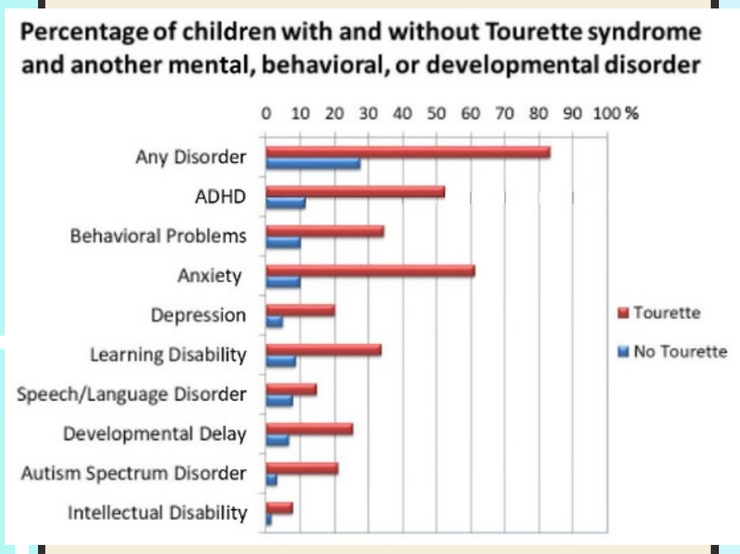
جامعة الشارقة
UNIVERSITY OF SHARJAH

A POTENTIAL WORLD WITHOUT TOURETTE'S

INTRODUCTION:

Sudden uncontrolled twitching, movements, or sounds are the main features of Tourette's syndrome. It is an early childhood neurological disorder that usually manifests before the age of 21 and is three times more common in males than females.(3) The tics intensify during strong emotions such as stress or excitement. According to the Centre of Arab Genomic Studies, the estimated prevalence in the Middle East is 10 per 1,000. (4) In every 6 children diagnosed with TS, 5 (83%) have at least one other mental, behavioral, or developmental disorder. (3)

GRAPH:



ETIOLOGY:

Despite intensive research, the underlying mechanisms and etiology of Tourette's syndrome (TS) remain unknown. Numerous neurotransmitters (dopamine, serotonin, norepinephrine, GABA, acetylcholine, glutamate) and each of them are thought to play a role in the development of the disease. (3) Both environmental factors and genes are likely responsible for the disease. (3) Currently identified genes associated with the development of TS are rarely involved, and no major gene has yet been identified. (4)

VS

OLD

STUDY OF DOPAMINE DEVELOPMENT (3):

Patients with TS have been found to have higher than normal levels of dopamine in the putamen. This increase is thought to play an important role in the pathogenesis of TS.

Two positron emission tomography (PET) scans were performed on 7 subjects with TS and 5 healthy subjects using [11C]raclopride as the radioactive tracer. Each subject received an intravenous injection of normal saline and an intravenous injection of amphetamine to determine dopamine levels after saline and amphetamine injection in the control group and in the TS group.

RESULTS(1):

After saline injection, both groups had similar dopamine levels. However, after amphetamine injection, the scan showed a 21% increase in intrasynaptic dopamine in the putamen compared to the saline injection, while the control group showed a less significant increase between the amphetamine and saline injections in comparison.

NEW

Currently available treatments for TS cause intolerable side effects that interfere with patients' daily lives. Although all current antidopaminergic treatments focus only on blocking D2 receptors, there is evidence that D1 receptors play a central role in the pathogenesis of TS. (1) Compared with D2 receptor antagonism, D1 receptors cause mild extrapyramidal side effects. (2) Ecopipam, an unsuccessful weight-loss drug, is currently being investigated as an alternative to D2 receptor blockers due to its ability to selectively block D1 receptors. (1)

ANIMAL STUDY (6):

A recent animal study in mice suggests that D1 receptors may be involved in the pathogenesis of Tourette's syndrome. Two groups of mice were used (saline-injected and IDPN-injected). Tourettes was induced in mice by injection of 3,3'-iminodipropionitrile (IDPN), a synthetic organic nitrile, a substance that induces vertical head shaking, random circling, hyperactivity, and increased acoustic startle response in rodents that resembles the symptoms of patients with Tourettes syndrome.

HALOPERIDOL:

Haloperidol, a D2 receptor antagonist, is a commonly used drug to reduce tics with an efficacy of 78-91%, which means that haloperidol is not a complete cure for TS. The main problem is hyperprolactinemia and EPS. The hyperprolactinemia can be reversed by stopping treatment, but the EPS may persist (4)

THE SIDE EFFECTS OF HALOPERIDOL ARE NUMEROUS AND INCLUDE:

- Weight gain
- Drowsiness
- Hyperprolactinemia (which is associated with amenorrhea, galactorrhea, and gynecomastia)
- Extrapyramidal side effects (dystonia, parkinsonism, akathisia, and tardive dyskinesia). (4)

D1 RECEPTORS:

ACTIVATION \ INHIBITION	D.S	S.N
D.S	saline-injected mice resulted in the exacerbation of stereotypic behaviors resembling symptoms of TS.	mice injected with saline showed no change in behavioral stereotypes.
S.N	Mice injected with IDPN significantly attenuated Tourette's associated behavioral stereotypes.	Mice injected with IDPN significantly attenuated Tourette's associated behavioral stereotypes.

D2 RECEPTORS:

ACTIVATION \ INHIBITION	D.S	S.N
D.S	mice injected with saline showed no change in behavioral stereotypes.	mice injected with saline showed no change in behavioral stereotypes.
S.N	Mice injected with IDPN significantly attenuated Tourette's associated behavioral stereotypes.	Mice injected with IDPN significantly attenuated Tourette's associated behavioral stereotypes.

These results suggest that D1 receptors may play a central role in the pathogenesis of Tourette's syndrome and that antagonism of D1 receptors may be a more precise drug target than antagonism of D2 receptors.

CLINICAL STUDY ON ECOPIPAM:

Forty patients aged 7 to 17 years with Tourette's syndrome were enrolled in a 4-week randomized, double-blind, placebo-controlled crossover study to determine the efficacy and safety of ecopipam. A Yale Global Tic Severity Scale (total tic score) was used to measure tic severity. All patients had a total tic score of 20 or more. Half of the patients took ecopipam, while the other half received a placebo for 30 days. This was followed by a 2-week washout period and then treatments were alternated for an additional 30 days. (5)

Results: Ecopipam showed a greater reduction in the total tic score compared with the placebo group, with no weight gain, extrapyramidal side effects, changes in the electrocardiogram, electrolyte tests, or vital signs. There were few adverse effects, which included dizziness, tiredness, and sleep problems (5)

REFERENCES

FUN FACT

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