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Letter to the Editors

Prolonged oro-facial dystonia in a 58 year old female following therapy with bupropion and St John's Wort

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Bupropion is widely used as an adjunct to stop smoking. The exact mode of action is unknown but it inhibits reuptake of dopamine, serotonin and norepinephrine in the central nervous system, as well as being a noncompetitive nicotine receptor antagonist [1]. Dystonia is reported as a rare side-effect, occurring in less than 1 in 1000 patients [2]. We are aware of only one previous case report of a dose-dependent, short-lived oro-facial dystonia following bupropion [3]. There have been no previous reports of interactions between bupropion and St John's Wort (*Hypericum perforatum*) [2]. We report the case of a patient who developed a persistant dystonia following bupropion, used in association with St John's Wort.

A 58 year old Caucasian female presented with a 2 h history of dystonic movements affecting the right side of her face, neck and right arm. She had been taking bupropion for the preceding 4 days at a dose of 150 mg day^{-1}. Her only other medications were St John's Wort at a dose of 300 mg once a day, which she had been taking for several years, and hormone replacement therapy in the form of Tridestra® (oestradiol and medroxyprogesterone). Her past medical history consisted of a completely resolved left Bells' Palsy 37 years previously. She smoked 15–20 cigarettes a day and drank alcohol occasionally. There was no family history of movement disorders.

Examination revealed episodic spasms of the right side of the face and right hand. During these attacks her eyes would roll back into her head and she was unable to communicate. These episodes occurred every 3 to 4 min and lasted approximately 45 s. In between attacks, neurological examination was unremarkable.

A diagnosis of acute facial dystonia secondary to bupropion was made. She was initially treated with parenteral chlorpheniramine, procyclidine and diazepam. This did not alter the duration of the dystonic movements but lengthened the spasm-free intervals.

CT scan of the brain was unremarkable. Her blood results showed she had subclinical hypothyroidism, with a raised TSH of 31.66 and a normal free T4 of 14.2. She was commenced on thyroxine. Her other bloods results, including biochemistry and screening for Wilson's disease, were unremarkable.

One week later she was discharged on oral chlorpheniramine, procyclidine and diazepam. On follow-up 2 weeks later she had persistant orofacial dystonia, although the periods between attacks had increased. Sodium valproate 800 mg twice daily was added with little effect. This was subsequently changed to carbamazepine 400 mg twice daily, with some response. The action of carbamazepine in dystonia is not clearly understood, whereas valproate has been shown to enhance GABA function in the brain, causing inhibition of the dopaminergic pathways that are involved in dystonia [4].

The oro-facial dystonia became less frequent over a 5 month period and eventually completely resolved. All medications were gradually withdrawn, with no recurrence of dystonia.

Bupropion was introduced as an antidepressant but was subsequently found to reduce the desire to smoke [1]. Its exact mode of action is unknown. It noncompetitively blocks nicotinic acetylcholine receptors, but also inhibits dopamine and norepinephrine reuptake, as well as inhibiting monoamine uptake. It seems likely that its effect in smoking is related to more than one receptor or transporter. It is also a weak serotonin reuptake inhibitor [5].

Dystonia is a syndrome of sustained muscle contractions that produces twisting and repetitive movements and postures. It is thought that this is due to serotonin-induced stimulation of dopaminergic pathways within the central nervous system [3]. It is a well recognised side-effect of several medications that affect dopamine concentrations, including antipsychotics and the selective serotonin re-uptake inhibitors (SSRIs) [6]. However, we could only find one case report of a dose-dependent, short-lived oro-facial dystonia in a patient receiving high dose bupropion [3].

St John's Wort is a herbal medication known to be a weak inhibitor of serotonin, norepinephrine and dopamine reuptake. There are several reports of St John's Wort interacting with SSRIs, resulting in various side-effects, including the serotonin syndrome. It is thought that these side-effects are due to an additive effect of the two agents, as they have a similar mode of action [7].

Dystonia is a rare side-effect of bupropion, possibly due to its weak serotonin reuptake inhibition, although the exact mechanism is unknown. We hypothesize that when it is used in combination with St John's Wort there is an additive effect on serotonin reuptake inhibition, making dopaminergic side-effects, such as dystonia, more likely to occur.

To our knowledge there are no reports of such a prolonged dystonia following bupropion, nor any cases of interactions between St John's Wort and bupropion.

This case highlights the need to be wary when prescribing bupropion in combination with other medications that affect serotonin reuptake. It is not recommended to use St John's Wort in combination with bupropion [2].

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