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Ambiguity aversion and familiarity bias: Evidence from behavioral and gene association studies

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Abstract It is increasingly recognized that decision making under uncertainty depends not only on probabilities, but also on psychological factors such as ambiguity and familiarity. Using 325 Beijing subjects, we conduct a neurogenetic study of ambiguity aversion and familiarity bias in an incentivized laboratory setting. For ambiguity aversion, 49.4% of the subjects choose to bet on the 50–50 deck despite the unknown deck paying 20% more. For familiarity bias, 39.6% choose the bet on Beijing's temperature rather than the corresponding bet with Tokyo even though the latter pays 20% more. We genotype subjects for anxiety-related candidate genes and find a serotonin transporter polymorphism being associated with familiarity bias, but not ambiguity aversion, while the dopamine D5 receptor gene and estrogen receptor beta gene are associated with ambiguity aversion only among female subjects. Our findings contribute to understanding of decision making under uncertainty beyond revealed preference.

Keywords Ambiguity aversion · Familiarity bias · Source dependence · Genetics · Neuroeconomics

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Many have attributed the study of probability to controversies on how best to engage in games of chance by Pascal and Fermat 400 years ago. The subject developed rapidly during the 18th century, but it was not until the work of Kolmogorov in the 20th century that we have a precise definition of probability in terms of the relative frequency of an event which can be repeated. Around the same time, Ramsey (1926) initiated another strand of probabilistic thinking that is based on decision making and is applicable to non-repeatable events. For instance, if one is indifferent between betting on whether the trailing digit of the Hang Seng Index will turn up odd or else even the next day, one might say that these two events are, subjectively speaking, equally likely. Subjective probability was given an axiomatic foundation by Savage (1954) building on the expected utility model of von Neumann and Morgenstern (1944).

Implicit in both the objective and the subjective views of probability is the notion that a lottery is fully described by its outcomes and associated probabilities. In this light, it is remarkable that Keynes had offered a contrarian view in 1921 by positing an additional psychological consideration—"If two probabilities are equal in degree, ought we, in choosing our course of action, to prefer that one which is based on a greater body of knowledge?" He illustrated this observation with an example of two urns, one containing 50 black balls and 50 red balls while another contains 100 balls of either color.

This example reappeared in Ellsberg (1961) who observed that people tend to be ambiguity averse in preferring to bet on the urn with known probabilities rather than one with unknown probabilities. The phenomenon of ambiguity aversion is puzzling. Since people tend to be indifferent between betting on red or black for either urn, drawing either color ought to have the same subjective probability of one-half, regardless of the urn used. Over the past decades, ambiguity aversion has inspired an active literature in decision theory beyond the subjective expected utility model, e.g., by using a non-additive generalization of probability (see, e.g., Schmeidler 1989) and by assuming that decision makers have a set of prior probabilities in the absence of unique well-defined subjective probability (Gilboa and Schmeidler 1989).

More recently, it is increasingly recognized that decision making under uncertainty depends not only on probabilities, but also on how uncertainty itself arises. This has been referred to as source dependence in Fox and Tversky (1995). In particular, they posit that people tend to prefer betting on risks arising from a more familiar source of uncertainty. Source dependence has given rise to another direction of research (see, e.g., Chew and Sagi 2008; Ergin and Gul 2009) in which the decision maker may have distinct attitudes towards risks arising from different sources of uncertainty. Here, a preference for betting on risks arising from a known or more familiar source may reflect a lesser degree of risk aversion than is the case for risks arising from an unknown or less familiar source of uncertainty.

Recently, ambiguity aversion and familiarity bias have been studied using neuroimaging (Chew et al. 2008; Hsu et al. 2005; Huettel et al. 2006). Over the past year, there is an embryonic literature combining experimental economics and behavioral genetics to explore the genetic basis of economic decision making. Two

recent twin studies, involving a Chinese and a Swedish population, suggest that genes may contribute significantly to economic risk taking (Cesarini et al. 2009; Zhong et al. 2009a). At the same time, findings of association between economic risk taking and well-characterized functional genes have been reported in Carpenter et al. (2011), Crisan et al. (2009), Dreber et al. (2009), Dreber et al. (2011), Frydman et al. (2011), Kuhnen and Chiao (2009), Roe et al. (2009), and Zhong et al. (2009b, c). However the neurogenetic basis of ambiguity aversion and familiarity bias remains unexplored.

Several polymorphic repeat regions near well-characterized brain-expressed genes are of significant interest in personality genetics, psychopathology and social cognition. The dopamine D5 receptor (DRD5) polymorphic repeat has been robustly linked to attention deficit hyperactivity disorder (ADHD), risky behavior (such as substance abuse and drunk driving) and comorbid anxiety and mood disorders (McGough 2005). The serotonin transporter (SLC6A4) is modulated by a polymorphic repeat, which has been shown to be associated with aversive behavior, neuroticism/harm avoidance and depression (Canli and Lesch 2007). Estrogen receptor alpha (ESR1) and estrogen receptor β gene (ESR2) are also characterized by polymorphic repeats associated with gender-specific anxiety traits perhaps mediated by brain serotonin levels (Imwalle et al. 2005). We hypothesized that these genes, linked to anxiety-related traits and characterized by polymorphic repeat regions, may contribute to ambiguity aversion and familiarity bias in decision making under uncertainty.

