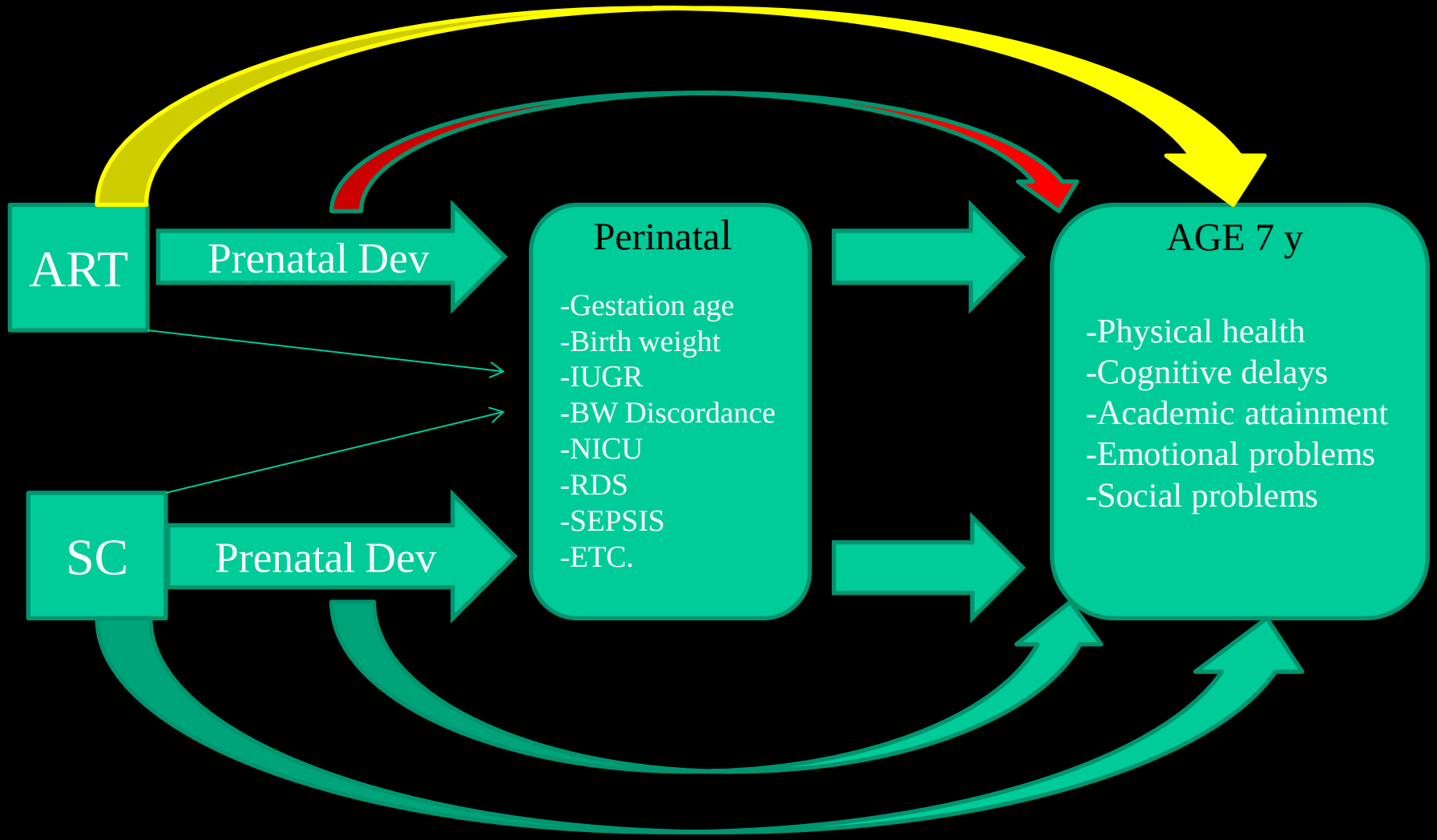
Prevention of Violence:
Lessons Learned from Genetics and Epigenetics

Richard E.Tremblay

Heracles' 10 labours (Hydra)
by Pollaiuolo


ART
Prenatal Dev
SC
Prenatal Dev
Perinatal
-Gestation age
-Birth weight
-IUGR
-BW Discordance
-NICU
-RDS
-SEPSIS
-ETC.
AGE 7 y
-Physical health
-Cognitive delays
-Academic attainment
-Emotional problems
-Social problems

Main research questions

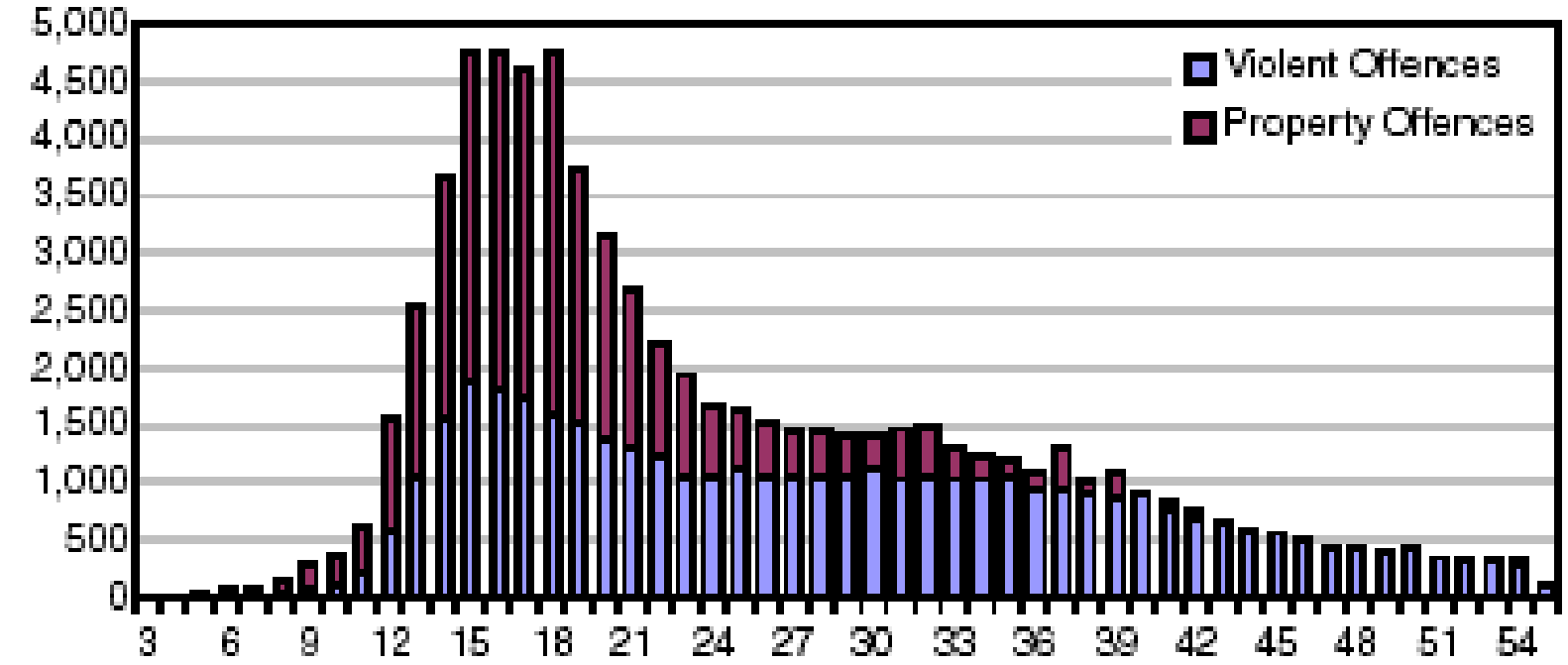
1. When do humans start to aggress?
2. What are the different developmental trajectories of aggression?
3. **What are the causes of these different developmental trajectories?**
4. **How can we prevent chronic physical aggression?**

AGE and Violent Offences

(Age-Crime Curve)

Figure 6

Younger youths less frequently accused of crime than older youths[1], 1999



Statistics Canada (2001)

