Affect Regulation in Prenatal Alcohol Exposure and FASD

Results from the Canadian National FASD Database

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Presenter Disclosures

The presenters have no conflicts of interest to disclose.

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Overview

- What is Affect Regulation (AR) impairment?
- How is it related to prenatal alcohol exposure?
- Comparing the attributes and outcomes of those with and without AR impairment
- AR as the 3rd Domain in FASD Diagnosis
- Summary and Key Points To Take Home
- Discussion

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What is Affect Regulation (AR)?

- The ability to control, modulate & regulate emotional reactions
- People with prenatal alcohol exposure (PAE) frequently have AR impairment

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How is AR related to prenatal alcohol exposure?

- In animal models, Dr. Joanne Weinberg (UBC) and others showed PAE results in changes to the hypothalamic-pituitary-adrenal (stress) axis
- These changes lead to increased dysregulation of the system that responds to stressors and...
- …in humans, **70-90%** with PAE have mental health problems by adulthood

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Alcohol as a Teratogen

- Teratogenic effects of alcohol exposure on the fetus may be direct or indirect
- They have an impact on the brain at a structural level, at a cellular level and at a neurochemical level
- PAE acts as a stressor and leads to dysregulation of the HPA axis throughout life, leading to increase in HPA tone or activity
- Dysregulation of the HPA axis is common in depression and anxiety

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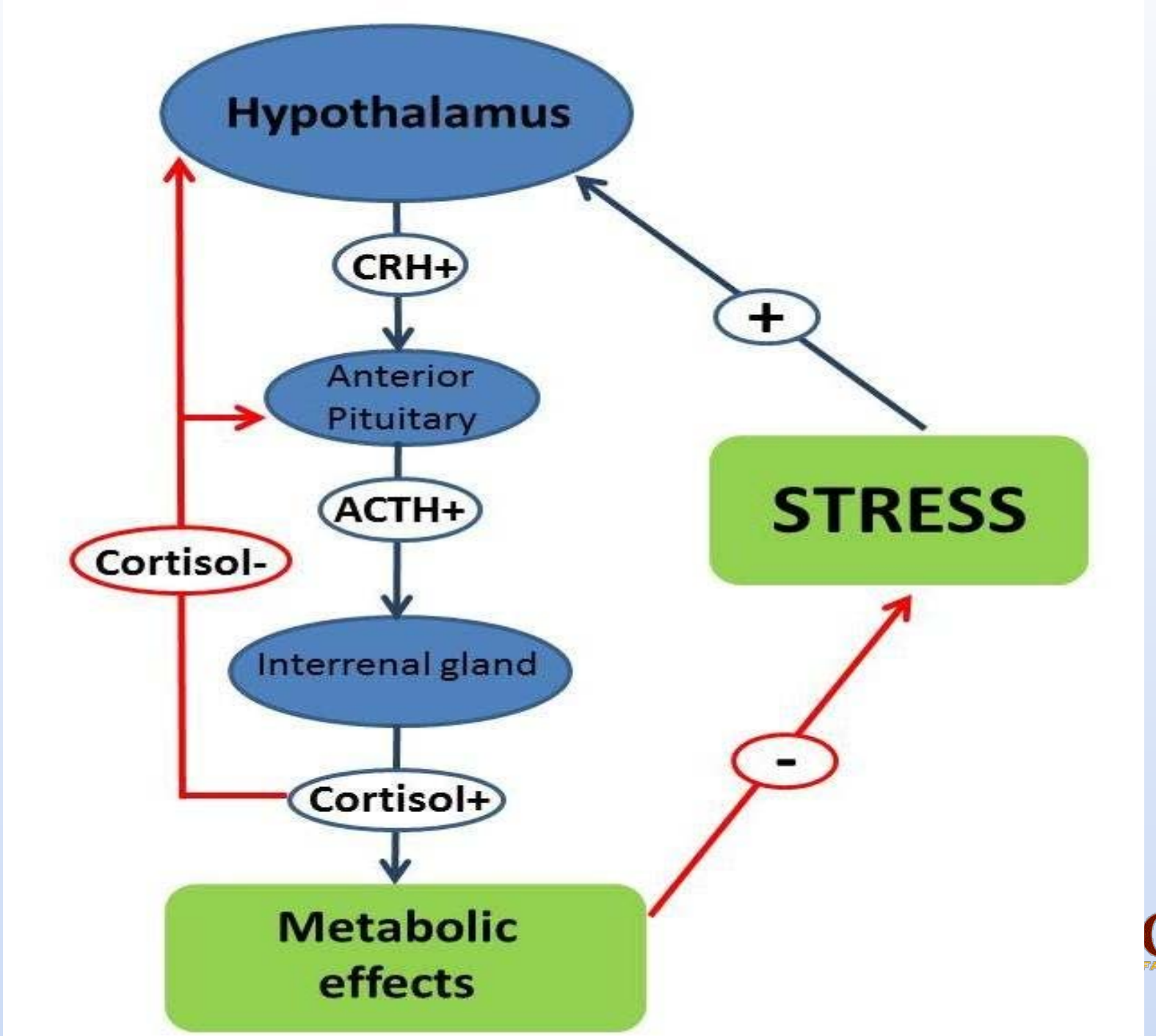