Using 325 Beijing subjects, we conduct a neurogenetic study of ambiguity aversion and familiarity bias in an incentivized choice setting. In the ambiguity task, subjects were asked to choose between betting on a known deck of 10 black and 10 red cards and betting on an unknown deck, comprising 20 cards with unknown numbers of the red and black cards, which paid 20% more. In the familiarity task, subjects were asked to choose between betting on whether the temperature on a historic day in Beijing was even or odd versus a corresponding bet with the Tokyo temperature for the same day, with the less familiar Tokyo bet paying about 20% more. We find strong evidence for both ambiguity aversion and familiarity bias—49.4% of the subjects chose to bet on the 50–50 deck despite the unknown deck paying 20% more and 39.6% of the subjects chose to bet on Beijing's temperature rather than Tokyo's temperature even though the Tokyo bet would pay 20% more. We genotyped subjects for anxiety-related candidate genes and test for their association with observed behavior in the ambiguity and familiarity tasks. We find the serotonin transporter polymorphism to be associated with familiarity bias but not ambiguity aversion, while the dopamine D5 receptor gene and estrogen receptor beta gene are both associated with ambiguity aversion only among female subjects. Our finding adds to recent findings of decision making under risk (Crisan et al. 2009; Dreber et al. 2009; Kuhnen and Chiao 2009; Roe et al. 2009; Zhong et al. 2009b, c; Frydman et al. 2011; Carpenter et al. 2011; Dreber et al. 2011) and contributes to a deeper understanding of decision making under uncertainty.

The paper is organized as follows. Section 1 introduces the methodology of behavioral genetics including a discussion on association studies using candidate genes. Section 2 presents the experimental design. Section 3 presents both behavioral and gene association results. Section 4 offers concluding remarks.

1 Behavioral genetics

A gene is the basic unit of heredity in a living organism. The gene concept is an empirical construct preceding the molecular biology era and based on breeding experiments in plants (first by Gregor Mendel in 1866) and animals. At the beginning of the 20th century Mendel's genes were identified with chromosomes. In 1944 the gene was identified with DNA and is now known to represent a sequence of four bases (A, G, C and T) arranged in a linear order, and as shown by Watson and Crick in 1953, the DNA molecule is a double helix held together by complementary pairings of bases (A = T, G = C) providing the mechanism for molecular replication and heritability. A human chromosome is a single DNA double helical molecule. There are an estimated 25,000 genes distributed on the 23 pairs of chromosomes. Individuals inherit half of their DNA from each parent. Some genes have various forms, known as alleles representing variations in the sequence of the DNA bases. For example, sickle cell anemia results from a particular allele coding for abnormal rather than normal hemoglobin and is due to a single base pair switch. Every individual has two separate copies of an allele at each locus, or location, on the chromosome, but each sperm or egg cell contains only one of these alleles. Thus a child has a 50% chance of receiving a particular allele from a particular parent.

In all organisms, genes encode protein in two major steps: First, the DNA is transcribed in the cell nucleus from DNA to messenger RNA; and, second, mRNA is translated into proteins in the cytoplasm. The process of producing a biologically functional molecule of either RNA or protein is called gene expression. Observable traits and behaviors of interest, referred to as phenotypes, are far downstream from the gene expression. While in some cases a single change in one letter of the DNA alphabet in a single gene alone can lead to a disease (such as sickle cell anemia), the vast majority of phenotypes are polygenic, meaning they are influenced by both multiple genes and different environmental factors.

Overall evidence that genes play a role in our ability to understand and manipulate social relationships mainly comes from studies of twins. The most common design compares monozygotic (MZ) and dizygotic (DZ) twins who were raised in the same family. MZ twins share all their genetic material, whereas DZ twins share approximately 50% of their genes. If we assume the environmental influences are the same for MZ and DZ twins for the phenotype of interest, then heritability is related to the difference in correlations between MZ twins and DZ twins. For the details of the twin method, readers can refer to Neale and Cardon (1992). Twin studies are informative regarding the percent of variance explained by genes, but not which specific genes or the number that contribute to the phenotype. For two decades the workhorse of human genetics has been genetic linkage combined with positional cloning which has produced remarkable success in identifying genes for rare Mendelian disorders. Today the completion of the Human Genome Project has allowed the use of the so-called SNP (single nucleotide polymorphism, a single change in one of the 4 DNA letters) map in testing association between phenotypes and genotype. Humans differ on the average every thousand base pairs (e.g. A→G) and this rich variation explains many differences in human behavioral traits. Another important source of variation in DNA are short-tandem repeat elements—regions of DNA that are variably repeated e.g.

$(GCGCGCGCGCGCGC)_n$. Finally, regions of DNA (>1 kb) that are either duplicated or deleted, so-called copy number variations, are now recognized as a third source of variation perhaps rivaling that of SNPs in overall importance.

