Interactions between Genes and Social Context

For Contraceptive Use in Adolescence and Young Adulthood

Guang Guo

Jonathan K. Daw

Department of Sociology, UNC-Chapel Hill

Introduction

Patterns of contraceptive nonuse have serious health consequences, pointing to a compelling need for basic and applied research on the full range of contributing factors involved. Rates of unintended pregnancy and STIs are high in the United States, and are highest among teens and young adults (Henshaw 1998). Differential rates of unintended pregnancy among racial and ethnic minorities contribute to disparities in socioeconomic and health prospects of both parents and children. Among sexually experienced teens and young adults, unintended pregnancies are the result of either contraceptive non-use or contraceptive failure (Brown & Eisenberg, 1995).

Our project will take advantage of previous work on patterns of contraceptive use and consistency across sexual relationships within current cohorts of teens and young adults. Noticeably absent from previous work on this subject are the likely contributions of predispositional genetic factors in contraceptive usage which interact with these environmental considerations. There are good reasons to believe that certain extensively studied genotypes may dispose individuals towards risky behavioral patterns (Caspi et al 2002, 2003; Guo and Tong 2006). The overall goal of this project is to remedy this imbalance and to identify genetic factors that interact with environmental and other non-genetic factors to influence patterns of contraceptive use.

Our project takes advantage of the data from the National Longitudinal Study of Adolescent Health (Add Health) Research Program whose goals are to understand how social contexts, experiences, and behaviors influence well-being in adolescence and early adulthood. Add Health's prospective, longitudinal design, its exceptionally large range of social, demographic, psychological, and behavioral information, and its sample size (projected Wave IV sample of 17,000 participants) will allow for the unprecedented investigation of how environmental factors interact with genetic factors to influence contraceptive among adolescents and young adults in the US population. We will assess these relationships for critical sub-populations, including by race/ethnicity (comparing Hispanics, non-Hispanic blacks and non-Hispanic whites), by age (comparing younger and older teens and young adults) and by gender (comparing females and males). Understanding patterns of contraceptive use/nonuse will help inform strategies to prevent unintended pregnancy and STIs.

Sample and Variables

For each wave, the effective sample are those members of the Add Health genetic sample who report having had sex at the time of interview. At Wave I this incorporates 853 individuals; at Wave II this includes 1159; at Wave III the sample is 2221.

The analyses presented in this abstract include four outcome variables – any effective contraceptive usage at most recent sex by wave ('all'), condom usage at most recent sex by wave, non-condom contraceptive method usage at most recent sex by wave ('other'), and any effective contraceptive usage at first sex (pooled across all wave subsets). The 'other' category is mutually exclusive from the recent condom usage category for analytical purposes. Contraceptive methods deemed 'effective' for our purposes include condoms, birth control pills,

vaginal sponges, forms, jellies, cremes, suppositories, diaphragms, IUDs, Norplant, rings, Depo Provera, and contraceptive films. Withdrawal and pull out are excluded.

In our statistical analyses, we model these outcome variables as functions of genotypes for the DRD2, DAT1, DRD4, MAOA, and SLC6A4 genetic loci, and for a series of demographic controls – race/ethnicity, gender, and age at interview. Future work will incorporate environmental measures to further isolate the genetic effects and explore possible gene-environment interactions for contraceptive usage.

Preliminary Results

Initial analyses support a view of adolescent contraceptive practice informed by individual, contextual, and genetic factors. Many polymorphisms display statistically significant bivariate relationships with different measures of contraceptive usage – effects whose nature interact strongly with gender and age.

To begin, we estimate a series of bivariate logistic regression models predicting contraceptive nonuse at last sex for each of three waves of Add Health, segregated by gender (table 1). Here we see that the 2R/- (for MAOA) and 9R/10R and 10R/10R (for DAT1) positively predict contraceptive nonusage at last sex, with significant effects showing up only in Wave I for the former and in Wave III for the latter. Furthermore, DRD2 183/183 and 304/304 genotypes negatively predict contraceptive nonusage in Wave III and, for 183/183, Wave II. All effects that varied by gender were limited to females only.

Next, we examine the nature of these effects by examining condom use at last sex and non-condom use at last sex (constructed mutually exclusively). These results are more difficult to interpret. In the condom usage models, some effects (DRD2 183/183, MAOA 2R) run in opposite directions from the 'all' results, and a number of new effects appear (DRD4 427/-,

SLC6A4 484/484). The 'other' usage models conform more strongly with the results for 'all,' as no directional genetic effects contrast. The main differences lie in the waves at which effects appear and the presence of a few novel effects vis-à-vis the 'all' models.

Clearly, statistical genetic effects on contraceptive nonusage are not a simple story, as behooves such a complex human behavior. This preliminary evidence suggests that any effects on condom usage are very different in nature from those for other contraceptive types. Our work for this project in the near future will necessarily address this apparent discrepancy.

Our next results are the estimated coefficients from a series of general estimating equation analyses (table 2), which utilizes each individual*wave unit as a separate observation, yielding 6663 total 'cases,' with all values missing for cases at which point the respondents were still virgins, resulting in 4233 nonmissing 'cases.' Here we see even more clearly the ways in which genetic contributions to contraceptive behaviors as a function of age, since we have the full range of age observations available to us. The DRD2 304/304 genotype shows a strong negative effect on contraceptive nonuse, with stronger effects for those older than 18. DAT1 9R/10R positively predicts nonuse, as before, but this effect is limited to females over 18. Although MAOA 2R/- predicts nonuse in a number of table cells, the gender*age effect is limited to females 18 or younger only. This last effect for the 'all' models is the only one preserved in the condom models. In the 'other' models, DRD2 304/304 again shows a number of statistically significant negative effects on contraceptive nonuse, and 183/183 negatively impacts contraceptive nonuse among females older than 18. Note that the coefficients for the GEE analyses are far more stable in direction and significance than were the logistic regressions by wave, and that all significant coefficients from the condom and 'other' models agreed with the 'all' model results when both effects were significant.