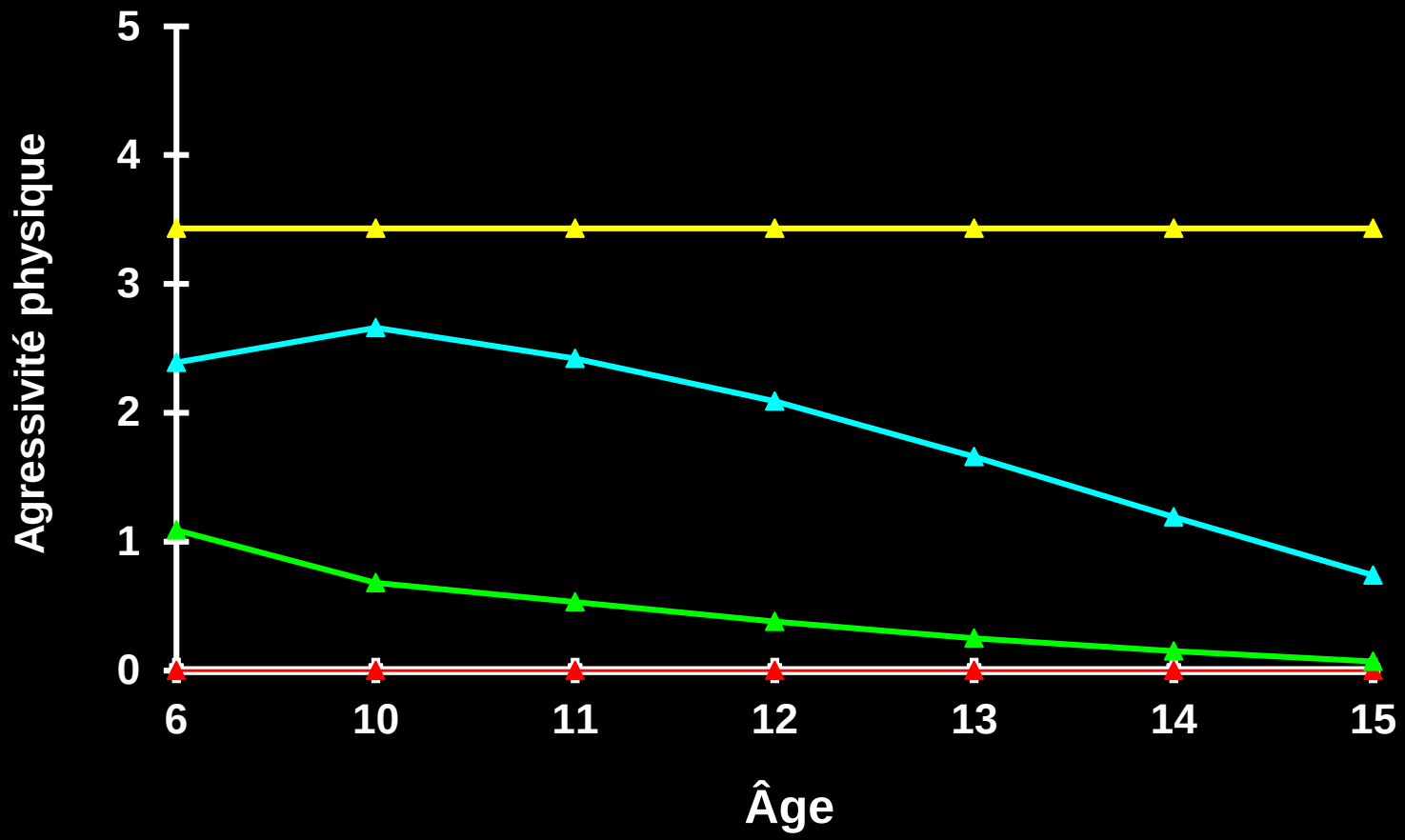
Panel on the Understanding and Control of Violent Behavior (1993)

"Modern Psychological perspectives emphasize that aggressive and violent behaviors are learned responses to frustration, that they can also be learned as instruments for achieving goals, and that the learning occurs by observing models of such behavior. Such models may be observed in the family, among peers, elsewhere in the neighborhood, through the mass media ...".

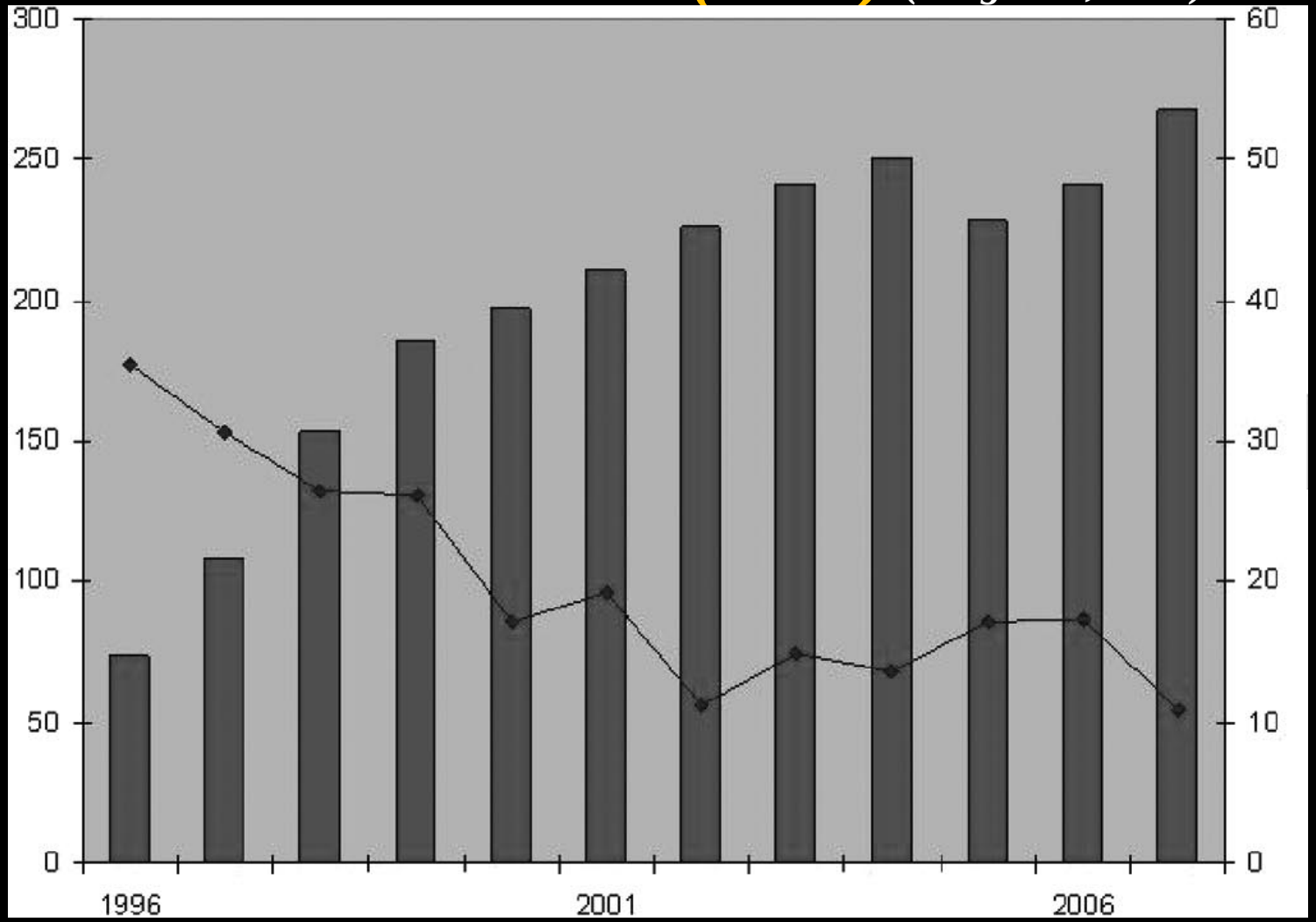
USA National Academy of Sciences
Reiss and Roth, 1993 p.7

PHYSICAL AGGRESSION TRAJECTORIES

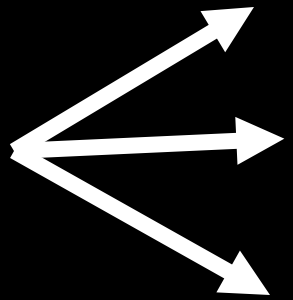
(Nagin & Tremblay, 1999)