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Stress-Diathesis Model

Fetal programming of the HPA axis by PAE alters neuroadaptive mechanisms that mediate the stress response, thus sensitizing the organism to stressors encountered later in life, and mediating, at least partly, the increased vulnerability to depression/anxiety disorders

Hellemans 2010

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PAE and Anatomical Brain Changes and MH

- PAE causes permanent structural alterations
- Common findings include reductions in parietal, temporal, frontal lobes, cerebellum, corpus callosum, basal ganglia
- Hippocampus and amygdala: regulation of emotion and affective expression
- White matter hypoplasia throughout the brain
- Gray matter increase in parietal and superior temporal lobes
- Frontal and parietal lobe anomalies: consistent with EF deficits

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Spadoni 2007

MH and EF

- EF is a cardinal deficit in FASD
- Executive System (ES): coordinates of a number of cognitive processes including goal-directed and task-oriented behaviours, self-regulation, behavior inhibition, planning, working memory, mental flexibility, response inhibition, impulse control, and monitoring of action
- ES is mediated by various networks. Most responsible is located in the frontal lobe (prefrontal cortex)
- Dopamine is the main neurotransmitter of the ES, mediating EF
- Dopaminergic system disturbance forms the basis of many psychiatric illness

Hosenbocus 2012

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Infancy and Early Childhood

Signs of neurological dysfunction in infants at birth after significant PAE include:

- Jitteriness, irritability, autonomic instability, hypotonia, slow habituation, low levels of arousal and disturbance in sleep pattern
- In early childhood, behavioural difficulties continue: poor attention, increased activity, increased emotional reactivity and irritability.

These behaviours leading to alterations in the Maternal - Child relationship may be one of the most significant impacts of PAE

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McGee 2007; Mattson 1998; Streissguth 1997

Infancy and Early Childhood

- Higher levels of PAE exposure shows higher levels of negative affect in mother-child interactions (cf. to infants with less PAE)
- Mothers in turn interact less in ways of responsiveness and stimulation to their babies
- Infants displayed higher levels of insecure attachment
- Findings could not be explained by other factors (cigarettes use, other drugs, caffeine or current alcohol use)

O'Connor 1992

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Infancy and Early Childhood

Follow up of these mother-child dyads in early childhood:

- Higher scores of depressive symptomatology (19% compared to prevalence of 1%)
- PAE and maternal depression has an additive predictive effect
- Association is stronger in girls than boys
- This is independent of mother's use of other substances

O'Connor 2000

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Infancy and Early Childhood

- PAE, maternal depression and low emotional support from the partner are associated with increased irritability at 5 months of age
- However at 17 years of age only the effects of PAE was found.

