Studying the association between *OXTR*, *MAOA* and *AVPR1* genes with cooperative behavior in a public good game with strategic method: Only the *AVPR1* and *MAOA* gene showed and effect

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Introduction

Twin studies have shown that prosocial and antisocial patterns of behavior are heritable to some extent. These findings are reinforced by studies that have found associations between patterns of human social behavior and genes that were previously known to participate in neural processes *(1-8)*. Together, this evidence suggests a causal link between certain genetic polymorphisms and patterns of social behaviors.

We studied the association between cooperative behavior and three candidate genes: the oxytocin receptor gene (*OXTR*), the arginine vasopressin 1a receptor gene (*AVPR1*), and the monoamine oxidase A gene (*MAOA*). One reason for choosing these genes is that they are involved in the expression of proteins that degrade or receive neurotransmitters, such as oxytocin, dopamine, norepinephrine, serotonin, and arginine vasopressin. Another reason for choosing these genes is that they have previously been associated to other forms of social behaviors, ranging from maternal sensitivity *(2)*, to antisocial alcoholism *(3)*, to allocations in a dictator game *(4,5)*.

To classify the subjects into strategic types of cooperative behavior, we observed their decisions in a public good experiment, a game in which an individual must choose between his own material interest and the material interest of his group *(9)*. According to their decisions, we classified the subjects into four strategic-types: free riders, conditional cooperators, hump shaped, and other. We then looked for associations between polymorphisms in these genes and the strategic heterogeneity observed in the subject pool.

Methods

192 undergraduate students from Universidad del Desarrollo volunteered as experimental subjects. 109 of the subjects were female. The experiment was carried out in a computer room equipped with z-Tree, a program for economic experiments *(10)*. We used a double-anonymous experimental design to reduce the social desirability bias *(11)*.

In the first stage of the experiment, the subjects participated in a **strategic public good game** *(12)*. At the beginning of the game, each subject was given an endowment of 20 tokens (1 token = CLP250 ≈ $0.44). Then the subjects were randomly assigned to groups of four players. Each player was asked the following questions:

A. How many tokens will you contribute to the public good if you are not previously informed of the other players' contributions?

B. How many tokens will you contribute to the public good if you are previously informed that the other players contributed an average of x token (for x = 0, 1, 2, 3, 4...20) ?

A player's answer to question A is his "uninformed contribution", while his answers to questions B.1 to B.21 constitute his "contribution scheme."

After the four players in the group made their decisions, the computer randomly chose three players and implemented their uninformed contributions. Then the computer calculated the average contribution of these players, and used that number to determine the contribu-tion of the fourth player, according to his contribution scheme.

Finally, the total contribution to the public good was multiplied by 2, and the result was divided in equal shares among the four players.

After playing the game, we collected saliva DNA samples from all subjects. DNA was extracted using the prepIT-L2P (Oragene Purifier) kit. The three polymorphisms of interest were amplified using PCR and confirmed by gel electrophoresis. The *OXTR* SNP rs53756G>A was identified using Sanger sequencing, and *AVPR1* SSR and *MAOA* u-VNTR using fragment analysis and capillary electrophoresis in ABI310.

