Toward an early developmental approach to substance use/abuse

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Canadian Academy of Health Sciences
Académie canadienne des sciences de la santé

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REPORT

The Royal Society of Canada &
The Canadian Academy of Health Sciences Expert Panel

Early Childhood Development

November 2012

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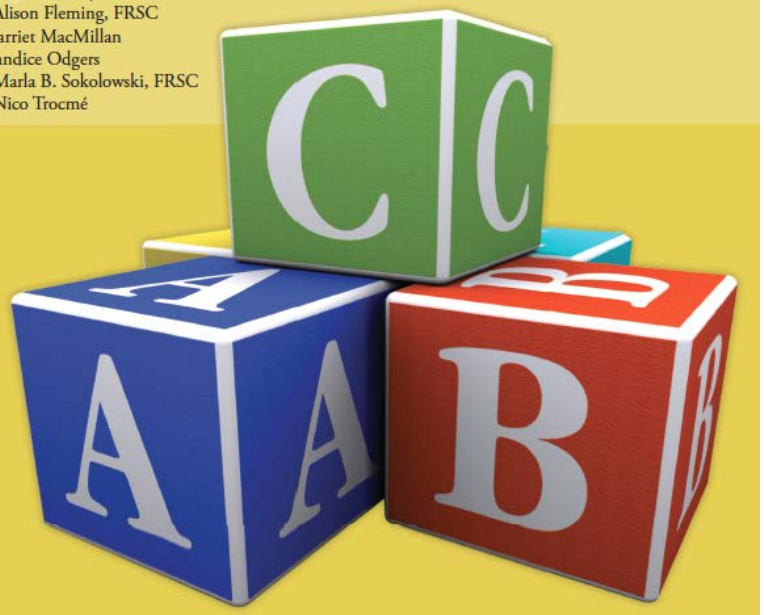
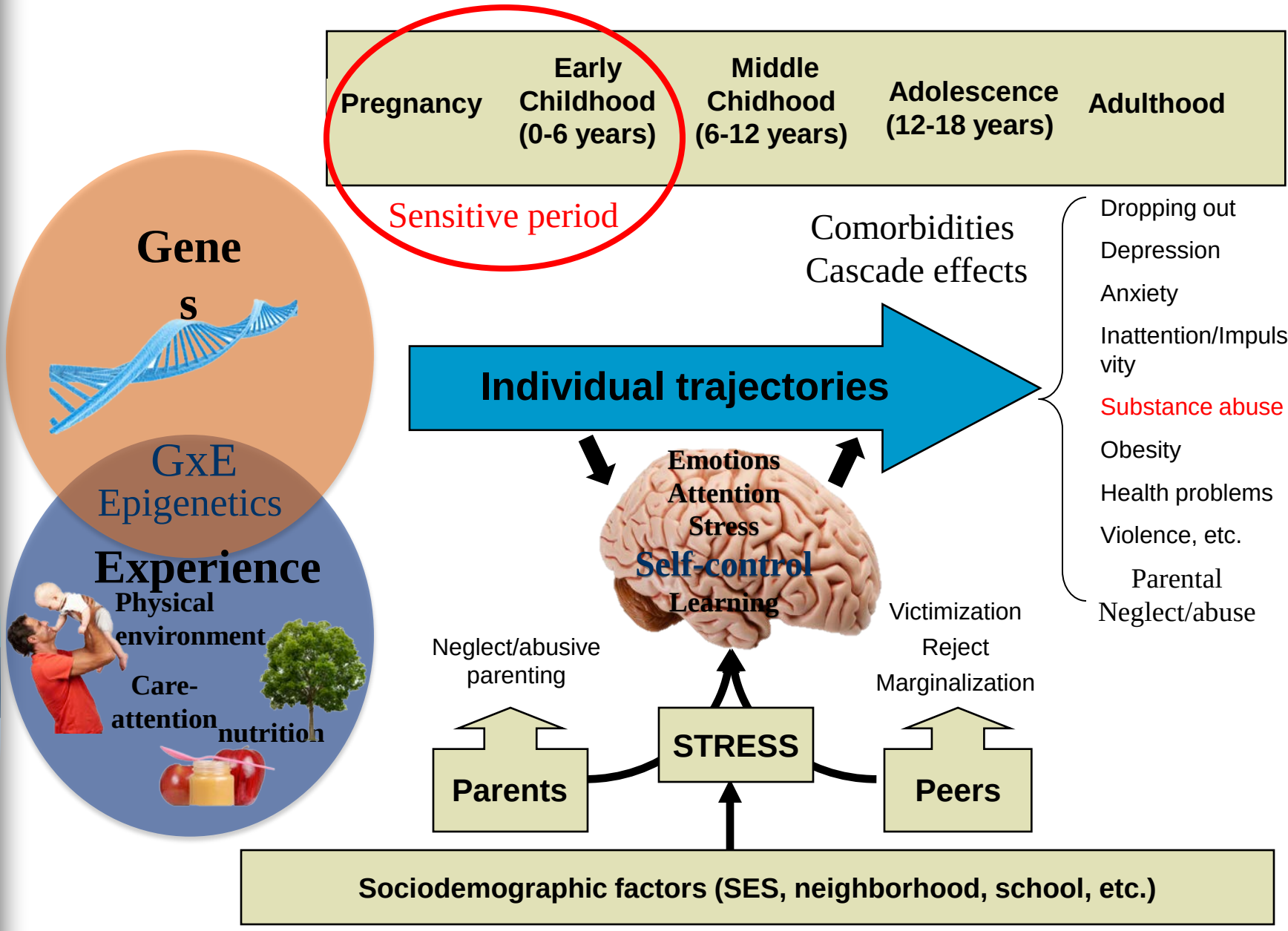


