Antidepressant Induced Apathy Responsive to Dose Reduction

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Abstract ~ Apathy has a significant negative impact on the quality of life. It can be a part of other axis I and axis III disorders such as depression. It has also been reported as a treatment emergent side effect of SSRI drugs. A 48 year old male with diagnosis of personality change due to medical condition and depressive symptoms was started on Sertraline. Although his depressive symptoms, impulse control and his irritability improved significantly he became quite apathetic. This responded positively to a reduction in the dose of Sertraline. Since apathy can be a residual symptom of depression it may be a valid consideration to increase the dose of the SSRI. However if apathy was not a significant part of depressive syndrome prior to SSRI treatment then antidepressant treatment emergent apathy needs to be considered and one option is to reduce the dose of the SSRI. Other options appear to be addition of other pharmacological agents such as stimulants, dopamine agonists, acetylcholinesterase inhibitors and NMDA antagonists.


Abbreviations ~ SSRI: Selective Serotonin Reuptake Inhibitor; NMDA: N-Methyl D-Aspartate; ACT: Auditory consonant trigrams; RBANS: Repeatable Battery for the Assessment of Neuropsychological Status; EEG: Electroencephalography.

Introduction

Apathy as an indifference and lack of concern for social, emotional and physical wellbeing is a negative state that can affect an individual's quality of life and their productivity significantly. It can be a part of the illnesses such as depression, schizophrenia and personality change after brain injury. However since the emergence and widespread use of SSRIs it became evident that even though these pharmacological agents were capable of treating most of the symptoms of depression, they may be leaving the apathy untouched or even precipitating the apathy. To this end some patients may feel that the quality of life had not improved as expected due to this apathy. We present a case of SSRI treatment emergent apathy that also responded positively to a reduction in the dose of the same SSRI.
CASE SUMMARY

A 48 year old married caucasian male presented to the mental health clinic with symptoms of depression, complaints of memory and behavioral problems, anger outbursts and road rage. He scored 32 on Beck depression inventory. He lacked any manic or psychotic spectrum symptoms. He reported panic attacks precipitated by crowded places and places with high perceptual stimulus. No suicidal or homicidal ideations were reported.

He has a complicated history which started more than 25 years ago when he was bitten by a spider and developed Reiter’s syndrome as a consequence. Subsequently he developed aortic insufficiency and underwent valve replacement 10 years ago. During that surgery he suffered a cardiac arrest which lasted approximately 3 minutes. Since that incident both he and his wife reported a change in his personality and his memory. He reported intermittent memory difficulties where he forgets a word mid sentence and also developed some naming difficulties. In addition to the memory problems he developed significant impulse control difficulties. He became quite uncharacteristically argumentative, becoming angry easily and displaying road rage. He also started to suffer from frequent and polymorphic headaches that were treated by the neurologists. The patient also stated that he has frequent panic attacks which are mostly triggered when he goes into malls or places which are very colorful where the subjective perceptual load is high. He had a neuropsychiatric assessment with an overall impression of a borderline visuo-spatial and problem solving scores. He had a normal awake EEG.

There is no significant past psychiatric history before the aortic valve replacement surgery. Patient reported uneventful childhood and normal schooling. He was gainfully employed but was retired on medical grounds following the development of Reiter’s syndrome. Prior to the onset of memory problems he described good memory function. He is married and has no children. He denied any past or present illicit substance use or any alcohol use to excess. He does not have any significant legal history. His medical history is significant for aortic valve replacement, chronic migraines, nephrolithiasis, hypertension and Reiter’s syndrome.

He had been seen elsewhere prior to this presentation and was tried on Valproate, Duloxetine and Bupropion but with inadequate response. After that he was switched to Sertraline. Since starting Sertraline at 50 mg daily he reported feeling very calm but reported complete apathy, indifference and complained of severe anhedonia. He denied any other cognitive or vegetative symptoms of depression other than apathy.
at this point. This was considered to be a response to treatment with Sertraline and this issue was discussed with him. He was willing to reduce the dose of Sertraline and the dose was reduced to 25 mg. After sertraline was reduced to 25 mg he came back to the clinic and reported that he was able to experience emotions again and that he was able to react to situations at home. He related how he restarted enjoying his family life and participating in the social events with friends and family which he was unable to do and unable to enjoy whilst on Sertraline at 50 mg daily. He continued to deny any pervasive sadness or other neuro vegetative symptoms of depression. He also denied any negative cognition such as hopelessness or helplessness.

**DISCUSSION**

Apathy for the clinical purpose was defined by Marin⁹ as primary absence of motivation that is not attributable to cognitive impairment, emotional distress or diminished level of consciousness. Apathy as a treatment emergent phenomenon may easily be confused with incomplete response to antidepressants. Current understanding of the cause of this apathy syndrome is unclear but a deficit of frontal lobe function was suggested.⁸ The serotonin system inhibits dopaminergic function at the level of the origin of the dopamine system in the midbrain as well as at the terminal dopaminergic fields in the forebrain.⁷,¹⁰ Dorsal raphe serotonin system and the ventral tegmental and substantia nigra dopamine system may act as mutual opponents.¹⁰ Clozapine produces a selective increase in dopamine release in rat prefrontal cortex mediated via activation of 5-HT₁A receptors.⁶ This explanation of apathy as a frontal dopamine deficit suggests the use of dopaminergic stimulation for its treatment.

In the circumstances where the treatment emergent apathy is clear options include reduction in dose, addition of stimulants, dopaminergic drugs as well as cholinesterase inhibitors. However in the circumstances where it is unclear whether one is treating incomplete response to medication or the treatment emergent apathy, safer option may be to consider increasing the dose of antidepressant. Apathy in these circumstances has been reported as dose dependant and reversible. It does carry the risk of worsening apathy but alternative of reducing the SSRI dose will put patient at risk of relapse of depression. If the apathy gets worse then it may clarify the clinical picture more in favor of treatment emergent apathy. Literature suggests that patients feel and describe the apathy as distinctly different to the lack of motivation as a part of depression.³,⁸,¹¹
A REPORT OF ANTIDEPRESSANT INDUCED APATHY RESPONSIVE TO DOSE ALTERATIONS

CONFLICT OF INTEREST

No conflict of interest exists for the above authors.

REFERENCES