Pair bonds, ancestry and the DRD4 gene

Assortative human pair-bonding for partner ancestry and allelic variation of the dopamine receptor D4 (*DRD4*) gene

Eisenberg, Dan T.A.^{1 -} dtae@dtae.net Coren Apicella^{2 -} apicella@fas.harvard.edu Benjamin C. Campbell³ - campbelb@uwm.edu Anna Dreber^{4,5} - anna.dreber@hhs.se Justin R. Garcia^{6,7} - jgarcia3@binghamton.edu J. Koji Lum^{6,7,8} - klum@binghamton.edu

¹Department of Anthropology, Northwestern University
²Department of Anthropology, Harvard University
³Department of Anthropology, University of Wisconsin-Milwaukee
⁴Department of Economics, Stockholm School of Economics
⁵Program for Evolutionary Dynamics, Harvard University
⁶Laboratory of Evolutionary Anthropology and Health, Binghamton University
⁷Department of Anthropology, Binghamton University
⁸Department of Biological Sciences, Binghamton University

Running Head: Pair bonds, ancestry and the DRD4 gene

Abstract:

The 7R allele of the dopamine receptor D4 gene has been associated with attentiondeficit hyperactivity disorder and risk taking. On the cross-population scale, 7R allele frequencies have been shown to be higher in populations with more of a history of longterm migrations. It has also been shown that the 7R allele is associated with individuals having multiple-ancestries. Here we conduct a replication of this latter finding with two independent samples. Measures of subjects' ancestry are used to examine past reproductive bonds. The individuals' history of inter-racial/ancestral dating and their feelings about this are also assessed. Tentative support for an association between multiple ancestries and the 7R allele were found. These results are dependent upon the method of questioning subjects about their ancestries. Inter-racial dating and feelings about inter-racial pairing were not related to the presence of the 7R allele. This might be accounted for by secular trends that might have substantively altered the decision-making process employed when considering relationships with individuals from different groups. This study provides continued support for the 7R allele playing a role in migration and/or mate choice patterns. However, replications and extensions of this study are needed and must carefully consider how ancestry/race is assessed.

Keywords: DRD4, assortative mating, race, ancestry, pair-bonds

Introduction

The cosmopolitan nature of humans is a defining characteristic of our evolutionary history and our present conditions. Mixing of human populations with accompanying political changes has long been recognized as a characteristic of historical and contemporary human populations . In characterizing human migration Charles Darwin went so far as to speculate that, "The restless who will not follow any steady occupation...emigrate to newly settled countries, where they prove useful pioneers" . Human mating patterns are well known to be influenced by geographical propinquity as well as homogamy .

While migration propensity is likely due to a suite of biological traits, cultural traits and genes, there is some evidence that particular traits and genes are of increased importance in explaining human migrations. In particular, the 7 repeat (7R) allele of the *48bp VNTR* site in the dopamine receptor D4 gene (*DRD4*) is present at higher frequencies in populations that have migrated farther in the past 1,000 to 30,000 years . The genetic structure of this same "migratory" 7R allele suggests that it originated and was positively selected for between 40,000 and 50,000 years ago . The 7R allele of the *DRD4* gene has been associated with behavioral traits such as attention deficit hyperactivity disorder (ADHD), impulsivity, financial risk taking and novelty seeking . It has also been shown that the 7R allele is associated with more nomadic lifestyles and potentially greater success in this nomadic lifestyle . Thus, the 7R allele might be related to decreased assortative mating via propinquity because of its association with migration and via homogamy because of its association with novelty seeking. Interracial romantic relationships face a number of cultural barricades , which 7R individuals might more readily overcome.

While a good case has been made that *DRD4* played a salient role in pre-historic population structure through its association with migration, it is less clear if *DRD4* is a correlate of current population structure. Key determinants of population structure that likely have salient behavioral components include migration and mating patterns. On the one hand, Chen and colleagues found no *DRD4* allele frequency differences between migrants and their source populations (however this analysis was exploratory and of

limited power). On the other hand Eisenberg and colleagues recently found that 7R alleles were associated with having multiple-ancestries in a group of U.S. (Binghamton, NY) undergraduates. This is consistent with other results that find that emigrants are more extraverted and open to experience than natives , and that Dutch couples born in different geographic regions and their offspring are more sensation seeking than those couples born in the same geographic region and their children . Similarly, in Finland, migration from rural to urban areas is associated with increased trait level sociability, while migration more generally is associated with increased trait level activity .