There are two general approaches today in genetic research of complex traits. One strategy is Genome Wide Association Studies (GWAS). The power of GWAS lies in it not being hypothesis driven. By default, GWAS engages the entire genome in the analysis. SNP frequencies are compared across cohorts or quantitative phenotypes to ascertain chromosomal regions that partially explain some of the phenotypic variance. A second widely-used approach is to start with candidate genes that are known to regulate specific proteins of interest and/or influence related behaviors that make 'biological sense.' For the studies of economic decision making, we shall focus on genes that affect neurotransmitter synthesis and reception, hormone regulation and transcription factors. Benjamin et al. (2007) provides an excellent overview of the molecular genetics of economic behavior.

Candidate gene We observe basic guidelines for conducting genetic association studies of behavioral phenotypes. Of significant interest are genes that encode elements of neurotransmitter systems, which have previously been shown to be associated with brain functions as well as normal or abnormal behavior. We also base our selection on common genetic variants that are present in the population.

Dopamine is the most well-studied neurotransmitter for decision making and reward processing. It has been shown that degree of ambiguity and unfamiliarity is negatively correlated with activation in the striatum, an important dopaminergic brain region (Hsu et al. 2005; Chew et al. 2008). We further examined clinical phenotypes that would offer hints, for dopaminergic candidate genes combined with behavioral features, relevant to ambiguity and familiarity bias. ADHD is an interesting phenotype found in about 5% of children, adolescents and adults and is characterized by increased risky behavior, impulsivity, anxiety-related personality disorders and deficits in social cognition. We hypothesized that genes associated with ADHD that have been shown to contribute to decision making biases might be biologically plausible candidates to also contribute to ambiguity aversion and source preference. Among dopaminergic genes linked to ADHD, DRD5, rather than DRD2, is robustly associated by meta-analysis with this disorder. Hence we chose to examine the DRD5 microsatellite for association with risk-related decision making attitudes. Notably, the DRD5 gene has been more strongly linked to characteristics of ADHD such as executive function (Lowe et al. 2004) than DRD2, making this polymorphism a particularly good choice in the current study.

DRD5 belongs to a group of dopamine receptors that stimulate the activation of adenylate cyclase through the coupling of G-proteins. A number of studies have investigated the association between a dinucleotide [CA] repeat polymorphism, located 18.5 kb from the 5'end of the DRD5 gene, and ADHD. Presumably the 148 bp allele is in linkage disequilibrium with a functional allele of this gene, although cis acting elements often act at great distances from the protein coding region of some genes. In a meta-analysis of published studies involving European and Asian populations, Li et al. (2006) show a strong association between the 148 bp allele and ADHD. Moreover, Vanyukov and his colleagues (2000) have shown association between the 148 bp allele with risky behavior such as substance abuse

and anti-social personality disorder and observed, interestingly, that the association was gender sensitive.

Another candidate would be the dopamine D4 receptor exon 3 polymorphism (DRD4), characterized by a highly polymorphic VNTR containing a 48 bp repeat 1. Its 7-repeat allele is known for contributing to individual differences in economic risk-taking (Dreber et al. 2009; Kuhnen and Chiao 2009; Carpenter et al. 2011; Dreber et al. 2011). Additionally, this gene along with DRD5 has been robustly associated by meta-analyses with ADHD. However, there is extensive evidence showing the low incidence of the DRD4 48 bp VNTR 7-repeat allele, the risk allele in ADHD, among Han Chinese (Ding et al. 2002). For our study, DRD4 was not included as a candidate since the allele frequency of its 7-repeat allele is 0.8%.

Serotonin is an important neurotransmitter for emotional regulation and has been implicated in anxiety disorders and depression. A number of imaging genetics studies support the link between serotonin and activation in the amygdala (Canli and Lesch 2007) which has been implicated in ambiguity aversion and familiarity bias in previous neuroimaging studies (Hsu et al. 2005; Chew et al. 2008). Transcriptional activity of the human serotonin transporter (SLC6A4) is modulated by several variations, including a repetitive sequence, the SLC6A4-linked polymorphic region (5-HTTLPR), which is composed of a short and a long version resulting in different gene expressions and functions (Canli and Lesch 2007). The contribution of SLC6A4 to individual differences in personality traits was initially explored in a population and family-based genetic study (Lesch et al. 1996), showing a significant association between the low-expressing 5-HTTLPR short variant and neuroticism. This trait is related to anxiety, stress reactivity and depression. In a recent study (Kuhnen and Chiao 2009), subjects with the short allele of 5-HTTLPR were significantly more risk averse in a portfolio choice setting. Meanwhile, Roiser et al. (2009) shows that subjects with the short allele of 5-HTTLPR are more sensitive to the effect of loss-gain framing in decision making under risk at both the behavioral and neural levels.

