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ASSOCIATION BETWEEN MONOAMINE OXIDASE A *(MAOA) GENE POLYMORPHISM AND VIOLENT BEHAVIOR*

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ABSTRACT

Practical portrayal thinks about uncovered that transcriptional action of the human monoamine oxidase A (MAOA) quality is balanced by a polymorphic redundant arrangement situated in 1.2 kb upstream of the ATG codon. To research the conceivable impact of the allelic variations of the MAOA quality in the hereditary inclination to forceful conduct, a case-control affiliation investigation of 31 mental patients and 26 solid controls was directed. Factual examination demonstrated no noteworthy contrasts in allele or genotype frequencies amongst control and patient gatherings. These discoveries recommend that either high or low action alleles of the MAOA-uVNTR 30-bp polymorphism are not related with standoffish conduct in mental patients.

Keywords: monoamine oxidase A, promoter polymorphism, antisocial behavior, psychiatric

INTRODUCTION

Hostility is the conveyance of an aversive boost starting with one individual then onto the next, with aim to hurt and with a desire of causing such damage, when the other individual is inspired to escape or maintain a strategic distance from the jolt (Geen.2011).

Animosity is considered as a positive side effect in numerous neuropsychiatric issue. Hereditary inclinations to viciousness, liquor abuse, introverted identity issue, and other related characteristics in criminal trials has been ascribed to a hereditary premise however particular genotyping proof has been presented on a to a great degree constrained premise the qualities and condition both impact forceful conduct and there is confirm that unpleasant life occasions can cooperate with particular hereditary variations (Craig and Halton, 2010, Al-Tayie*et al.2016).*

The Research in behavioral hereditary qualities gave solid proof that hereditary polymorphisms are hazard factors for the improvement of viciousness and mental issue (Baker *et al*, 2008).

Biology's role in behavior is obvious because all conduct is controlled by the cerebrum and the nervous system. qualities arrange the improvement of the mind through interpretation and interpretation of DNA into proteins (Bloom *et al*., 2000). Neurotransmitters, known as chemical transporters are having aninternal cause or origin chemicals that enable neurotransmission (Lodish *et al*., 2017)

The right working of the mind requires amounts of chemical messengers or neurotransmitters, change in the vital extents or even a little sore in delicate zones can affect the mindset, acting, responding, and feeling. At the point when the generation of neurotransmitters is unnecessary, inadequate or non-existent certain ailments that fundamentally influence the adjust of the living being can cause mental issues (Narvaes, 2014).

The dopaminergic system is associated with behavioral initiation, inspired conduct and reward handling. It likewise assumes a dynamic part in the regulation of forceful practices (Dongju *et al*., 2008).

The Serotonergic Pathway The neurotransmitter serotoninhave main function and an important role in a multitude of biological functions and has been involved in more behavioral, physiological and pathological mechanisms (Stolerman, 2010).

The political, social, or economic causes of violence are very much contemplated, yet more as of late the mindfulness has developed that organic causes, which may clarify singular contrasts in inclination to viciousness, additionally should be examined. Conduct hereditary research offers researchers an approach to investigate both hereditary and Environmental impacts on human practices and identity attributes (Bloom, 2006).

Which Several investigations in people and creatures have related monoamine oxidase (MAOA) with animosity. MAOA is known as mitochondrial protein that catalyzes the oxidative deamination of neurotransmitters serotonin, dopamine, which are associated with the control of forceful conduct. The quality encoding MAOA is situated on the Xp11.23-p11.4 chromosome containing a polymorphism (MAOA-uVNTR) found 1.2 kb upstream of the MAOA coding successions. MAOA -uVNTR polymorphism comprising of a 30-base match rehashed arrangement. Six allele variations containing 2, 3, 3.5, 4, 5, or 6 rehashes duplicates have been distinguished. These diverse uVNTR variations are related with various transcriptional exercises of the MAOA promoter, which thus result in various articulation levels of the MAOA

quality. As far as articulation, the MAOA quality was separated into two gatherings: a low MAOA action gathering and a high MAOA action gathering. The low MAOA movement bunch comprised of the 2, 3, and 5 rehashes alleles, while the high MAOA action gather comprised of the 3.5-rehash allele and the 4-rehash allele. The low action alleles were observed to be related with animosity and impulsivity (Galal El-Din *et al*., 2014)