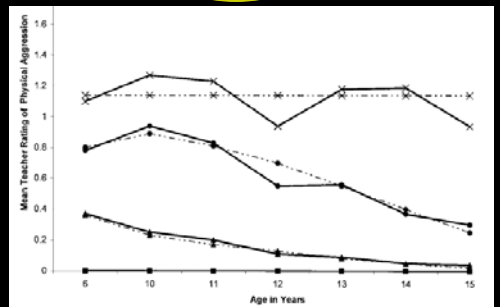


Serious Violent Crimes by Youth and Video Game Sales (USA) *(Ferguson, 2013)*



Boys' Childhood Chronic Physical Aggression

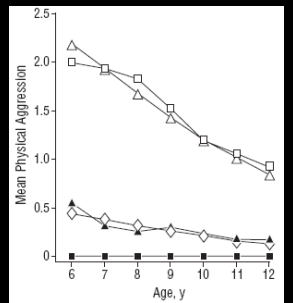


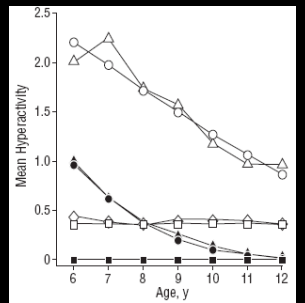


- School Failure
- Tobacco
- Alcohol
- Drugs
- Early Sex
- Violence
- Depression
- Unemployement
- Poverty

Girls' Childhood Chronic Physical Aggression And/Or Hyperactivity

- Tobacco Abuse
- School Failure
- Early Sex
- Partner Aggression
- Depression
- Teenage pregnancy
- Welfare

