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

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The 7 repeat (7R) allele of the dopamine receptor D4 gene has been associated with attention deficit 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 long-term 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 interracial/ancestral dating and their feelings about this are also assessed. Tentative support for an association between multiple ancestries and the 7R allele was found. These results are dependent upon the method of questioning subjects about their ancestries, with only finer-scale measures of ancestry being associated with 7R. Interracial dating and feelings about interracial pairing were not related to the presence of the 7R allele. This study provides continued support for a role for the 7R allele in migration and/or mate choice patterns. However, replications and extensions of this study are needed and the way ancestry/race is assessed must be carefully considered.

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 historic and contemporary human populations (Boas, 1909). 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' (Darwin, 1977). Human mating patterns are well known to be influenced by geographical propinquity (Peach and Mitchell, 1988; Rosenberg *et al.*, 2005) as well as homogamy (Kalmijn, 1998; Smits *et al.*, 1998).

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 1000 to 30 000 years (Chen *et al.*, 1999).

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 (Wang *et al.*, 2004). The 7R allele of the *DRD4* gene has been associated with behavioral traits such as attention-deficit hyperactivity disorder (ADHD) (Li *et al.*, 2006), impulsivity (Eisenberg *et al.*, 2007), financial risk-taking (Dreber *et al.*, 2009; Kuhnen and Chiao, 2009) and novelty seeking (Kluger *et al.*, 2002; Schinka *et al.*, 2002; Savitz and Ramesar, 2004). It has also been shown that the 7R allele is associated with more nomadic lifestyles (Chen *et al.*, 1999) and potentially greater success in this nomadic lifestyle (Eisenberg *et al.*, 2008). 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. Further, interracial romantic relationships face a number of cultural barricades (Harris and Kalbfleisch, 2000), which 7R individuals might more readily overcome.

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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 (Nalls *et al.*, 2009). On the one hand, Chen and colleagues (1999) 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 (2007) recently found that 7R alleles were associated with having multiple ancestries in a group of US (Binghamton, NY) undergraduates. This is consistent with other results that found that emigrants are more extroverted and open to experience than natives (Ciani *et al.*, 2007; Jokela, 2009). For example, Dutch couples born in different geographic regions and their offsprings are more sensation seeking than those couples born in the same geographic region and their children (Rebollo and Boomsma, 2007). Similarly, in Finland, migration from rural to urban areas is associated with increased trait level sociability, and migration more generally is associated with increased trait level activity (Jokela *et al.*, 2008).

The dopamine system has also been implicated in sexual (Melis and Argiolas, 1995; Dominguez and Hull, 2005; Melis *et al.*, 2006; Succu *et al.*, 2007) and pair bonding behaviors (Gingrich *et al.*, 2000; Curtis and Wang, 2005; Fisher *et al.*, 2005; Aragona *et al.*, 2006; Smeltzer *et al.*, 2006), including romantic love in humans (Fisher, 2004). *DRD4* has specifically been associated with sexual desire, sexual arousal, sexual function (Zion *et al.*, 2006), sexual novelty (Hamer, 2002), and age at first sexual intercourse (Miller *et al.*, 1999; Guo and Tong, 2006; Eisenberg *et al.*, 2007). Additionally, 7R alleles have been associated with a desire for children and marriage earlier in life (Eisenberg *et al.*, 2007).

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 findings of gene association studies (Lucentini, 2004), replications, like that 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 ages of 18 and 23 years (mean 20.07) and the second includes 181 undergraduate students (118 females and 63 males) from Binghamton University, State University of New York between the ages of 18 and 28 years (mean 20.11). Harvard subjects were all male because an aim of gathering the dataset was to analyze correlates of testosterone levels (Apicella *et al.*, 2008). Harvard University participants were recruited by fliers distributed on the Harvard campus, as well as via e-mail 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 deficit 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 questions 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 were 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^{TM} 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 (Feigelson *et al.*, 2001) 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 (Boom *et al.*, 1990) previously described by Lum *et al.*, (1998).

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 (Ding *et al.*, 2002). 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 (Van Tol *et al.*, 1992; Asghari *et al.*, 1995; Schoots and Van Tol, 2003; Van Craenenbroeck *et al.*, 2005; Czermak *et al.*, 2006), with some heterogeneity (Asghari *et al.*, 1994; Jovanovic *et al.*, 1999; Watts *et al.*, 1999; Oak *et al.*, 2001; Cho *et al.*, 2006). 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 (Hutchison *et al.*, 2003; Hamarman *et al.*, 2004; Brody *et al.*, 2006; Hutchison *et al.*, 2006; McGough *et al.*, 2006). The *DRD4* gene codes for a receptor for dopamine that is particularly expressed in the prefrontal cortex (Lahti *et al.*, 1995; Matsumoto *et al.*, 1996; Meador-Woodruff *et al.*, 1996; Defagot and Antonelli, 1997; Mulcrone and Kerwin, 1997; De la Garza and Madras, 2000; Zhang *et al.*, 2002; Callier *et al.*, 2003; Durston *et al.*, 2005; Diamond, 2005; Noain *et al.*, 2006; Beazely *et al.*, 2006).

