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The Relationship between Intelligence and Mitochondrial DNA Polymorphism at Site of 15925 Base Pairs

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

Intelligence has a huge influences and is very closely related with human's life. Because intelligence is indefinable, scholars have specified it through testing tools and named it intelligence quotient (IQ). In measuring IQ, researchers have found that IQ has a wide distribution and tried to find out the reasons by assessing the brain's functional level and environmental and genetic factors. One study reported an association between IQ and mitochondrial DNA (mtDNA) sequence 15,925, and this study investigated the association in Koreans. The number of participants was 57 in the mental retardation group without chromosomal abnormalities and 148 in the normal group, respectively. PCR technique and direct sequencing analysis were used to know participant's mtDNA sequences. At 15,925 base, all participants had only wild type C and no variant type of m.15,925 C > T. We further studied variants in mtDNA sequences 15,926-15,927. At 15,926 base, the variant type of 15,926 C < T was found in only one case (0.7%) in the control group. At the 15,927 base, variant type of 15,927 G < A was found in 9 cases (6.1%) in the control group and 1 case (1.8%) in the retardation group, respectively. As a result, the polymorphisms of mtDNA sequences at bases 15,925-15,927 had no statistical significance in the Korean control and mental retardation group.

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Keywords: Intelligence; mitochondrial DNA; polymorphism; variation.

ABBREVIATION

IQ and mtDNA 15925 SNP.

1. INTRODUCTION

Intelligence is the ability to apply knowledge to manipulate the environment or to think abstractly based on objective criteria. However, the practical meaning of intelligence has always been controversial. There have been attempts to define intelligence in a variety of ways, including logic, understanding, self-awareness, learning, emotions, reasoning, planning, creativity, and problem solving. However, there are some common features of definitions of intelligence: Intelligence is a property that individual agents have as they interact with their environment, adapt to different goals, achieve goals, and solve problems they face [1].

Intellectual disability, also known as general learning disability or mental retardation, means IQ score below 70. Mentally retarded children reach developmental milestones such as walking and talking much later than the general population. These children typically have difficulties with communication, forming social relationships, learning academic skills. These children have particular difficulties with communicating, forming social relationships, and learning academic skills. To evaluate the genetic influence of mental retardation, gene studies have been performed [2]. Loss-of-function variations in DPP6 which is associated with autosomal dominant mental retardation [3]. Many autosomal or X-linked mental retardation genes have been identified, with FMR1 being one of the most common inherited monogenic causes of intellectual disability. To date, a few genes (PRSS12, CRBN, CC2D1A, GRIK2, TUSC3, TRAPPC9, TECR, ST3GAL3, MED23, MAN1B1, NSUN1) for autosomal-recessive forms of non-syndromic mental retardation have been identified and established in various families with intellectual disability [4, 5].

Mitochondrial DNA (mtDNA) variations have impact on occurrence of diseases. In the past decades, several types of somatic mtDNA variations have been identified in cancer. One of the cancer hallmarks is energy metabolism reprogramming. Underlying mechanism of energy metabolism reprogramming is mitochondrial dysfunction [6]. Mitochondrial reactive oxygen species (ROS) amplify the tumorigenic phenotype and generate additional variations that lead to metastatic behavior [7]. As many genetic researches are being boosted, mitochondrial DNA (mtDNA) have been considered as one of the important materials to solve the secret of human intelligence. A study raised a theory that the polymorphism in mitochondrial DNA can be associated with IQ [8]. The SNP which they thought as a key DNA was an Msp1 restriction site (CCGG) at 15,925 base pairs of the complete mitochondrial genome in a gene that codes for the transfer RNA for threonine. They noticed a bizarre finding emerged for the expressed sequence tag(EST) 00083 restriction fragment length polymorphism: Not a single heterozygote genotype was detected, unlike any of the other DNA markers that they had studied. Therefore, this study was conducted to determine whether this mtDNA variation is related to mental retardation in Koreans.