Materials and Methods

Subjects: The number of samples collected was 57 samples, 26 healthy and 31 samples Collected from the specialized psychological center in Al-Zahra Hospital in Wasit Governorate, from people with mental illness and a criminal case under the supervision of a specialist doctor. DNA was extracted then the polymorphisms analysis achieved by Polymerase Chain Reaction (PCR) in the laboratories of the Faculty of Science, Wassit University. Then Determined the size of *MAOA* VNTR polymerphism by gel electrophoresis

Blood Samples: Blood samples 3 to 5ml were collected in EDTA tubes from each subject in the study and stored frozen at -20°C until analysis.

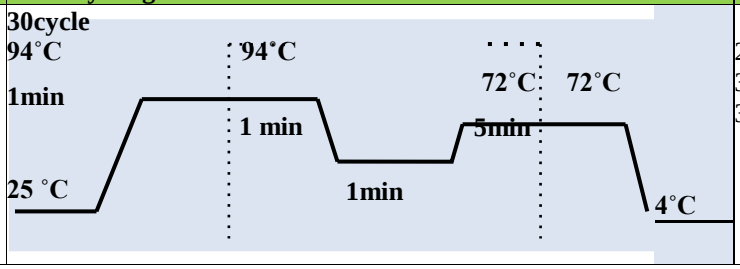
Genotyping

DNA Extraction: Each frozen blood specimen was thawed; genomic DNA was then extracted direct by use FAVORGEN genomic DNA extraction kit (Taiwan). DNA purity and concentration were determined by a spectrophotometer (Nanodrop).

PCR Amplification Primers:

Target	Primer Sequence (5´-3´)		Origin	Reference
MAOA	**F:5'ACAGCCTGACCGTGGAGAAG-3'**	°	Bioneer (Korea)	Butovskaya et al.,2013(B)
	R:5'-GAACGTGACGCTCCATTCGGA-3'	**Mean of two tm pleas**		

Table 3.1: The PCR amplification conditions for MAOA gene

Gene	PCR Cycling Profiles	Product Size bp	Reference
MAOA		291,321, 336,351, 381	Butovskaya *et al*., 2013

Intensified items were examined by electrophoresis in 2.5 % agarose gel recolor with ethidium bromide, at 5-7 V/cm for 2 hours, then envisioned under UV light utilizing bright Gel documenttation. DNA stepping stool (100bpPromega) was utilized as a relative (Table 1).

Statistical analysis: Differences between genotype frequencies were tested using the 2χ test. Analyses were calculated by comparing allele frequencies in control group versus Patients groups.

RESULTS AND DISCUSSION

distribution of sample: In this study 57 sample divided to 31 Sample from male have history in aggressive and drugs trading whilst 26 sample from healthy males (Control), to analyze the association MAOA VNTR polymorphisms with behavior in male human.

Age Distribution: The over mean ages of control groups were 32.58 ± 12.20 and case group 26.48 ±7.64 years old. Age is confounding in regard to changing response and actual levels of hormones in this study, the maximum age was 63 years within age group >50 as listed in table 2, the maximum number of the case was found within age group 20-29 years (70.96%).

Table 3.2: Age disterbution of studied individual **P value ≤ 0.05*

	control No = 26		patients No = 31	
	N	%	N	%
<20	0	0%	3	9.67%
20-29	15	57.69%	22	70.96%
30-39	4	15.38%	4	12.90%
40-49	3	11.53%	2	6.45%
>50	4	15.38%	0	0%
total	26	100%	31	
X^2	68.33			
Sig.	0.009*			

3.3 Concentration and Purity of DNA: Geno-mic DNA was successfully axtacted from all blood samples. The concentration and purity of DNA rang from 30 to 180µg/ml and 1.6 to 2 respectivly mentioned in Figure 1.