Since our initial analysis as well as prior research (Croson and Gneezy 2009) provides evidence that women show greater ambiguity aversion and familiarity bias than men, we also examine two estrogen receptor genes. Estrogen receptor alpha (ESR1) has a TA repeat located upstream from exon 1 which may influence its tissue specific expression. This repeat has been associated with high anxiety scores in men, conduct disorder (Comings et al. 1999), and neuroticism in women (Westberg et al. 2003). The human estrogen receptor β gene (ESR2) with a polymorphic CA repeat in intron 5 has been shown to be associated with menopausal complaints including mood disturbances, anxiety and depression (Takeo et al. 2005). In rat pharmacological studies the anxiolytic properties of estrogens are ESR2 mediated (Lund et al. 2005). Similarly, in the absence of functional ESR2 receptors (ESR2 knockout), regardless of the presence of circulating estradiol in plasma, female mice exhibited enhanced anxiety and decreased concentrations of serotonin or dopamine in several brain regions (Imwalle et al. 2005). These animal studies are consistent with some investigations involving human subjects. The short CA repeats have also been associated with osteoporosis suggesting that they are associated with less expression (Geng et al. 2007).

We hypothesized that these genes, linked to anxiety-related traits and characterized by polymorphic repeat regions, may contribute to ambiguity aversion and

familiarity bias in decision making under uncertainty. Since women show greater ambiguity aversion and familiarity bias than men in the previous studies as well as the current one, these four genes, all associated with gender-sensitive phenotypes, are particularly attractive candidates.

2 Experimental design

2.1 Subjects

350 subjects were recruited in Beijing through the internet, posters, and word of mouth. The first group was recruited in July 2007; the second group was recruited in February 2008. Demographics of the subjects are summarized as follows: mean age 28.2 +/− 10.8 (s.d.); 162 male, 188 female; 123 non-student subjects, 227 student subjects; 67 subjects with high school education, 194 subjects with college education, 89 subjects with postgraduate education; 325 Han Chinese, 25 non-Han Chinese. We did not do genotyping for the 25 non-Han Chinese, and only the 325 Han Chinese are included in analysis for current study to have a better control of population.

This study was approved by the Internal Review Board of the Hong Kong University of Science and Technology. Prior to running the experiment, subjects were each given a written informed consent form for donation of blood samples and for participation in the behavioral experiment. Subsequently, subjects participated in the behavioral experiment as described below. After the experiment, subjects donated 10 cc of blood each for genotyping, taken by nurses and doctors from hospitals in Beijing.

2.2 Experimental paradigm

Most experimental studies on the original Ellsberg paradox involve choosing between betting on the unknown deck versus betting on the known deck where betting correctly in either case would pay the same, in which case people tend to bet on the known deck. For our association study, in order to generate a more even split of individuals between those preferring to bet on the known deck versus those preferring to bet on the unknown deck, we increase the payoff associated with betting on the unknown deck. This calls for a judicious choice of a threshold difference. In the ambiguity aversion task, subjects choose between betting on a "known" deck consisting of 10 red cards and 10 black cards, and an "unknown" deck consisting of 20 cards without knowing the composition of the red and black cards. For the known deck, a correct bet pays Y10 (about USD1.4). For the unknown deck, a correct bet pays Y12 with an increase of Y2 as a result of pretests.

In Fox and Tversky's (1995) experiment on familiarity bias, the bet is on whether the temperature in San Francisco/Istanbul is above/below a specific temperature. However, subjects may have different information about the cities, which could be a confounding factor for familiarity bias. Recently Abdellaoui et al. (2011) use the Chew and Sagi (2008) notion of exchangeability to elicit equal chance for the

possible temperature range for cities. Chew et al. (2010) adopt an odd-even design which captures exchangeability more directly to investigate source preference over almost objective events (Machina 2004) such as whether the trailing digits of Dow Jones would be odd or even. We apply this design in this paper for bets on whether the temperature at a specific historical day in Beijing (Tokyo) would be odd or even. This procedure induces the same unambiguous probability of one half for odd versus even regardless of the city chosen. As with the case for ambiguity aversion, to generate an even split between those betting on Beijing and those betting on Tokyo, a correct bet on the Beijing temperature pays Y11 which is Y2 less than the payout for a correct bet on the Tokyo temperature.

2.3 Genotyping

The genotyping method is in Appendix I. The allele frequency of DRD5 is presented in Table 1. The allele frequency of 5-HTTLPR is presented in Table 2, and it is in Hardy-Weinberg Equilibrium ($p<0.9998$). For ESR1, 16 alleles (178–208 bp) and for ESR2 15 alleles (141–169 bp) were identified and the distribution of allele frequencies is similar to previous reports (e.g., McIntyre et al. 2007). The allele frequency is presented in Figs. 1 and 2 respectively.

3 Results

At the behavioral level, our specific choice of threshold payoffs induced 50.6% of the subjects to bet on the unknown deck in the card-deck task, and 60.4% of the subjects to bet on Tokyo in the temperature task. We find significant gender dependence with female subjects being significantly more likely to bet on Beijing (t-test, $p<0.019$) in the temperature task and to bet on the known deck (t-test, $p<0.011$) in the card-deck task. This is consistent with prior findings on the gender difference of decision making under uncertainty (Croson and Gneezy 2009). We do not find significant association between ambiguity aversion and familiarity bias (corr = 0.020, $p>0.719$), a finding consistent with evidence from Hsu et al. (2005) (corr = −0.143, $p>0.579$, from Table S6 in Hsu et al. 2005). This suggests that familiarity bias and ambiguity aversion are distinct phenomena at the behavioral level.