2. MATERIALS AND METHODS

Peripheral blood DNA samples were obtained from 57 mental retardations without chromosome anomaly and 148 healthy controls. Mental retardation samples without chromosomal abnormalities were previously used for APOE allele analysis [9]. PCR and sequencing analysis were used to identify sequence changes at the subject's mtDNA sequence 15,925. Primers for amplification were designed using Primer3Plus. Materials for PCR including buffer, blend Taq, dNTP were products from TOYOBO Blend Taq Plus. The forward primer’s sequence for PCR was 5’ –AGG ACA ACC AGT AAG CTA CC – 3’ (20mer) and reverse primer’s sequence was 5’ – AGC TTT GGG TGC TAA TGG TG – 3’(20mer). PCR was performed by using a thermal cycler(Applied Biosystems, USA) in the order as follow: 1 cycle of 2 minutes at 94°C for predenaturation, 40 cycles of 30 seconds at 94°C for denaturation, 40 cycles of 30 seconds at 55°C for annealing, and 40 cycles of 1 minute at 72°C for extension. Final extension was performed at 72°C for 10 minutes. PCR was performed by thermal cycler (T100TM thermal cycler, Bio-Rad Inc, Singapore). The electrophoresis was performed on agarose gel to detect PCR product. To determine the sequences of the DNA samples, direct sequencing was performed on the ABI Prism 3100 Genetic Analyser (Applied Biosystems, USA). The data were analyzed using SPSS(ver. 24.0. IBM, USA). A chi-square test was performed to see how variations in nucleotide sequence differ between normal and intellectual disabilities.

Table 1. Frequency of each identified nucleotide polymorphism in normal and intellectual disability groups

location	Base change		Normal	Intellectual Disability	P value
15,925	C → T	**C**	148(100.0)	57(100.0)	invaluable
		T	0(0.0)	0(0.0)	
15,926	C → T	**C**	147(99.3)	57(100.0)	0.534
		T	1(0.7)	0(0.0)	
15,927	G → A	**G**	139(93.9)	56(98.2)	0.198
		A	9(6.1)	1(1.8)	

3. RESULTS

At 15,925 nucleotide, only the major allele C appeared in both the normal group and the intellectual disability group, there was no value of analyzing the relationship between intelligence and 15,925 mtDNA sequence (Table 1). At 15,926 nucleotide, minor allele T was found in only one case (0.7%) in the normal group, but it was not significant in the two groups. At 15,927 nucleotide, minor allele A was found in 9 cases (6.1%) in the normal group and in 1 case (1.8%) in the intellectual disability group, but there was no significant difference at 15,927 nucleotide.

4. DISCUSSION

Intelligence is a big part of human life. People with intellectual disabilities have difficulty performing basic functions such as cognition, learning, communication, and self-care skills. They are more likely to be isolated from society. As the aging society progresses along with the low birth rate, it is important to secure a productive population. If the secret of intelligence could be revealed, intellectual disabilities could be reduced or treated. In this context, anthropologists and geneticists have been conducting experiments related to intelligence.

Many trials and documents about new genetic and functional links to intelligence have been published to identify the origin of intelligence. Researchers have attempted to confirm genetic correlations in intellectual differences and health related outcomes including Alzheimer's disease, ADHD and other psychiatric disorders [10]. MspI recognizes the four nucleotide base sequence: CCGG. EST00083 (GenBank M62027) was shown to be a mitochondrial polymorphism by MspI at the 15,925 base pair of the mitochondrial genome. A loss of an MspI cut site at 15925 bp would result in a new allele 2. This polymorphism yielded a significant frequency difference between low and high IQ groups, so the polymorphism at position 15,925 was proposed as a candidate marker for IQ [8].

The frequencies of the two alleles (called A1: MspI-cleavage 1 and A2: MspI-non-cleavage 2) are expected to vary depending on race. The frequencies of A1 and A2 were similar to the frequencies of 85% and 14% in Caucasians, respectively [8, 11-13]. Meanwhile, in a Japanese study, the A2 allele was found in 3 out of 116 individuals (2.6%) [14]. Although the A2 allele was not found in our study, it may appear at similar frequencies in Japanese and Koreans.

This study showed that only C nucleotide instead of T appeared at mtDNA sequence 15,925 in normal and intellectually disabled groups of Koreans. The P values comparing variants in the 15,926 and 15,927 mtDNA sequences with intelligence were 0.534 and 0.198, respectively, indicating no significant association between these two variants and IQ. Therefore, this study suggests that the mtDNA polymorphism at position 15,925 does not exist in Koreans and is not associated with IQ.

This study has a limitation. The number of participants in this study was not large enough to compare mtDNA differences between the intellectual disability and normal groups. Although a single allele was present at mtDNA 15,925 in the participants of this study, a large-scale investigation of in-depth genetic background must be performed before mtDNA variants in Koreans can be used in experiments and medicine.

5. CONCLUSIONS

In this study, we investigated a polymorphism at mitochondrial nucleotide 15,925, which is thought to be associated with IQ. This study suggests that mtDNA polymorphism at 15,925 is not associated with IQ in Koreans.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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