PAE results in an enduring vulnerability having a long lasting influence

Lemola 2009

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Infancy and Early Childhood

- Looking at a cumulative risk model in young children with PAE, living in single home environments and poverty showed higher levels of insecure attachments with higher levels of PAE
- “Supportive Presence” by the mother reduces the deleterious effects of PAE on the child’s security of attachment in preschool years

O’Connor 2009

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Middle Childhood

- Children with PAE have higher levels of internalizing and/or externalizing behaviours
- Number of studies: Identify high levels of mood disorders, anxiety, ADHD, ODD and Conduct Disorders
- Having better social skills and living with married biological parents seem to ameliorate some of the effects of PAE
- Higher levels of anxiety with PAE
- Anxiety symptoms are worse in children not in their biological homes

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Walthall 2008

Behaviour Regulation

Children with PAE:

- More likely to perceive some social interactions as hostile and formulate aggressive physical solutions, classifying them as conduct disordered by their parents
- Children without PAE do the same but are not classified as CD

Though all children formulate aggressive solutions to perceived social slights, children with PAE are more likely to act on these leading to a CD diagnosis

O'Connor 2008

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Adolescents and Young Adults

- High Levels of Mental Health Disorders (up to 90%)
- Depression and Anxiety
- Psychotic disorder
- Passive aggressive personality disorder
- Antisocial Personality
- Addictions
- High degree of suicide risk: suicide risk and attempted suicides

O'Connor 2009

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PAE and MH

- Evidence supports that PAE is a significant factor in MH issues in individuals with FASD
- Evident even when other factors are controlled for
- Caused by several different mechanisms
- Manifests differently across the life span
- Can be partially mitigated by early diagnosis, appropriate environmental and family support, SES etc
- Likely more common and evident at a younger age than our data suggests

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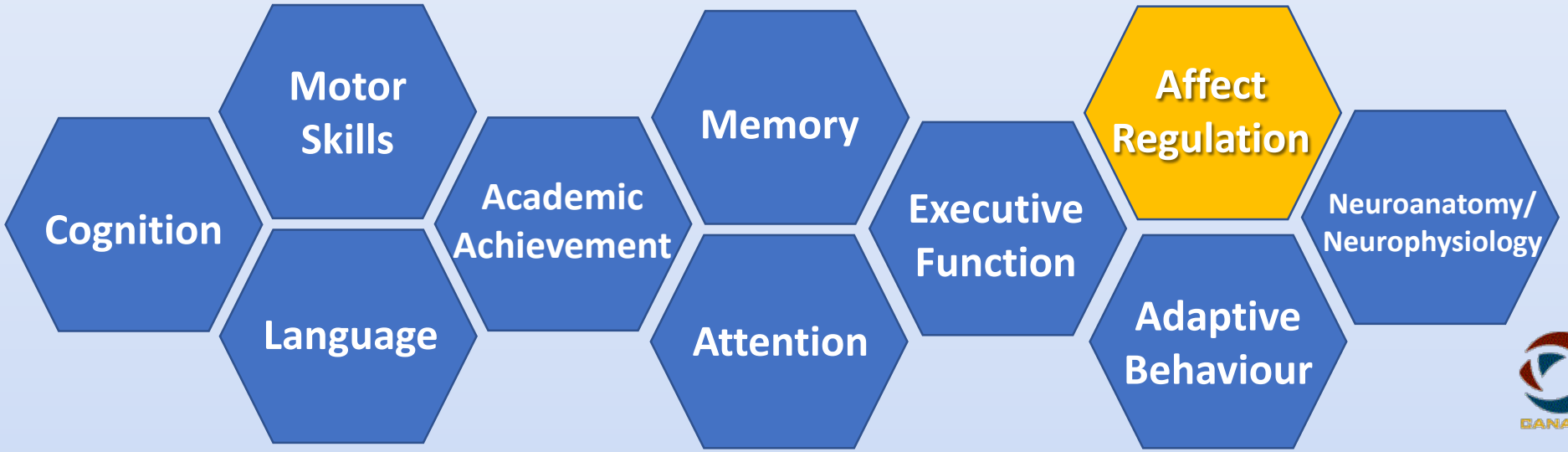
Affect Regulation Impairment in FASD Diagnosis