The dopamine system has been implicated in sexual and pair bonding behaviors, including romantic love in humans. The *DRD4* gene codes for a receptor for dopamine that is particularly expressed in the prefrontal cortex. *DRD4* has specifically been associated with sexual desire, sexual arousal, sexual function, sexual novelty, age at first sexual intercourse in. Additionally, 7R alleles have been associated with a desire for children and marriage earlier in life.

Here we explore the previous findings of an association between *DRD4* and assortative mating for partner ancestry in two new datasets. In addition to evaluating whether *DRD4* is related to past cross-cultural pairing (having ancestors from multiple geographic regions/cultures), we also examine whether current/recent pair-bonding behaviors as well as planned future pair bonding behaviors are related to *DRD4*. Given abundant failures to replicate the findings of gene association studies , replications, like conducted here, are very important.

Methods:

Data collection

This study incorporates participants from two separate samples: the first includes 98 male undergraduates from Harvard University between the age of 18 and 23 years (mean 20.07) and the second includes 181 undergraduate students (118 females, 63 males) from Binghamton University, State University of New York between the ages of 18-28 (mean 20.11). Harvard subjects were all male because an aim of gathering the dataset was to analyze correlates of testosterone levels . Harvard University participants were recruited by fliers distributed on the Harvard campus, as well as via email solicitation to undergraduate residential houses. Harvard subjects were excluded if they responded affirmatively to questions about current use of psychotropic medication or having been diagnosed with bipolar depression, pathological gambling and/or attention deficient

hyperactivity disorder (ADHD). Harvard subjects completed the study in small group sessions (between one and twelve individuals) at a central location in the Department of Anthropology During spring 2007. Harvard subjects answered the question in privacy and were told that all data would be confidential. Binghamton University participants were recruited from the Department of Psychology's Human Subject Pool. Data was collected in a reserved lecture hall where measures were taken to ensure participant privacy. All participants from both samples were asked to complete questionnaires and provide a saliva buccal wash sample using 10 ml of Scope[™] mouthwash for later DNA extraction. Research procedures were conducted under the respective approval of Harvard University's Institutional Review Board and Binghamton University's Human Subjects Research Review Committee. Written consent was obtained from all subjects before participating in the study.

Genotyping

Buccal cell samples for DNA analysis were obtained from participants and processed in the Laboratory of Evolutionary Anthropology and Health at Binghamton University, New York. DNA was extracted using an abbreviated version of the silica extraction protocol previously described by Lum et al. .

DRD4 VNTR:

The *DRD4 48-bp VNTR* polymorphism is in exon 3 of the gene coding for the dopamine receptor D4. The *VNTR* polymorphism varies between 2 and 11 repeats of a similar *48 bp* coding region sequence, with a tri-modal distribution of 2, 4 and 7 repeat alleles (2R, 4R and 7R) in most, but not all, populations . Although the functional significance of the *DRD4 VNTR* polymorphism has not been definitively characterized, long alleles (typically 7R as opposed to 4R) have been generally found to be functionally less reactive in in-vitro expression experiments , with some heterogeneity . Additionally, in vivo human pharmacological studies are also generally consistent with the notion that 7R alleles are associated with less responsive D4 receptors than 4R alleles