As discussed in a recent study (Jakobsdottir et al. 2009), there are two basic statistical approaches for evaluating markers. The risk-based approach models risk as a function of marker(s), often with adjustment for covariates, and is commonly applied in genetic studies. In case–control studies, this is done with logistic regression, and the markers with the strongest effect on disease risk are those

Table 1 Allele and genotype frequency of DRD5

Allele frequency		Genotype frequency		
148 bp	others	148 bp/148 bp	148/others	others/others
30.1%	69.9%	11.0%	38.1%	50.8%

Table 2 Allele and genotype frequency of 5-HTTLPR

Allele frequency		Genotype frequency		
short	long	short/short	short/long	long/long
69.8%	30.1%	51.7%	36.2%	12.1%

Short and long represent the repeat length of 5-HTTLPR

associated with the smallest p-values and most extreme odds ratios (ORs). The current investigation uses the latter method which is most commonly employed in genetic association studies. To test the effect of genotypes on our binary data, we use logit regression with robust standard error for genotype association analysis with Stata 8.0. Gender, age, and student status have been included as independent variables.

DRD5 Although *DRD5* is not significantly associated overall with ambiguity aversion ($p>0.212$) nor familiarity bias ($p>0.928$), significant association is observed for ambiguity aversion in female subjects ($p<0.01$) with the 148 bp allele contributing to ambiguity seeking (Fig. 3b). The results are reported in Table 3.

5-HTTLPR The short allele of *5-HTTLPR* contributes significantly to familiarity bias ($p<0.005$) (Fig. 3a). This association is robust with respect to gender (*male*, $p<0.057$; *female*, $p<0.043$). No association is observed between *5-HTTLPR* and ambiguity aversion ($p>0.315$). These results are reported in Table 4.

ESR1 Figure 1 displays the distributions of *ESR1* alleles, which were each divided into two groups of approximately the same size. For *ESR1*, 178–188 bp (48.2%) were classified as short (S), and 190–208 bp were classified as long (L). No significant association is observed between *ESR1* and ambiguity aversion ($p>0.497$) or familiarity bias ($p>0.801$). These results are reported in Table 5.

ESR2 Figure 2 displays the distributions of *ESR2* alleles, which were each divided into two groups of approximately the same size. For *ESR2*, 141–157 bp (about

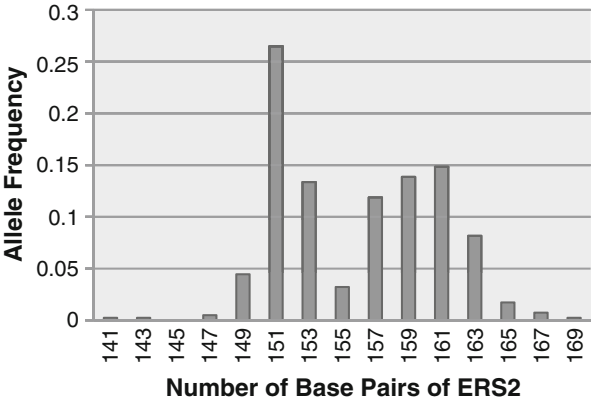

Fig 1 Allele frequency of ESR1

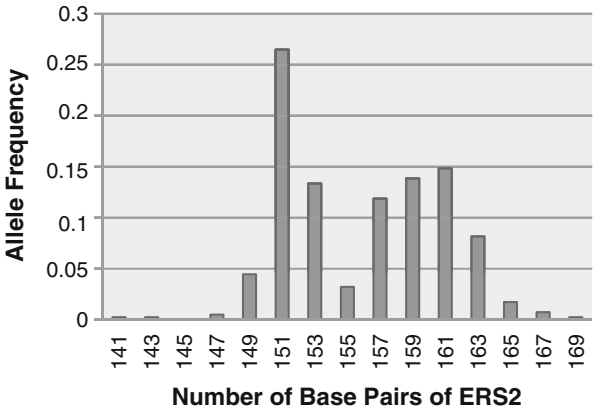

Fig 2 *Allele frequency of ESR2.* The x-axis is the number of base-pair, and the y-axis is the percentage of the allele

