

Dystonias and Dyskinesias of the Jaw Associated with the Use of SSRIs

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KEY WORDS—SSRIs; 5HP; dopamine; dyskinesia; dystonia; orofacial dyskinesia

INTRODUCTION

The 5HT reuptake inhibiting antidepressants (SSRIs) were introduced into clinical practice in the late 1980s. From the time of their introduction a series of reports have appeared indicating that they were liable to produce motor (extrapyramidal) side-effects (Meltzer *et al.*, 1979; Bouchard *et al.*, 1989; Baldwin *et al.*, 1991), including dystonias (Brod, 1989; Reccoppa *et al.*, 1990), dyskinesias (Budman and Bruun, 1991; Fallon and Liebowitz, 1991; Wils, 1992; Arya and Szabadi, 1993; Scheepers and Rogers, 1994) or restlessness (Lipinski *et al.*, 1989; Creaney *et al.*, 1991; Rothschild and Locke, 1991). There are theoretical grounds for suspecting that such reactions might occur, given that there is a modulatory interaction between the serotonergic and dopaminergic systems (Tricklebank, 1989; Baldessarini and Marsh, 1990; see Arya (1994) for review). Given such reactions one concern must be whether the SSRIs are liable to produce long standing dyskinetic or dystonic reactions.

In 1993, Ellison and Stanziani reported four cases of SSRI-associated nocturnal bruxism, following treatment with sertraline or fluoxetine. These conditions resolved in three cases with co-administration of buspirone and in the fourth after decreasing the dose of the SSRI. In 1993, Micheli and colleagues also reported that antidopaminergic drug exposure could lead to bruxism and provided details of eight cases. In the former paper, SSRIs appeared to produce nocturnal bruxism, which the authors postulated might stem from an exacerbation of the nocturnal bruxism found normally in

association with REM sleep or else it might be related to the alteration in sleep patterns, brought about by SSRIs, leading to an inappropriate release of bruxism. Micheli and colleagues, by contrast, reported the presence of diurnal bruxism, that was alleviated by sleep, which they accordingly attributed to a tardive dystonic reaction to treatment. These latter cases responded poorly to interventions.

We report on six cases of SSRI-associated bruxism, occurring diurnally in five of the six, which have persisted in two subjects despite discontinuation of treatment and which have had significant consequences for either the general or dental health of those affected.

CASE REPORTS

Case 1

EJ, a 73-year-old lady, with a longstanding anxiety disorder, was referred for rationalization of her medication which was nitazepam 10 mg *nocte*, diazepam 5 mg per day, flupenthixol 0.5 mg t.d.s., lofepramine 140 mg *nocte* and betahistidine 8 mg per day. She had a 30-year history of treatment for anxiety. Routine physical investigations on referral, and subsequently, were normal.

She was switched from lofepramine to sertraline with beneficial effects on her mood. Eight months later she became more depressed and her sertraline was increased to 100 mg per day and her flupenthixol reduced to 1 mg per day. Within two weeks of this change she began to grind her teeth. It was

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sufficiently uncomfortable to lead to her removing her false teeth, and although with effort she could control obvious signs of toothgrinding, she was unhappy to answer phone calls or her hall door, with consequent effects on her confidence and mood. She had sore gums and a sore roof to her mouth.

EJ's flupenthixol was reinstated at 1.5 mg per day and sertraline was changed to paroxetine. The tooth-grinding eased but did not clear and she became more restless especially in the evening. Procyldine 5 mg b.d. alleviated her restlessness. Halting flupenthixol aggravated her tooth-grinding and her depression.

Over 18 months, paroxetine was increased to 40 mg/day and flupenthixol 1 mg/day was restarted, which alleviated the tooth-grinding but not her depression; fluvoxamine was started with an improvement in her mood but at a cost of inducing restlessness and tooth-grinding; flupenthixol was changed to remoxipride, which reduced her restlessness but aggravated the tooth-grinding and gum tenderness.