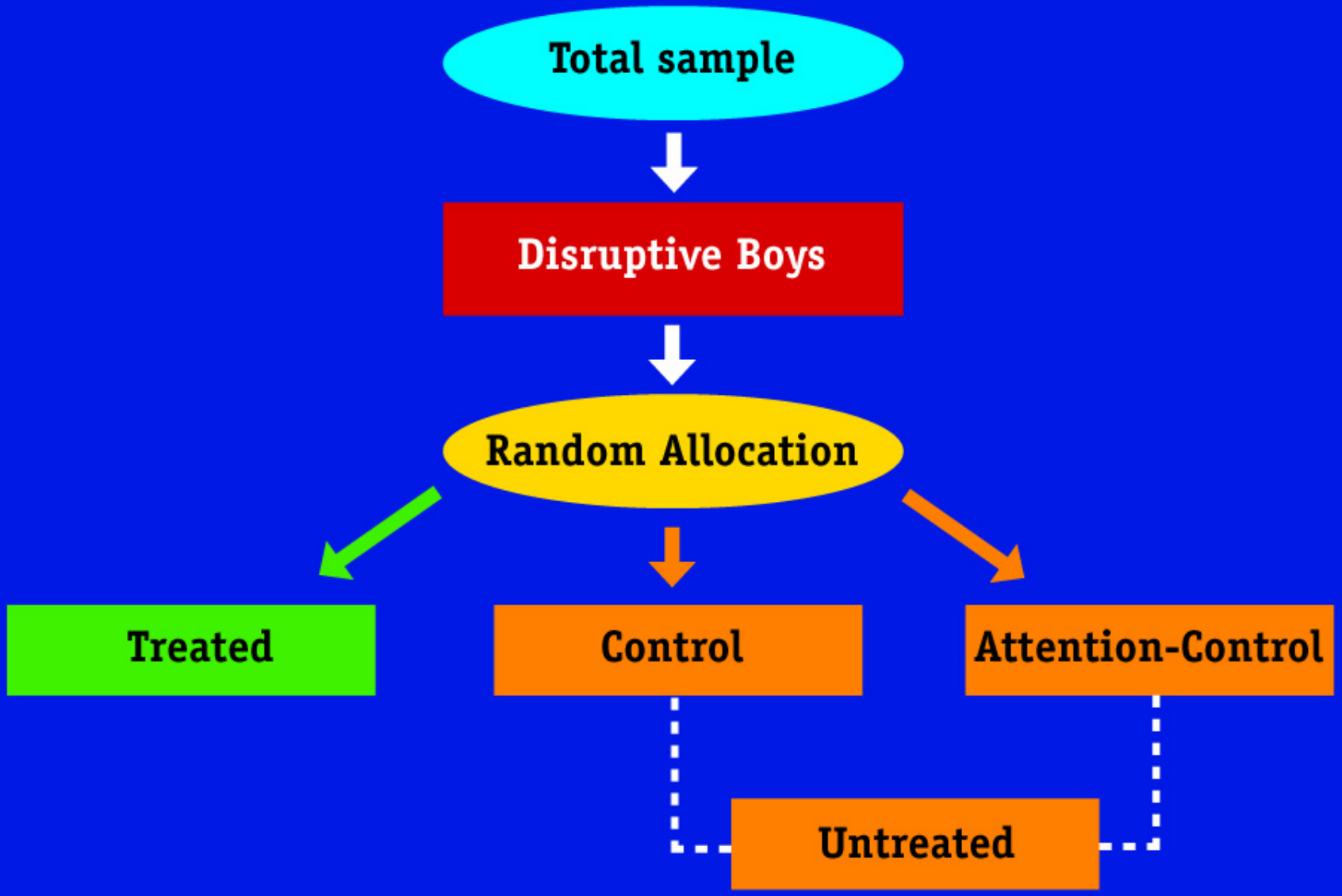




Fontaine et al., 2008, AGP

Prevention of delinquency starting at School Entry

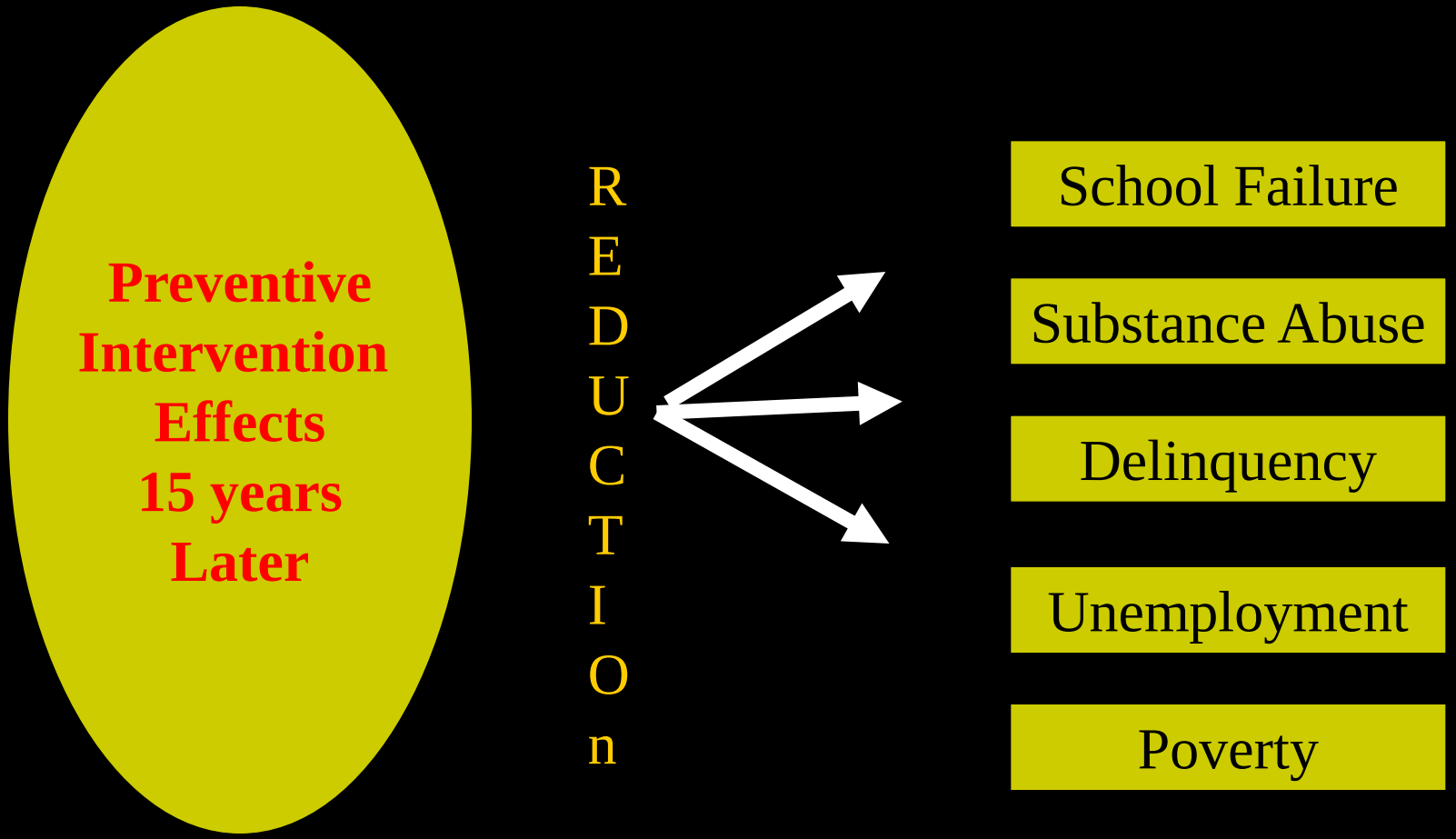
MLES EXPERIMENTAL DESIGN



Preventive Intervention

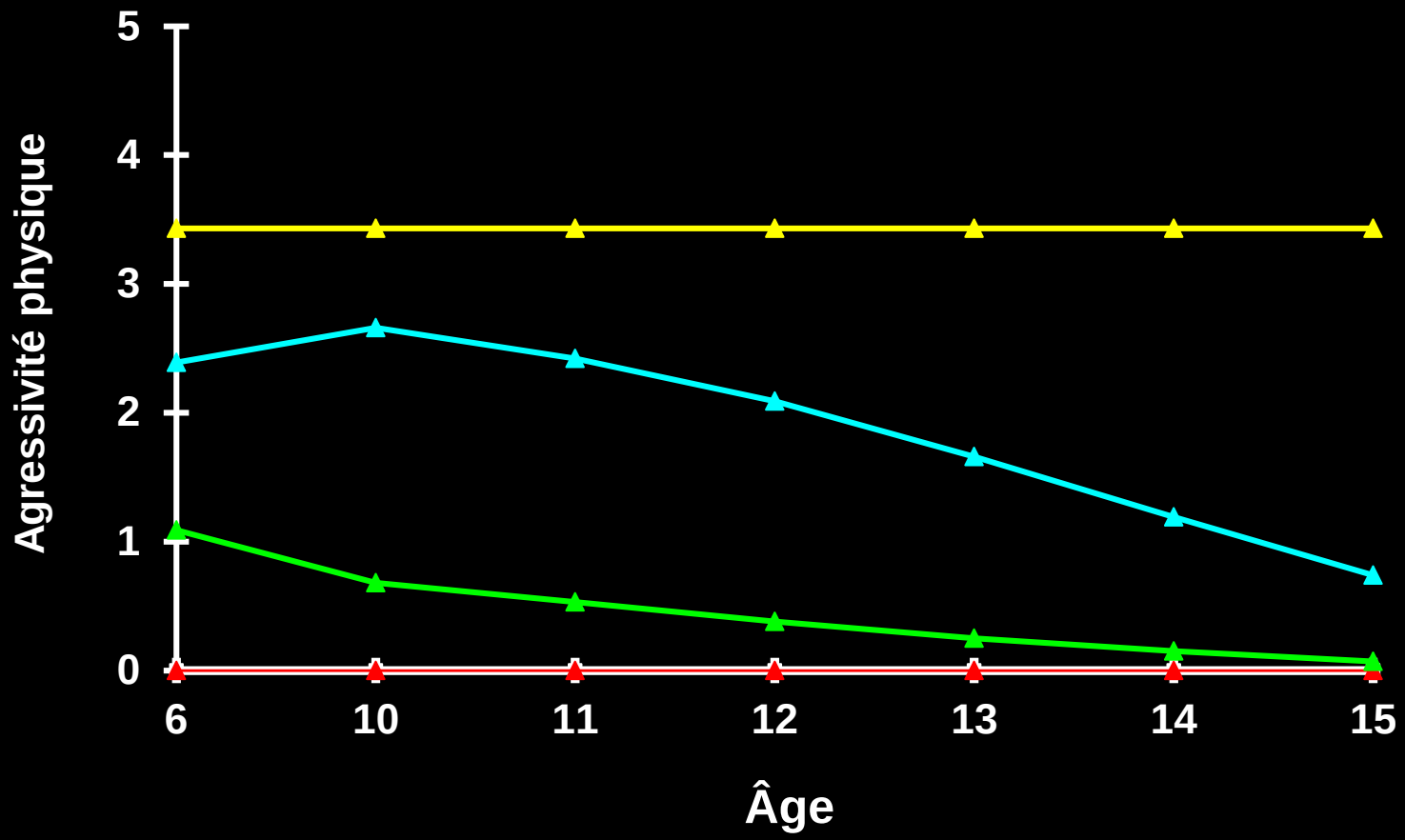
From 7 to 9 years

- Home visits for parent training (2 times per month)
- Social skills training at school with prosocial peers (2 years)
- Teacher support at school (2 years)



BUT NOT VIOLENCE

When Does Physical Aggression Start?



Québec Longitudinal Study of Children

Subjets : 2,223 children representing births in 1997-98 (twins: 600 pairs)

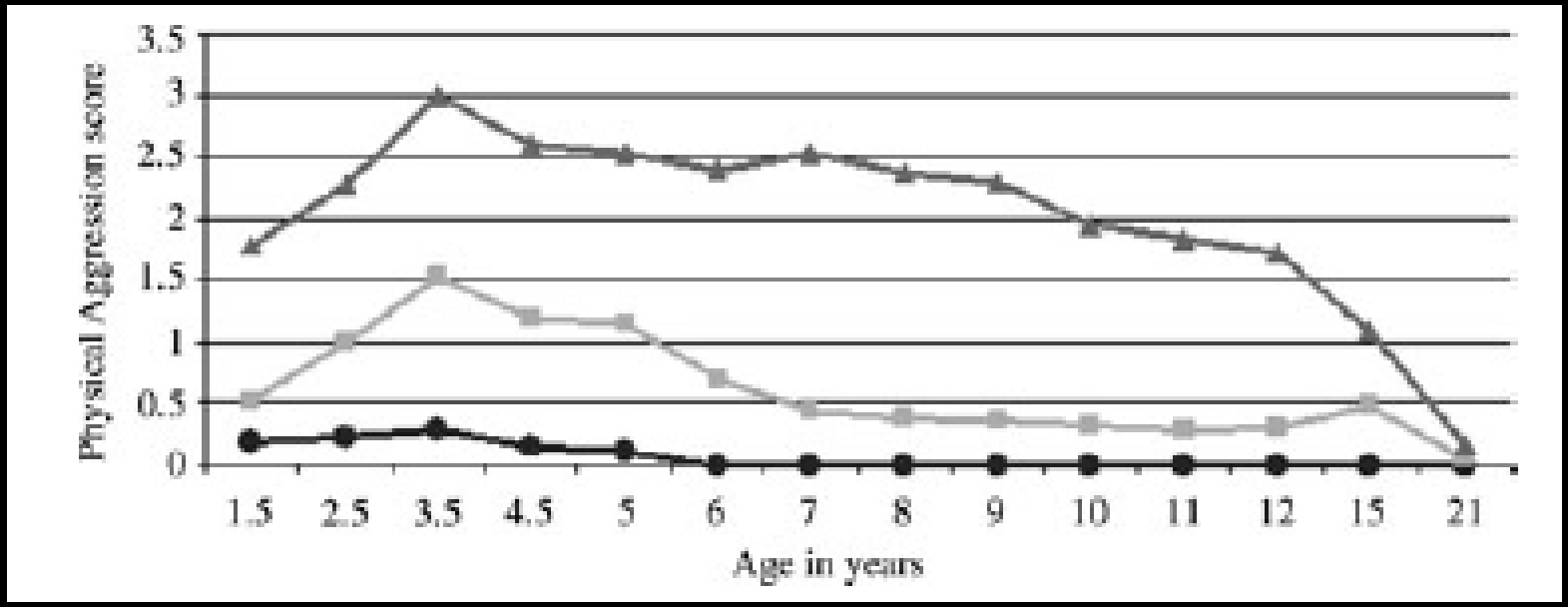
Age at evaluations : 5, 17, 30, 42 months, 5, 6, 7, 8, 9, 10, 12 years

Sources of info : Parents, child care provider, teachers, peers, children, official files. Observations at home, in day care, at school, in the laboratory.