Main questions

1. Are there identifiable early adverse childhood experiences (ACE) that lead to poor mental health and unhealthy behaviours?
   - Is there evidence that they have their effects through changes to brain structure and function?
   - Do these factors operate together to produce their changes?
   - Are there factors that mitigate the influence of adverse early experiences?

1. What is the evidence for the effectiveness of a variety of interventions to mitigate the adverse effects of environmental influences.

Bio-social model of human development (maladjustment)



Substance use/abuse: defining features of a developmental framework

1. Substance use/abuse implies identified brain pathways and systems (e.g., the dopamine system; Koob & Volkow, 2010)

2. Substantial contribution of genetic factors
   - alcoholism, cocaine, opiate addiction (Goldman et al., 2005)
   - gambling problems (Slutske et al., 2010)

3. Substantial co-occurrences across forms of substance use
   - Co-occurrences associated to common genetic factors
     - set of biological vulnerabilities for a general syndrome (Wareham & Potenza, 2010)?
       1. Behavioural disinhibition? (Iacono et al., 2008)?
       2. Self-control? (Moffitt et al., 2012)?

Substance use/abuse: defining features of a developmental framework

4. Links with early adversity?

Yes (prenatal alcohol/nicotine, low SES, and maltreatment), but developmental processes are not clear.

- Twin and adoption studies failed to document an environmental pathway in substance use/abuse across generations (Haber et al., 2005; Waldron et al., 2009; Goodwin et al., 1973; Cadoret et al., 1987)

- Some early preventive interventions have shown positive effects on substance use (e.g., Perry preschool program; Montreal Longitudinal and Experimental Study; Nurse-family partnership; Chicago Longitudinal Study of Child-Parent Centres)

Three additional points for a full and refined developmental approach to substance use/abuse

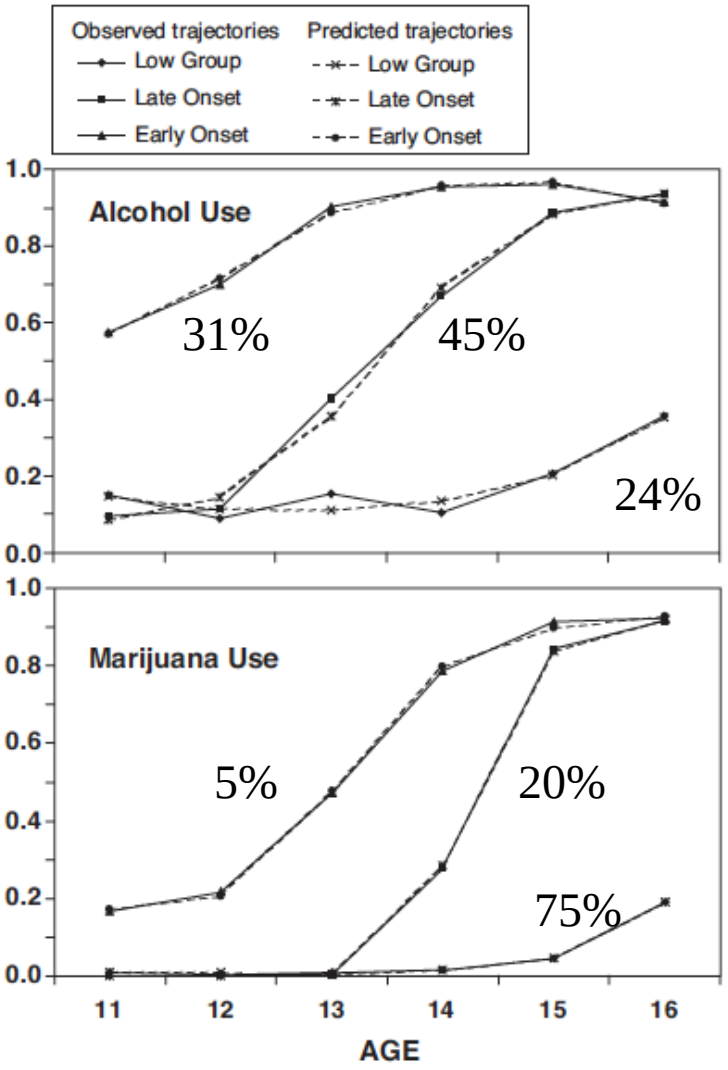
1. Substance use/abuse as a developmental construct;
   - The story is in the developmental trajectories (versus episodic assessments);
2. Early risk factors should be documented;
   - Substance use can be traced back to early developmental trajectories reflecting low self-control and disinhibition;
3. Gene-Environment interplay should be tested more systematically.

