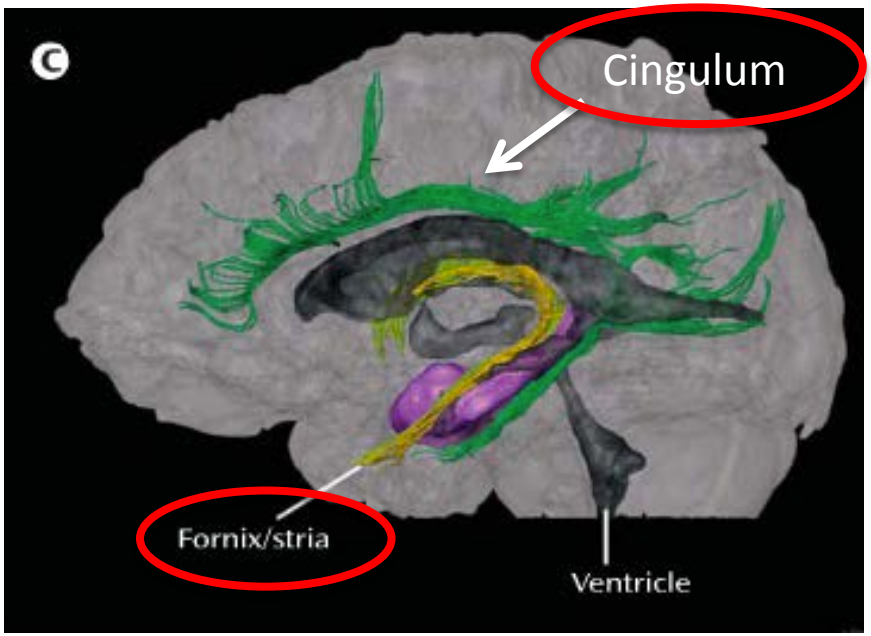
Arcuate Fasciculus

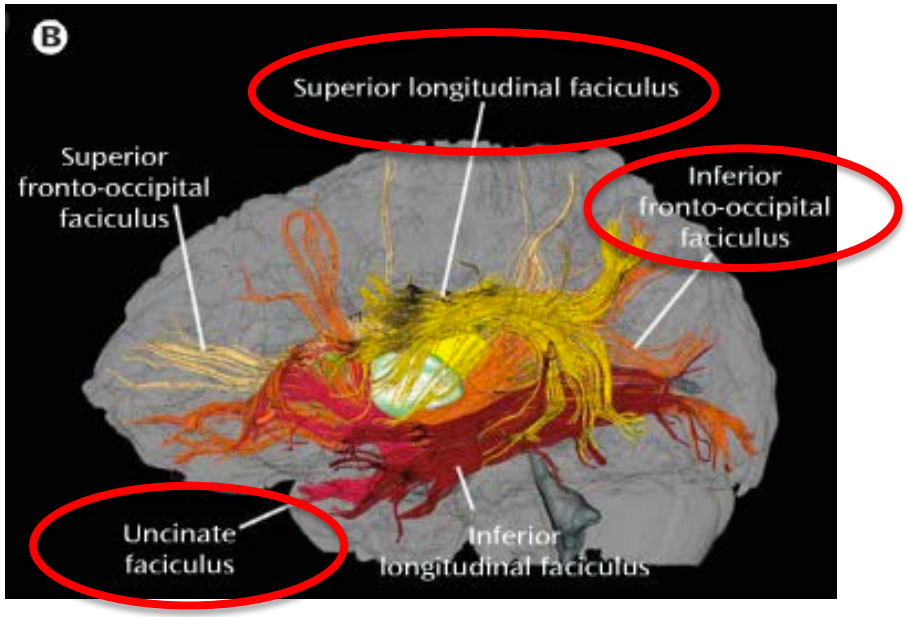


Voineskos et al. 2013;Rowland et al. 2009

Therefore, we investigated white matter integrity in FEP patients with PNS

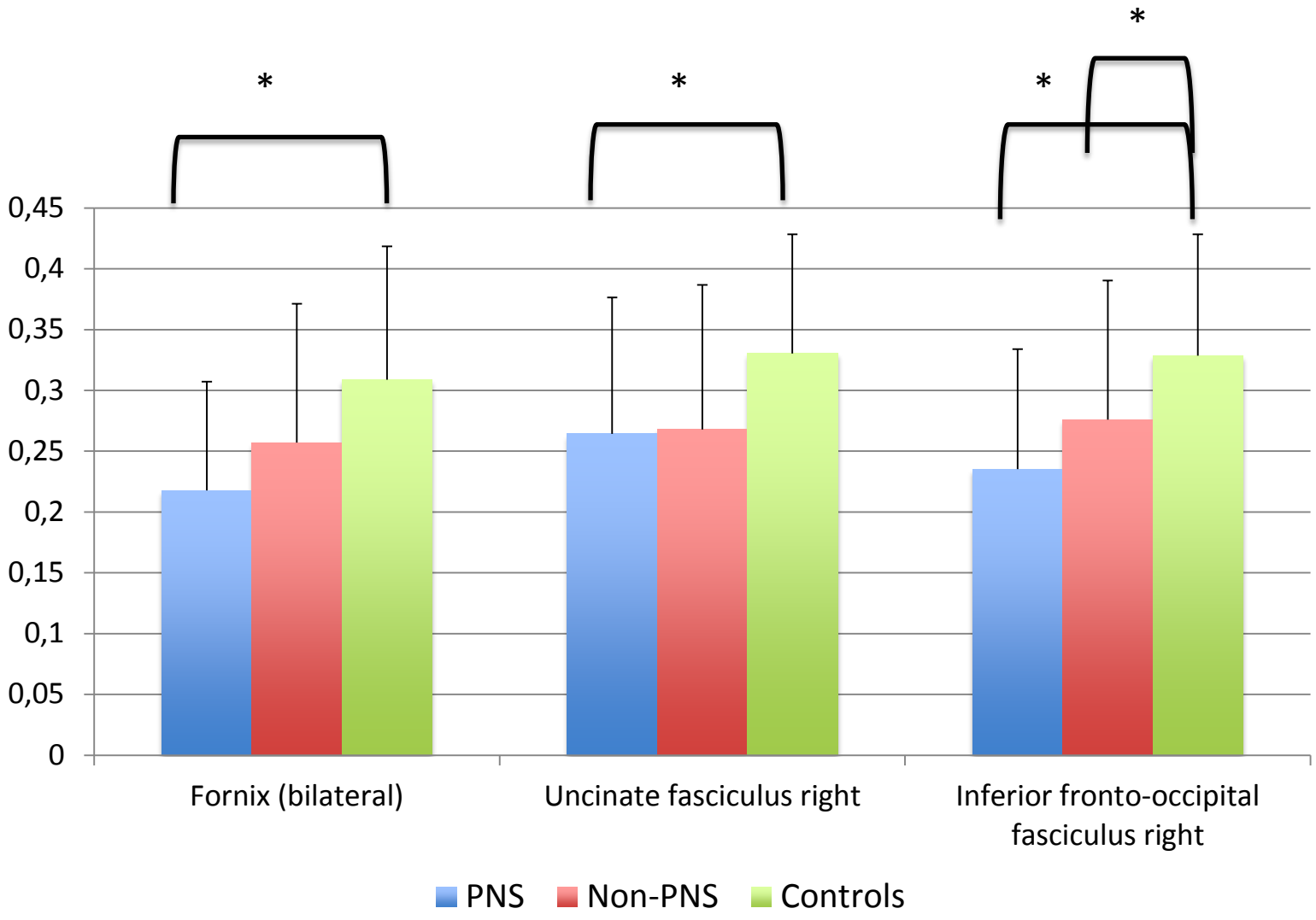
METHODS: WHITE MATTER ALTERATIONS IN PNS





We measured FA values in these regions of interest in FEP patients with PNS (12), without PNS (52) and controls (52)

PRELIMINARY FINDINGS



* p< 0.05

PRELIMINARY FINDINGS

1. Uncinate Fasciculus: Connects orbitofrontal cortex and temporal lobe

2. Uncinate Fasciculus: Critical structure in emotion and memory

3. Lower FA in UF correlated with negative symptom severity and verbal memory impairments (Szesko et al. 2008)

4. Fornix: Connects the hippocampal formation to the prefrontal cortex

CONCLUSIONS

Improve with cognitive remediation?

