



Role of HLA-A in Handedness

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Abstract

A relationship exists between cerebral dominance and right or left handedness. Left-hemisphere dominance occurs in 97% of right-handed people and in 70% of left-handed people. The other 30% of left-handed individuals have anomalous or right-hemisphere dominance. Both environmental and genetic factors have been proposed to explain the human handedness. Aim of this study was to determine the effect of genetic factor of human leukocytes antigens (HLA-A) on development of left handedness. A cross-sectional case control comparative study included thirty Iraqi Arab Muslims individuals with left handedness between September -2013 to June -2014. The second control group consisted from thirty individuals with right handedness. HLA-A typing was done to both groups using SSOP method. There was no significant difference between different alleles regarding HLA-A left handed compared with the control group. Genetic factor regarding HLA-A typing had no role in development left handedness.

Key Words: HLA, handedness, genetic

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Introduction

Left handed individuals are those persons who used their hand for writing and working comfortable. It had been found that handedness affect the behavior of the individual [1] and right handed are more skillful than left handed when performing tasks [2]. In addition to that Geschwind and Galaburda [3-5] suggested an association between brain laterality and immune disorders. Left handed had a specific immunologic parameters that effect both cellular and humoral immune system, the left-handed group demonstrated a significant decrease in the inflammatory cell types T cellCD3+, T helper CD4+and MHC class II- HLA-DR, CD19+ B-cells and CD16/CD57+ cells NK cells suggesting an association between cerebral hemispheric specialization and the immune system [6]. Other found that high level of testosterone is supportive of general immunity and leads to greater incidence of left handed and deviation from normal cerebral function (anomalous dominance) and increased incidence in autoimmune diseases than right handed [7].

The left handedness occurs in about 8% of the individuals reasons why some people are left-handed and other are right handed are not clear, but they seem to depend on a mixture of genetic, and environmental factors. Left-handedness does seem to run in families and genetic rather than environmental is the causative agent, the gene for handedness are the pseudoautosomal region of the X chromosome [8]. Other environmental reasons for left-handedness are birth trauma, exposure to high levels of testosterone in the uterus and maternal smoking during pregnancy and low Apgar score between 2-6 can significantly increase risk for left-handedness population [9]. There is a strong association of left handedness with various neurodevelopment conditions like schizophrenia, autism, Rett syndrome [10, 11]. Regarding the genetic factor, the human leukocyte antigen (HLA) is one of genetic factor that may be responsible for the development of left handedness. HLA region is located on chromosome 6p21.3 and encodes genes for the major histocompatibility complex (MHC). It contains hundreds of genes that encode proteins with important role in immunity, including antigen processing and presentation, and self-recognition by immune cells. The MHC complex is divided into three subgroups (classes I, II, and III). The class I region is located at the telomeric end of the MHC and is divided into classical (HLA-A, -B, -C) and non-classical (HLA-E, -F and -G) genes. HLA-A genes are highly polymorphic and constitutively expressed by most somatic cells and are co-dominantly expressed on the cell surface and responsible for presenting endogenous antigens to CD8+ cytotoxic cells [12].

In this study we aimed to analyze the association between the genetic factor (Human Leukocyte antigens –class I- HLA-A) typing and left handedness individuals in sample of Iraqi Arab Muslims population.

Patients and Methods

A cross-sectional case control comparative study included thirty Iraqi Arab Muslims individuals with left handedness between September -2013 to June -2014. Age of study group was ranged from 17-25 years and Male to female ratio was 2:1 in the study group. The second control group consisted from thirty individuals with right handedness. Both of them were from students of Al-Kindi college of Medicine. The control group was ethnically similar to study group, their ages were ranged from 17-24 years. Male to female ratio in the control group was 2:1.

The Scientific and Ethical Committee of Al-kindy medical college had approved the study. Informed consent was obtained from both groups.

HLA genotyping: Peripheral venous blood samples from study and control groups were collected in ethylenediaminetetraacetic acid-containing tubes and then stored at -20°C until testing for class II- HLA-A. Genomic DNA was extracted using Qiagen DNA extraction Kit-Germany. DNA product was verified by electrophoresis in a 2% agarose gel containing ethidium bromide and was visualized under UV light. Locus- and allele-specific amplification of genomic DNA were performed for HLA-A. Amplification and Hybridization was performed using a panel of sequence-specific oligonucleotide probes (SSOP) using HLA-A amplification and hybridization kits (SSO HLA type A plus and Mastermix for HLA type A Amp plus kits -Innogenetics-Belgium) using automated method by AutoLipa-48 Innogenetics-Belgium. The results were interpreted using LiRas version-5.0 software-Innogenetics-Belgium.