Domains : Physical, emotional, cognitive, social development

Physical Aggression Trajectories

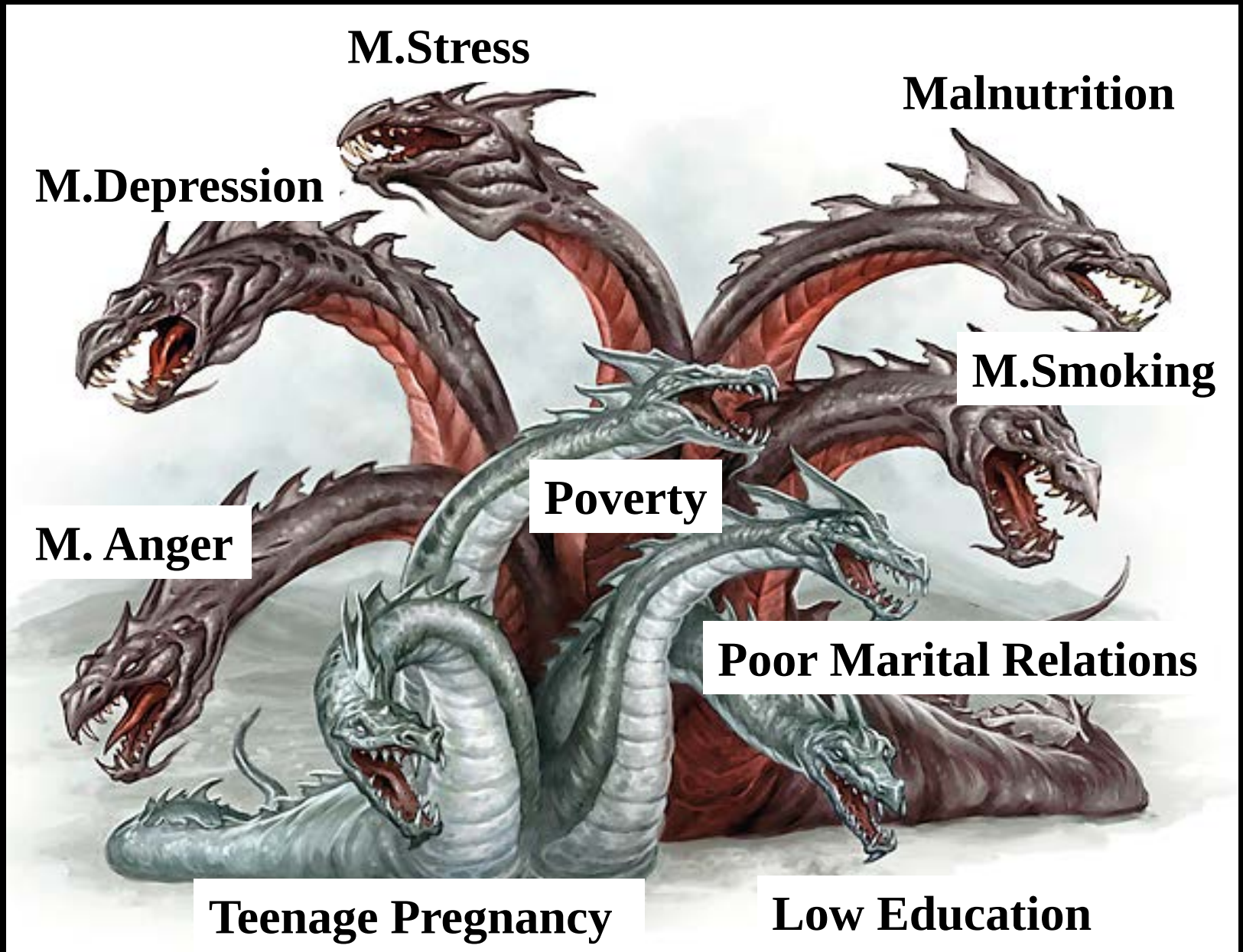
1.5 to 21years

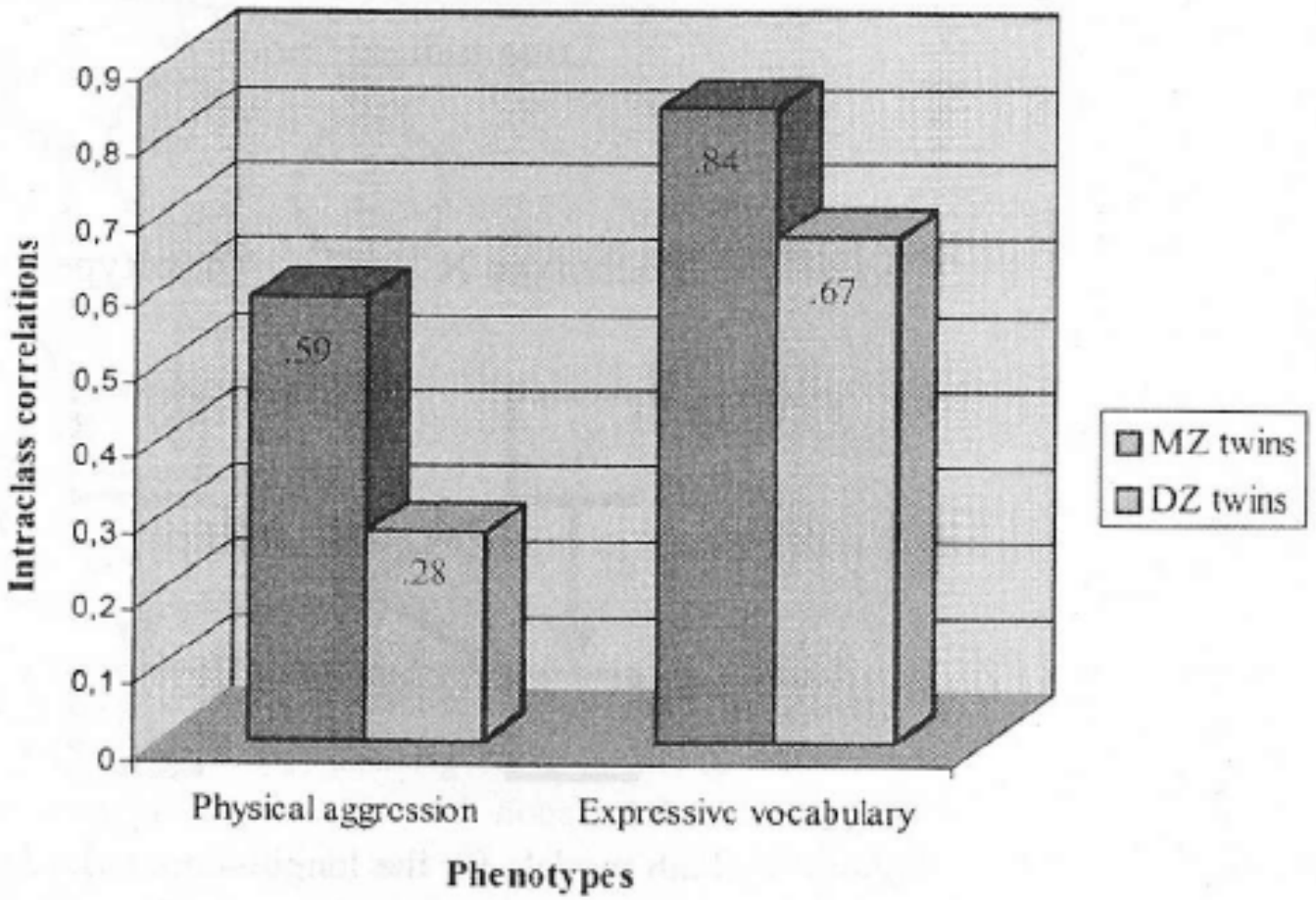


CAUSAL MECHANISMS?