Substance use as a developmental construct

Developmental trajectories of alcool and marijuana use in early to middle adolescence (Wanner et al., AB, 2006)

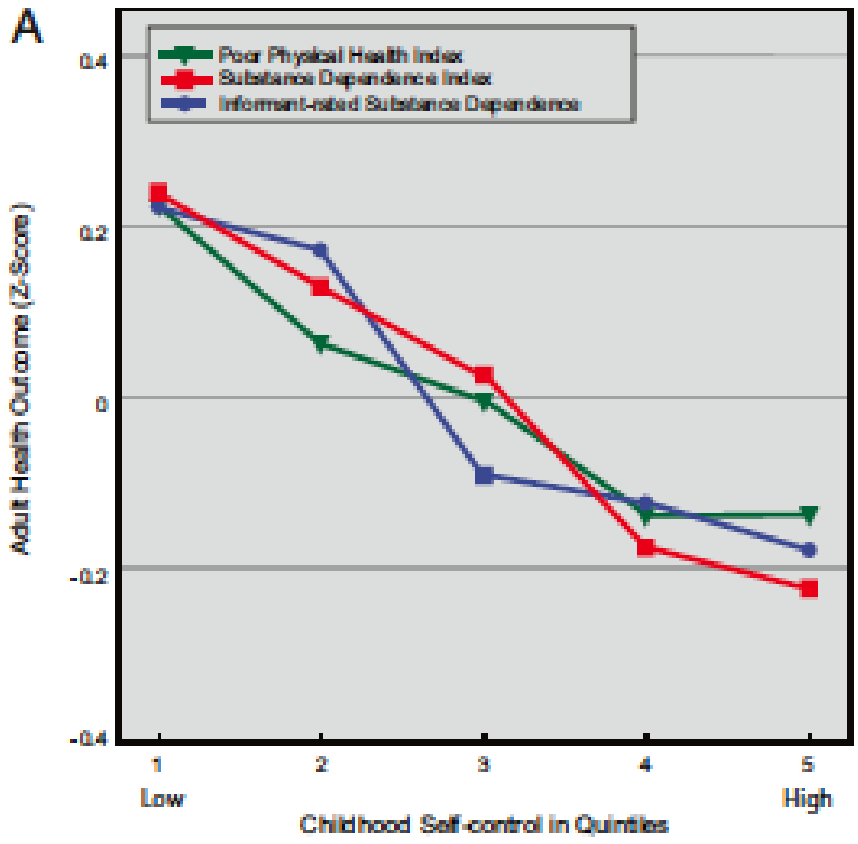
- N = 903 from a Montreal cohort of 1037 French-speaking kindergarten boys of low SES background followed longitudinally

- Children self-assessments of alcohol and marijuana use between ages 11 and 16.



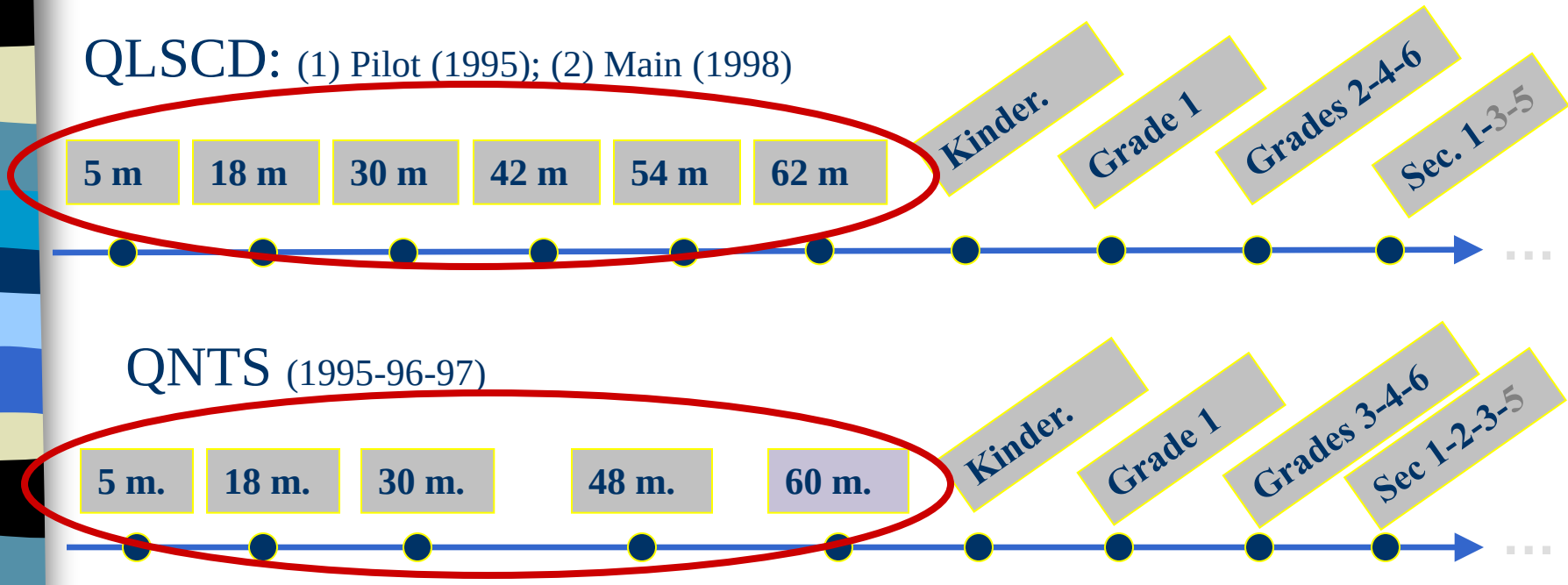
Early risk factors

Childhood self-control predicts substance dependence (Moffitt et al., PNAS, 2012)



Self-control?

