Unmasking idiopathic Parkinson disease with the use of the atypical antipsychotics for symptoms of depression and anxiety in older adults: a case series

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Introduction

- The differential diagnosis of parkinsonism includes degenerative, drug-induced, and less commonly vascular, traumatic, or infectious etiologies[1]
- Parkinsonism in the setting of antipsychotic use is insufficient to make a diagnosis of drug-induced parkinsonism (DIP) as antipsychotics may unmask degenerative parkinsonism[2]
- Features suggestive of degenerative parkinsonism include an asymmetry of parkinsonian signs on examination and non-motor symptoms including REM behavior disorder (RBD), hyposmia, and autonomic dysfunction, all atypical in DIP
- Late-life onset anxiety and depression (after age 40) are both also increasingly recognized as non-motor features of degenerative parkinsonian syndromes[3]
- Dopamine transporter single-photon emission computed tomography (DaT-SPECT) showing asymmetric reductions in basal ganglia dopamine transporter concentration can also aid in differentiating degenerative parkinsonism from DIP[4]

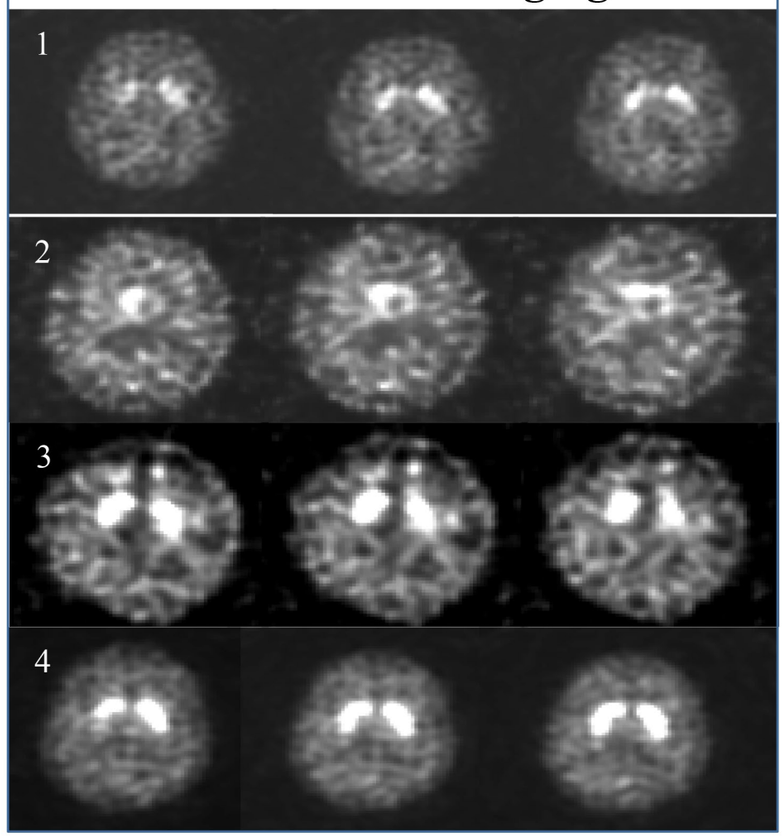
Methods

- This series reviews four cases of patients who underwent neurological evaluation, including DaT-SPECT imaging for parkinsonism while undergoing treatment with off-label second generation antipsychotics (SGAs) for late life depression and anxiety from 2014-2016.

Results

- Two women and two men (age range 46-66) presented with parkinsonism in the setting of off-label SGA use for late-life onset depression and anxiety
- All patients had asymmetric parkinsonism on examination
- Other features suggestive of degenerative parkinsonism included RBD, hyposmia, and orthostatic hypotension (OH)
- DaT-SPECT imaging results were suggestive of a degenerative parkinsonian syndrome in all cases
- Results were conveyed and recommendations made to discontinue the SGA and try alternative approaches for treatment of mood and anxiety
- Patients 1, 2, and 4 were managed with optimization of antidepressant or mood stabilizer therapy resulting in reasonable control of mood symptoms
- Patient 1 demonstrated resolution in rigidity and improvement in bradykinesia and tremor with discontinuation of aripiprazole
- Patient 2 had minimal improvement in bradykinesia and tremor following discontinuation of olanzapine
- Patient 4 had a resolution of her rest tremor and improvement in bradykinesia with discontinuation of asenapine

DaT-SPECT Imaging



Results (continued)

- Patient 3 had a complete resolution of motor symptoms with discontinuation of aripiprazole. He experienced a recurrence of mood symptoms off antipsychotic therapy and low dose quetiapine was added to his regimen with good control of mood symptoms and no return of motor symptoms

Conclusions

- The off-label use of SGA monotherapy for depression and anxiety has increased, though low level evidence supports the efficacy of SGAs in the treatment of these symptoms[5]
- Late-life onset mood symptoms in our cohort likely represented pre-motor symptoms of a degenerative parkinsonian syndrome that was unmasked with off-label SGA use
- Clinicians treating patients with SGAs should be aware of the potential for these agents to induce parkinsonism and should be aware that, among the SGAs, quetiapine and clozapine are less commonly associated with extrapyramidal effects[6]
- Further studies are needed to estimate the frequency of off-label SGA use to treat anxiety and depression in older adults and to determine the prevalence of DIP in the population
- Future research should strive to understand the relationship between these agents and motor dysfunction in this population. Parkinsonism may be a reversible side effect in some patients or the unmasking of an underlying neurodegenerative disease in others. However, the notion that SGAs may actually cause or contribute to a neurodegenerative process should also be considered.

Patient	Age	Gender	Antipsychotic	Symptom Treated	Parkinsonian Features	Imaging Findings
1	66	M	Aripiprazole	Depression	Asymmetric rigidity and bradykinesia; mild right rest tremor; RBD; hyposmia	Diffusely reduced basal ganglia radiotracer uptake, most prominent in right caudate
2	46	F	Olanzapine	Bipolar disorder, anxiety	Asymmetric tremor and bradykinesia	Reduced radiotracer uptake, most prominent in left putamen
3	55	M	Aripiprazole	Depression	Asymmetric rest tremor; possible RBD	Reduced left striatum radiotracer uptake
4	61	F	Asenapine	Anxiety	Asymmetric tremor and bradykinesia; OH	Asymmetric reduction of radiotracer uptake in the right putamen

References:

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