Genes, Environment, Epigenetics

Best Early Predictors of Chronic Physical Aggession



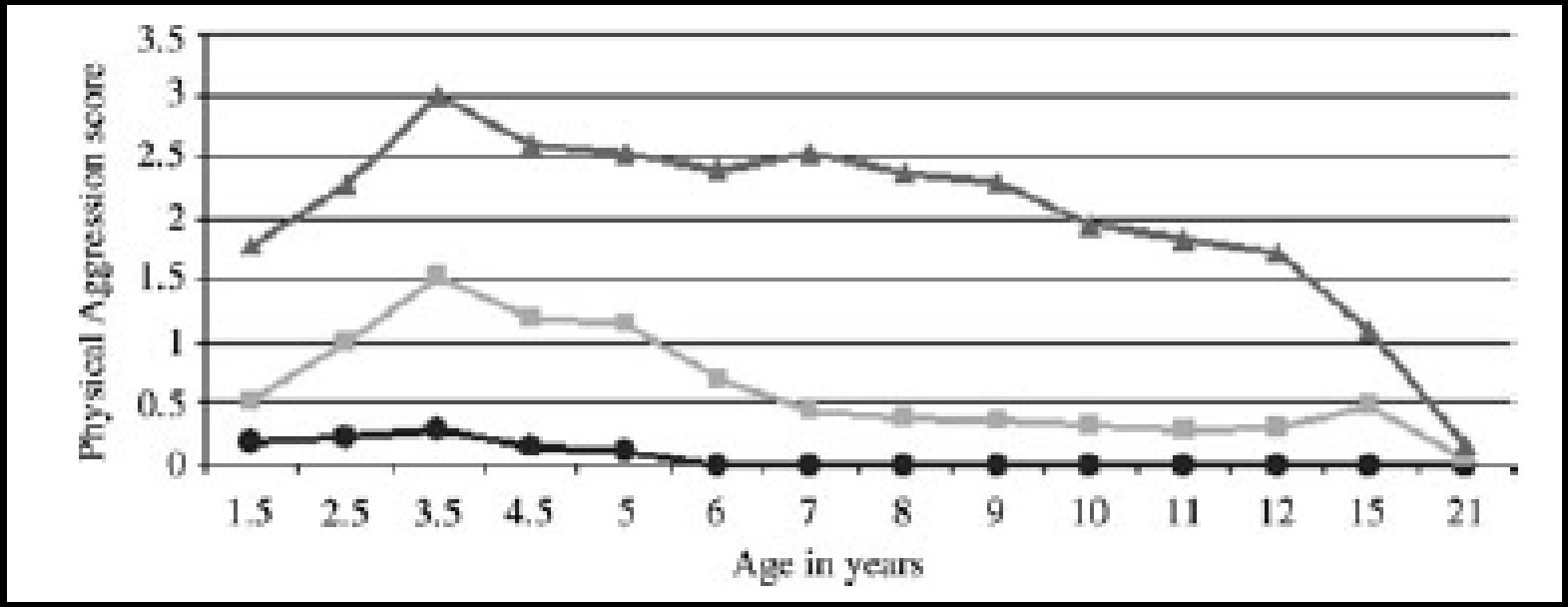


Intraclass MZ and DZ correlations and ACE Model for Physical Aggression and Expressive Vocabulary at 18 Months

A	C	E
82%	0%	18%

Dionne et al., 2003

Strong genetic effects
explain individual differences in frequency of aggression
but …
frequency decreases substantially with age
We are not doomed to aggress because of our genes!



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(Age-Crime Curve)

Figure 6

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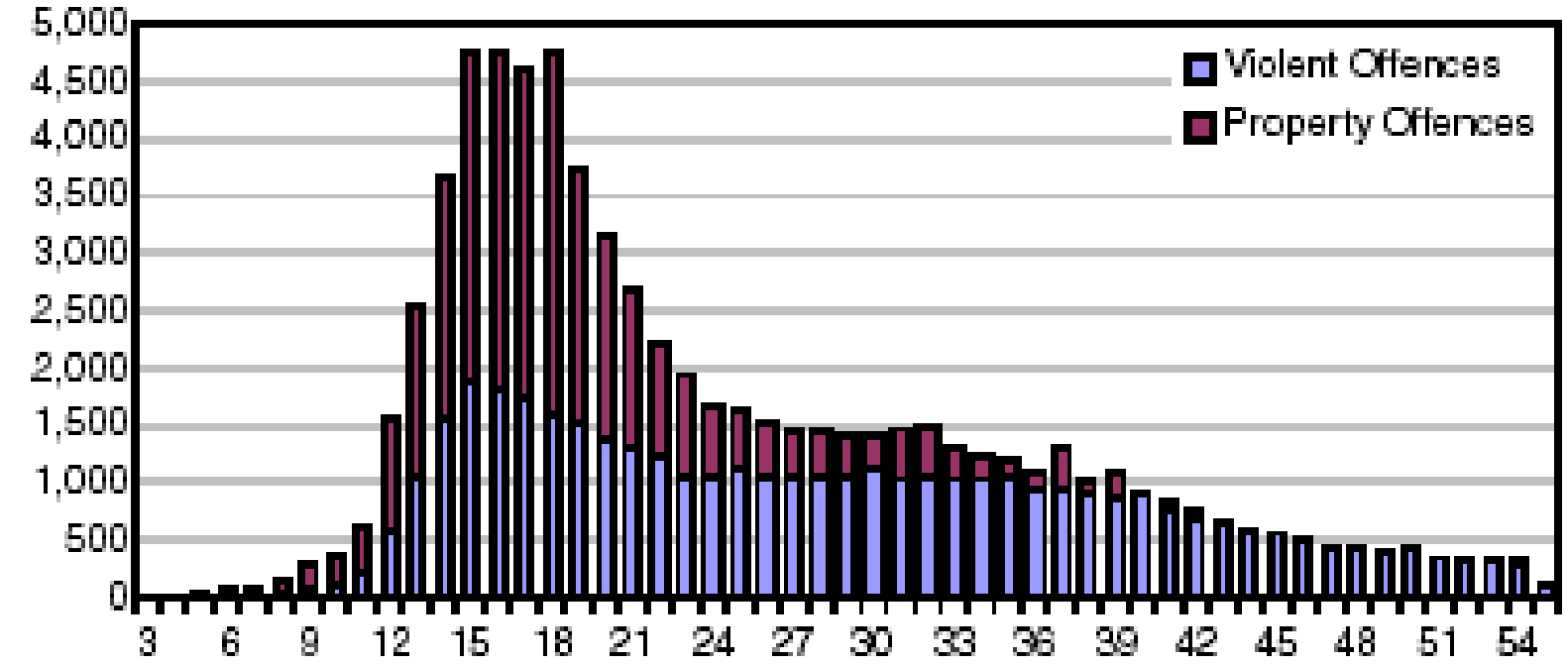


Statistics Canada (2001)

Strong genetic effects
explain individual differences in frequency of aggression
but …
within pair correlation for MZ (who share the same genes)
is only .59