Patients with PNS

Present before onset of psychosis??

Poorer verbal memory in FEP

1) Reduced GM in frontal and parahippocampal gyrus in FEP
2) Reduced white matter integrity in FEP specific to fronto-temporo-limbic structures

Poorer functional outcome in FEP

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FRSQ for providing me with my doctoral funding

EXTRA SLIDES

Douglas McGill PEPP MONTRÉAL

PEPP LONGITUDINAL STUDY

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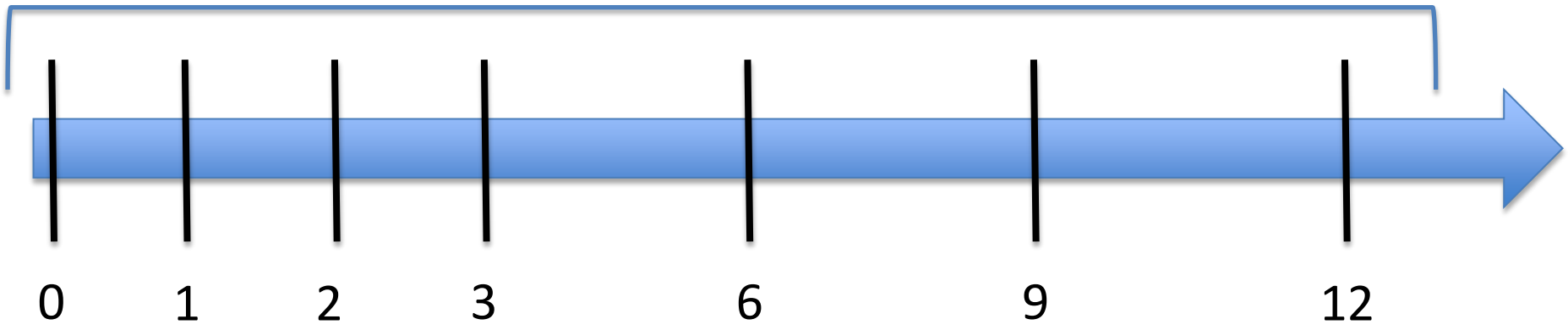
Assessment of clinical symptoms



SOFAS
Neuropsychological Evaluation
MRI/DTI

SOFAS
Neuropsychological Evaluation
MRI/DTI

HOW ARE NEGATIVE SYMPTOMS DEFINED?