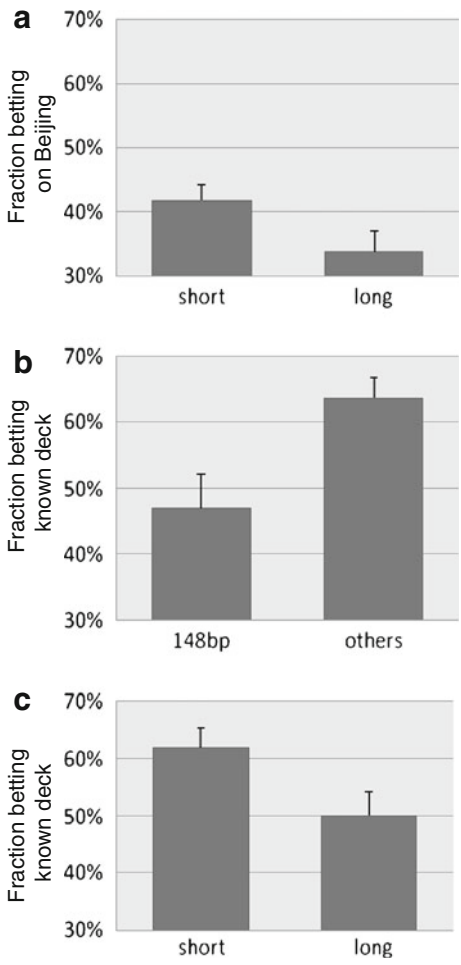

Fig. 3 **a** *5-HTTLPR and familiarity bias*. Subjects with short allele tend to bet on Beijing. **b** *DRD5 and ambiguity aversion in females.* Female subjects without 148 bp allele tend to bet on the known deck. **c** *ESR2 and ambiguity aversion in females.* Subjects with short allele tend to bet on the known deck

Table 3 Association results for DRD5 and ambiguity aversion as well as familiarity bias

	All		Male		Female	
	Ambiguity	Familiarity	Ambiguity	Familiarity	Ambiguity	Familiarity
DRD5	0.801	0.982	1.298	0.785	0.551**	0.155
	(0.142)	(0.201)	(0.358)	(0.269)	(0.127)	(0.285)
Female	0.460***	0.567**				
	(0.11)	(0.154)				
Age	1.006	0.923***	1.012	0.908***	0.994	0.935**
	0.016	(0.018)	(0.022)	(0.025)	(0.024)	(0.026)
Student	0.774	2.075**	1.126	2.247	0.462	2.091
	(0.272)	(0.758)	(0.489)	(1.152)	(0.249)	(1.137)
Observations	299	299	140	140	159	159
R-squared	0.035	0.188	0.006	0.215	0.049	0.155

Odd ratios are without parentheses, and robust standard errors are in parentheses: ***$p<0.01$, **$p<0.05$, *$p<0.1$

58.0%) were classified as short (S), and 159–169 bp were classified as long (L). Significant association was observed between *ESR2* and ambiguity aversion ($p<0.023$) with the short allele contributing to ambiguity aversion (Fig. 3c), but no association was observed between *ESR2* and familiarity bias ($p>0.672$). As anticipated, *ESR2* contributes significantly to ambiguity aversion in female subjects ($p<0.046$), but not for male subjects ($p>0.262$). These results are reported in Table 6.

In sum, we find subjects with the short 5-HTTLPR allele tend to bet on Beijing (familiar), while female subjects without the DRD5 148 bp allele were more likely to bet on the known deck as were female subjects with the ESR2 [CA] short alleles.

Table 4 Association results for 5-HTTLPR and ambiguity aversion as well as familiarity bias

	All		Male		Female	
	Ambiguity	Familiarity	Ambiguity	Familiarity	Ambiguity	Familiarity
5-HTTLPR	1.189	0.595***	1.202	0.559*	1.213	0.622**
	(0.196)	(0.111)	(0.295)	(0.171)	(0.279)	(0.146)
Female	0.562**	0.540**				
	(0.128)	(0.143)				
Age	1.001	0.932***	0.994	0.930***	1.002	0.934**
	(0.015)	(0.017)	(0.020)	(0.023)	(0.023)	(0.026)
Student	0.812	2.232**	1.134	2.277	0.583	2.188
	(0.272)	(0.823)	(0.499)	(1.155)	(0.301)	(1.203)
Observations	323	323	147	147	176	176
R-squared	0.019	0.183	0.005	0.189	0.015	0.162

Odd ratios are without parentheses, and robust standard errors are in parentheses: ***$p<0.01$, **$p<0.05$, *$p<0.1$

Table 5 Association results for ESR1 and ambiguity aversion as well as familiarity bias

	All		Male		Female	
	Ambiguity	Familiarity	Ambiguity	Familiarity	Ambiguity	Familiarity
ERS1	1.1084	0.95831	1.16543	1.06703	1.04765	0.88052
	(0.168)	(0.162)	(0.266)	(0.271)	(0.214)	(0.201)
Female	0.515***	0.566**				
	(0.12)	(0.151)				
Age	1.00394	0.929***	1.00288	0.922***	0.9993	0.935*
	(0.016)	(0.018)	(0.021)	(0.025)	(0.023)	(0.025)
Student	0.76427	2.145**	1.04115	2.411*	0.54109	2.01281
	(0.258)	(0.781)	(0.452)	(1.217)	(0.280)	(1.072)
Observations	310	310	141	141	169	169
R-squared	0.0244	0.1808	0.0025	0.2025	0.0151	0.1513

Odd ratios are without parentheses, and robust standard errors are in parentheses: ***$p<0.01$, **$p<0.05$, *$p<0.1$