Documenting early development: A family of birth cohorts from Québec

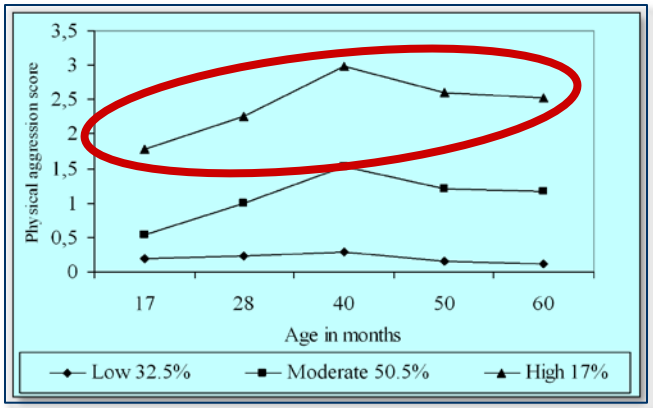


LSCDQ (ÉLDEQ): A prospective longitudinal study of 2000 children, starting at the age of 5 months, who were sampled to be representative of all infants between 59 and 60 gestational weeks of age in 1998 in the province of Quebec. Supported $$ by the Government of Québec, the L&A Chagnon Foundation, GRIP, and piloted by ISQ.

QNTS (ÉJNQ): A prospective longitudinal study of 630 families of twins of the greater Montreal region. Financed par GRIP: Michel Boivin, Mara Brendgen, Ginette Dionne, Daniel Pérusse, Philippe Robaey, Richard Tremblay, Frank Vitaro et al. (MSSSQ, ISQ-SQ, IRSC, PNRDS, CRSHC, FRSQ, CQRS, FCAR, CLLRnet)

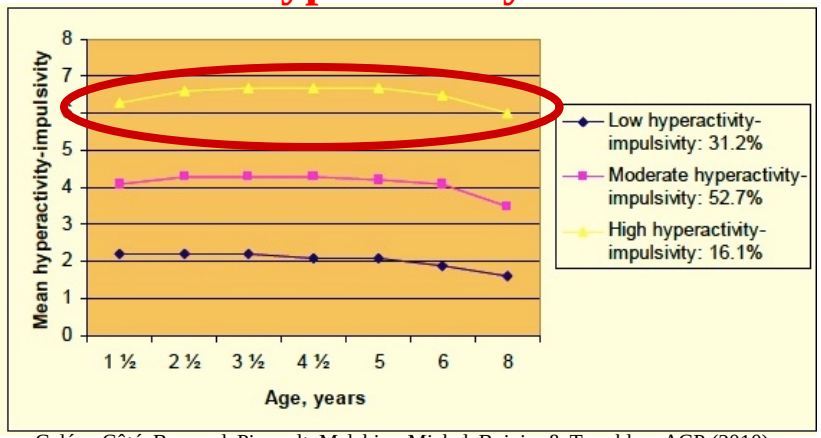
Trajectories of emotional and behavioural difficulties appear very early in life

Physical aggression



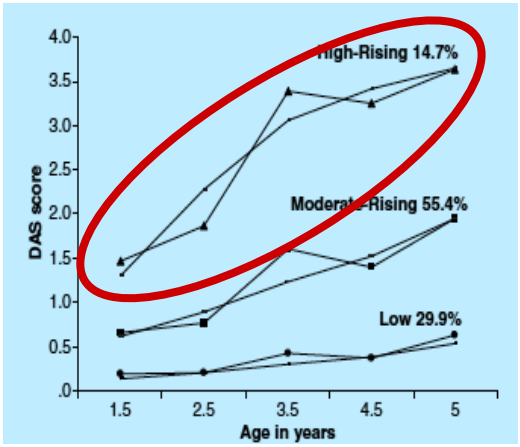
Côté, Boivin, Nagin, Japel, Xu, Zoccolillo, Junger, & Tremblay, AGP (2007).

Hyperactivity



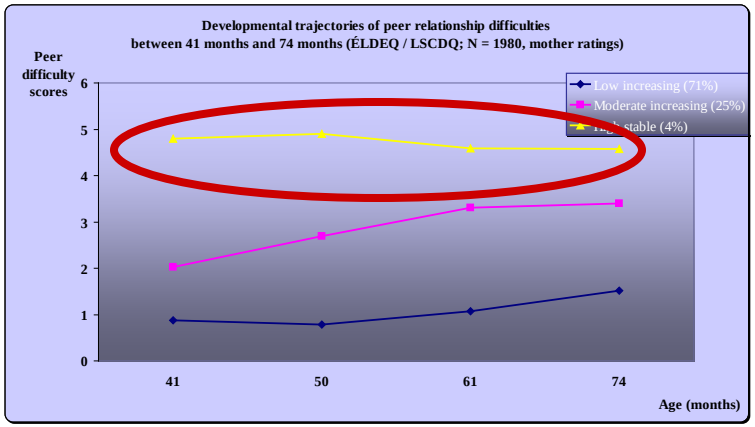
Galéra, Côté, Bouvard, Pingault, Melchior, Michel, Boivin, & Tremblay, AGP (2010).