Results

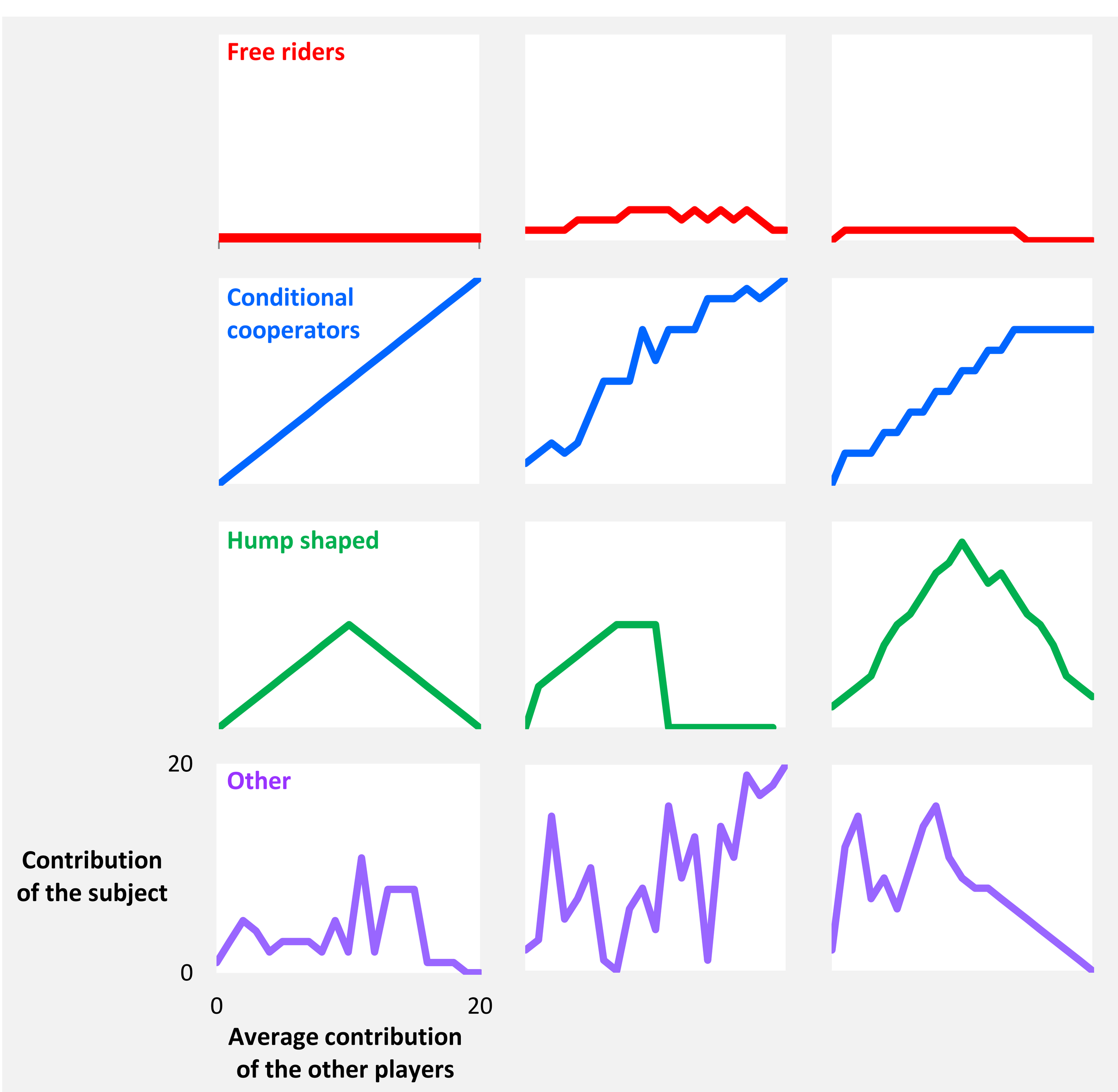

Figure 1: Sample of contribution schemes. We classified the subjects into the different strategic types using the following algorithm. If a subject's contribution was always ≤ x%, we classified that subject as a free rider (we used three alternative criteria to classify free riders: x% = 10%, 20%, and 30%). Otherwise, we classified the subject into one of three strategic types: conditional cooperator, hump shaped, or "other". If the subject's contribution scheme had a positive spearman rank-correlation (p-value ≤ 0,001), we classified the subject as a conditional cooperator. If his contribution scheme had a positive Spearman correlation up to a point where the correlation turned negative, we classified the subject as a hump shaped. Otherwise, we classified him as other. Subjects who were classified both as conditional cooperators and hump shaped were reclassified as other.