- Based on research in humans and animals, new guidelines (2016) for FASD diagnosis in Canada include AR as 1 of 10 domains for neurodevelopmental assessment
- AR is operationalized as meeting DSM-5 diagnostic criteria for a mood or anxiety disorder



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Our AR Research Questions

Are there *differences* between those with and without AR impairment?

What *outcomes* are associated with AR impairment?

Has the domain of AR allowed for more diagnoses of FASD? Is it used as the *3rd domain*?

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Method: Canadian National FASD Database

- Collects information about FASD assessments from 26 clinics across 9 provinces/territories
- Includes our geographic, cultural, urban/rural diversity
- Collected through the diagnostic assessment process
- Data is input to REDcap by clinics using a secure online portal

Study Question 1: Are there differences between individuals with and without AR impairment?

<u>Criteria</u> for cases included from National Database:

1. Data input January 2016 to March 2018
2. Diagnosed with FASD or given “PAE - At Risk” designation
3. AR was assessed at the clinic (those with missing data not included)

Total sample number = 404

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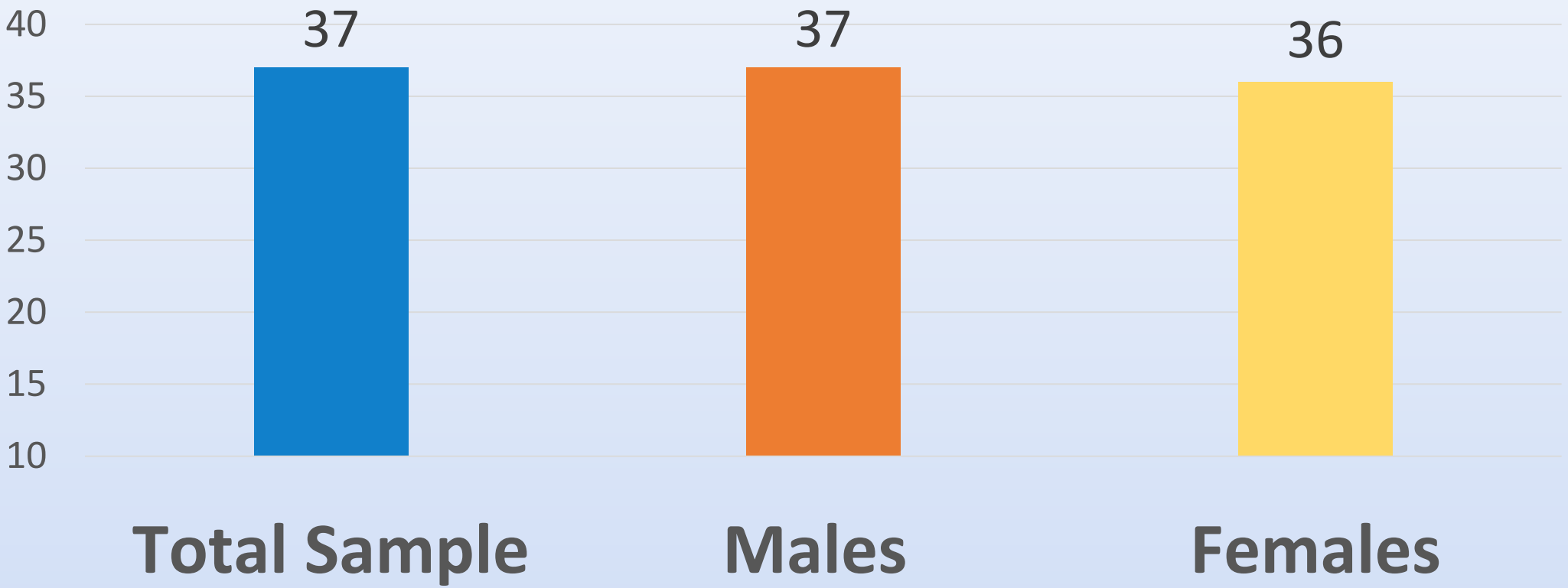
Results for rates of AR impairment: No difference in the percent (%) of males and females with AR impairment