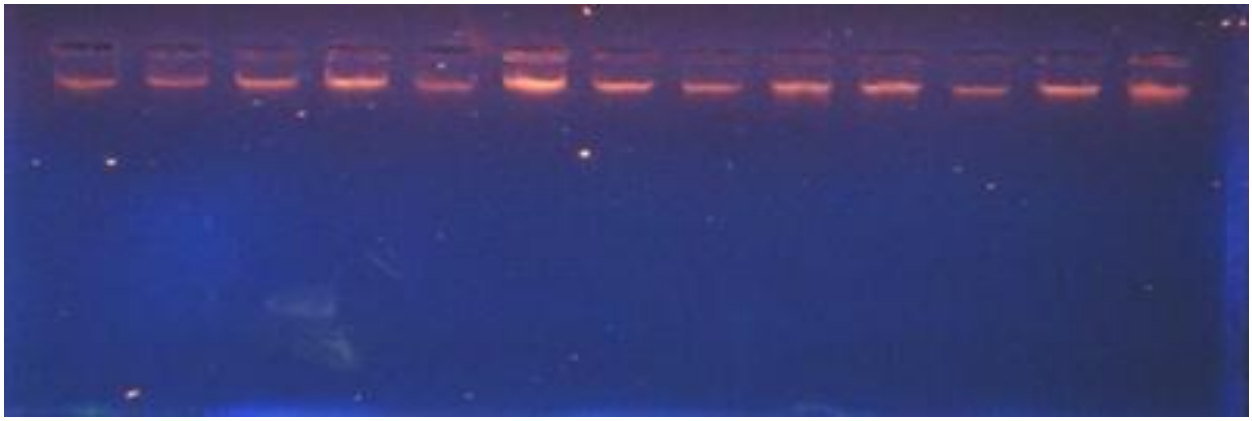


Figure 1: Gel electrophoresis of DNA extracted from blood samples, 1% agarose gel, 5volt for1 hour.

Analysis of MAOA VNTR polymorphism: The MAOA gene contains 30bp VNTR polymorphism in the promoter region this polymorphism varies from 2 to 5 copies the PCR product included 321bp (3 repeat allele), 351bp (4-Repeat allele), 381bp (5– Repeat) the different fragment size was determining by comparison to molecular length standard and confirmed by software analysis (gel analyzer 2010) (figure 2)

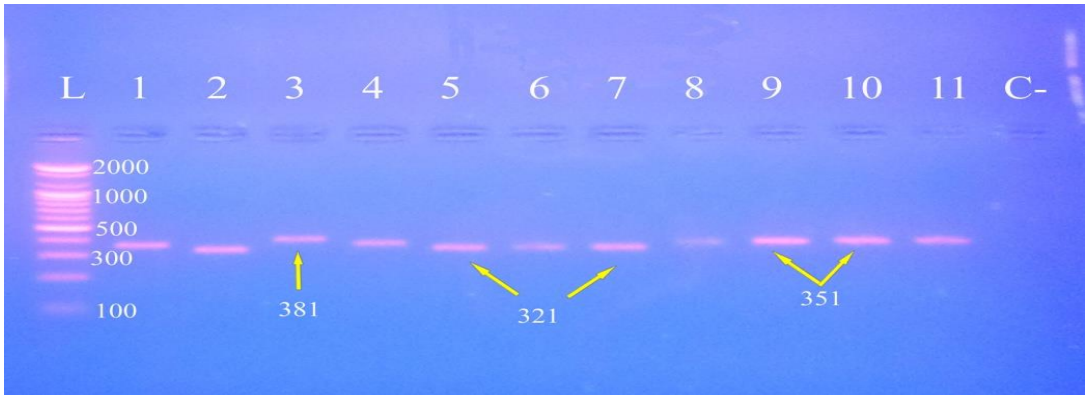


Figure 3.3: Electrophoresis pattern of PCR product for MAOAgene products were representing the VNTR polymorphism for gene in 2.5% agarose ,50 V, for 2h (15 µl of PCR product loaded in each well). lanes 1-8 were case and lanes 9-11 were control

- *Lane L: DNA ladder (100bp); Lane 2,5,6,7: band 321 bp, represent the homozygote genotype 3/3 repeat*
- *Lane 1, 4,8,9,10,11: Band 351 bp, represent the homozygotes genotype 4/4 repeat.*
- *Lane 3: Band 381 bp, represent the homozygotes genotype 5/5 repeat.*
- *Lane C-: The negative control.*

The*MAOA* VNTR serves as a requirement in re gulation of gene expression at Transcriptional level, alleles with 3.5 or 4 repeats identified as the optimal length for regulatory region should be the wild the type among a variety of common among apopultions (Pai *et al.*,2007)

The genotypes distribution of MAOA VNTR Polymorphism with allele frequency in control and case gropes: The distribution of the observed MAOA VNTR genotype and allele frequencies in the control and case gro-ups shown in table 3.

