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Short communication

Preliminary evidence for the interaction of the oxytocin receptor gene (oxtr) and face processing in differentiating prenatal smoking patterns

Suena H. Massey[a,b,*], Ryne Estabrook[b], T. Caitlin O'Brien[c], Daniel S. Pine[d], James L. Burns[b], Suma Jacob[e], Edwin H. Cook[f], Lauren S. Wakschlag[b,g]

[a] Department of Psychiatry and Behavioral Sciences, Northwestern University Feinberg School of Medicine, 676 North Saint Clair Street, Suite 1000, Chicago, IL, USA
[b] Department of Medical Social Sciences, Northwestern University Feinberg School of Medicine, 633 North Saint Clair Street, 19th Floor, Chicago, IL, USA
[c] Department of Psychology, Illinois College, 1101 West College Avenue, Jacksonville, IL 62650, USA
[d] Laboratory of Affective & Developmental Neurosciences, NIMH Intramural Research Program, 15K North Drive, MSC-2670, Bethesda, MD 20892, USA
[e] Department of Psychiatry, University of Minnesota, F256/2B West, 2450 Riverside Avenue, Minneapolis, MN 55454, USA
[f] Institute for Juvenile Research, Department of Psychiatry, University of Illinois at Chicago, 1747 West Roosevelt Road, Chicago, IL, USA
[g] Institute for Policy Research, Northwestern University, 2040 Sheridan Road, Evanston, IL 60208, USA

HIGHLIGHTS

- Prenatal smoking patterns may reflect differences in maternal empathic capacity.
- Relation between face processing and prenatal smoking depended on genetic context.
- Enhancing empathy may improve prenatal smoking cessation for selected individuals.
- Oxytocin functioning may be a biological substrate in prenatal smoking behavior.

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ABSTRACT

Prenatal smoking cessation has been described as an empathic action "for the baby," but this has not been empirically demonstrated. We capitalized on a genetically-characterized extant dataset with outstanding measurement of prenatal smoking patterns and maternal face processing data (as an indicator of empathy) to test this hypothesis, and explore how empathy and smoking patterns may be moderated by a genetic substrate of empathy, the oxytocin receptor gene (OXTR). Participants were 143Caucasian women from the East Boston family study with repeated prospective reports of smoking level, adjusted based on repeated cotinine bioassays. Salivary DNA and face processing (Diagnostic Analysis of Nonverbal Accuracy-2) were assessed 14 years later at an adolescent follow-up of offspring. Two-thirds of participants reported smoking prior to pregnancy recognition. Of these, 21% quit during pregnancy; 56% reduced smoking, and 22% smoked persistently at the same level. A significant interaction between face processing and OXTR variants previously associated with increased sensitivity to social context, rs53576GG and rs2254298A, was found ($\beta = -.181$; $p = .015$); greater ability to identify distress in others was associated with lower levels of smoking during pregnancy for rs53576(GG)/rs2254298(A) individuals ($p = .013$), but not for other genotypes ($p = .892$). Testing this "empathy hypothesis of prenatal smoking cessation" in larger studies designed to examine this question can elucidate whether interventions to enhance empathy can improve prenatal smoking cessation rates.

* Corresponding author at: 676 North Saint Clair Street, Suite 1000, Chicago, IL 60611, USA. Tel.: +1 202 577 9286/312 695 6479; fax: +1 312 695 5502.
E-mail addresses: suena.massey@northwestern.edu (S.H. Massey), restabrook@northwestern.edu (R. Estabrook), tcobrien@northwestern.edu (T.C. O'Brien), pined@mail.nih.gov (D.S. Pine), james-l-burns@northwestern.edu (J.L. Burns), sjacob@umn.edu (S. Jacob), edcook@uic.edu (E.H. Cook), lauriew@northwestern.edu (L.S. Wakschlag).

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1. Introduction

Maternal smoking during pregnancy remains a common preventable risk factor for poor pregnancy and birth outcomes [1] and putatively, for externalizing problems across the lifespan [2] despite decades of attempts to reduce its prevalence [3]. While there is a great need to understand how to motivate pregnant smokers to quit and stay abstinent through delivery, most research has focused on psychosocial risks associated with continued smoking rather than modifiable psychological characteristics related to successful cessation [4].

Most women who do successfully quit smoking during pregnancy appear to merely suspend smoking during gestation, then resume after delivery [5] suggesting that motivation to change smoking behavior upon recognition of a pregnancy may be driven by the perceived harm of smoking to the baby, rather than perceived risks to personal health [6]. Moreover, pregnancy involves a change in identity as viewed by others [7]; pregnant women are visibly carrying, and face pressures to conform to societal expectations to assume healthy behaviors [8]. Thus, beyond variations in nicotine dependence [9], differences in prenatal smoking behavior may also reflect important psychological differences among smokers [10], in particular, processes related to concern for others, and differences in sensitivity to social context [11–13]. We aimed to provide an initial empirical foundation for the conceptualization of prenatal smoking behavior change as an empathic behavior, moderated by genetic indicators of sensitivity to social context, with the ultimate goal of identifying targets for future interventions [14].