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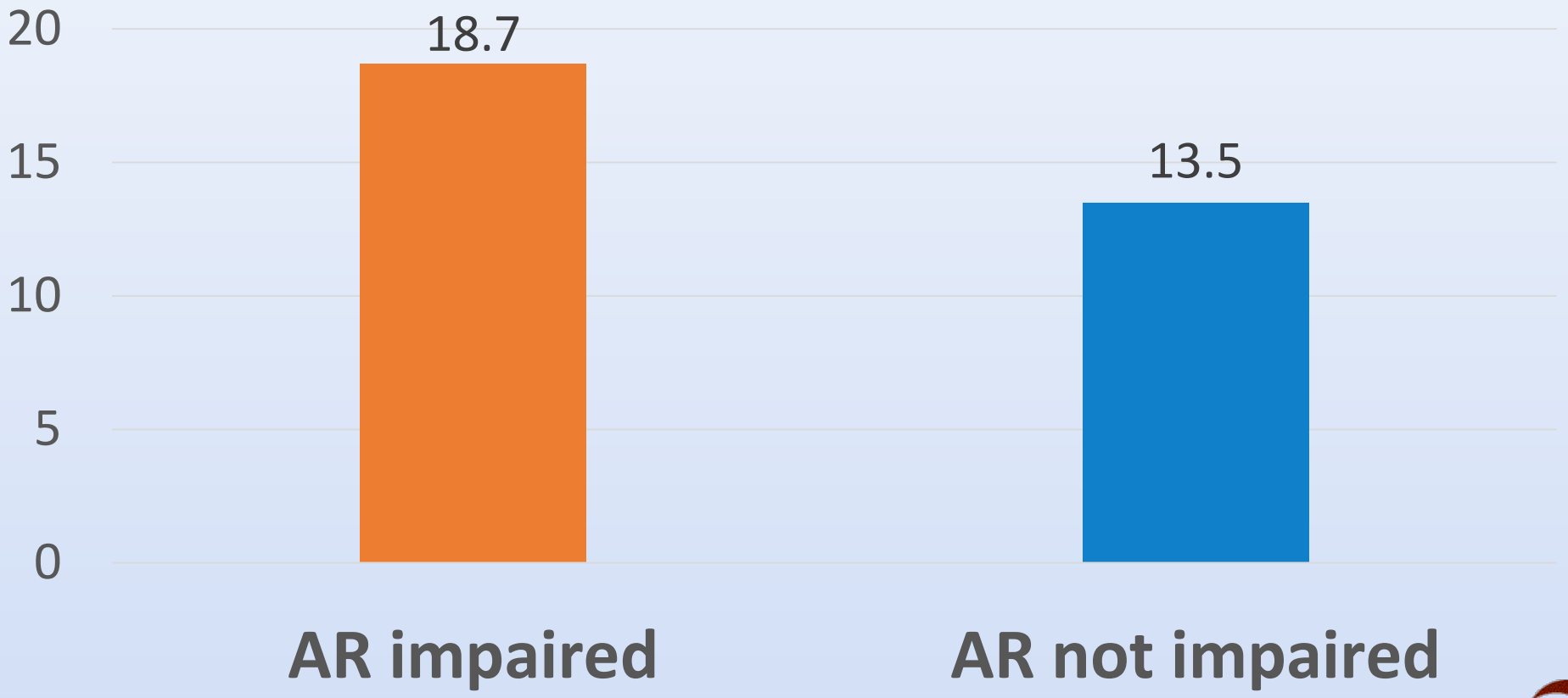
Results for Age:
AR impaired group were significantly older (years) at the time of FASD Diagnosis



