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LETTER TO THE EDITOR

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Duloxetine for pathological laughing and crying

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Pathological laughing and crying (PLC) is a condition characterized by frequent, sudden outbursts of uncontrollable crying and/or laughing that are disproportionate or incongruent to underlying feelings or external triggers (Wortzel *et al*. 2008). Alternative terms often used to describe this syndrome are pseudobulbar affect, emotional incontinence, emotional or affective lability, organic or pathological emotionalism and involuntary emotional expression disorder. The condition is associated with various neurological disorders, such as stroke, multiple sclerosis, Parkinson's disease, traumatic brain injury, dementia and amyotrophic lateral sclerosis (ALS). PLC can be socially and occupationally disabling and is a source of distress for affected patients and their families. However, it is largely under-recognized or misdiagnosed in clinical settings. An important first step in the recognition and accurate measurement of PLC has been accomplished with the introduction of specific rating scales, such as the interviewer administered Pathological Laughter and Crying Scale validated for use with stroke victims (Robinson *et al*. 1993) and the self-report Center for Neurologic Study – Lability Scale (CNS-LS) validated for use with ALS and multiple sclerosis patients (Moore *et al*. 1997). Treatment of the PLC syndrome has included, with varying success, behavioural interventions and pharmacological agents. This case-report highlights the potential usefulness of duloxetine in the treatment of PLC symptoms in ALS, a fatal disorder with a reportedly high prevalence (up to 49%) of PLC.

Case report

Ms. M, a 52-yr-old female, manifested 18 months ago gradually worsening muscle weakness and wasting in the upper and lower limbs, night cramps, muscle fasciculations, and difficulty walking. One year later, the patient additionally exhibited dysphagia, dysarthria, nasal speech and frequent, unpredictable outbursts of uncontrollable crying or laughing either spontaneously or in response to non-specific or trivial and often inappropriate emotionally laden stimuli. On presentation, she was depressed, felt helpless, and complained of low energy and non-refreshing sleep. Embarrassment about emotional outbursts had led to social withdrawal. Neurological examination provided evidence of upper and lower motor neuron degeneration (bilateral corticospinal tract signs, peripheral muscle weakness and atrophies, signs of bulbar palsy, no sensory changes). Electromyography displayed widespread fibrillations and fasciculations, i.e. active denervation, in all four limbs, paraspinal and facial muscles with normal nerve conduction studies. Brain and cervical spine MRI scans as well as routine laboratory tests provided no evidence of other disease processes that might explain the observed clinical and electrophysiological signs; therefore, a diagnosis of ALS was made (Brooks *et al*. 2000). The patient had no symptoms of cognitive dysfunction (Mini-Mental State Examination score 29/30) but scored 23 on the 17-item Hamilton Depression Rating Scale ($HAMD_{17}$). The severity of PLC symptoms was measured with the CNS-LS, which comprises seven items rated from 1 'never applies' to 5 'applies most of the time' and includes a 4-item labile laughter (LL) subscale and a 3-item labile tearfulness (LT) subscale; a total score of 24 was recorded with respective subscale scores of 11 and 13 (crying outbursts prevailed). A previous 3-month trial with 20 mg/d citalopram prescribed by a general practitioner only minimally alleviated depressive and PLC symptoms and had been discontinued. Duloxetine (60 mg/d) was initiated. One week later, the patient had impressive improvement in PLC symptoms, especially in crying spells; affective outbursts became much rarer, briefer and less intense (CNS-LS score 14; LL 8, LT 6). Six weeks after treatment initiation, her mood, sleep and overall functioning were considerably improved ($HAMD_{17}$ score 10) and PLC symptoms were further relieved (CNS-LS score 10; LL 6, LT 4).

The basic mechanisms implicated in affective lability are not well understood. Presumably, PLC results from interruption of cortical inhibition of postulated laughing and crying centres in the upper brainstem or from lesions in the cerebro-ponto-cerebellar pathways involved in appropriate

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adjustment to social/cognitive context. Furthermore, the monoaminergic neurotransmitter systems, which appear to be implicated in the regulation of both mood and affective expressions, are thought to have a role in the manifestation of PLC episodes (Wortzel *et al*. 2008). Although both depression and PLC, especially crying spells, are highly responsive to serotonergic agents, PLC usually responds first to treatment (often in 1–3 d); this difference in response rates suggests that PLC and depression are distinct entities, although they frequently co-occur in neurological disease (Nahas *et al*. 1998).

Selective serotonin reuptake inhibitors (SSRIs) are recommended as first-line pharmacotherapy for PLC (Nahas *et al*. 1998). When SSRIs are ineffective or poorly tolerated, agents acting solely or additionally on the noradrenergic and/or dopaminergic neurotransmitter systems, such as nortriptyline (Robinson *et al*. 1993) and other tricyclic antidepressants, L-dopa (Udaka *et al*. 1984), psychostimulants (methylphenidate, dextromethorphan/quinidine; Rosen, 2008), lamotrigine (Ramasubbu, 2003) and novel dual-action antidepressants [venlafaxine (Smith *et al*. 2003), mirtazapine (Kim *et al*. 2005)] have been reported as second-line PLC treatments. Therefore, it is not surprising that duloxetine, a novel serotonin norepinephrine reuptake inhibitor (SNRI), acted rapidly and was highly effective in the treatment of PLC symptoms, in particular pathological crying, in the present case.

Further controlled studies are warranted to investigate the efficacy of duloxetine in the management of PLC symptoms, as well as its differential effect on crying *vs*. laughing outbursts in patients with ALS or other neurological disorders, with or without comorbid depression. Finally, it is unknown whether duloxetine or other dual-action antidepressants are better than SSRIs for PLC treatment in a subgroup of patients with specific biological or clinical characteristics.

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None.

Statement of Interest

None.

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