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 (for more details on genotyping issues at this locus see: Hamarman *et al.*, 2004; Eisenberg *et al.*, 2007; Eisenberg *et al.*, 2008). The PCR reaction consisted of 1× Q-Solution (Qiagen), 1× Buffer (Qiagen), 1 μM Primer 1 (5′ GCGACTACGTGGT CTACTCG 3′), 1 μM Primer 2 (5′ AGGACCCTCATGG CCTTG 3′), 200 μM dATP, 200 μM dTTP, 200 μM dCTP, 100 μM dITP, 100 μM dGTP, 0.3 units HotStar Taq (Qiagen), and 1 μl of DNA template, in a total volume of 10 μl. The PCR profile began with 15 min at 95°C for enzyme activation and denaturing of template DNA followed by 40 cycles consisting of 1 min denaturation at 94°C, 1 min annealing at 55°C, 1.5 min extension at 72°C, and finished with a 10 min 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 (Hosking *et al.*, 2004). While HWE 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 disequilibrium instead of genotyping error.

Table 1 *DRD4* allele and genotype frequencies by each independent sample

	Harvard		Binghamton		
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

Since the Binghamton sample is in Hardy–Weinberg disequilibrium, expected genotype percentages are given. ∼ 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: (i) ancestral partnering patterns, (ii) current/recent partner patterns and (iii) expected future partnering patterns.

Ancestral partnering patterns. These 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 not to 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 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 to that of above (ancestry I), and 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. 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 (Eisenberg *et al.*, 2007, unpublished data), this error

likely decreases power to detect a *DRD4* multiple-ancestry association and might even bias the analysis (e.g. if lack of a free-response option changes subjects' selection). Subjects in the Binghamton survey were also asked to respond freely by 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 tend to also measure more fine-grained differences across countries (e.g. having Irish and German roots). It is important to note that ancestry I is the measure that most closely parallels the measure used in the only previous study of *DRD4* and multi-racial ancestry (Eisenberg *et al.*, 2007).

Recent partnering patterns. These 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. This measure parallels ancestry I, in that ethnic groups are assessed in the same manner and it tends to measure partnering across continents/regions.

Expected future partners. Subjects were asked to rate their agreement with two statements on a 1–5 scale (1 being strongly disagree and 5 strongly agree): (i) 'I would be willing to have a romantic relationship with someone from a different race than myself.' and (ii) '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 (Eisenberg *et al.*, 2007), a questionnaire with 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 (J. Brzustowski, http://www2.biology.ualberta.ca/jbrzusto/hwenj.html) using a Markov Chain algorithm (Guo and Thompson, 1992). All other statistical analyses utilized STATA/IC 10.0. Distributions in regressions were homoskedastic (using the Breusch–Pagan/Cook–Weisberg test for heteroskedasticity). *DRD4* genotypes were parsed by the number of 7R alleles for regressions and 7R− *vs* 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 α 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 are available upon request or from www.dtae.net.

RESULTS

Pair-wise correlations between measures of assortative mating for ancestry are given in Table 2 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 (Table 2), 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

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

Harvard study		1	2	3	4		
1	Ancestry I	1.000	–	–	–	–	–
2	Recent partners	0.249*	1.000	–	–	–	–
3	Future romantic	0.134	0.226*	1.000	–	–	–
4	Future marriage	0.156	0.187	0.645*	1.000	–	–
Binghamton study		1	2	3	4	5	6
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

In 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.
*$P < 0.05$.

identifying as having multiple ancestries are unlikely to meet people of the same multiple ancestries as themselves. Correlations between variables are generally consistent between the Harvard and Binghamton (Table 2) subsamples (e.g. significant correlations between ancestry 1 and recent partners, recent partners and future romantic, and future romantic and future marriage), suggesting that these measures and populations are generally similar.

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 3; $n = 95$, one-sided Fisher's Exact, $P = 0.562$) or the Binghamton dataset using an effectively multiple-choice measure (ancestry I; Table 3; $n = 173$, one-sided Fisher's Exact, $P = 0.104$).