Sufficient DNA for *DRD4* PCR amplification was extracted from 166 Binghamton University and 95 Harvard University buccal cell samples. All samples that were initially scored as homozygotes were reanalyzed two additional times with different starting template concentrations to decrease the likelihood of allelic dropout and other errors . The PCR reaction consisted of 1x Q-Solution (Qiagen), 1x Buffer (Qiagen), 1 µM Primer 1 (5' GCGACTACGTGGTCTACTCG 3'), 1 µM Primer 2 (5' AGGACCCTCATGGCCTTG 3'), 200 µM dATP, 200 µM dTTP, 200 µM dCTP, 100 µM dITP, 100 μ M dGTP, 0.3 units HotStar Taq (Qiagen), and 1 μ l of DNA template, in a total volume of 10 μ l. The PCR profile began with 15 minutes at 95°C for enzyme activation and denaturing of template DNA followed by 40 cycles consisting of 1 minute denaturation at 94°C, 1 minute annealing at 55°C, 1.5 minute extension at 72°C, and finished with a 10 minute extension at 72°C. Amplicons were electrophoresed through 1.4 – 2.0% agarose gels containing ethidium bromide and genotypes were determined by comparison with a 100 bp ladder.

DRD4 allele and genotype frequencies are given in Table 1. *DRD4* in the Harvard dataset was consistent with Hardy-Weinberg Equilibrium (HWE; Markov Chain algorithm, p = 0.717), while in the Binghamton subject pool HWE was violated (Markov Chain algorithm, p = 0.006). Some caution should be used in interpreting the Binghamton results because its deviations from HWE might suggest genotyping errors . While HW violations have been shown to have the potential to bias results in case-control studies, it seems less likely that this would bias the current type of association study. Since HWE assumes a large, randomly mating population, our use of a small sample of a relatively narrow cohort of young individuals who might assortatively mate with respect to the allele in question might account for the HW disequilbrium instead of genotyping error.

Table 1. *DRD4* allele and genotype frequencies by each independent sample.Since the Binghamton sample is in Hardy-Weinberg disequilibrium, expected genotypepercentages are given.

	Harvard		Binghamton		amton
Allele/Genotype	n	%	n	%	expected %
Allele					
2	24	12.6	38	11.0	
3	6	3.2	9	2.6	
4	129	67.9	246	71.1	
5	4	2.1	4	1.2	
6	2	1.1	0	0.0	
7	25	13.2	47	13.6	
9	0	0.0	2	0.6	
Total	190	100.0	346	100.0	
Genotype Classification					
2/2	1	1.1	7	4.0	1.2
2/3	1	1.1	1	0.6	0.6
2/4	20	21.1	22	12.7	15.6
2/7	1	1.1	1	0.6	3.0

3/3	0	0.0	1	0.6	0.1
3/4	3	3.2	6	3.5	3.7
3/7	2	2.1	0	0.0	0.7
4/4	41	43.2	90	52.0	50.5
4/5	3	3.2	4	2.3	1.6
4/6	2	2.1	0	0.0	0.0
4/7	19	20.0	33	19.1	19.3
4/9	0	0.0	1	0.6	0.8
5/7	1	1.1	0	0.0	0.3
7/7	1	1.1	6	3.5	1.8
7/9	0	0.0	1	0.6	0.2
7-	71	74.7	132	76.3	
7+	24	25.3	41	23.7	
Total	95.0	100.0	173.0	100.0	~99.5

~ does not sum to 100% because expected frequencies of genotypes not found in the sample are not shown

Measures of cross-cultural pairing:

Three different types of measures of assortative mating for ancestry were used: [1] ancestral partnering patterns, [2] current/recent partner patterns and [3] expected future partnering patterns.

1. Ancestral partnering patterns were evaluated with different means in each dataset. In the Harvard dataset subjects were asked the ethnicities of each of their four grandparents (ancestry I). They were instructed to not answer if they did not know and to circle as many choices for each grandparent as necessary. Choices were semi-structured with options: European, East Asian, Hispanic/Latino, African American and an Other category that allowed for free responses. Only one subject reported more than two ancestries and he was combined with those reporting two ancestries for analysis. In the Binghamton survey subjects were given a question identical that of above (ancestry I), except because of a printing error, the "other" category contained a very small area for free-responses that subjects did not take advantage of or realize the purpose of (Harvard participants consistently filled in free-responses in their questionnaires where this error did not appear). This question was thus effectively a simple multiple choice question. Subjects in the Binghamton survey were also asked to free respond listing their "Ethnic group background/identification (please be as specific as possible)". The number of mutually exclusive categories listed was then counted (ancestry II). Ancestry II was also reduced to a dichotomous variable representing having

multiple ancestries or not (ancestry III). Those who only listed their ethnic group as "American" were not analyzed. Ancestry I tends to measure partnering patterns across continents/regions, while ancestry II and III tends to also measure more fine grained differences across countries (e.g. having Irish and German roots).