1.1. Processing of negative facial emotions as a predictor of empathic behavior

One way to measure empathic capacity directly is to assess the ability to accurately identify distress in others through processing of facial expressions [15]. Face processing ability, particularly regarding distress in others, has been shown to be predictive of prosocial (helping) behaviors [16], and individuals lacking in concern for others show deficits in processing facial expressions of fear, sadness, and anger [17]. In this study, we draw on available face processing data as an indicator of empathy, and the tendency to act on behalf of other's needs, in this case, the needs of the fetus.

1.2. Oxytocin receptor polymorphisms and sensitivity to social context

The nanopeptide neurohormone oxytocin has been extensively studied in relation to the tendency to exhibit concern for others, the development of early maternal behaviors [18], neurodevelopmental disorders characterized by social deficits [19,20], and more recently, individual responses to addictive substances [21]. Two single nucleotide polymorphisms (SNPs) in the third intron of the oxytocin receptor gene (OXTR), rs53576 (G/A) and rs2254298 (G/A), have been the subject of intense inquiry as they relate to individual differences in empathy and prosocial behaviors [22]. While the effect of these SNPs on gene functioning are unknown, and they are unlikely to confer main effects individually, there is recent evidence linking the combination of the rs53576GG and rs2254298A variants to face processing ability in children [23]. Moreover, as with the monoamine oxidase gene [24], the serotonin transporter gene [25], and dopamine-related genes [26], these OXTR variants may interact with environmental or other factors to influence psychological outcomes.

For example, relative to A carriers, individuals with the rs53576GG genotype show greater sympathetic reactivity to social stress [27] and increased vulnerability toward attachment problems if exposed to childhood maltreatment, yet seem to benefit more from the stress-buffering effects of social support [28]. Thompson et al. demonstrated that girls who were A carriers at rs2254298 had higher anxiety and depressive symptoms if exposed to early adversity, but had lower levels under favorable environmental conditions [29]. Hence, rather than conferring risk or protective main effects, rs53576GG and rs2254298A in combination may potentiate an individual's sensitivity to social context in a 'for better or for worse' fashion [30].

Within the conceptualization of prenatal smoking cessation as an empathic behavior related to concern for fetal health, moderated by sensitivity to social context, we analyzed an extant genetically-characterized pregnancy cohort with ideal measurement of smoking patterns and available maternal face-processing data to provide an initial empirical foundation for this line of inquiry. We predicted that among women with the GG/A genotype at OXTR rs53576 and rs2254298, greater empathic capacity would be associated with lower levels of smoking during pregnancy. Limitations of utilizing this sample are noted; face processing was assessed in mothers many years later when offspring were adolescents and the sample is relatively small. However, as many larger studies do not have in-depth measurement of these constructs, the current investigation represents a first step toward larger prospective studies specifically designed to examine this question.

2. Material and methods

Participants were from a prospective pregnancy cohort recruited from a neighborhood health clinic in East Boston before 20 weeks of gestation, enrolled in the Maternal Infant Smoking Study of East Boston (MISSEB) between 1986 and 1992 [31] who then participated in a follow-up study of their offspring, the East Boston Family Study (EBFS) [32]. Sample details and study procedures have been described previously [24]. For the current paper, only Caucasian mothers from whom saliva was obtained for genotyping and from whom face-processing data were obtained were included in analyses (Fig. 1). Mothers with face-processing data did not differ from those without in terms of smoking during pregnancy or other variables, described below.

2.1. Pregnancy smoking

Smoking was assessed at each prenatal visit (mean of 6.4 ± 1.7 visits; range = 2–12) by self-report using timeline follow-back methodology [33] combined with blood and urine cotinine radioimmunoassays [34]. Smoking patterns were established via a 'best-estimate' approach such that non-disclosure and underreporting were corrected based on serum cotinine values, employing statistical methods previously described [35]. A continuous corrected mean serum cotinine measure of average cigarettes per day across pregnancy was used as the dependent variable.

2.2. OXTR genotyping

Salivary DNA was collected using DNA Genotek Oragene self-collection kits and quantitated with a fluorescent Quant-iT PicoGreen dsDNA Assay (Invitrogen, Carlsbad, CA, USA) after extraction, then normalized to 10 ng/μL. SNP markers were genotyped using TaqMan® SNP Genotyping Assays (Applied Biosystems, Foster City, CA, http://www.appliedbiosystems.com). TaqMan® PCR reactions were done with Universal Master Mix Amperase® UNG, 0.25 μL Taqman probe mix and 2.25 μL water for a 5 μL total volume. PCR conditions (PerkinElmer 9700 Thermocycler) (Applied Biosystems, Foster City, CA) were: one AmpErase® step at 50.0 °C for 2 min, one enzyme activation step at 95.0 °C for 10 min, 40 alternating cycles of denaturation at 92.0 °C for 15 s, and reannealing and extension at 58.0 °C for 1 min. Fluorescence intensity