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Freezing of gait and major depressive disorder responding both to electroconvulsive therapy

Freezing of gait (FOG) is an episodic absence or marked reduction of forward progression of the feet despite the intention to walk [1]. During episodes of freezing, patients feel as if their feet 'are being glued to the floor'. FOG is common in patients with Parkinson's disease and atypical parkinsonism, and is associated with greater disease severity [2]. Stress, anxiety, a depressive mood and cognitively challenging situations are notorious for provoking or increasing the severity of FOG [3]. Here, we present a patient who clinically presented with a major depressive disorder (MDD) that was accompanied by FOG, and whose freezing showed a remarkable response to electroconvulsive therapy (ECT).

A 70-year-old-man with a somatic history of hypertension, angina pectoris and benign prostatic hyperplasia was admitted to the inpatient psychiatric clinic of GGZ inGeest because of suicidality. At the time of admission, he was treated with amlodipine 5 mg/day, carbasalate calcium 100 mg/day, rosuvastatine 10 mg/day, pantoprazole 20 mg/day, persantin XR® 400 mg/day, isosorbide mononitrate 30 mg/day, clonazepam 2 mg/day, Xanax XR® 2 mg/day and alprazolam 2 mg/day. His psychiatric history showed recurrent episodes of psychotic depression. Both the patient and his wife felt that the current episode differed greatly from previous depressions. In particular, the current episode started with persistent hyperventilation, overall stiffness and the episodic feeling that his feet were glued to the floor when walking, which he had never experienced previously. He reported that these symptoms had started immediately after he had bumped into a door several months ago. A depressed mood at onset of symptomatology was denied, but his mood did deteriorate gradually after the event. Several weeks prior to admission, suicidal thoughts occurred. Upon admission, he also experienced sleeping problems, anxiety, excessive worrying and hyperventilation (VIDEO I). Unambiguous episodes of FOG, with alternating trembling of the legs, was frequently provoked by gait initiation and turning (VIDEO II). Despite various neurological examinations prior to admission, no somatic diagnosis could be established. An MRI-scan during admission showed limited cortical atrophy (grade I) and focal white matter lesions in the parietal and frontal regions, but no lacunar infarcts or microbleeds, particularly not in the basal ganglia.

Supplementary video related to this article can be found at https://doi.org/10.1016/j.parkreldis.2019.07.002.

Because of suicidal thoughts, right unilateral ECT, twice weekly, was started. ECT was administered using Thymatron System IV (maximum energy 200%, 1008 mCoulombs) using a titration dosing protocol in which the dose was raised in the presence of a motor seizure less than 20 seconds [4]. After ECT, there was a remarkable improvement of his mood (Montgomery Asberg Depression Rating Scale at admittance: 34/60; after one ECT: 15/60; after 3 ECTs: 5/60, at discharge: 2/60). Facial gesticulation showing profound anxiety at admission, normalized. Remarkably, his FOG also disappeared after ECT, to an extent that even turning around no longer provoked FOG (VIDEO III). Only one ECT session markedly improved his gait, but during the days after ECT, symptoms gradually worsened again. In total, eight sessions of ECT were given to achieve a stable remission, in terms of both his mood and FOG. In order to prevent a relapse, nortriptyline and lithium were started after ECT. The patient was referred to the general practitioner for follow-up, who reported no relapse of depression or FOG during follow-up, and no new neurological symptoms developed. Two years after discharge, he died because of complications of a coronary artery bypass grafting surgery.

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Three mechanisms may explain the presence of FOG in this patient. First, this patient probably had a major depressive disorder and he may have manifested FOG in the context of psychomotor retardation, which is one of the main symptoms of a major depressive disorder. Psychomotor retardation includes disturbances in speech, facial expression, fine motor behavior, gross locomotor activity or ideation [5]. However, overt FOG has never before been described, perhaps because FOG can easily be missed during a routine motor examination in clinical practice (the anxiety associated with being examined typically suppresses the phenomenon), and certainly when the exam does not include rapid turning in place (this is the best test to provoke FOG in clinic) [6]. Based on brain imaging studies, it has been suggested that bradykinesia in melancholic depression (nowadays classified in DSM-V as a major depressive disorder) could be due to dopamine deficiency in the basal ganglia [7]. Such a striatal dopamine deficiency might hypothetically also result in FOG, which – at least in the setting of Parkinson's disease – is usually responsive to dopamine replacement therapy [2]. Further work in larger patient groups, and using dedicated turning tests to provoke FOG, is now needed to establish whether FOG should be considered as a true manifestation of major depressive disorder. Second, both the FOG and the depression could have been the very first symptoms of Parkinson's disease. However, this is unlikely for several reasons. Depression can indeed often be a presenting symptom of PD [8], but FOG is typically not [2]. Some patients present with FOG as their first and main presenting symptom (this is referred to as primary progressive freezing of gait), but this rarely responds so dramatically to any type of intervention. Moreover, the fact that both the symptoms of depression and the FOG were so reversible, without need for maintenance ECT, makes Parkinson's disease less plausible as the underlying pathology. Finally, no new neurological symptoms developed in the two years following discharge. Third, we considered the possibility that the cerebrovascular lesions, even though the basal ganglia per se were spared, contributed to both the depression [9] and FOG [10], perhaps by disconnecting cortical motor regions from brainstem locomotor regions. Again, the dramatic and prolonged response to ECT would argue against this explanation. Note that, irrespective of the underlying explanation, this case report illustrates the strong interaction between gait and mood [11].

Why did this patient respond so well to ECT? ECT has been suggested to activate the mesocorticolimbic dopaminergic system [12],

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including enhancement of the sensitivity of dopaminergic receptors [13]. Hence, ECT might have reversed the assumed dopamine deficiency, as can be seen in a major depressive disorder. Another possibility is that this patient did have underlying Parkinson's disease, and ECT can improve the motor signs of parkinsonism when given to treat severe depression [13]. Further work is now needed to establish whether more patients have FOG that responds favorably to ECT, in the setting of either major depressive disorder or Parkinson's disease.

Declaration of interest

All authors of this article have NO affiliations or involvement in any organization or entity with any financial interest, or non-financial interest in the subject matter or materials discussed in this manuscript.

Contribution to the manuscript

Dr D. Rhebergen collected the data and critically revised the draft.
M.Ph.C. Klok wrote the first draft of the manuscript.
Dr J. Nonnekes, Prof. B.R. Bloem and Dr M.L. Stek critically revised the draft.

Ethical approval

As stated in our manuscript, the patient is unfortunately diseased. We therefore cannot obtain written informed consent. Please note that all videos have been anonymised, such that the patient cannot be recognized from the videos.

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