Anxiety and depression



Côté, Boivin, Liu, Nagin, Zoccolillo & Tremblay, JCPP (2009)

Interpersonal difficulties



Barker, Boivin, Brendgen, Bissonnette, Arseneault, et Tremblay (AGP, 2008)

…and are associated with ++ risk factors reflecting adversity

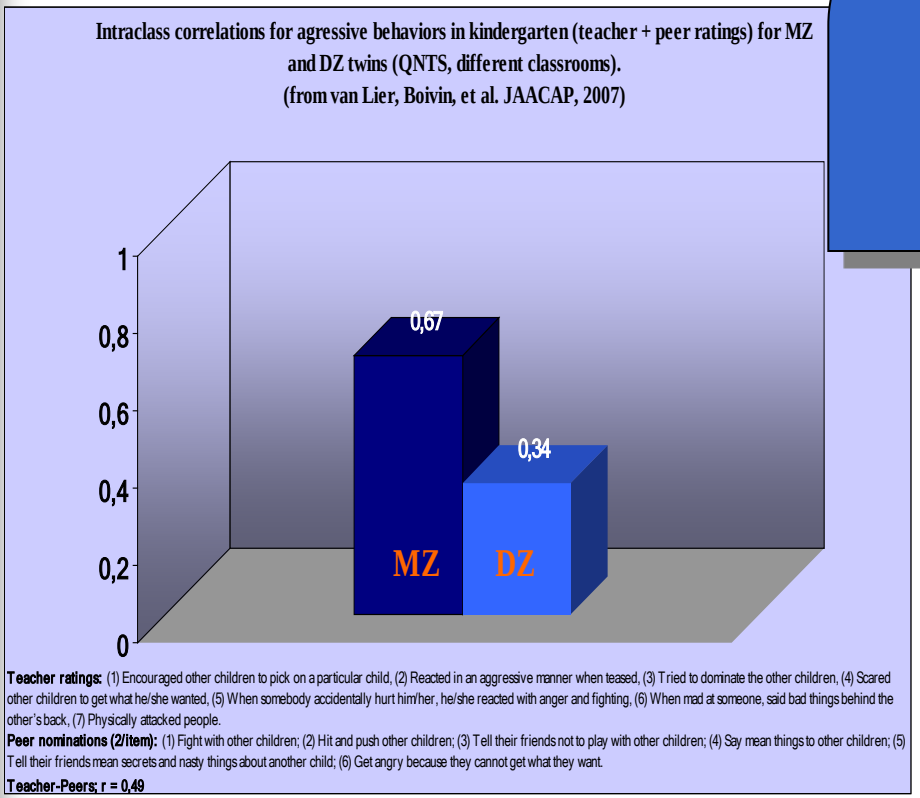
Predictors of a high trajectory of physical aggression

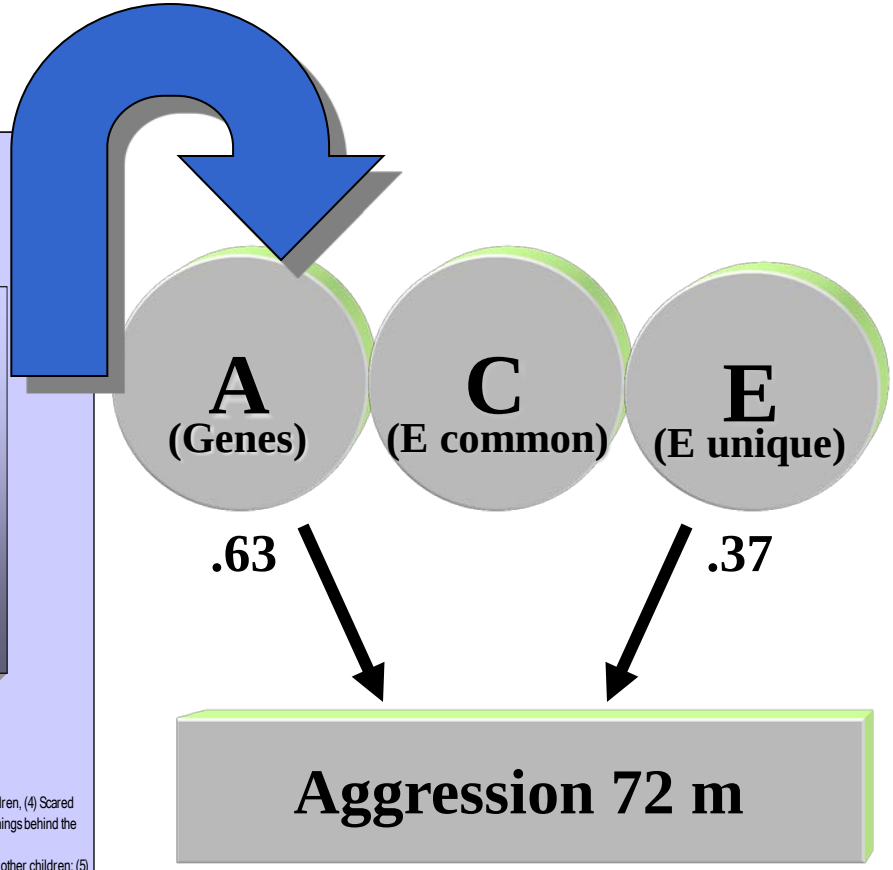
- Male*** (+ genetic risk)
- Maternal depression***
- Conduct problems (mother)***
- Alcohol use (mother)***
- Low perceived self-efficacy***
- Mother not working before 9 months*** (Note: before parental leave policy)
- Having a brother/sister***
- Insufficient income***
- Family dysfunction***
- Other predictors: Poor health at birth*, No high school diploma*, Separated/divorced*.