A number of non-SSRIs were subsequently tried. Mianserin alleviated tooth-grinding but was associated with a deterioration in mood and excessive sedation. Phenelzine had no clear effect on mood and produced marked insomnia. Neither dothiepin or lofepramine helped EJ's mood compared with what she remembered the effects of 5HT reuptake inhibitors to have been. Sertraline was, therefore, reinstated and again was helpful but at the cost of aggravating the tooth-grinding. Propranolol was added into the regime, on the basis of a suggestion that it might reverse the dyskinetic effects of drugs active on the 5HT system (Power and Cowen, 1992). This appeared to ease the tooth-grinding and restlessness consequent on the combination of sertraline and flupenthixol but in its own right brought about fatigue and limb heaviness and was, therefore, stopped.

Clomipramine was started two years after the initial script for a 5HT reuptake inhibitor. This had beneficial mood effects and was associated with restlessness and tooth-grinding at a lesser degree of intensity. On the hypothesis that some 5HT reuptake inhibition was necessary for mood stability, in this lady, but excess aggravated a propensity to dyskinesia, imipramine 50 mg *nocte* was instituted with gratifying effects on her mood at a cost of minimal tooth-grinding. The addition of buspirone subsequently appeared to make no difference to either her mood or her tooth-grinding.

Case 2

JP, a 28-year-old woman, was referred for the management of mood instability associated with a diagnosis of borderline personality. She had a prior history of extensive treatment with a range of neuroleptics, antidepressants and minor tranquillisers, without apparent dyskinetic or dystonic problems.

She was started on fluoxetine 20 mg/day. Within one week she began tooth-grinding by day and night and developed jaw clenching and tender, bleeding gums, as well as yawning. She spontaneously discontinued the fluoxetine, which according to her self-report alleviated her tooth-grinding, but she restarted it owing to a recrudescence of her original anxieties and depression. Restarting aggravated her tooth-grinding and gum tenderness. She reported the problem six weeks later, specifically attributing the side-effect to the treatment, despite having awareness of a history of nocturnal bruxism in childhood.

She was subsequently tried successively on paroxetine 20 mg/day, sertraline 50 mg/day and fluvoxamine 100 mg/day, which did nothing to ease her tooth-grinding, although their use alleviated her gum tenderness. Dental consultation found that her teeth had been ground down, sufficient to lead to the removal of one tooth. The grinding of her teeth could be controlled for limited periods of time by conscious effort. JP restarted on fluoxetine, to which propranolol was added. Her tooth-grinding intensified and gum tenderness re-emerged but she was happy to continue with treatment given the positive effects on her mood.

In early 1993, she discontinued all treatment after becoming pregnant. The tooth-grinding continued but gradually decreased in intensity during the subsequent year. She continued to have gum tenderness but it was uncertain whether this was the original complaint or was related to pregnancy. In August 1994, she restarted fluoxetine and this led to an exacerbation of her tooth-grinding and gum tenderness. The addition of buspirone 5 mg b.d. alleviated the bruxism but was found to be excessively sedating and therefore discontinued. She continues with treatment.

Case 3

MH, a 67-year-old lady, had a 10-year history of brief paranoid reactions, which typically responded within 4–5 days to modest doses of trifluoperazine—1–6 mg per day. As she was depressed on referral,

her neuroleptic was discontinued and she was commenced on paroxetine 20 mg *mane*, which helped. Four months later following stress at home, she had a recurrence of paranoid feelings and trifluoperazine 5 mg per day was added to this. She recovered, discontinued her trifluoperazine and remained well for seven months before presenting again with diurnal tooth-grinding and jaw clenching. Her gums ached and bled and on a number of occasions she awoke to find her mouth filled with brown fluid.

Paroxetine was discontinued but within two weeks she became more depressed and paranoid feelings re-emerged. Chlorpromazine 25 mg b.d. helped her paranoid feelings but not her mood. It was associated with restlessness and gum tenderness although her tooth-grinding stopped. Six months later, she was recommenced on paroxetine but this had to be discontinued owing to a re-emergence of intense tooth-grinding. Dental consultation revealed that five of her bottom front teeth were dramatically worn down. Four were 'built up' but one had to be crowned. The problem cleared on discontinuing paroxetine.