There is increasing awareness that it is difficult to replicate findings in genetic association studies due to multiple testing and publication bias. For instance, while DRD4 and novelty seeking have been well studied, meta-analysis (Munaf et al. 2008) suggests there is lack of overall association with novelty seeking. Since we examined 4 polymorphisms in the current study, the strict Bonferroni correction significance could only be established at $p<0.0125$. In a sense, only the association between 5-HTTLPR and familiarity bias ($p<0.005$), and the association between DRD5 and ambiguity aversion in females could survive the correction in this level, but the association between ESR2 and ambiguity aversion in females ($p<0.046$)

Table 6 Association results for ESR2 and ambiguity aversion as well as familiarity bias

	All		Male		Female	
	Ambiguity	Familiarity	Ambiguity	Familiarity	Ambiguity	Familiarity
ERS2	1.451**	1.083665	1.304434	0.8608273	1.590*	1.299864
	(0.238)	(0.206)	(0.309)	(0.259)	(0.370)	(0.329)
Female	0.502***	0.574**				
	(0.117)	(0.151)				
Age	1.004275	0.929***	0.999787	0.925***	1.005565	0.936**
	(0.016)	(0.017)	(0.021)	(0.025)	(0.023)	(0.025)
Student	0.81529	2.120**	1.067599	2.471*	0.646822	2.116113
	(0.273)	(0.762)	(0.473)	(1.260)	(0.326)	(1.103)
Observations	316	316	144	144	172	172
R-squared	0.0359	0.1767	0.0066	0.1953	0.0325	0.1531

Odd ratios are without parentheses, and robust standard errors are in parentheses: ***$p<0.01$, **$p<0.05$, *$p<0.1$

would not. If we further take into account multiple testing with two phenotypes, only the association between 5-HTTLPR and familiarity bias could survive Bonferroni correction.

For the exploratory analyses, we did not use this overly conservative Bonferroni correction owing to the increased risk of making Type 2 errors. In addition, the range of odds ratio in our study from 1.45 to 2 is similar to the effect sizes for other behavioral traits (Jakobsdottir et al. 2009). As with genetic association findings often reported in the literature, the findings of the current report should be considered provisional at the current stage and their validation awaits replication in independent samples.

4 Concluding remarks

The remarkable works of Keynes, Knight, and Ramsey in the 1920s have enhanced our understanding of the nature of decision making under uncertainty with the suggestion that people may be ambiguity averse in preferring bets involving known probabilities to those based on contingencies without known probabilities. This was further studied in Ellsberg (1961) and subsequently extended to source dependence (Heath and Tversky 1991; Fox and Tversky 1995), which encompasses the phenomenon of familiarity bias in which people tend to prefer bets arising from a familiar source of uncertainty than those arising from an unfamiliar source.

Our odd-even design to elicit familiarity bias has the advantage of inducing the same unambiguous probability of half for each subject in both bets. A preference for the Beijing bet paying less than the Tokyo bet would support the idea that subjects strictly prefer betting on a more familiar source of uncertainty. This behavior is not compatible with non-expected utility models of decision making that are based on the hypothesis of global probabilistic sophistication, i.e., lotteries are fully captured by their underlying probabilities and outcomes (Machina and Schmeidler 1992; Chew and Sagi 2006). These include betweenness conforming preferences (Chew 1983; Dekel 1986; Chew 1989) and rank-dependent preferences (Quiggin 1982; Green and Jullien 1988). While Choquet expected utility (Schmeidler 1989) can account for ambiguity aversion via a non-additive capacity, this model reduces to Quiggin's rank-dependent utility in the presence of known probabilities if equally probable events assume the same capacity value. In this case, Choquet expected utility is incompatible with having a 'bias' in favor of one 50–50 lottery from a familiar source of uncertainty to another 50–50 lottery from a less familiar source and pays less. While this observation applies to cumulative prospect theory which is defined in terms of Choquet expected utility, Tversky and Kahneman (1992, page 302) raised the intriguing possibility of the function, linking the non-additive capacity to an underlying probability, may itself depend on the source of uncertainty. Another strand of the literature that can account for Ellsbergian behavior involves the idea of multiple priors, e.g., Gilboa and Schmeidler (1989). For this approach to account for the nature of familiarity bias reported in this paper, one would need to assume that the event of odd or even has non-unique priors.

Our study links ambiguity aversion and familiarity bias to three common polymorphisms which have been associated with anxiety-related traits and gender-

sensitive phenotypes. Our results show that DRD5 (microsatellite marker) and ESR2 (CA repeat) are associated with ambiguity aversion, while SLC6A4 (5-HTTLPR indel) is associated with familiarity bias. Our results corroborate the view proposed in Ellsberg (1961) and Fox and Tversky (1995) that lack of competence and confidence contributes to ambiguity aversion and familiarity bias, specifically, that DRD5 (microsatellite marker) and ESR2 (CA repeat) are associated with ambiguity aversion while SLC6A4 (5-HTTLPR indel) is associated with familiarity bias. Taken together, our findings suggest distinct neurogenetic mechanisms modulating familiarity bias and ambiguity aversion. This corroborates the lack of significant correlation between ambiguity aversion and familiarity bias at the behavioral level.