GE interplay in development

The challenge of complexity and inter-individual variability

The case of aggressive behaviours: G accounts for within-family similarities and E, for within-family differences





(vanLier, Boivin et al., JAACAP, 2007)

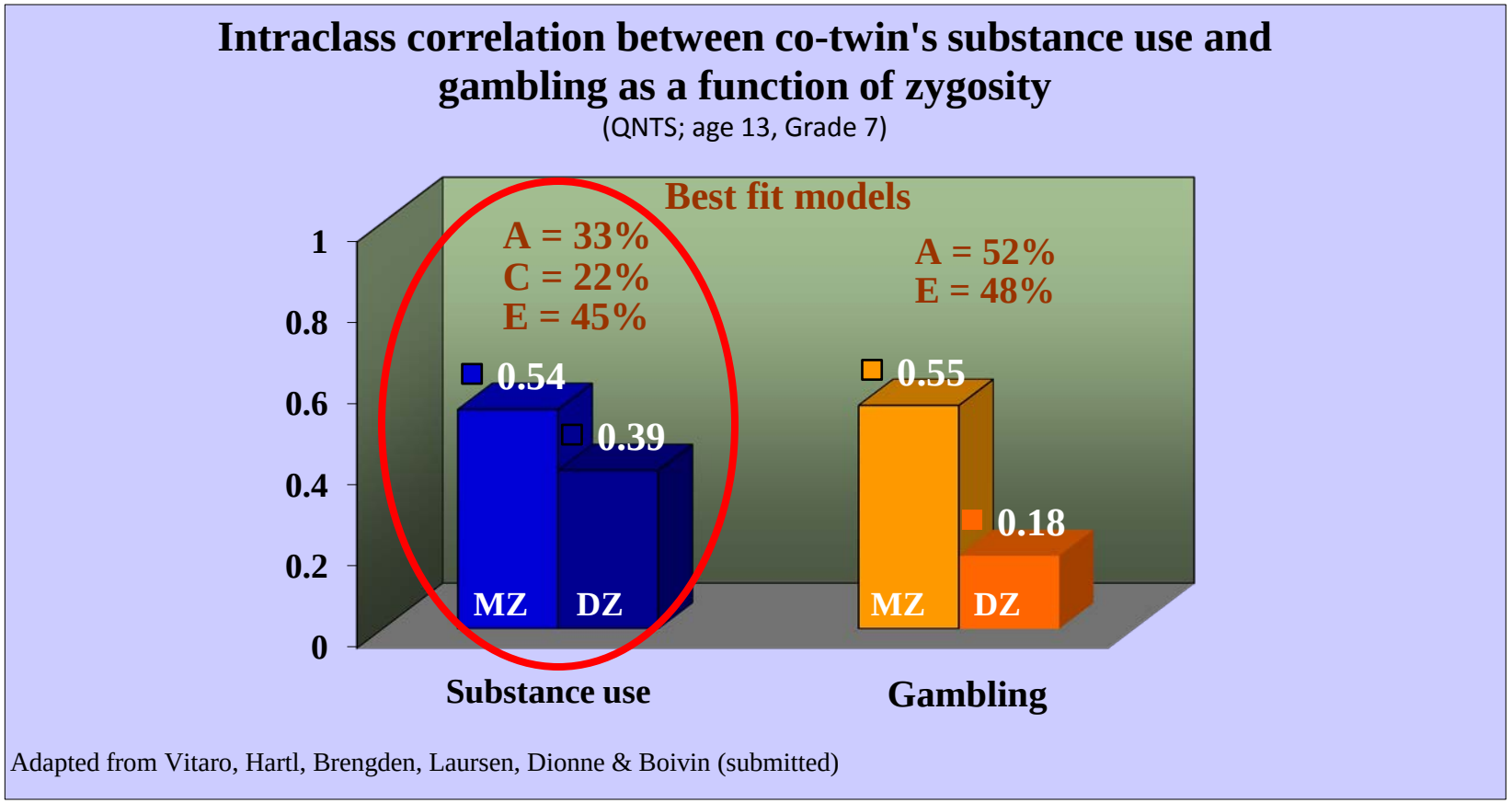
Need to qualify the genetic contribution to substance use as a function of context