We found far fewer statistically significant effects for contraceptive nonusage at first sex than for recent use. Bivariate logistic regression analyses showed positive effects for DAT1 genotypes including no 9R or 10R alleles, for both males and females. The DRD4 379/- and 379/379 genotypes both positively predict contraceptive nonusage at first sex for all individuals, but not males and females individually (likely a function of cell sizes). The GEE analysis for this variable (results not shown) yields only one statistically significant coefficient, for MAOA 2R/-. Clearly, the statistical evidence suggests that contraceptive usage is structured less strongly by one's genotype than in later sexual experiences.

Future Analyses and Conclusion

We recognize that contraceptive usage is a very complex human behavior, influenced by and intertwined with a huge range of individual and social factors. Clearly much work remains to be done to understand the nature of the genetic associations our results document. We need to examine a greater range of environmental-, individual-, and relationship-level variables than these preliminary analyses incorporate in order to rule out the possibility that these results are the result of statistical conflation, and to examine possible interactive avenues through which genetic effects might operate. We also wish to more fully explore more complete measures of contraceptive nonusage, such as variables indicating patterns of consistency in contraceptive usage.

On the genetic side of things we have more work to do as well. We plan to conduct haplotype analysis once novel genotyping becomes available. In addition to gene-environment interactions, gene-gene interactions must also be considered. And to account for possible confounding effects of population structure, we will employ sibling-based QTDT, a statistical

package for use in genetic linkage analyses. Even more, the results of future work will likely suggest additional work that needs to be done.

To conclude, while the authors of this research are themselves very interested in human biology, our primary motivation for this research lies in an interest in traditional demographic and sociological realms of research. We believe that investigating biological factors in human behavior serves not only its own purposes, but helps us as social scientists to attain a fuller appreciation of the range of influences on human action, and helps to isolate the pure effects of individual and environmental factors whose estimated coefficients predicting contraceptive behavior may have been distorted by a lack of controls for genetic factors in previous research.

References

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Table 1 – Genetic Effects on Contraceptive Usage at Recent Sex by Wave and Gender1

	Wave I			Wave II			Wave III		
ALL	All	Male	Female	All	Male	Female	All	Male	Female
DRD2 (vs het):									
183/183	---	---	---	---	---	-0.4321	-0.2102	---	
304/304	---	---	---	---	---	---	-0.6242	---	-0.8852
DAT1 (vs. 9R/9R):									
9R/10R	---	---	---	---	---	---	---	---	0.8733
10R/10R	---	---	---	---	---	---	---	---	0.7965
MAOA (vs. only 3.5R & 4Rs)									
2R/-	1.0148	---	1.1937	---	---	---	---	---	---
CONDOM									
DRD2 (vs het):									
183/183	---	---	---	---	---	---	---	---	.3351
MAOA (vs. only 3.5R & 4Rs)									
2R/-	---	---	---	---	---	---	-.7840	-1.3257	---
DRD4 (vs. 475/-)									
427/-	---	---	---	---	---	---	---	.5828	---
SLC6A4 (vs. 528/528)									
484/484	---	---	---	---	---	---	.2730	---	.4135
OTHER									
DRD2 (vs het):									
183/183	---	---	---	---	---	---	-.2304	---	-.4350
304/304	---	---	---	---	---	---	-.4173	---	-.7314
DAT1 (vs. 9R/9R):									
9R/10R	1.2067	1.9837	---	---	---	---	---	---	---
MAOA (vs. only 3.5R & 4Rs)									
2R/-	---	---	---	---	---	---	1.2699	---	---
DRD4 (vs. 475/-)									
619/619	---	---	---	---	---	---	---	.9263	---
427/-	---	---	---	---	-1.0886	---	---	---	---
SLC6A4 (vs. 528/528)									
484/528	---	---	---	---	---	-.7502	---	---	---

[1] All coefficients shown are statistically significant at the .05 level in bivariate logistic regressions. Rows without any significant effects are omitted in the interests of space.

Table 2 – Genetic Effects on Contraceptive Usage at Most Recent Sex, by Gender and Age Group, General Estimating Equations

	All			Males			Females		
ALL	All2	<=18	>18	All	<=18	>18	All	<=18	>18
DRD2 (vs het):									
183/183	---	---	---	---	---	---	---	---	---
304/304	-.4957	---	-.7309	-.4509	---	---	-.5480	---	-.9542
DAT1 (vs. 9R/9R):									
9R/10R	---	---	---	---	---	---	.5487	---	.7569
MAOA (vs. only 3.5R & 4Rs)									
2R/-	.5869	.9046	---	---	---	---	.8186	1.3042	---
Ctrl (3R,5R)	---	---	---	.2358	---	.3066	---	---	---
CONDOM									
MAOA (vs. only 3.5R & 4Rs)									
2R/-	---	---	---	---	---	---	---	.9887	---
OTHER									
DRD2 (vs het):									
183/183	---	---	---	---	---	---	---	---	-.2836
304/304	-.4701	---	-.5397	---	---	---	-.6684	---	-.8009

Table 3 – Genetic Effects on Contraceptive Usage at First Sex, by Gender

	All	Male	Female
DAT1 (vs. 9R/9R):			
No 9Rs or 10Rs	0.8640	1.5755	1.5755
DRD4 (vs. 475/-):			
379/-	0.3779	---	---
379/379	1.4931	---	---

[2] Controls: Age, age squared, and dummy variables for african american, hispanic, asian american, and native american status. Controls for the analyses by age category drop the age controls.