Statistical analysis was done using MiniTab version 3.0 software. The distribution of HLA alleles in study and control groups were compared using chi-square for continuous variable. Fisher's exact test was used when necessary. In each comparison, the odds ratio (OR) along with the 95% confidence interval (95% CI) was used. P-value less than 0.05 was considered statistically significant.

Results

Control and study groups were typed for identifying the HLA-A alleles using DNA-based methodology (PCR-SSOP). Allele's frequencies of HLA-A for left handed and control group (right handed) is shown in table-1-. There was no significant difference between different alleles regarding HLA-A left handed compared with the control group.

Discussion

Handedness runs in families and there is increase chance of the child to being left handed when both his parents were left handed [13]. Thus, genetic factor plays an important role in etiology of handedness. HLA typing is one of genetic factor that may play an important role in causation left handed individuals. In our study, we did not found a significant association between HLA-A typing and handedness. A mutation can lead to dextral allele that biasing to right handed and control of speech toward the left cerebral hemisphere. Other study found deviation from right handed due to developmental instability due to polygenic homozygosity and particular HLA alleles could be an important factor [14]. There is an association between left handed and immune disorders like autoimmune disease, celiac disease and allergy [15]. Other authors found an association between left handed and multiple sclerosis [16] due to exposure to sex hormones in utero [17]. Left handed is associated with increased risk of breast cancer [18], colorectal cancer [19] and inflammatory bowel disease [20]. Other study showed that HLA alleles are associated with an increased risk of diseases among left-handed individuals due to elevated levels of circulating autoantibodies, total T-cells, and T-helper cells in left-handed as compared to right-handed individuals[21].

Annett 1981 [22] demonstrated the genetic basis of handedness. Single gene theories indicate the prevalence of handedness while linkage studies have failed to identify a single locus responsible about handedness and there were different regions of the genome, including 2p12-q11, 10q26, 12q21-23 and Xq21 [23-26].

Therefore, further examination of HLA alleles class I and class II to assess the relationship between HLA and left handedness with larger group study.

Table 1. Human leukocytes antigens (HLA-A) alleles frequencies in left handed individuals and right handedness control group.

HLA-A* alleles	Left handed group n=30		Right handed control group n=30		Odd ratio (95% confidence interval)	P- value
	No.	%	No.	%		
0101	6	20	10	33.33	0.5 (0.1547 to 1.6163)	0.5
02	6	20	6	20	1.0 (0.2822 to 3.5437)	1
0201	0	0	2	33.3	na	na
0204	0	0	4	66.6	na	na
0219	2	33.3	0	0	na	na
0256	4	66.6	0	0		
03	0	0	10	33.33	na	na
0301	0	0	6	60	na	na
0302	0	0	4	40	na	na
1101	6	20	2	6.6	3.5 (0.6454 to 18.9807)	3.5
23	4	13.33	2	6.6	2.15	2.15
					0.3634 to 12.7639	na
2304	2	50	0	0	na	na
2308	0	0	2	100	na	na
2310	2	50	0	0	na	
24	16	53.33	12	40	1.71 (0.6159 to 4.7719)	1.71
2002	0	0	10	83.3	na	na
2404	2	12.5	0	0	na	na
2409	2	12.5	0	0	na	na
2410	4	25	0	0	na	na
2417	2	12.5	0	0	na	na
2418	4	25	0	0	na	na
2423	0	0	2	16.6	na	na
2428	2	12.5	0	0		na
2501	4	13.33	0	0	na	na
26	4	13.33	0	0	na	na
2601	2	50	0	0	na	na
2612	2	50	0	0	na	na
2907	2	6.66	0	0	na	na
30	4	13.33	2	6.6	2.15 (0.3634 to 12.7639)	2.15
3001	0	0	2	100	na	na
3011	4	100	0	0		
3101	0	0	2	6.6	na	na
3201	0	0	2	6.6	na	na
3301	0	0	4	13.3	na	na
3604	4	13.3	0	0	na	na
68	2	6.66	8	26.66	0.19 (0.0378 to 1.0198)	0.19
6801	0	0	2	25	na	na
6802	0	0	4	50	na	na
6805	2	100	0	0	na	na
6806	0	0	2	25		
7403	2	6.66	0	0	na	na

na=not applicable

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Conflict of interests

The authors have no conflicts of interest.

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