A subsequent depression with paranoid feelings was managed with lofepramine 140 mg *nocté* and stelazine 5 mg per day without any further problem. Risperidone 1 mg b.d. given subsequently had to be discontinued after a month because of akathisia. Sulpiride 200 mg *mane* has been helpful but after three months of treatment a mild tooth-grinding has re-emerged and her gums have become tender. Buspirone has had no beneficial effects.

Case 4

LD, a 41-year-old lady, with no previous psychiatric history, was treated by her general practitioner for depression with fluoxetine 20 mg/day. Within a week she developed painful clenching of her teeth, with tension in her jaw and associated muscles but she did not have tenderness of her gums. The painful sensation in her teeth was present continuously and was not relieved by analgesics. She inferred that the problem persisted through sleep because she was in considerable pain when she woke up. She attended an osteopath, because of spreading pain to her neck muscles, who commented that her neck muscles were too tight to manipulate. After 12 weeks her GP informed her that her symptoms might be related to medication and discontinued her fluoxetine. She was switched to dothiepin. The symptoms stopped within 24 h and no further problems were encountered.

Case 5

FO, a 30-year-old lady, with no previous psychiatric history, was treated by her general practitioner for depression with fluoxetine 20 mg/day for six months. Toward the end of this period, she became aware of nocturnal tooth-grinding and painful teeth. She consulted her dentist, who noted that her lower teeth had been ground down and recommended that she wear a gum shield. At no point did she have obvious gum tenderness. The problem continued. A month after halting fluoxetine, she was re-started on it, at which point the tooth-grinding became more intense—although it remained confined to night-time. The medication was discontinued, since when the tooth-grinding has continued but is less severe.

Case 6

TW, a 61-year-old man, with a previous history of major depressive disorder following treatment for a cancer of the bladder and desertion by his wife, was referred for treatment of depression. On presentation, he was taking dothiepin 225 mg *nocte*, nitrazepam 5 mg *nocte* and haloperidol 0.5 mg t.d.s. He had been on a comparable regime for five years with haloperidol replacing flupenthixol 0.5 mg b.d. in April 1993 and dothiepin replacing doxepin in September 1991 in an attempt to control weight gain. After the first consultation, his haloperidol was stopped and his dothiepin increased to 250 mg *nocte*. There was no complaint of and no evidence for tooth-grinding or clenching or jaw stiffness or tenderness.

Dothiepin was subsequently switched to fluoxetine 20 mg *mane*, as his mood remained flat. This caused poor sleep, stomach churning and some increase in anxiety, although his mood was otherwise helped to some extent. He persisted with this until one weekend, four months later, his fluoxetine ran out and he took some dothiepin to tide him over and found that his stomach churning and sleep improved considerably.

Approximately one month before this, he became aware of teeth clenching and grinding. A dental plate, which normally stayed in place with one application of dentifrice per day, now needed to be secured twice per day. His teeth hurt although his gums were not tender. His jaw muscles hurt, particularly in the morning. His temporomandibular joints began to click uncomfortably. He did not associate these problems with fluoxetine as they

continued after it was halted. Six months after the last dose of fluoxetine, the intensity of the problem appears to have eased marginally. He can control his tooth clenching for limited periods of time when in company. Buspirone was tried but made no difference.

DISCUSSION

Two sets of case reports in a short period of time (Ellison and Stanziani, 1993; Micheli *et al.*, 1993), along with these reports, suggests that bruxism occurs with some frequency as a complication of psychotropic drug treatment but that it has been unrecognized hitherto, or at least unreported. All three sets of reports suggest that, quite apart from the question of frequency, these side-effects when they occur may have significant consequences for the dental health of patients affected and indirectly for the management of their psychiatric conditions. In these reports the question of causation is complicated by the fact that four of the subjects had prior exposure to a neuroleptic, although only one was actually on a neuroleptic at the time the problem started. In one subject (EJ), there appeared to be an almost dose-response relationship between the amount of 5HT reuptake inhibition and the degree of tooth-grinding. Two subjects EJ and JP reported some relief with the 5HT-1 antagonist propranolol, although it did not clear the problem up. Buspirone produced no benefits in the three subjects for whom it was prescribed but did help one.