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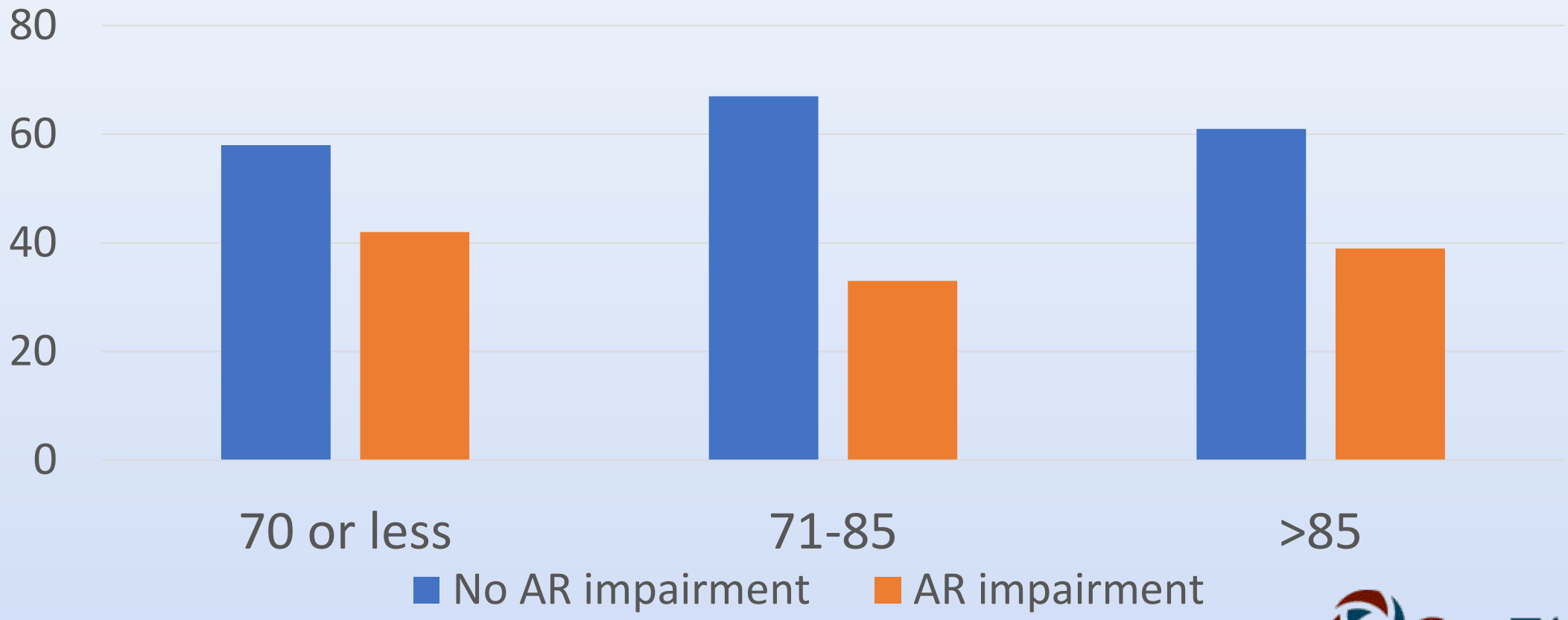
Results for IQ (%): No difference in IQ scores for AR impaired vs. not AR impaired



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Study Question 2: Odds of AR Impairment in Each