- Heritability points to vulnerability/resilience, not to destiny;

- Heritability estimates are not fixed entities; they may not apply
  - To all developmental period; e.g., early adolescence (when initiating),
  - to specific societal groups where adversities may override genetic influence;
  - in contexts where the environment may constrain individual choices (Koopmans et al., 1999; Legrand et al, 2008; Rose et al, 2001);

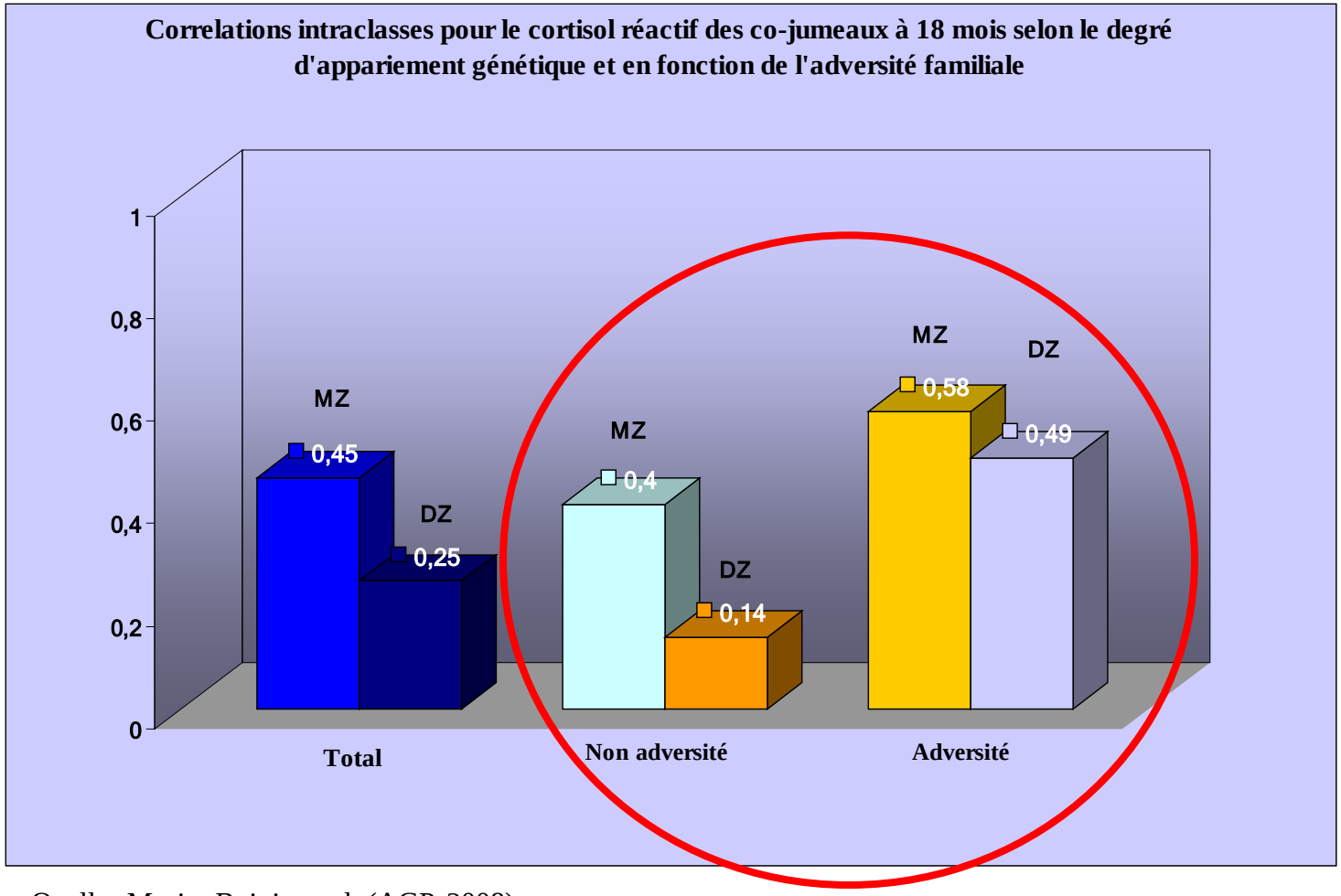
- Heritability likely hide the role of environment in more complex gene-environment transactions, such as G-E correlations (e.g., Cleveland et al., 2005) and GxE interactions in development.
    - Only stating to be documented

Shared and unique E may be more important during early adolescence



Adapted from Vitaro, Hartl, Brengden, Laursen, Dionne & Boivin (submitted)

Familial aggregation of the cortisol response at 18 months according to genetic relatedness and family adversity.



Ouellet-Morin, Boivin et al. (AGP, 2008)

The challenges of the «new» science of ECD for understanding substance use.