The problem does not appear specific to any one SSRI in that the reactions occurred in subjects taking paroxetine, sertraline and fluoxetine and in two of the subjects JP and EJ it was present to a similar extent with each of the SSRIs, including clomipramine in the case of EJ.

Are these difficulties mediated through the serotonergic or dopaminergic systems? It seems clear that there are modulatory interactions between these two systems (Tricklebank, 1989; Baldessarini

and Marsh, 1990; Arya, 1994). Of note also is that two SSRIs, paroxetine and CGP 6085A have been reported to induce an oral hyperkinesis in one species of monkey (Johnson, 1992; Korsgaard *et al.*, 1985). It may be also pertinent that amphetamine (Ashcroft *et al.*, 1967) and l-dopa (Magee, 1970) can cause tooth-grinding. In addition as noted in the Introduction, there have been a series of reports of extrapyramidal reactions of varying kinds following the use of SSRIs.

It would seem possible that Ellison and Stanziani (1993) and Micheli *et al.* (1993) are describing related conditions but one group suggests their patients were suffering from an exaggeration of normal functioning, while the other viewed the problem in terms of extrapyramidal dysfunction. Our cases appear to span the divide between these two groups. It is not clear that our group of subjects are homogeneous as regards the type of conditions associated with SSRI use. One of our subjects (FO) appeared to have the kind of bruxism, described by Ellison and Stanziani (1993), in that it was nocturnal only, but it did not clear on discontinuation of treatment. Another (LM) appeared to have a disorder characterizable as an acute dystonia. It would have been of interest to see if this responded to an anticholinergic agent (it did clear on switching from fluoxetine to dothiepin, which has anticholinergic properties). A third case (JP), involving jaw clenching, began within a week of the onset of treatment and hence cannot be described as a tardive dystonia, although other dystonic reactions occurring this quickly after the start of treatment have been termed tardive (Burke *et al.*, 1982). Equally unlike LM, JP's condition persisted for over a year after the discontinuation of treatment. MH, TW and EJ had more classic tardive dystonic features, in that the problem appeared several months after the start of treatment. In contrast to the cases reported by Micheli *et al.* (1993), however, the problem in these cases appears to have persisted through the night and to have had a mixture of

Table 1. Relevant clinical features of patients with tooth-grinding

Subject	Diurnal/ <i>nocte</i>	Concomitant neuroleptic	Drug/ naive	SSRIs	Dyskinesia/ dystonia	Response to buspirone	Persisting
EJ	24 h	Yes	No	All	DK/DT	No resp.	Mild
JP	24 h	Yes	No	All	DK/DT	Resp.	Yes
MH	24 h	Yes	No	Paroxetine	DK	No resp.	Yes
LD	24 h	No	Yes	Fluoxetine	DK/DT	N/a	No
FO	<i>nocte</i>	No	Yes	Fluoxetine	DK	N/a	Yes
TW	24 h	Yes	No	Fluoxetine	DK/DT	No resp.	Yes

dystonic (clenching) and dyskinetic (grinding) features and in the case of EJ the problem cleared up on discontinuing SSRIs even in the face of continuing neuroleptic treatment.

The group reported by Micheli *et al.* (1993) were of mixed sex (five males and three females) and were all drawn from an older age bracket (56–76). In contrast, the cases reported by Ellison and Stanziani were all female, with ages ranging from 30 to 43. This difference in age range and sex mix may be related to the use of neuroleptics in one case and SSRIs in the other. Our cases span this age range (29 to 73) but the sex ratio resembles that reported by Ellison and Stanziani (1993). It would seem too early at this stage to pick out either sex or a particular age group as being particularly at risk.

In summary, these cases and those reported by Ellison and Stanziani (1993) suggest that SSRIs may induce oro-facial dystonic or dyskinetic reactions, that may in turn have significant consequences for the physical or mental well-being of those affected. Against this, it is yet not clear that these reactions occur unduly frequently, nor is it clear that they outweigh the physical and mental effects of tooth decay brought about as a consequence of tricyclic antidepressant associated xerostomia. In addition, it seems worth noting that three of our subjects benefitted substantially from the SSRIs implicated in precipitating their problem to the extent of being prepared to continue treatment in the face of these difficulties.

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