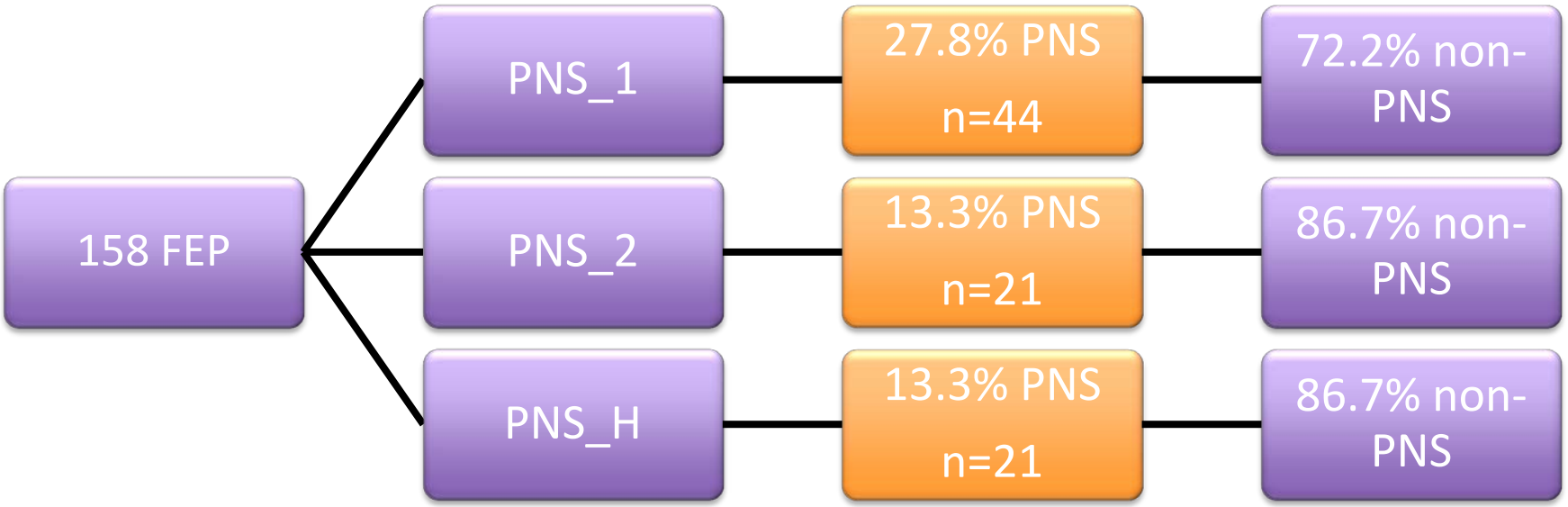
Deficit Syndrome

- Well-defined
- Prevalence: 15-20%
- Primary negative symptoms
- Present for a min of 12 months
- Identified using the Schedule for Deficit Syndrome (min of 2 out of 6)

Persistent NS

- No clear criteria
- Prevalence: 15-40%
- Primary or secondary negative symptoms
- Present for a min of 6 months
- Identified using any validated negative symptom scale