Overall, alleles associated with familiarity bias and ambiguity aversion are the same alleles in many human studies, including studies using experimental economics paradigms (Crisan et al. 2009; Kuhnen and Chiao 2009; Roiser et al. 2009), that are also associated with more avoidant personality types, especially neuroticism or harm avoidance (Cloninger 1986). Personality is a continuous trait and women score higher on harm avoidant traits than men (Zion et al. 2006) underpinning the idea that source dependence may have a link to this basic human personality trait. This notion is corroborated by current findings in personality neurogenetics. Intriguingly, the neurogenetic evidence appears to support a distinction between ambiguity aversion and familiarity bias at the specific gene level, since ESR2 and DRD5 are associated solely with ambiguity bias whereas SLC6A4 is solely associated with familiarity bias. To summarize, we suggest that avoidant personality underlies source dependence which in turn drives familiarity bias and ambiguity aversion through partially distinct genetic mechanisms. Future studies would profitably examine other common polymorphisms and their role in source dependence.

In an imaging study of ambiguity aversion and familiarity bias, Hsu et al. (2005) found that the amygdala was more activated under the ambiguity (unfamiliarity) condition than under the risk (familiarity) condition. Chew et al. (2008) conducted a subsequent fMRI experiment on familiarity bias using an odd-even design that is close to what we use in the current study, and replicated amygdala activation in modulating familiarity bias. The emerging evidence regarding the role of 5-HTTLPR in mediating amydagla activation (Hariri et al. 2002; Roiser et al. 2009), together with the present study, suggests a neurobiological mechanism from 5-HTTLPR, amygdala activation, to familiarity bias. Specifically, genetically driven variation in brain activation may respond to human emotion arising from familiarity bias. This suggests that differential excitability of the amygdala to unfamiliar sources of uncertainty may contribute to an increased fear and anxiety associated with the short allele of 5-HTTLPR.

In their 1991 paper, Heath and Tversky suggest a link between familiarity bias and the home market bias in finance—"investors are sometimes willing to forego the advantage of diversification and concentrate on a small number of companies with which they are presumably familiar." More recent empirical studies, e.g., Huberman (2001), reveal an intriguing domestic "home bias" in terms of systematic under-diversification of stock holdings in companies that are closer to home even when all of them are US based. Through the Heath-Tversky observation, it would be of interest for future studies to investigate whether 5-HTTLPR modulates home market bias in the setting of a field experiment.

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Appendix I. Genotyping method

The polymorphism for the SLC6A4 44 bp deletion/insertion (5-HTTLPR) in the promoter region was characterized using PCR amplification procedure with the following primers: F5′-GGCGTTGCCGCTCTGAATTGC-3′, R5′-GAGGGACT GAGCTGGACAACC-3′. PCR reactions were performed using 5 μl Master Mix (Thermo scientific), 2 μl primers (0.5 μM), 0.6 μl Mg/Cl2 (2.5 mM), 0.4 μl DMSO 5% and 1 μl of water to total of 9 μl total volume and an additional 1 μl of genomic DNA was added to the mixture. All PCR reactions were employed on a Biometra T1 Thermocycler (Biometra, Güttingem, Germany). PCR reaction conditions were as follows: preheating step at 94.0°C for 5 min, 34 cycles of denaturation at 94.0°C for 30 s, reannealing at 55°C for 30 s and extension at 72°C for 90 s. The reaction proceeded to a hold at 72°C for 5 min. All reaction mixtures were electrophoresed on a 3% agarose gel (AMRESCO) with ethidium bromide to screen for genotype.

Amplification of the DRD5, ESR1 and ESR2 microsatellites was achieved using the following primers: DRD5: forward: 5′- CGTGTATGATCCCTGCAG -3′; reverse: 5′- GCTCATGAGAAGAATGGAGTG -3′; ESR1 (corresponds to the TA dinucleotide repeat in the 5′ promoter region): forward 5′- AGACGCATGATA TACTTCACC -3′; reverse 5′- GTTCACTTGGGCTAGGATAT -3′. ESR2 (corresponds to the CA dinucleotide repeat in intron 5): forward (fluorescent) 5′- GGTAAAC CATGGTCTGTACC -3′; reverse 5′- AACAAAATGTTGAATGAGTGGG -3′. PCR reactions were performed using 5 μl Master Mix (Thermo scientific), 0.5 μl primers (0.5 μM), 0.4 μl Mg/Cl2 (2.5 mM) and 3.1 μl of water to total of 9 μl total volume and an additional 1 μl of genomic DNA was added to the mixture. All PCR reactions were employed on a Biometra T1 Thermocycler (Biometra, Güttingem, Germany). PCR reaction conditions were as follows: preheating step at 95.0°C for 5 min, 30 cycles of denaturation at 95.0°C for 30 s, reannealing at 55°C for 30 s and extension at 72°C for 40 s. The reaction proceeded to a hold at 72°C for 10 min. The PCR product was analyzed on an ABI 310 DNA Analyzer.

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