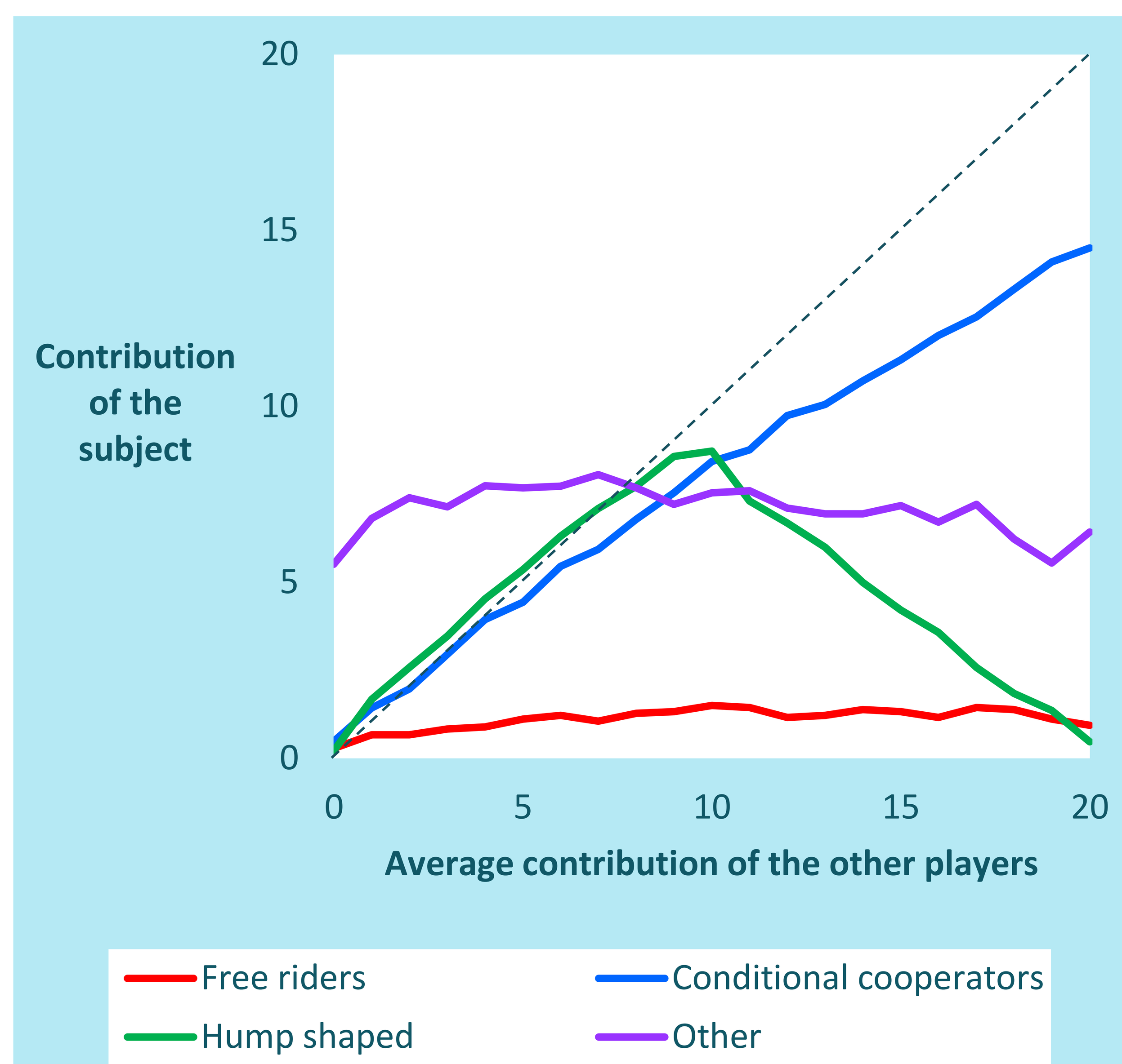

Figure 2: Average contribution schemes for each type of player. In this figure, subjects were classified as free riders if their contribution was always ≤ 20%. The 45° line represents the contribution scheme of a perfect conditional cooperator. As in previous studies, the average condi-tional cooperator exhibits a self-serving bias: he always wants to contribute less than the other players of his group.

Table 1a: Distribution of strategic types among women, by free rider classification criterion			
	Maximum contribution of free riders		
Strategic type	10%	20%	30%
Free riders	4	10	19
Conditional cooperators	53	50	46
Hump shaped	11	11	9

Table 1b: Distribution of strategic types among men, by free rider classification criterion			
	Maximum contribution of free riders		
Strategic type	10%	20%	30%
Free riders	6	8	17
Conditional cooperators	45	45	38
Hump shaped	8	8	8
Other	24	22	20

Table 2a: Distribution of genotypes among women

OXTR rs53756	n	*AVPR1* RS3	n	*MAOA* u-VNTR	n
GG	49	long/long	51	4.5/4.5	38
GA	42	long/short	43	4.5/3.5	44
AA	18	short/short	13	3.5/3.5	10

Note: 2 samples for *AVPR1* and 17 for *MAOA* could not be amplified.

Table 2b: Distribution of genotypes among men

OXTR rs53756	n	*AVPR1* RS3	n	*MAOA* u-VNTR	n
GG	41	long/long	21	4.5	32
GA	33	long/short	49	4.5	39
AA	9	short/short	9		

Note 1: *MAOA* is located in the X chromosome, so men only have one allele.
Note 2: 4 samples for *AVPR1* and 12 for *MAOA* could not be amplified.

Figure 3: Distribution of strategic types for each genotype by gender. In this figure, subjects were classified as free riders if their contribution was always ≤ 20%. The *AVPR1* RS3 polymorphism shows a significant effect on the distribution of strategic types, but only for women (see details in Tables 3a to 5b). Women that carried the short/short genotype were more likely to behave as conditional cooperators, and less likely to behave as hump-shaped or other. The *MAOA* u-VNTR polymorphism also has a significant effect on the distribution of strategic types, but only for women. Women that carried two alleles with 3.5 repeats were less likely to behave as hump shaped.

