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# Drug-induced stuttering: a review of the French Pharmacovigilance Database



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J. Béné<sup>1</sup>, M. Auffret<sup>1</sup>, S. Fedrizzi<sup>2</sup>, M. B. Valnet-Rabier<sup>3</sup>, J. Caron<sup>1</sup>, S. Gautier<sup>1</sup>  
and the French Association of Regional Pharmacovigilance Centres.

<sup>1</sup> Centre Hospitalier Régional et Universitaire de Lille, Centre Régional de Pharmacovigilance, Lille, France

<sup>2</sup> Centre Hospitalier Universitaire de Caen, Centre Régional de Pharmacovigilance, Caen, France

<sup>3</sup> Centre Hospitalier Universitaire de Besançon, Centre Régional de Pharmacovigilance de Franche Comté, Besançon, France

## INTRODUCTION

Stuttering is a disturbance in the normal fluency and time patterning of speech. There are two main types of stuttering, developmental (the more common) and acquired.

The aim of this study is to review the reports of stuttering as an adverse drug reaction (ADR) recorded in the French Pharmacovigilance Database (FPVD).

## METHOD

- All cases of “stuttering” recorded in the FPVD between 1985 until June 2014 were researched and reviewed.
- We selected all the cases where only one drug was suspected.
- Data on drug involved, characteristics of patients (age, sex and underlying disease) and ADR (seriousness, delay in occurrence, evolution, imputability and other etiologies) were collected.

## RESULTS

A total of 51 cases of stuttering were recorded in the FPVD until June 2014.

Behind these cases, 36 in which only one drug was suspected were selected.

The male:female sex ratio of the patients included in these reports was 2.4 and the mean age was 40 (min-max: 3-89) years.

The drug suspected were mainly psychoactives: seven cases with antiepileptic drug, six cases with neuroleptic drug (particularly clozapine and olanzapine) and five cases with antidepressive agent. Two cases involved antihistaminic and antineoplastic agents. Other classes of drug were also involved (one case for each class: TNF- $\alpha$  antagonist, vaccine, antibiotics, immunosuppressive agent...).

The mean time from drug suspected introduction to stuttering onset was 80 days (range: 1 day to 3 years). The drug suspected to be involved in the stuttering was withdrawn or the dosage was reduced in 32 cases. Improvement was observed in 29 cases. The drug was maintained in 2 cases but the evolution was not known. In four cases a positive rechallenge was observed (the drugs suspected were rasagiline, olanzapine, carbamazepin and maprotiline).

Causality was rated as possible for 22 cases, probable for 9 cases, likely for 5 cases.

Another concomitant cause of stuttering was suspected in 3 cases (psychotic etiology).

## DISCUSSION

Acquired stuttering can begin at any age. It has a sudden onset and is almost always associated with gross impairment of brain function. Neurogenic and psychogenic acquired stuttering are described. Multiple neurotransmitter systems seem to be involved in stuttering and drug induced imbalance in these systems may account for speech disturbance.

In literature, drug induced stuttering has been reported with psychotropic medications, including selective serotonin reuptake inhibitors, tricyclic antidepressants, phenothiazines, theophylline, lithium, olanzapine and clozapine, in accordance with our results. In few cases stuttering was clearly a dose-related side effect.

PET studies using 6-fluorodopa (6-FDOPA) as a marker of presynaptic dopaminergic activity showed significantly higher 6-FDOPA uptake in patients with moderate to severe developmental stuttering than in non stuttering control subjects. This uptake included ventral limbic cortical and subcortical regions. This is compatible with the hypothesis that stuttering is associated with an overactive presynaptic dopamine system in regions of the brain that modulate verbalization. In an interesting way, haloperidol and risperidone are the only two medications that have shown efficacy via double-blind studies in controlling stuttering symptoms. A case series suggest also that olanzapine may be a pharmacologic option in the management of stuttering.

## CONCLUSION

Despite the limits of a voluntary reporting database (such as under-reporting), this study confirms that several drugs may induce stuttering in humans. The pathogenesis of developmental, as well as acquired or neurogenic, stuttering is unclear (a part of seizure activity or a variant of movement disorder).

Our work also indicates that drug-induced stimulation of central ways is involved in stuttering in humans.

### References

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