RESULTS - PREVALENCE



METHODS- PNS DEFINITIONS

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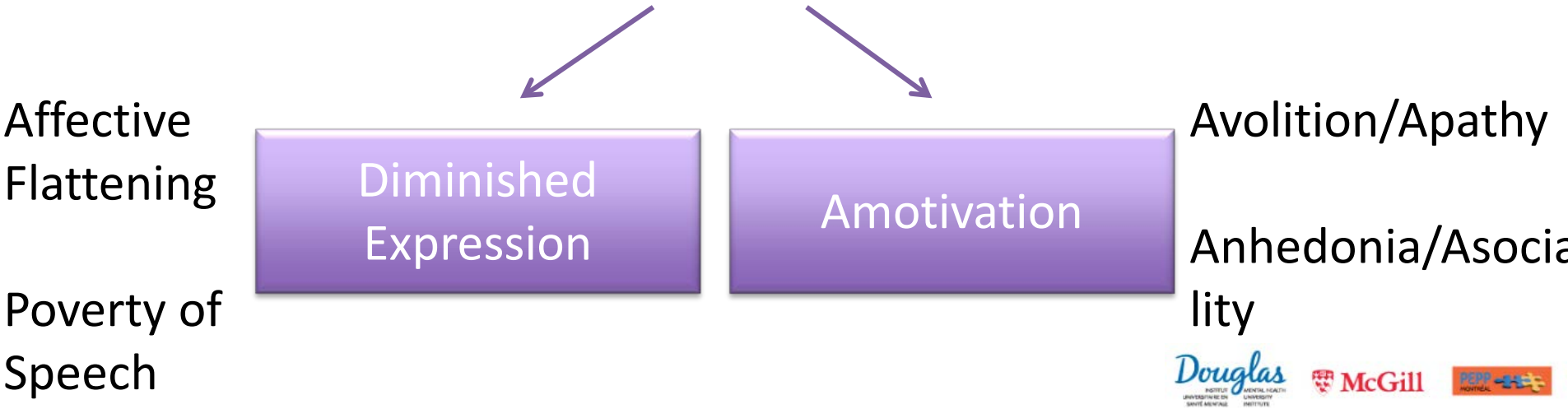
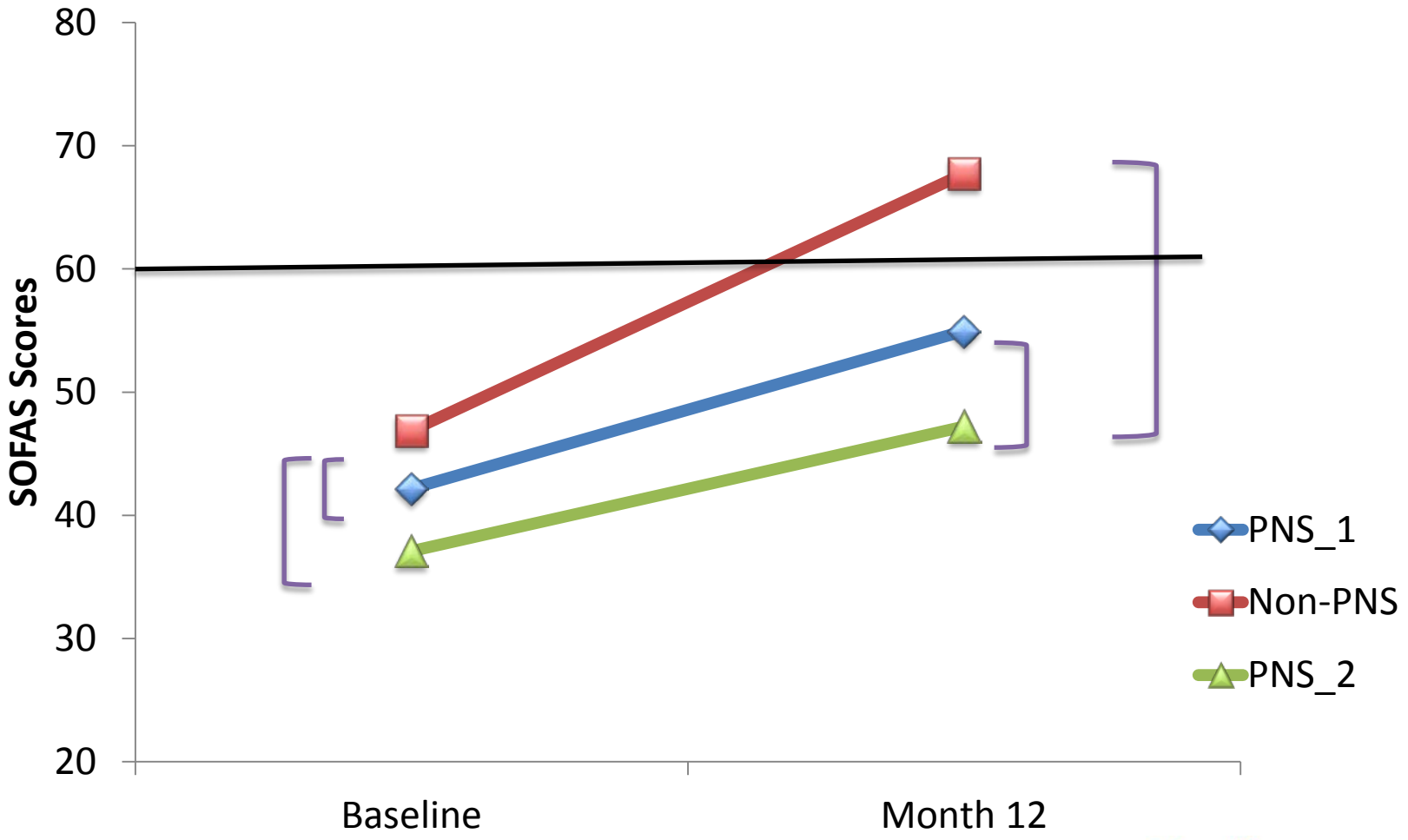
1) PNS_1: score of ≥3 on *at least 1 global item* of the SANS (Malla et al., 2004)

2) PNS_2: score of ≥3 on *at least 2 global items* of the SANS (Edwards et al., 1999)

3) PNS_H (Hybrid): score of ≥3 on either one or both of the subdomains (Foussias and Remington, 2010):



