Minority Stress and Substance Abuse Disparities among Young African American Men: Does DNA Methylation in the Oxytocin Receptor Gene Play a Role?

14th Annual Texas Conference on Health Disparities

Social Epigenomics & Health Disparities

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Steve Kogan

– Human Development and Family Science
– Center for Family Research
– Basic longitudinal studies on risk and resilience in development
– Bioecological hypotheses: Integrating biomarkers into prospective studies

No Lab Coat Needed
Agenda

• Brief introduction to epigenetics
• $OXTR$ DNA methylation ($OXTRm$)
• The African American Men’s Project
• Modeling $OXTRm$ as a stress mechanism
The social brain meets the reactive genome: neuroscience, epigenetics and the new social biology

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The Limits of Genetic Determinism
Genetic Determinism
The Reactive Genome
Molecular Epigenetics

- Study of mitotically and or meiotically heritable changes in gene functions that cannot be explained by changes in DNA sequence
- Long term alterations of DNA that don’t involve changes in the DNA sequence itself
Epigenetic Control of Gene Activity

Genes can be turned “on” or turned “off” through epigenetic changes
DNA Methylation

- Most commonly studied mechanism
- Addition of a methyl group to a DNA base that can silence or attenuate gene expression
Molecular Epigenetics

- Developmental plasticity
- Intermediate process by which a fixed genome can respond in a dynamic way to the solicitations from a changing environment and produce different phenotypes from a single genome
Molecular Epigenetics

- Some modifications can be maintained throughout life whereas others are susceptible to change later in life under certain circumstances
- Some epigenetic states appear to be transmissible inter-generational
DNA Methylation: Case example

- Meaney et al

A pup that is raised by an anxious, low-nurturing mother becomes an anxious adult.

A pup that is raised by a relaxed, high-nurturing mother becomes a relaxed adult.
The biological embedding of the social environment: DNA Methylation as a Mechanism:
Integrating DNA Methylation into Behavioral Research

• Richly characterized, prospective data
• Engaging participants in genetic research
• Working in transdisciplinary teams
A longitudinal investigation of risk and protective mechanisms associated with high risk sexual behavior and substance use among young Black, rural men.
The African American Men’s Project:
1. 3 Waves
   1. Age 19.5
   2. Age 21 (Saliva specimen)
   3. Age 22.5
2. Self-report data
   1. Concurrent and childhood environments
   2. Prosocial ties
   3. Contextual stressors
   4. Substance use
OXTR DNA Methylation

- OXT – oxytocin
- OXTR – oxytocin receptor
- OXTR – oxytocin receptor gene
- OXTRm – oxytocin receptor gene methylation
Why *OXTR* DNA Methylation?

- OXT and *OXTR*m exhibit associations with early life stress and contemporaneous stressful environments in animal and human studies.

    
Why OXTR-m?

- OXT system in general and OXTRm in particular, have been linked with social cognition, emotion regulation, and response to stress.
Why OXTR-m?

- OXT system is a putative mediator of stress buffering processes
OXTR DNA-m

• T2 saliva sample

Study 1: OXTRm and Substance Abuse Symptomology

- Low levels during adolescence
- Rapid increase among emerging adults
- Despite late onset, increased negative consequences
Study 1: Constructs

- Social environment
  - Childhood trauma (CTQ)
  - Prosocial ties in emerging adulthood (index; relationships with parents, romantic partners, peers)
- $OXTR_m$ index of 13 contiguous sites
- Substance abuse symptomatology
Study 1

Prosocial Ties

Childhood Trauma

Substance Use Problems

OXTR Methylation

Substance Use Problems

Time 1

Time 2

Time 3
Study 1

Retrospective

Time 1

Prosocial Ties

-0.15**

-0.15**

Childhood Trauma

-0.04

OXTR Methylation

-0.04

Substance Use Problems

Time 2

0.20**

Substance Use Problems

Time 3

0.19***

0.09*

Center for Family Research

The University of Georgia
Study 1: Follow Up

- Childhood Trauma → OXTR Methylation
- OXTR Methylation → Substance Use Problems
- Prosocial Ties → Prosocial Ties
- Prosocial Ties → Substance Use Problems

Correlation Coefficients:
- Childhood Trauma to Prosocial Ties: -.28***
- Childhood Trauma to Substance Use Problems: .22***
- Prosocial Ties to OXTR Methylation: -.12*
- Prosocial Ties to Substance Use Problems: .21**
- Substance Use Problems to Prosocial Ties: .11*
- Substance Use Problems to OXTR Methylation: -.03
Study 2: *OXTRm* and Father Involvement (Brown, Kogan, et al)

- Father subsample (N=192)
- Social environment
  - Childhood trauma
  - Social instability (residential instability, school/work disengagement, vocational engagement, economic distress)
- Outcomes
  - Relationship with child’s mother
  - Father involvement
Study 2: Brown, Kogan, et al

Time 1:
- Social Instability
- Childhood Trauma

Time 2:
- OXTR Methylation

Time 3:
- Father Involvement
- Relationships w/ Mother

Relationships w/ Mother
Study 2: Brown, Kogan, et al

Social Instability

Childhood Trauma

.22**

.19**

Social Instability

.19**

OXTR Methylation

.19**

.19*

Relationship w/ Mother

Father Involvement

.47**

-.19**

Time 1

Time 2

Time 3
Discussion

• Potential mediator of the effects of contemporary prosocial ties and social instability
  – Not associated with childhood adversity
  – Childhood adversity is linked to methylation via contemporary social environments

• OXTRm forecasts substance use symptomology and low levels of father involvement
  – Directions of effect?
  – Stability of methylation
Proof-of-Principle Studies

- Integrating methylation into developmental models
- Single time point
- Unknown time frame for malleability for stability
- Single region of single gene
Stress Modulation: Moderational analyses
Limitations/Directions

- Directions of effect and stability
  - Follow-up time point
- Use of saliva vs blood sample
- Self-report method bias
Implications of Epigenetics

• Pharmacological treatments
• Hidden vulnerabilities and intervention development
  – Downstream risks and “biological residue”
  – Intervention impact
The Center for Family Research

• An NIH-funded research center at the University of Georgia
• +20 years of basic and prevention studies with rural African American families
Drop me a line

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