- Recent partnering patterns were evaluated by asking, "What are the ethnicities of your three most important sexual partners (most important first)?". Choices were: European, East Asian, Hispanic/Latino, African American and Other. Partner ethnicities were matched to the subjects' ethnicities and scored dichotomously as all partners congruent with subject ancestry, or not.
- 3. *Expected future partners*: Subjects were asked to rate their agreement with two statement on a 1-5 scale (1 being strongly disagree and 5 strongly agree): [a] "I would be willing to have a romantic relationship with someone from a different race than myself." and [b] "I would be willing to get married to someone from a different race than myself?".

It should be noted that the questions in the Binghamton study came after a long series of questions about sexual behaviors, sexual expectations and sexual feelings. This may have affected responses to our measures of cross-cultural pairing. A previous study has shown that *DRD4*/7R- individuals are less likely to answer the Sociosexual Orientation Inventory , a questionnaire with many fewer and less in depth questions about sexual behaviors. If this is a factor, it seems most likely that it would bias the sample by producing more missing values in 7R- individuals. However, this is not seen in our analysis of missing values (not shown).

Data Analysis

HW equilibriums were tested with the HWE program using a Markov Chain algorithm . All other statistical analyses utilized STATA/IC 10.0. Distributions in regressions were homoscedastic (using the Breusch-Pagan/Cook-Weisberg test for heteroskedasticity). *DRD4* genotypes were parsed by the number of 7R alleles for regressions and 7R- versus 7R+ in cross-tabulations. In cross-tabulations Pearson chi-square tests were used when expected cell frequencies exceeded 10, and Fisher's exact tests when below 10. An alpha value of 0.05 was used throughout. Since we have clear a priori predictions, one-sided significance values are used where appropriate to the statistical test.

Due to the complexity of parsing ethnicity, as well as *DRD4* genotypes, the raw data used for this analysis is available upon request or from <u>www.dtae.net</u>.

Results

a.

Pair-wise correlations between measures of assortative mating for ancestry are given in Tables 2a and 2b for the Harvard and Binghamton studies respectively. The remainder of the analysis looks at these traits individually in an exploratory fashion because correlations are generally not high, and the measures likely represent distinct facets of the traits of interest. Of important note, in the Binghamton study (2b), ancestry I is barely correlated with ancestry II or ancestry III. Ancestry I has a strong correlation with recent partners in both studies, probably because subjects identifying as having multiple ancestries are unlikely to meet people of the same multiple ancestries as themselves.

Table 2. Pair-wise correlations between measures of assortative mating for ancestry.

a. Harvard study and b. Binghamton study. In b. Binghamton study, ancestry I is from the multiple choice measure, ancestry II from the free-response measure and ancestry III is a dichotomized version of ancestry II. * indicates p < 0.05

		<u>1</u>	<u>2</u>	<u>3</u>	<u>4</u>		
1	ancestry I	1.000					
2	recent partners	0.249*	1.000				
3	future romantic	0.134	0.226*	1.000			
4	futuremarriage	0.156	0.187	0.645*	1.000		
b.		<u>1</u>	<u>2</u>	<u>3</u>	<u>4</u>	<u>5</u>	<u>6</u>
1	ancestry I	1.000					
2	ancestry II	0.014	1.000				
3	ancestry III	0.010	0.849*	1.000			
4	recent partners	0.505*	-0.110	-0.088	1.000		
5	future romantic	0.038	0.094	0.025	0.261*	1.000	
6	future marriage	0.024	0.140	0.087	0.280*	0.847*	1.000

Ancestral partnering patterns:

There was no association between having diverse ancestry and being 7R+ in the Harvard dataset using the semi-structured measure (ancestry I; Table 3a; n = 95, one sided Fisher's Exact, p = 0.562) nor the Binghamton dataset using an effectively multiple-choice measure (Table 3b; n = 173, one sided Fisher's Exact p = 0.104). However, this first evaluation means is in doubt in the Binghamton dataset because of an error in data

collection. When subjects indicated a grandparental ancestry of other, the free response line was printed so small that subjects generally did not specify what this category meant. This is contrary to the Harvard study where the free-response line was of sufficient length (data not shown). Since those indicating an "other" ancestry are also more likely to have multiple ancestries than the general sample populations in both the Harvard dataset (not shown) and previous study, this error likely decreases power to detect a *DRD4*- multipleancestry association and might even bias the analysis (e.g. if lack of a free-response option changes subjects selection).

Using the second ancestral partnering evaluation means in the Binghamton survey (ancestry II), simply asking subjects for their ethnic background in one free-response question, ancestry varies from one reported ancestry to seven with a median of one. Those who were 7R+ in the Binghamton dataset were more likely to have diverse ancestries (ancestry III; Table 3c; n = 170, Pearson chi-square = 4.83, p = 0.028). Results were similar when the diversity of ancestry was regressed against the number of 7R alleles (ancestry II; n = 170, t = 3.73, beta = 0.321, $R^2 = .022$, one sided p = 0.028). Each additional 7R allele was associated with reporting 0.321 more ancestry groups. Similarly, when the sample was restricted to only those with ancestry in Europe, in an effort to eliminate the effect of dramatically different DRD4 allele frequencies in places such as Asia and South America, a stronger relationship was found, despite decreased power (n =115, t = 2.32, beta = 0.450, $R^2 = .05$, one sided p = 0.011). When the scale of ancestral diversity was categorized by whether diversity occurred at the intra-continental or intercontinental scales, we found that there was a near significant trend towards increasing 7R allele frequencies with an increasingly large scale of ancestral diversity (n = 169, t = 1.62, beta = 0.145, R^2 = .016, one sided p = 0.054).

Table 3. Relationships between DRD4 and ancestral diversity.

a. uses the semi-structed ancestry I measure in the Harvard study, b. a multiple choice version of ancestry I in the Binghamton study and c. a free response measure (ancestry III) in the Binghamton dataset.

		<u>7R-</u>	<u>7R+</u>	<u>Total</u>
<u>1</u>				
<u>ancestry</u>	obs	63	21	84
		62.	21.	
	exp	8	2	84
<u>>1</u>				
<u>ancestry</u>	obs	8	3	11
	exp	8.2	2.8	11
<u>Total</u>		71	23	95

a.

```
One sided Fisher'sexact = 0.562
```

b.

				<u>Tota</u>
		<u>7R-</u>	<u>7R+</u>	1
1				
<u>ancestry</u>	obs	102	36	138
		105.		
	exp	3	32.7	138
<u>>1</u>				
<u>ancestry</u>	obs	30	5	35
	exp	26.7	8.3	35
<u>Total</u>				

One sided Fisher'sexact = 0.104

с.

				<u>Tota</u>
		<u>7R-</u>	<u>7R+</u>	1
<u>1</u>				
<u>ancestry</u>	obs	93	22	115
	exp	87.3	27.7	115
<u>>1</u>				
<u>ancestry</u>	obs	36	19	58
	exp	41.7	13.3	58
<u>Total</u>		132	41	173
Pearson c	hi-squa	re = 4.8	3,p=(0.028

Recent partnering patterns

Incongruities in ancestries between subjects and their past/present sexual partners were near significantly related to the presence of 7R alleles in the Harvard study (Table 4a; one-sided Fisher's exact, p = 0.081), but not in the Binghamton study (Table 4b; Pearson chi-square = 0.432, p = 0.511). It should be noted that the current/recent partnering patterns from the Binghamton survey are based upon the same partially flawed question as above in Table 3b. That is, because subjects specifying a grandparent from an *other* category generally did not specify what this *other* category was, we were unable to distinguish whether these subjects matched their partners or not. Table 4. Relationship between current/recent partnering patterns and DRD4

a. Harvard study and b. Binghamton study.