Table 3a: Marginal effects of the *OXTR* rs53756 polymorphism on the distribution of strategic types among women, by free rider classification criterion

		Maximum contribution of free riders		
Strategic type	Genotype	10%	20%	30%
Free riders	GG	-8% **	-3%	4%
	GA	0%	-1%	14%
Conditional cooperators	GG	11%	8%	3%
	GA	8%	9%	3%
Hump shaped	GG	-1%	8%	-1%
	GA	-2%	8%	-6%
Other	GG	-2%	-4%	-6%
	GA	-6%	-6%	-10%

Baseline: AA genotype.

Table 3b: Marginal effects of the *OXTR* rs53756 polymorphism on the distribution of strategic types among men, by free rider classification criterion

		Maximum contribution of free riders		
Strategic type	Genotype	10%	20%	30%
Free riders	GG	94%	-14%	-26%
	GA	99%	-9%	-22%
Conditional cooperators	GG	-66%	-70%	-58%
	GA	-61%	-71%	-59%
Hump shaped	GG	-14%	-14%	-15%
	GA	-16%	-18% *	-18%
Other	GG	-14%	99%	99%
	GA	-21%	99%	99%

Table 4a: Marginal effects of the AVPR1 RS3 polymorphism on the distribution of strategic types among women, by free rider classification criterion

		Maximum contribution of free riders		
Strategic type	Genotype	10%	20%	30%
Free riders	long/long	2%	0%	3%
	short/short	6%	-2%	16%
Conditional cooperators	long/long	-4%	2%	1%
	short/short	32% **	36% **	21%
Hump shaped	long/long	-1%	-1%	-2%
	short/short	-12% ***	-12% ***	-9% **
Other	long/long	-5%	-2%	-2%
	short/short	-27% **	-22% **	-28% ***

Baseline: short/long genotype.

Table 4b: Marginal effects of the AVPR1 RS3 polymorphism on the distribution of strategic types among men, by free rider classification criterion

		Maximum contribution of free riders		
Strategic type	Genotype	10%	20%	30%
Free riders	long/long	-2%	-3%	-6%
	short/short	0%	0%	-20% ***
Conditional cooperators	long/long	-11%	-13%	-10%
	short/short	18%	16%	31% *
Hump shaped	long/long	5%	5%	4%
	short/short	2%	2%	2%
Other	long/long	8%	12%	12%
	short/short	-20%	-17%	-13%

Table 5a: Marginal effects of the *MAOA* u-VNTR polymorphism on the distribution of strategic types among women, by free rider classification criterion

		Maximum contribution of free riders		
Strategic type	Genotype	10%	20%	30%
Free riders	4.5/4.5	-1%	-1%	-1%
	3.5/3.5	-5% *	-2%	-12%
Conditional cooperators	4.5/4.5	19%	17%	11%
	3.5/3.5	12%	15%	17%
Hump shaped	4.5/4.5	-2%	-2%	-3%
	3.5/3.5	-12% ***	-12% ***	-10% **
Other	4.5/4.5	-15%	-13%	-6%
	3.5/3.5	5%	-1%	5%

Baseline: 4.5/3.5 genotype.

Table 5b: Marginal effects of the MAOA u-VNTR polymorphism on the distribution of strategic types among men, by free rider classification criterion

		Maximum contribution to the public good		
Strategic type	Genotype	10%	20%	30%
Free riders	4.5	-1%	-2%	7%
Conditional cooperators	4.5	-2%	-2%	-12%
Hump shaped	4.5	3%	3%	3%
Other	4.5	0%	1%	1%

Baseline: 4.5 genotype.

*** = 1% significance, ** = 5% significance, * = 10% significance.
All marginal effects where calculated using multinomial linear regressions.

Conclusions

- The *OXTR* rs73756 polymorphism showed no effect on the strategic types of players in the public good game.
- Women that carried two short alleles of *AVPR1* RS3 polymorphism were more likely to behave as conditional cooperators, and less likely to behave as hump shaped or other.
- Women that carried two alleles with 3.5 repeats of the *MAOA* u-VNTR polymorphism were less likely to behave as hump shaped.
- The negative effect of the short/short genotype on conditional cooperativeness seems to contradict previous studies that report positive associations of this genotype to prosocial behaviors *(4)*. This apparent contradiction disappears if conditional cooperativeness is interpreted as an expression of negative reciprocity. According to this interpretation, conditional cooperators punish free-riders by ceasing to cooperate, which qualifies as an antisocial behavior.

References

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Acknowledgments

CONICTY: Project "Anillo en Complejidad Social" SOC-1101.
Universidad del Desarrollo: Proyecto interfacultades 2012 "Genetic basis of social behaviour in collective action problems"

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