The highest genotype in patient 4/4R (51.61 %) followed 3/3R (29.03%) then 5/5R (19.35 %) in control the highest genotyping 4/4R (73.07%) followed 3/3R (19.23%) then 5/5R (7.69 %). Two common allele 4R and 3R and less allele 5R were observed in ours sample the result pointed out that there was no differ-rence ($p>0.05$) among all genotypes between control and case group.

Table 3.3: Genotypes distributions of MAOA VNTR polymorphism and association in control and case groups.

Genotype	Control		Patients		X^2	Sig.	OR	C.I.
	N	%	N	%				
5R	2	7.69%	6	19.35%	2.00	0.16	Reference	
3R	5	19.23%	9	29.03%	1.31	0.25	0.67	3.89-0.18
4R	19	73.07%	16	51.61%	0.81	0.36	3.56	5.23-1.98
Total	26	100%	31	100%				

Sig*: Statistical significance*; X2: *Chi-squared*; OR: *Odds ratio*; CI: *Confidence level.*
NS: *Not significant*.

This result was consistent with the other studies which suggested not difference between the healthy and psychiatric patient group (Frazzetto*, et al.,* 2007*)* and the other two meta analysis studies which suggested that the maoa VNTR does not play any major role in the manifestation of violent in Schizophernia patient (Norton et al., 2002, Li and He , 2008).

The relationship between the MAOA uVNTR polymorphism and antisocial behavior is still controversial. The localization of MAOA on chromosome X might in part explain this observed homozygote male, because have single X chromosome in women can be heterozygous or homozygous for MAOA (Samochowiec, *et al*., 2015).

These distinctive uVNTR variations are related with various transcriptional exercises of the MAOA promoter, which thus result in various articulation levels of the MAOA quality. As far as articulation, the MAOA quality was isolated into two gatherings: a low MAOA action gathering and a high MAOA action gathering. The high articulation allele (H-allele) incorporate 3.5 and4 rehashes and the low articulation alleles (L-allele) incorporate 2,3,5, repeats (Salem *et al*., 2013). The distribution of the observe red MAOA geno-type and allele frequencies in the control and case group are shown in table 4.

In control the highest expression the 4R (H allele) 73.07% and low expression the 3R,5R (L allele) 26.92% In case group H allele (51.61%) and L allele (48.38%) The results is no signification between case and control for all allele frequency ($p>0.05$). This text need more regulation pleas.

Table 4: Genotypes distributions of MAOA VNTR polymorphism with high and low allele frequency in control and case groups

Genotype	Control		Patients		^2X	Sig.	OR	C.I.
	N	%	N	%				
L- allele	7	26.92%	15	38.35%	2.91	0.08	Reference	
h-allele	19	73.07%	16	51.61%	0.89	0.36	0.56	1.71-0.12
Total	26	100%	31	100%				

This result was in agreement with they revealed that no significant difference in the MAOA-L activity either in offenders or psychiatric patients compared to control P= 0.11 and 0.22, respectively. Moreover, no significant difference was observed in either offenders or psychiatric patients with MAOA-H activity compared to control P= 0.35 and 0.23, respectively (Galal El-Din *et al.,* 2014). And the same result was found by Huang *et al.,* (2004) and De Luca et al., (2006).

Conclusion

All available data refer to a convoluted factors and structure for the most part imprudent animosity, with the MAOA u-VNTR share in just a little measure of change in hazard. Along these lines, despite the fact that MAOA isn't a (violence gene) such capacity alleles may incline to advancement toward animosity. which, in mix with different components, show to the advancement of withdrawn conduct. Thought about autonomously from these components, legacy of the MAOA allele is totally good with mental wellbeing. The primary utility of the right now perceptible qualities approach is along these lines less in the claim to have isolated hereditary hazard factor that without anyone else deterministically foresee psychopathology, than in utilizing such variations as devices to find neural frameworks connected to rash savagery at last. The relationship between the nearness of low action alleles and incautious and aggressive conduct came about because of most reduced level of promoter movement.

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