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Clinical Evaluation of Latrophilin 3 (LPHN3) Gene in Children with Attention Deficit Hyperactivity Disorder (ADHD)

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Abstract

This Disorder (attention deficit hyperactivity disorder) is a neurodevelopmental disorder defined by impairing levels of inattention, disorganization, and/or hyperactivity impulsivity. Inattention and disorganization entail inability to stay on task, seeming not to listen, and losing materials, at levels that are inconsistent with age or developmental level. Hyperactivity-impulsivity entails overactivity, fidgeting, inability to stay seated, intruding into other people's activities, and inability to wait symptoms that are excessive for age or developmental level.Attention-Deficit Hyperactivity Disorder is the most commonly diagnosed psychiatric disorder, occurring in 5-7% of children world wide.This study aimed to evaluate the association between LPHN3 gene and attention deficit hyperactivity disorder . Methods: The subjects were 2 groups*;* Group (I): included 30 patients with attention deficit hyperactivity disorder . And Group (II): included 30 apparently healthy individuals as a control group. The polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP) method was used to determine the genetic association of attention deficit hyperactivity disorder with the LPHN3 gene polymorphis (rs2349039). Results: The attention deficit hyperactivity disorder group included 20 male (66.7%) and 10 females (33.3%), the mean age was 9.8±1.8 years. there was a statistically significant difference in the distribution of genotypes of the LPHN3 rs2349039 polymorphism in the attention deficit hyperactivity disorder and control groups, (p=0.01). In attention deficit hyperactivity disorder group; individuals with CG genotype were 5.8 folds to have attention deficit hyperactivity disorder than CC individuals. Also, those with GG genotype were about Six times more likely to have attention deficit hyperactivity disorder than CC ones.

Keywords: Gene (RS2349039), hyperactivity.

1. Introduction

This disorder is a social disorder. The worldwide-pooled prevalence of attention deficit hyperactivity disorder was estimated to be 5.29% in 2007 [1].

However, the prevalence estimates exhibit rising trends in the recent years to about 11% highlighting the increasing burden of Attention Deficit Hyperactivity DISORDER on health care systems [2].

This Disorder has been found to be associated with significant morbidity, surpassing diabetes mellitus and Intellectual Disability in terms of years lived with disability in males aged 10–14 years [3].

Nosological redefining of Attention Deficit Hyperactivity Disorder as a neurodevelopmental disorder emphasizes the importance of gaining insights into the etiological mechanisms. Despite almost two centuries of research, the exact etiopathogenesis of this disorder is still an unanswered question. Accumulating global research focuses on various arenas like epidemiology, etiological aspects as genetics, neurobiology, biomarkers for attention deficit hyperactivity disorder − hormonal, nutritional, neurochemical and electrophysiological parameters, medical and psychiatric comorbidity associated with attention deficit hyperactivity disorder and diverse pharmacological and non-pharmacological interventions [3].

This Disorder is a behavioural description based on criteria that are sensitive to subjectivity and cognitive biases [4].

Unfortunately, confusing naming and explaining is a common error with regard to behavioural problems. Seeing Attention Deficit Hyperactivity Disorder as a brain defect causing problematic behaviour may be tempting: one cause, one solution [5].

Although there is no single medical, physical, or genetic test for Attention Deficit Hyperactivity Disorder , a diagnostic evaluation can be provided by a qualified mental health care professional or physician who gathers information from multiple sources [6].

These sources include attention deficit hyperactivity disorder symptom checklists, standardized behavior rating scales, a detailed history of past and current functioning, and information obtained from family members or significant others who know the person well. Some practitioners will also conduct tests of cognitive ability and academic achievement in order to rule out a possible learning disability [6].

This disorder cannot be diagnosed accurately just from brief office observations or simply by talking to the person. The person may not always exhibit the symptoms of attention deficit hyperactivity disorder during the office visit, and the diagnostician needs to take a thorough history of the individual's life. A diagnosis of attention deficit hyperactivity disorder must include consideration of the possible presence of co-occurring conditions [7].

Clinical guidelines for a diagnosis of the disorder are provided by the American Psychiatric Association in the diagnostic manual Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-4). These

established guidelines are widely used in research and clinical practice. During an evaluation, the clinician will try to determine the extent to which these symptoms currently apply to the adult and if they have been present in childhood. In making the diagnosis, adults should have at least five of the symptoms present. These symptoms can change over time, so adults may fit different presentations from when they were children [8].

This study aimed to evaluate the association between LPHN3 gene and attention deficit hyperactivity disorder

2. Patients and methods

This study was done to assess the link between attention deficit hyperactivity disorder

and LPHN3 gene.

The participating children were divided into Group one: included 25 patients who will be diagnosed by corners assessment as attention deficit hyperactivity disorder . Group two : included 25 apparently healthy individuals age and sex matched as a control group.

2.1 Inclusion criteria

Age:- 6-10 years

2.2 Exclusion criteria

Patients significant medical disease or other psychological disorder

2.3 Ethical considerations

All subhect undergo history clinical assessment and PCR for detect gene

Statistical analysis

The mean pain score recorded at 24 hours for group A and group B was the same, no statistical significant difference between the two groups. Similarly at 1 month, no difference had been found in pain score in both groups of ICBN. However there is significant decrease of pain, numbness and paraesthesia in group A as compared with group B at 3 month (P<0.001). This shows that over a period time (3 months) the pain was significantly decreased in group A as compared with group B.

3. Results

we have 30 boys and 20 girls in two groubs, group one: included 25 patients who will be diagnosed by corners assessment as attention deficit hyperactivity disorder . Group two : included 25 as normal subject

Table (1) Characters of the attention deficit hyperactivity disorder.