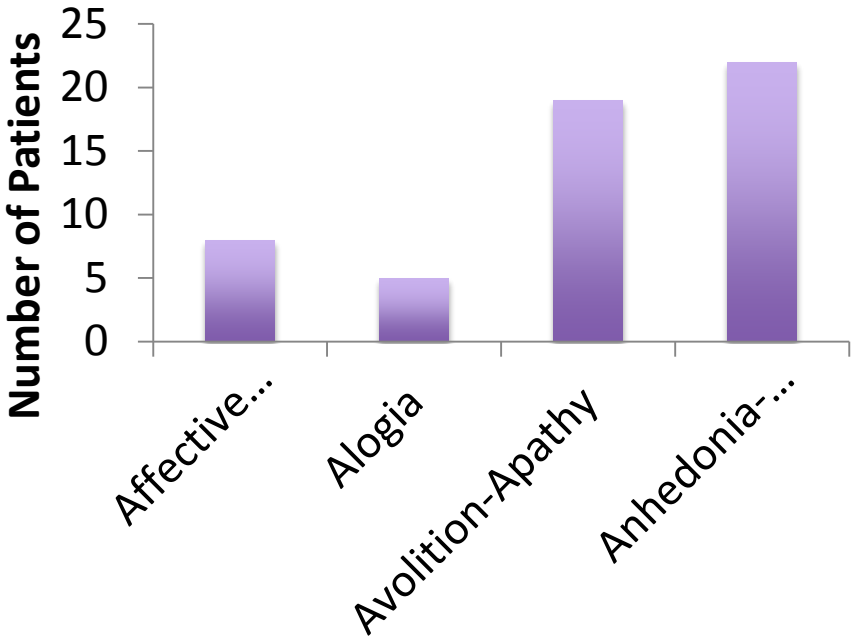
RESULTS


80
70
60
50
40
30
20
SOFAS Scores
Baseline
Month 12
PNS_1
Non-PNS
PNS_2

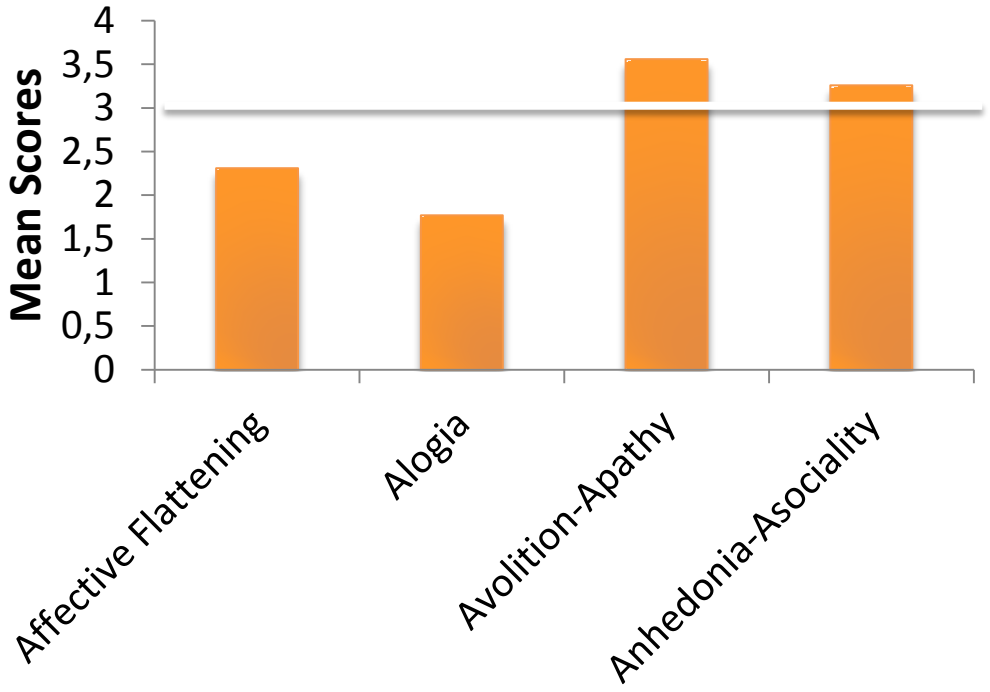
FEP PATIENTS IN PNS GROUP

INTERVENTION PRÉCOCE ET PRÉVENTION DES PSYCHOSES
EARLY INTERVENTION IN PSYCHOSIS

Frequency



Mean SANS scores



HOW ARE PNS DEFINED?

Author	PNS Definition Applied
Galderisi et al. 2012	PANSS score > 3 on a min of 1 NS item
Stauffer et al. 2012	PANSS score > on min of 3 NS items
Buchanan et al. 1998	Total score of ≥ 20 OR a score of ≥2 on at least 1 SANS global item
Edwards et al. 1999	SANS HI score of ≥3 on 2 or more of global subscales SANS LOW score of ≥2