ONLINE RESOURCES

# Dopamine receptor D4 (*DRD4*) gene polymorphism among Gaddi tribe of Himachal Pradesh

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## Introduction

Dopamine is one of the most important neurotransmitters in the brain. D4 receptor of dopamine shows the largest number of polymorphisms among all the dopamine receptors and is one of the most polymorphic of all the genes studied (Chang *et al.* 1996). *DRD4* gene is reported to be associated with personality associated traits like novelty-seeking. The polymorphism in *DRD4* is revealed in the variable number of imperfect 48 bp tandem repeats in exon 3, ranging from two to 11 repeat units, with over 67 different haplotype variants (Ding *et al.* 2002; Grady *et al.* 2003). In most geographical locations, the 4R allele is the most common, whereas 2R and 7R allele frequencies vary widely (Chang *et al.* 1996; Ding *et al.* 2002). The 4R and 7R repeats are the most common worldwide (Chang *et al*. 1996). 4R and 2R alleles are common in Indian subcontinent (Chen *et al.*1999). 7R is absent among most of the Indian tribes and rare among caste groups of India. (Saraswathy *et al.* 2013). This study is an attempt to find out the distribution of *DRD4* variants among Gaddis, a transhumant population of northern India. Transhumance is seasonal and short term (for 2–4 months) micro-migration with livestock due to unfavourable change in environment.

## Materials and methods

### *Subjects*

A total of 152 random blood samples of healthy individuals (males and females), aged 25–75 years were collected from Gaddi population of Bharmour region of Chamba, Himachal Pradesh. Care was taken to avoid blood relatives up to the first cousin during the sampling. Informed written consent was taken from all the subjects before collecting the samples. The study was approved by the ethical committee, Department of Anthropology, University of Delhi.

### *Genotyping*

Genomic DNA was isolated using salting-out method (Miller *et al.* 1988). *Drd4* was genotyped by allele specific method (Eisenberg *et al.* 2008). PCR products were genotyped by agarose gel electrophoresis and genotypes were visualized under long wave UV light after staining with ethidium bromide.

### *Statistics*

Genotype and allele frequencies were calculated by gene counting method using PopGene software (Yeh *et al.* 1999). Conformity to Hardy–Weinberg equilibrium (HWE) was performed by goodness of fit chi-square test. Statistical significance was checked at 5% level of probability.

## Results

The distribution of different combination of repeats among Gaddis showed that 4R/4R is in highest frequency (67.76%), followed by 4R/2R (20.39%), 4R/5R (7.89%), 4R/7R (1.31%), 2R/2R (1.31%) (table 1). From frequency distribution calculations, it was found that Gaddi population has only five repeat alleles out of all 10 repeats reported in *DRD4* gene worldwide and out of six repeats reported in Indian populations. Allele frequencies of 4R, 2R, 5R, 7R and 3R were 0.83, 0.11, 0.04, 0.01 and 0.01, respectively (table 1).

## Discussion

Only 4R and 2R are found in homozygous condition in the present population. 4R is found in heterozygous condition with all the other repeats (2R, 3R, 5R and 7R), whereas 2R is found only with 4R. However 4R and 2R alleles are the most frequent, 7R allele which is absent in Indian tribal populations is found in a low frequency among the Gaddi

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**Table 1.** Distribution of 48 bp variable number tandem repeats polymorphic variants of *DRD4* gene among Gaddi tribe of Himachal Pradesh, north India.

| | Genotype | Number | Percentage | Allele | Allele frequency |
|---|---|---|---|---|---|
| 1 | 2R/2R | 2 | 1.31 | 2R | 0.11 |
| 2 | 4R/2R | 31 | 20.39 | 3R | 0.01 |
| 3 | 4R/3R | 2 | 1.31 | 4R | 0.83 |
| 4 | 4R/4R | 103 | 67.76 | 5R | 0.04 |
| 5 | 4R/5R | 12 | 7.89 | 7R | 0.01 |
| 6 | 4R/7R | 2 | 1.31 | | 1.00 |
| Total | | 152 | 100 | | |

$\chi^2 = 2.94$; $P = 0.98$; df = 10.

population. 7R in heterozygosity with 4R is present in 1.31% of individuals. Such presence of 7R among Gaddi population could either be attributed to gene flow from Eurasia, where 7R is frequent or to the selection conducted on it due to the transhumant nature of Gaddis. Absence of 7R allele among the tribal population of India could possibly attribute to a settled nature and hence replaced by its functional derivative, 2R (Chen *et al.* 1999; Ding *et al.* 2002, Wang *et al.* 2004). However, among the Gaddi tribe, the mere presence of 7R, though in very low frequency could be due to their transhumant nature which is consistent with the studies that migratory populations have a higher proportion of long alleles (Chen *et al.* 1999). But in recent years, Gaddis opted for settled lifestyle (agriculture, jobs etc.) which could be attributed to low frequency of 7R. This suggest that transhumance of Gaddis affect the selection of 7R repeat of *DRD4*, as migration (macro or micro) may affect selection of this repeat.

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