1. Describing developmental processes from birth; HUGE undertaking
   - Longitudinal birth/pregnancy cohorts

2. The challenge of complexity; understanding the processes…
   - G-E interplay;
   - «Biological embedding» of early experience (epigenetics);
     - How much? When? Where? How predictive?
   - The multiple levels of biosocial integration;

3. Building an early developmental (i.e., 0 to 6) framework for prevention;
   - Understanding what works in intervention;

4. How do we integrate this “new” knowledge to inform policy and services?

Acknowledgements

Edward D. Barker, Ronald G. Barr, Thomas Boyce, Mara Brendgen, Sylvana M. Côté, Ginette Dionne, Alison Fleming, Nadine Forget-Dubois, Cédric Galéra, Marie-Claude Geoffroy, Clyde Hertzman, Mireille Jetté, Jean-Pascal Lemelin, Harriet MacMillan,
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Québec MSSS, MFA
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Participants of LSCDQ and QNTS

Causes for concern…

Alcohol and drug use among adolescents are still serious problems (Health Canada, 2012)

- The use of marijuana, other illicit drugs and alcohol by Canadian youth (15-24 years of age) **is down since 2004**,
- BUT prevalence among youths remains high…
  - cannabis (25%), 3 times higher than rates for adults (8%);
  - other illicit drugs (7.0%): 9 times higher (adult: 0.8%)
  - heavy frequent drinking (9%): 3 times higher (adult: 3.3%).

Reviews and Overv

Genetic Sensitivity to the Environment: he Case of the Serotonin Transporter Gene and Its Implications for Studying Complex Diseases and Traits

Avshalom Caspi, Ph.D.
Ahmad R. Hariri, Ph.D.
Andrew Holmes, Ph.D.
Rudolf Uher, Ph.D., M.R.C.Psych.
Terrie E. Moffitt, Ph.D.

Evidence of marked variability in response among people exposed to the same environmental risk implies that individual differences in genetic susceptibility might be at work. The study of such Gene-by-Environment (GxE) interactions has gained momentum. In this article, the authors review research about one of the most extensive areas of inquiry: variation in the promoter region of the serotonin transporter gene (*SLC6A4*; also known as *5-HTT*) and its contribution to stress sensitivity. Research in this area has both advanced basic science and generated broader lessons for studying complex diseases and traits. The authors evaluate four lines of evidence about the *5-HTT* stress-sensitivity hypothesis: 1) observational studies [illegible] polymorphic region (*5-HTTLPR*), stress sensitivity, and depression in humans; 2) experimental neuroscience studies about the *5-HTTLPR* and biological phenotypes relevant to the human stress response; 3) studies of *5-HTT* variation and stress sensitivity in nonhuman primates; and 4) studies of stress sensitivity and genetically engineered *5-HTT* mutations in rodents. The authors then dispel some misconceptions and offer recommendations for GxE research. The authors discuss how GxE interaction hypotheses can be tested with large and small samples, how GxE research can be carried out before as well as after replicated gene discovery, the uses of GxE research as a tool for gene discovery, the importance of construct validation in evaluating GxE research, and the contribu- [illegible] to the public understanding of genetic science.

(*Am J Psychiatry 2010; 167:509–527*)

The moderation by the serotonin transporter gene of environmental adversity in the aetiology of mental illness: review and methodological analysis

R Uher and P McGuffin

Medical Research Council (MRC) Social, Genetic and Developmental Psychiatry Research Centre, Institute of Psychiatry, King's College London, London, UK

Serotonin transporter allelic variation in mothers predicts maternal sensitivity, behavior and attitudes toward 6-month-old infants

V. Mileva-Seitz[†], J. Kennedy[‡,§], L. Atkinson[¶],

greater early care quality scored higher on ratings of their *perceived attachment* to their baby ($F_{(5,125)} = 3.27$;

Molecular Psychiatry (2008) 13, 334–347

www.nature.com/mp

ORIGINAL ARTICLE

Interaction between a functional *MAOA* locus and childhood sexual abuse predicts alcoholism and antisocial personality disorder in adult women

F Duc [illegible] M Catena[2], RW Robin[3] and D Goldman[1]

Development and Psychopathology 19 (2007), 1039–1046
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Printed in the United States of America
DOI: 10.1017/S0954579407000521

Parenting quality interacts with genetic variation in dopamine receptor D4 to influence temperament in early childhood

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GxE

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84/08 $30

GxE

Gene-Environment Interaction of the Dopamine D4 Receptor (DRD4) and Observed Maternal Insensitivity Predicting Externalizing Behavior in Preschoolers

Influence of Life Stress on Depression: Moderation by a Polymorphism in the 5-HTT Gene

Avshalom Caspi,[1,2] Karen Sugden,[1] Terrie E. Moffitt,[1,2]*
Alan Taylor,[1] Ian W. Craig,[1] HonaLee Harrington,[2]

PSYCHOLOGICAL SCIENCE

Research Article

SOCIOECONOMIC STATUS MODIFIES HERITABILITY OF IQ IN YOUNG CHILDREN

Eric Turkheimer, Andreana Haley, Mary Waldron, Brian D'Onofrio, and Irving I. Gottesman
University of Virginia

Development and Psychopathology 19 (2007), 1047–1072

Printed in the United States of America
DOI: 10.1017/S095457940707065

Gene × Environment interactions in speech sound disorder predict language and preliteracy outcomes

LAUREN M. McGRATH,[a] BRUCE F. PENNINGTON,[a] ERIK G. WILLCUTT,[b] RICHARD BOADA,[c] LAWRENCE D. SHRIBERG,[d] AND SHELLEY D. SMITH[e]
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