Toward an early developmental approach to substance use/abuse

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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)

- Pregnancy
- Early Childhood (0-6 years)
- Middle Childhood (6-12 years)
- Adolescence (12-18 years)
- Adulthood

Sensitive period

Comorbidities
Cascade effects

- Dropping out
- Depression
- Anxiety
- Inattention/Impulsivity
- Substance abuse
- Obesity
- Health problems
- Violence, etc.

Individual trajectories

- Emotions
- Attention
- Stress
- Self-control
- Learning

Parental Neglect/abuse
- Emotions
- Stress
- Self-control
- Learning

Victimization
- Reject
- Marginalization

Peers

- Parents

Sociodemographic factors (SES, neighborhood, school, etc.)

- Gene
- Experience
- GxE
- Epigenetics
- Care-attention
- Nutrition
- Physical environment

- Dropping out
- Depression
- Anxiety
- Inattention/Impulsivity
- Substance abuse
- Obesity
- Health problems
- Violence, etc.

Parental Neglect/abuse

Epigenetics
GxE
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 alcohol 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)
**QLSCD**: (1) Pilot (1995); (2) Main (1998)

**QNTS** (1995-96-97)

**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

Hyperactivity

Anxiety and depression

Interpersonal difficulties

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

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

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

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
Intraclass correlations for aggressive behaviors in kindergarten (teacher + peer ratings) for MZ and DZ twins (QNTS, different classrooms).
(from van Lier, Boivin, et al. JAACAP, 2007)

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

Teacher ratings: (1) Encouraged other children to pick on a particular child, (2) Reacted in an aggressive manner when teased, (3) Tried to dominate the other children, (4) Scared other children to get what he/she wanted, (5) When somebody accidentally hurt him/her, he/she reacted with anger and fighting, (6) When mad at someone, said bad things behind the other’s back, (7) Physically attacked people.

Peer nominations (2/10): (1) Fight with other children; (2) Hit and push other children; (3) Tell their friends not to play with other children; (4) Say mean things to other children; (5) Tell their friends mean secrets and nasty things about another child; (6) Get angry because they cannot get what they want.

Teacher-Peers; r = 0.49

Intraclass correlations for agressive behaviors in kindergarten (teacher + peer ratings) for MZ and DZ twins (QNTS, different classrooms).
(from van Lier, Boivin, et al. JAACAP, 2007)

A
(Genes)

C
(E common)

E
(E unique)

.63

.37

Aggression 72 m

(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

Intraclass correlation between co-twin's substance use and gambling as a function of zygosity
(QNTS; age 13, Grade 7)

Best fit models

A = 33%
C = 22%
E = 45%

A = 52%
E = 48%

Substance use
Gambling

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);
   - 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

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%).
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

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

GxE

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