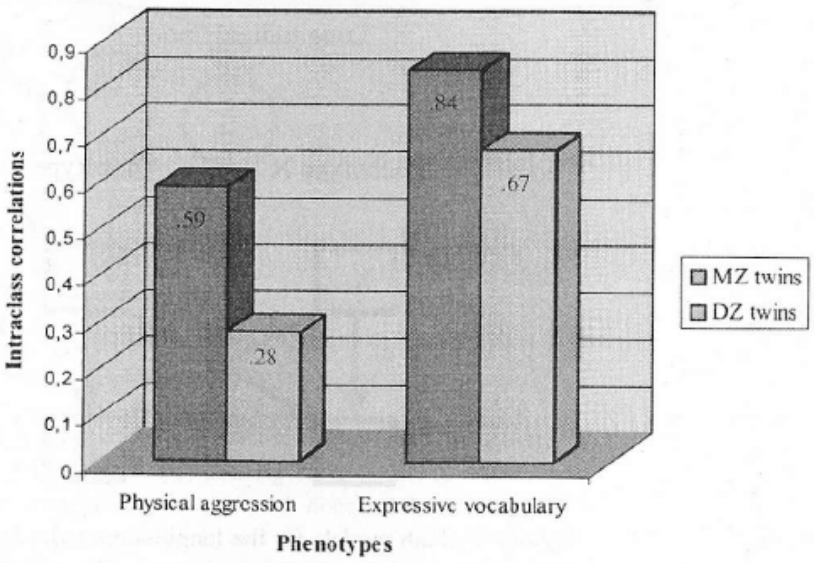
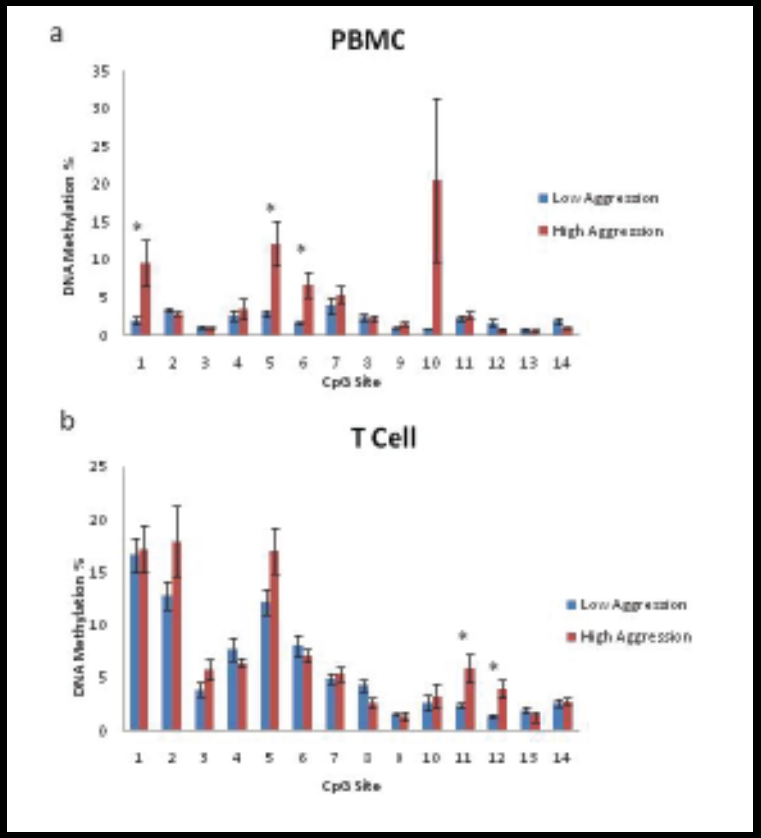


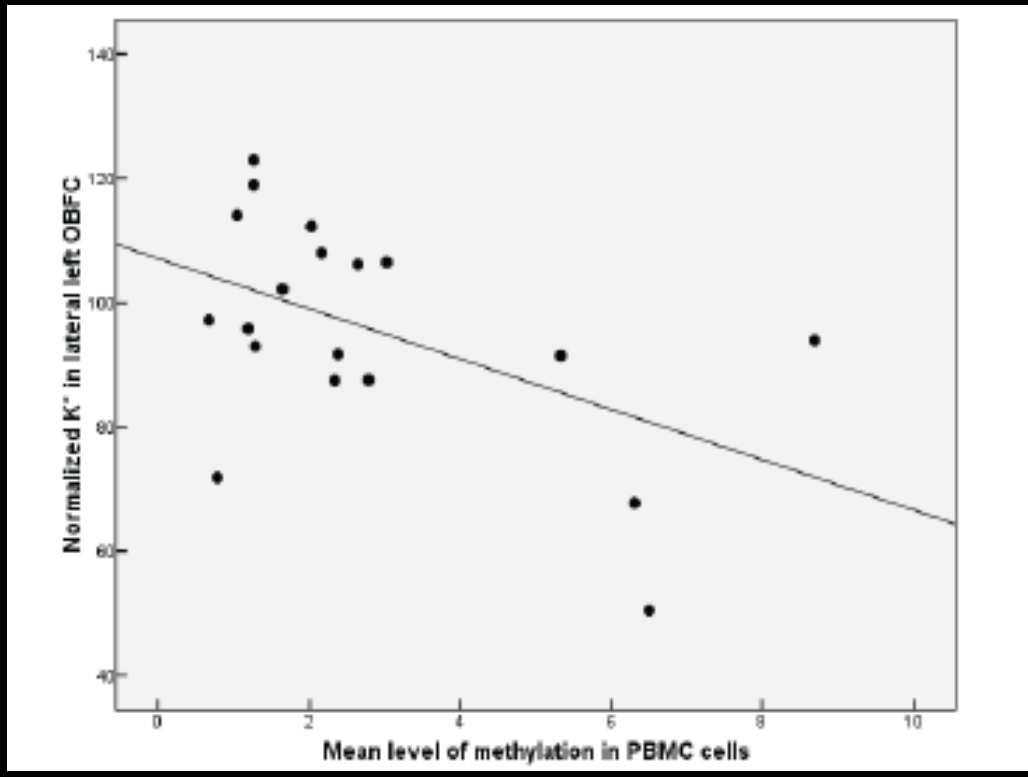
Figure 4. Intraclass monozygotic (MZ) and dizygotic (DZ) correlations for expressive vocabulary and physical aggression.

Epigenetics

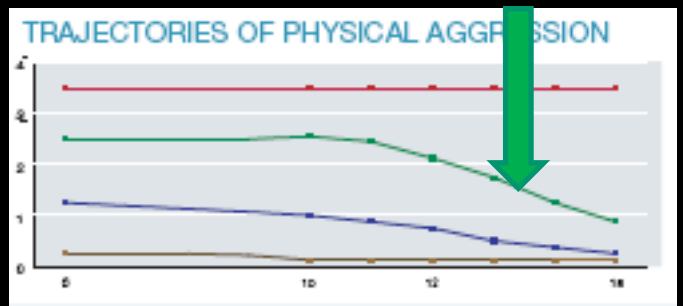
Chemical modification of GENES
by the ENVIRONMENT
(Switching genes on & off)

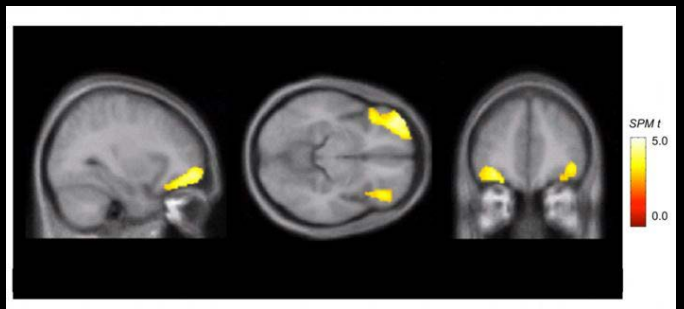
DNA methylation of blood cells, physical aggression and brain serotonin synthesis (Wang et al., 2012, PLoS ONE)





5-HT synthesis & PMBC methylation (r=-0.50, p=0.03)





When and what type of environment creates these DNA methylation differences between the aggressives and not aggressives?

1. A consequences of their chronic aggression? (Injuries, isolation, etc)
2. A consequence of their environment? (e.g. peers, parents)
   -during adolescence?
   -during middle childhood?
   -during early childhood?
   -in utero?
3. A consequence of their genetic endowment?

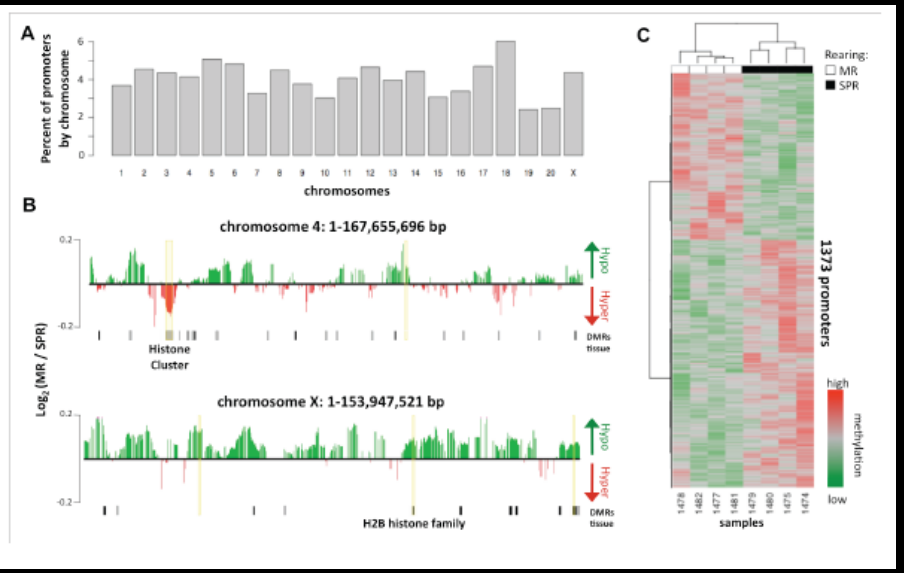
To answer we need experiments that are sensitive to the environment, to its timing and to the genetic code.