In the Binghamton survey, using the second ancestral partnering evaluation (ancestry II) means 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 3; $n = 170$, 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; $n = 170$, $t = 3.73$, $\beta = 0.321$, $R^2 = 0.022$, 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 ($n = 115$, $t = 2.32$, $\beta = 0.450$, $R^2 = 0.05$, one sided $P = 0.011$). When the scale of ancestral diversity was categorized by whether diversity occurred at the intra-continental or inter-continental scales, 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 $P = 0.054$). Ancestry II and ancestry III variables were not available in the Harvard survey.

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 4; one-sided Fisher's exact, $P = 0.081$), but not in the Binghamton study (Table 4; 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 seen above in Table 3. 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 3 Relationships between *DRD4* and ancestral diversity

		Harvard study (using the semi-structured ancestry I measure)			Binghamton study (using a multiple-choice version of ancestry I)			Binghamton dataset (using a free-response measure (ancestry III)		
		7R–	7R+	Total	7R–	7R+	Total	7R–	7R+	Total
1 ancestry	Obs.	63	21	84	102	36	138	93	22	115
	Exp.	62.8	21.2	84	105.3	32.7	138	87.3	27.7	115
>1 ancestry	Obs.	8	3	11	30	5	35	36	19	58
	Exp.	8.2	2.8	11	26.7	8.3	35	41.7	13.3	58
Total		71	24	95	132	41	173	132	41	173
		One-sided Fisher's exact = 0.562			One-sided Fisher's exact = 0.104			Pearson's chi-square = 4.83, $P = 0.028$		

Table 4 Relationship between current/recent partnering patterns and *DRD4*

		Harvard study			Binghamton study		
		7R–	7R+	Total	7R–	7R+	Total
Matched	Obs.	29	6	35	57	22	79
	Exp.	25.7	9.3	35	58.7	20.3	79
Unmatched	Obs.	37	18	55	47	14	61
	Exp.	40.3	14.7	55	45.3	15.7	61
Total		66	24	90	104	36	140
		One-sided Fisher's exact = 0.081			Pearson's 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 either 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, $P = 0.747$), or 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 Eisenberg *et al.* (2007) 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 differences in question phrasing and layout.

Ancestral partnering was not associated with 7R in the Harvard dataset and only associated with 7R by the finer scale measure of ancestry in the Binghamton dataset. We note that the finer scale ancestry measure used in the Binghamton dataset (ancestry II/III) was not available in the Harvard dataset. Recent relationships with partners from differing ancestries was near significantly associated with 7R+ in the Harvard study, but not in the Binghamton one (however, a finer scale measure for recent relationships analogous to ancestry II/III was not available in either study). 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 interracial pairing was a greater reflection of traveling out of one's country, while multicultural college communities afford much more mixing.

The variation of results by different ancestry measures as well as their low correlations (Table 2) warrant further discussion. 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 the measure used in previous study (Eisenberg *et al.*, 2007) in that it was better able to quantify multiple ancestries from different countries and cultures in the same continent (the measure used in the 2007 study most closely parallels the ancestry I measure). If the ancestry II variable was assessed in the Harvard study, the results between surveys likely would have been more consistent with our hypothesis.

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 tend to be highly correlated with geographical distance between populations (isolation by distance) as well as exhibiting genetic discontinuities between continents (Peach and Mitchell, 1988; Rosenberg *et al.*, 2005), measuring ancestral differences across both the intra- and inter-continental scales is likely an important distinction to retain.

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 where these studies were conducted), rather than implicit biases and actual behavior (e.g. Cronk, 1999, p. 9). It is also likely that actual behaviors have changed much over the past few generations, such that interracial dating and marriage are currently much more acceptable/prevalent (Johnson *et al.*, 1980; Ahern *et al.*, 1983; Nalls *et al.*, 2009; however linear trends should not be assumed: Halpin and Chan, 2003). 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 (Blascovich *et al.*, 2001; Olsson *et al.*, 2005).

From these two studies of *DRD4* and ancestry and the previous one (Eisenberg *et al.*, 2007), 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' etc.) and instructed to be as specific as their knowledge allows.

It might also be beneficial to explore family histories more deeply to understand the contexts that lead to partnering patterns (e.g. Gal, 1979). 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* influences mating patterns via altering affective conditioning (Livingston and Drwecki, 2007).

Genetic measures of individual admixture (e.g. heterozygosities) might also provide a more objective measure of multiple ancestries (Nalls *et al.*, 2009). We predict that these genetic measures will correlate more strongly with *DRD4*/7R alleles than more subjective and 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 R^2 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 (Richerson and Boyd, 2005). While the theoretical and evolutionary implications of this corpus of literature is compelling for the understanding of human diversity and our evolutionary history (e.g. the implications of assortative mating for multi-level selection and altruism as in Sober and Wilson, 1998), we are not aware of any legitimate (never-mind moral) policy or other practical implications of this line of research.

Conflict of Interest

None declared.

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