Variable		No. (N=30)	% (100%)
Type of attention deficit hyperactivity disorder	Hyperactive	6	20.0
	Inattentive	5	16.7
	Combined	19	63.3
Comorbidity	Non	6	20.0
	Anxiety disorder	3	10.0
	Conduct disorder	9	30.0
	Mood disorder	5	16.7
	Oppositional deviant disorder	7	23.3
Age of onset (ys)	Mean±SD	4.7±1.15	
	Range	2-6	

This table shows the characters of attention deficit hyperactivity disorder Disease; the mean age of onset was at 4.7±1.15 years. Regarding the type of attention deficit hyperactivity disorder ; 20% of cases were hyperactive, 16.7% of cases were inattentive, and 63.3% of cases were combined. Regarding associated comorbidity; 6 patients (20%) had no associated comorbidity, 3 patients (10%) had anxiety disorder, 9 patients (30%) had conduct disorder, 5 patients (16.7%) had mood disorder, and 7 patients (23.3%) had Oppositional deviant disorder.

Table (2) Comparing the studied groups regarding lab investigations.

Variable	attention deficit hyperactivity disorder group (n=30)			Control group (n=30)			St."t"	P
	Mean	± SD	Range	Mean	± SD	Range		
Hb (mg/dl)	11.0	1.33	9-13	10.5	1.52	9-13	1.35	0.18 (NS)
WBCs (x10^3)	7.40	1.33	4.96-9.72	7.00	1.25	5.1-9.25	1.19	0.24 (NS)
AST	21.5	6.82	11-34	22.3	7.66	11-33	0.45	0.65 (NS)
ALT	43.1	11.14	29-62	44.4	11.86	27-61	0.46	0.64 (NS)
Creatinine	0.68	0.12	0.5-8	0.67	0.11	0.5-0.8	0.22	0.82 (NS)
Urea	13.8	4.94	6-20	11.7	4.15	5-18	1.78	0.08 (NS)

Hb: hemoglobin; WBCs: white blood cells; ALT: alanine aminotransferase, AST: aspartate aminotransferase. St."t": student t-test; NS: non significant.

This table shows comparison between studied groups regarding laboratory investigations; there was no statistical difference between two groups regarding Hb, WBCs, AST, ALT, Creatinine, or urea.

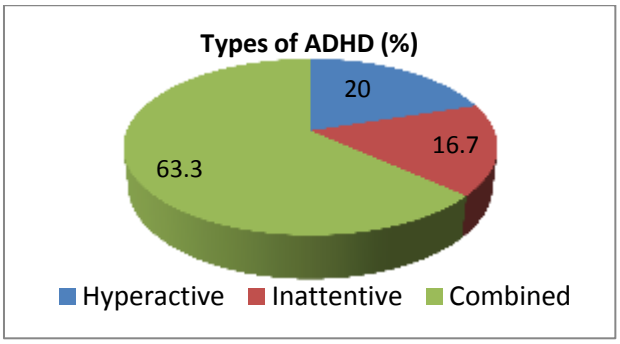

Fig (1) Pie chart showing % of attention deficit hyperactivity disorder types among the studied patients

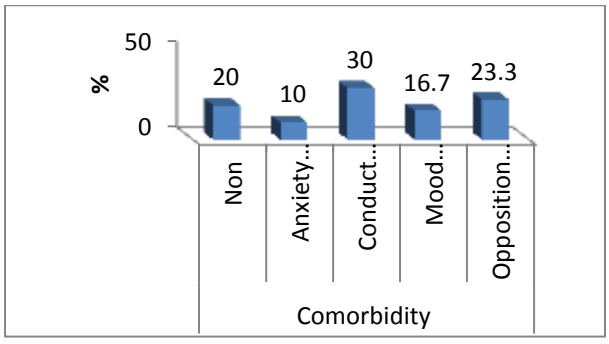

Fig (2) Bar chart showing comorbidities among the studied patients

4. Discussion

This disorder is a social disorder Inattention and disorganization entail inability to stay on task, seeming not to listen, and losing materials, at levels that are inconsistent with age or developmental level. Hyperactivity-impulsivity entails overactivity, fidgeting, inability to stay seated, intruding into other people's activities, and inability to wait symptoms that are excessive for age or developmental level [9].

The Disorder is highly comorbid with other psychiatric disorders, including (seasonal) depression, anxiety, and circadian rhythm disturbances. Childrens with attention deficit hyperactivity disorder usually suffer from short sleep duration due to insomnia, which has been associated with delayed onset of melatonin. Short sleep duration, binge eating, and skipping meals are all associated with obesity [10].

Numerous attention deficit hyperactivity disorder susceptibility molecular genetics studies have been conducted using several approaches. Candidate gene studies focused primarily on genes involved in monoamine systems. Altogether, these studies have identified many variants, generally of small effect, which do not explain the great attention deficit hyperactivity disorder heritability [9].

The search for candidate genes associated with attention deficit hyperactivity disorder susceptibility and response to medication remains an active area of investigation. Recently, a new gene has been associated with attention deficit hyperactivity disorder susceptibility, the latrophilin 3 gene (LPHN3) [11].

In this study, there was no statistical difference between types of gene polymorphism and Hb, WBCs, ALT, AST, creatinine, or urea.

Similarly Acosta et al. (2016), concluded that ADGRL3 not only is not spurious, but also is associated with a more severe form of attention deficit hyperactivity disorder . And Ribases et al., (2011), reported that LPHN3 contributed to combined type attention deficit hyperactivity disorder , and specifically to the persistent form of the disorder.

5. Conclusion

Work reveals a link between latrophilin 3 gene (RS2349039) and attention deficit hyperactivity.

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