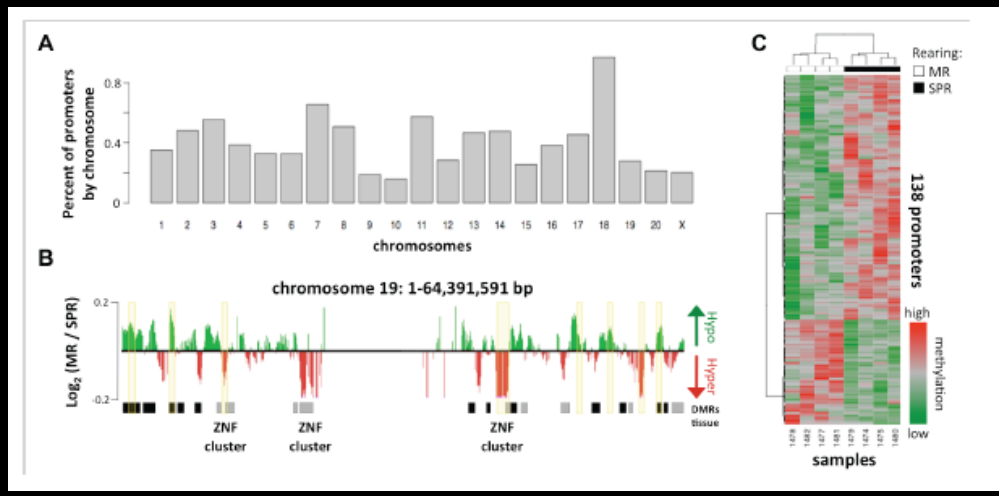
Randomized Controlled Trials

THE SIGNATURE OF MATERNAL REARING IN THE METHYLOME IN RHESUS MACAQUE PREFRONTAL CORTEX AND T CELLS

Nadine Provençal*[1,2,3], Matthew J. Suderman*[1,2,4], Claire Guillemin[1,2,3], Dongsha Wang[2,3], Angela Ruggiero[6], Allyson J. Bennett[5], Peter J. Pierre[5], David P. Friedman[5], Sylvana M. Côté[3], Michael Hallett[4], Richard E. Tremblay[3], Stephen J. Suomi[6&] and Moshe Szyf[1,2&].

J. Neuroscience, 2012





Prefrontal Cortex

T Cells

Back to Humans

- Can we do the monkey experiments with humans?
- Yes, by enriching the environment of deprived families during pregnancy and infancy

Preventive Interventions -9m to 5y

Parent and Surrogate Parent Support

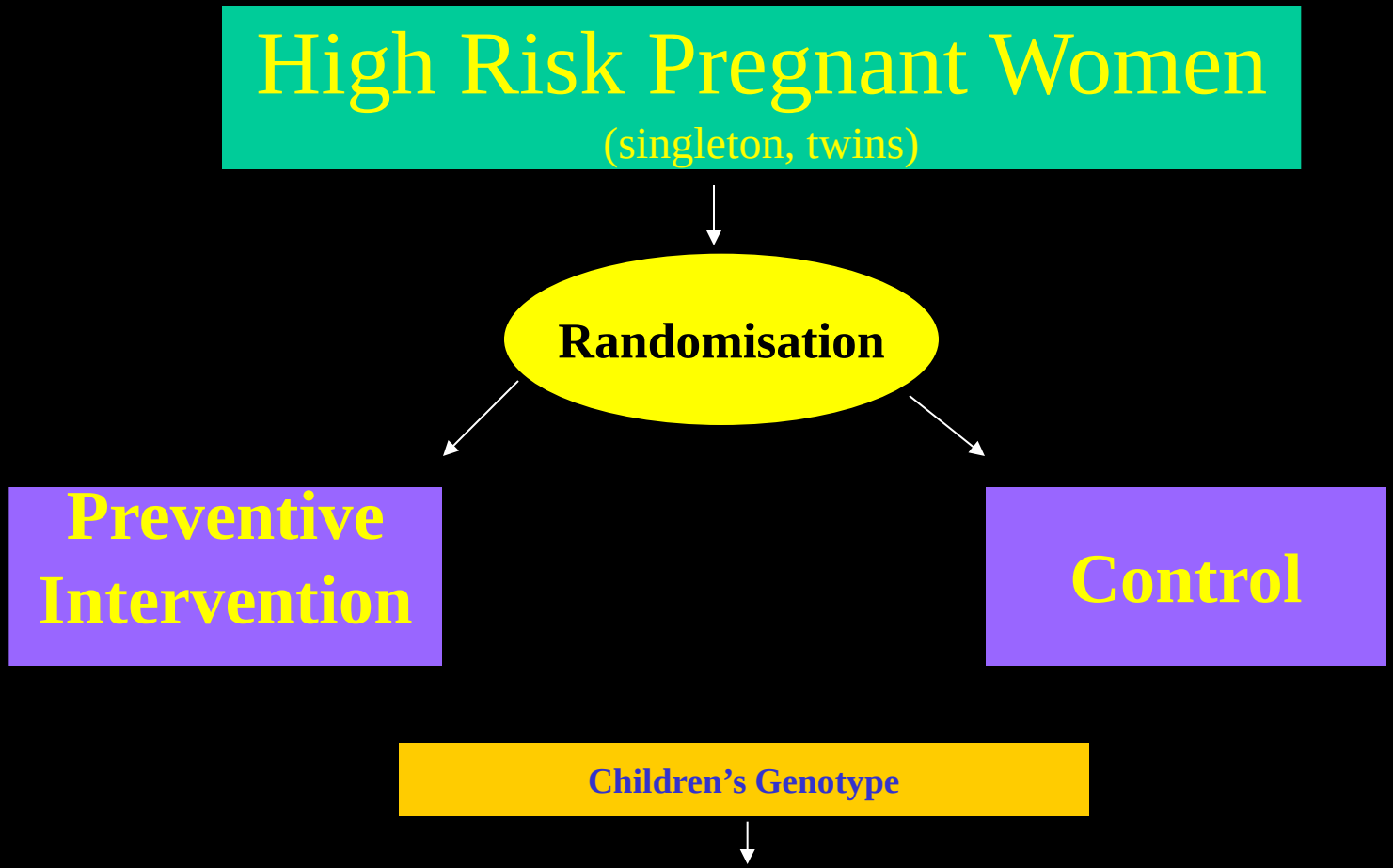
- **Mother's life style during pregnancy**
- **Parenting sensitivity and care**
- **Language development**
- **Executive function development**
- **Play-fighting**
- **Discipline**
- **Prosocial skills**
- **Nutrition**

New tools, new perinatal experiments

- The perinatal experiments from 20+ years ago show long term impacts (e.g. Elmira; Infant Health Dev Program).

BUT

- Not planned to prevent violent behaviour
- No knowledge of early bio-psycho-social **mechanisms** and the **timing** of the effects



Outcomes: 3 Phenotypic Levels

-DNA methylation development
-Brain Development (ex. 5HT synthesis)
-Behavior development (ex. aggression)

Conclusions

1. **Epigenetic analyses have started to identify the mechanisms by which the environment substantially impacts human development.**
2. **Environments (mothers, fathers, nutrition) can modify genetic programming better than attempts to directly manipulate genes.**
3. **By enriching the environment at the appropriate time and intensity we should have system wide impacts on gene expression.**

Conclusions

4. **Environmental effects on human development, like genetic effects, appear strongly intergenerational and highly linked to maternal development.**

5. **If this is true, prevention of chronic aggression and other developmental problems needs to take an intergenerational perspective and start in early pregnancy, at the latest.**

Conclusions (ctnd)

6. **This means that although chronic physical aggression is largely a male problem, its early prevention requires giving the best services to pregnant women and families of new born,**

   because this targets the natural intergenerational bio-chemical-psycho-social systems.

Nkomeshya Mukamambo II
Chief of the Soli people, Zambia

« When you educate a man, an individual is educated.

When you educate a woman, you educate her children - and thus the nation. »

OBRIGADO