a.						
		<u>7R-</u>	<u>7R+</u>	<u>Total</u>		
<u>matched</u>	obs	29	6	35		
	exp	25.7	9.3	35		
<u>unmatched</u>	obs	37	18	55		
	exp	40.3	14.7	55		
<u>Total</u>		66	24	90		
One sided Fisher'sexact = 0.081						
b.						
		<u>7R-</u>	<u>7R+</u>	<u>Total</u>		
<u>matched</u>	obs	57	22	79		
	exp	58.7	20.3	79		
<u>unmatched</u>	obs	47	14	61		
	exp	45.3	15.7	61		
<u>Total</u>		104	36	140		

Pearson chi-square = 0.432, p = 0.511

Expected future partners

The distribution of the two Likert Scale questions, "I would be willing to have a romantic relationship with someone from a different race than myself" and "I would be willing to get married to someone from a different race than myself?" were heavily skewed towards complete agreement with the respective statements. For this reason and because the scale is ordinal, Kruskal-Wallis tests were used to test if scores differed by 7R allele presence. No significant or near significant associations were found between 7R+ presence and willingness to have romantic relationships with those from different races (Harvard: n = 93, df = 1, chi-square = 1.218, p = 0.270; Binghamton: n = 168, df = 1, chi-square = 0.104, p = 0.747), nor to marry those from different races (Harvard: n = 93, df = 1, chi-square = 0.048, p = 0.827; Binghamton: n = 168, df = 1, chi-square = 0.607, p = 0.436).

Discussion

The findings of this study of two independent samples coupled with the similar past study of suggest partial support for the hypothesis that *DRD4*/7R is associated with having multiple-ancestries. The current study particularly illustrates the difficulties of measuring ancestry and how sensitive results can be to seemingly minor differences in question phrasing and layout.

Ancestral partnering was not associated with 7R in the Harvard dataset and only by one of two primary measures in the Binghamton dataset. Recent relationships with partners from differing ancestries was near significantly associated with 7R+ in the Harvard study, but not in the Binghamton one. It should be noted that *DRD4* genotype associations with subjects' ancestries are actually proxy measures for the associations of the behaviors of the subjects' ancestors with *DRD4* genotypes. Since a subject with a 7R allele by definition had more ancestors with 7R alleles, the subject's genotype serves as a rough proxy for ancestral genotypes. Expected future partnering patterns were not related to *DRD4*/7R. The fact that only ancestral partnering patterns and not recent partnering or planned future partnering were significantly associated with *DRD4* suggests some explanations including: type II error, that most measures were insufficiently specific, that the nature of mating based upon ancestry has become less taboo in recent years, or perhaps that ancestral diversity is a greater reflection of traveling out of one's country, while multi-cultural college towns afford much more mixing.

The variation of results by different ancestry measures as well as their low correlations (Fig 2b) warrant further discussion. The Harvard sample size might be underpowered to detect the given effect. It is also possible that the Harvard sample of elite Ivy League students represents a substantively different population than the Binghamton sample of state school students. As noted above, the first measure of multiple ancestries in the Binghamton dataset (ancestry I) was likely inadequate because it did not leave space for subjects to define their ancestry in a free-response. As such, we believe that the second ancestry measure (ancestry II) was superior in that it elicited a finer scale response of ancestral backgrounds. In fact this free response method is probably superior to previous study in that it was more able to quantify multiple-ancestries from different countries and cultures in the same continent. Regardless of the validity of ancestry scales I and II, the low pair-wise correlations between the two suggests that they are measuring substantively different factors. Since marriage practices and genetic similarities between populations tends to be highly correlated with geographical distance between populations

(isolation by distance) as well as exhibiting large genetic discontinuities between continents, measuring ancestral differences across both the intra- and inter-continental scales is likely important.

We note that the young age of participants limits the conclusions we can draw from the ancestries of their past sexual partners. Sexual partners at this age might more reflect experimentation than who a subject will actually have children with. Similarly, self-reported feelings about romantic relationships and marriage with those of other races might be a greater reflection of explicit social norms (especially on the relatively liberal college campuses these studies were conducted in) of what opinions are acceptable to express, rather than implicit biases and actual behavior . It is probably far easier to theoretically date and marry someone from a different race, culture or religion than to actually manage (or benefit from) differences of opinion, background and family disapproval that might come from the actual behavior. It is also likely that actual behaviors have changed much over the past few generations, such that inter-racial dating and marriage is currently much more acceptable/prevalent . In support of the notion that there might be a secular trend in inter-ethnic partnering, there is evidence that "close, positive interracial contact" decreases racial prejudice .