	N	Odds Ratio	95% C I	p-value
Language Disorder	250	**.6**	.4 - 1.2	.20
Intellectual Disability	278	**1.0**	.6 - 1.7	.82
Attention Deficit	317	**1.5**	.8 - 2.5	.15
Conduct Disorder	169	**4.8**	2.1 - 10.9	<.001
Attachment Disorder	189	**4.9**	2.2 - 10.9	<.001
PTSD	140	**7.4**	2.6 - 20.6	<.001
Prior Suicide Attempt	176	**9.1**	4.1 - 20.2	<.001

Implications

- Individuals with AR impairment are MUCH more likely to develop PTSD and attempt suicide
- Can we identify AR impairment early in life?
- Can we target interventions to specific group to try and avoid these outcomes?

Study Question 3: Has adding the AR domain allowed for more FASD diagnoses?

Criteria for cases included:

1. Entered January 2016 to October 2018 including FASD, no FASD and PAE-At Risk
2. Data divided into three groups:
   a) Cases with 2 or fewer domains of impairment
   b) Cases with exactly 3 domains of impairment
   c) Cases with 4 or more domains of impairment

Total sample number = 769

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Logistic Regression Analysis: Model 1

What are the odds of having…….

AR as one of two domains of impairment
+ No FASD

vs.

AR as one of three domains
+ YES FASD diagnosis

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Results and Implications of Model 1

- The odds of having AR, three domains of impairment, and FASD was higher (OR 1.9), p=.058
- Interpretation: AR deficits are twice as likely to be present in the three domain group compared to the two domain group.
- From the 769 cases assessed, a total of 335 FASD diagnoses were made; 16 of these had AR as one of three domains.
- This means using the new Guidelines 16 more FASD diagnoses were made than would have been possible previously.

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Logistic Regression Analysis: Model 2

What are the odds of having…….

AR as one of two domains of impairment
+ No FASD

vs.

AR as one of four or more domains
+ YES FASD diagnosis

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Results and Implications of Model 2

- The odds of having AR, four or more domains of impairment, + FASD was higher (OR 6.1), $p<.001$
- Interpretation: AR deficits are 6 times more likely to be present in the four domain or more group.
- This means AR impairment is MUCH more likely to be present in more severely impaired individuals (i.e. those with more domains of impairment)

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Summary and Key points from research

- **AR impairment is associated with** suicide attempts, PTSD, Conduct and Attachment disorder
- **AR impairment is not related to IQ or gender**
- **The AR domain has increased FASD diagnoses …. a little** about 16/335 extra diagnoses can be directly attributed to the AR domain
- **Early identification of AR** may help with support recommendations and interventions

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Notes for discussion -MM

- We note that in the new DSM-5 criteria for ND-PAE, self-regulation and behavior form one of the major domains to be assessed.
- Includes attention and impulse control (components of EF) which are also associated with emotional and cognitive processes needed to regulate affect/mood
- Implication: ongoing inflated relationship between FASD/PAE and affect regulation confounding the exact relationship
- Proposed mechanism involves affecting neuro-adaptive mechanisms that mediate the stress response, which can lead to hyper-reactivity to stress across the lifespan
- Human studies are still associational and not causative, thus PAE is at best significant risk factor for AR

Olson 2015

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Notes for discussion -MM

- Note other potential factors confounding PAE-AR relationship that has not be separated in humans – ADHD, Trauma, PTSD, somatization and eating disorders Dvir et al 2014
- ADHD may be related to deactivation of the default mode network
- Implication for service: could an algorithm be developed to assist teams with no mental health expertise in identifying likely contribution to AR in those with suicide attempt, more than 4 domains, PTSD, attachment and conduct problems especially in older subjects.
- We need to develop more reliable assessment tool rather than the current practice of adding disparate diagnoses to the exclusion of obvious affect regulation disorders such as borderline PD and other cluster B PDs, and bipolar disorder

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