From these two studies of *DRD4* and ancestry and the previous one, we are struck by how carefully researchers must phrase questions about ancestry in order to gain the necessary information. We suggest that future studies that analyze ancestry for similar purposes use free response questions to ask specifically about the ancestry of each grandparent. Subjects should be given examples of possible answers (e.g. "Western European", "Scottish-Irish-German", "Ashkenazi Jewish", "Korean") and instructed to be as specific as their knowledge allows.

It also might be beneficial to explore family histories more deeply to understand the contexts that lead to partnering patterns. Did grandparents and parents of different ancestries meet because one or both partners were traveling/immigrating? What roles if any do the stigmatization or positive-prejudices of out-groups play? What about the economic status of partners? How do these patterns in past generations compare and contrast with those seen today? Differences in *DRD4* responses to different races should be further analyzed. Perhaps *DRD4* acts via altering affective conditioning.

Genetic measures of individual admixture (e.g. heterozygosities) might also provide a more objective measure of multiple-ancestries. We predict that these genetic measures will correlate more strongly with *DRD4*/7R alleles than more subjective and historical memory constrained self-report measures.

We wish to be clear that while genetic factors might play a role in behavioral differences in human populations and propensities for cross-population mating, this does not preclude the importance of other developmental, political, economic and social factors. Given the small effect sizes and R² values observed here, it is clear that *DRD4* accounts for only a small part of the additive variance (if any). We suspect that other factors might be more important proximate determinants that in some cases feedback and select for particular genes . While the theoretical and evolutionary implications of this corpus of literature is compelling for the understanding of human diversity and our evolutionary history , we are not aware of any legitimate (never-mind moral) policy or other practical implications of this line of research.

It is possible that the 7R, risk-conferring allele, is more adaptive in dynamic environments. In a dynamic social environment or changing ecological environment, ideas acquired from family members may be less innovative and adaptive than those ideas acquired from a broader survey of society. Perhaps consistent with wider surveying for ideas, DRD4 7R+ individuals have increased propensities for noveltyseeking, cognitive flexibility, higher activity levels, better sexual functioning and may have faster response times. Especially notable, while externalizing behaviors are normally negatively related to IQ, among 7R+ subjects (but not 7R-) there is no relationship between externalizing behaviors and IQ. 7R+ individuals may be characterized by putting less value on familial influences and being more readily able to take advantage of dynamic social environments. Evidence of younger desired age at first reproduction, earlier first sexual intercourse and more multi-racial ancestries among 7R+ individuals is generally consistent with a higher mating effort and lower offspring investment strategy suiting a dynamic social environment with less dependable family influences. Marriage with those from different ancestries could provide new networks of kin support, and avenues for learning to take advantage of new environments.

Acknowledgements:

DTAE is funded by a National Science Foundation Graduate Research Fellowship and AD by the Jan Wallander and Tom Hedelius Foundation. The Binghamton study and all genotyping was supported in part by the Binghamton University Foundation's Research Awards to JRG and by startup funds to JKL from Binghamton University. The authors thank Peter Ellison for his help in making this study possible and Richard Zamore, Edward Aller, and Rita Spathis for valuable laboratory assistance. The Newton Free Library provided research assistance.

Author contributions:

DTAE conceived of this research question, drafted survey questions utilized here, conducted all analyses and wrote the manuscript.

CA helped conduct and conceive of the Harvard study, entered and cleaned data. BCC helped conduct and conceive of the Harvard study, entered and cleaned data AD helped conduct and conceive of the Harvard study, entered and cleaned data. JRG helped conceive and ran the Binghamton study and helped genotype samples JKL helped conceive the Binghamton study and oversaw genotyping. All authors read and approved the final manuscript.

Works Cited: