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Mini Review

Personal medicine and micro-dosing: A novel interpretation of adverse reactions to SSRIs in the treatment of depression.

Mark R Dadds[1]*, Stanley Catts[2]

*[1]*Department of Psychology, School of Psychology, University of Sydney, Australia*

[2]*Department of Psychology, Department of Psychiatry, University of Queensland, Australia*

***Corresponding author:** Mark R Dadds, Department of Psychology, School of Psychology, University of Sydney, Australia.

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Adverse reactions to SSRIs in the treatment of depression are common, increase with dosage, and in combination with data showing therapeutics benefits are achieved at lower doses, drive the mandate to start low and go slow in terms of dosage [1]. Where the side effects include rapid onset of activation, agitation and anxiety [2], SSRIs are often discontinued and investigation for bipolar spectrum disorder may be pursued [3]. Here we present a case showing that an alternative interpretation of such an adverse reaction might be warranted. Specifically we present preliminary data to indicate that a subset of patients might be unusually sensitive to SSRIs and actually benefit from doses currently considered significantly below therapeutic range.

Case A was a 62 year old male with a history of depression first identified in adolescence. Depression was noted in the maternal grandmother, a nephew, and at least one other sibling. Symptoms included feelings of despair, sleep disturbance, social withdrawal, anxiety, and a range of somatic symptoms. Other medical features included a 25 year history of Hashimotos managed with thyroxine and mild psoriatic arthritis; otherwise health was good with normal weight and other functions. Treatment for the depression had included self-administered St Johns Wort which was ineffective, and three trials of SSRIs, all of which had been terminated due to intolerable side effects. The most recent in 2013 involved 10mg Lexapro. After 3 days the patient reported severe anxiety, akathisia, mental confusion, and agitation. (muscle movement? technical terms?). A similar reaction had been noted in a nephew who was then recommended a trial on Lithium but refused the treatment (no evidence of bipolar emerged over the subsequent 9 years). Evidence was noted of unusual sensitivity to other medications; for example, 4mg Doxylamine Succinate reliably induced 8 hours deep sleep (recommended dose 25-50mg). Thus, it was decided to test the idea that the side effects were associated with high sensitivity to SSRIs which may in fact, be beneficial at greatly reduced doses.

This hypothesis was tested in an open-trial multiple baseline design with alternating on and off medication phases of 12.5mg Sertraline. In phase 1 the medication was compounded into 12.5 capsules, but subsequently, 50mg tables were halved and taken every second day. St Johns Wort 1800mg qd was substituted in the off-medication phases. Phase changes were implemented when stable trends were visible. Daily self-reported records of morning and evening depression levels were kept. Morning levels were generally higher and highly convergent with evening levels (r = .91) thus we show morning levels here. Data are shown in (figure 1). Microdose Sertraline was associated with clinically significant reductions in depression compared to off-medication phases. No side effects were noted. The absence of depression and side effects continued in the 14 months since these data were collected.

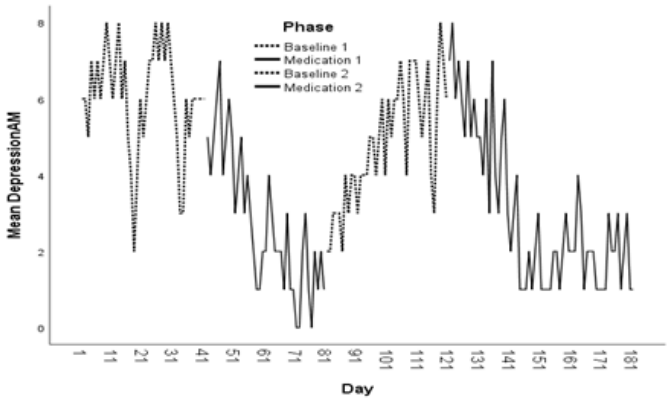

Figure 1: Daily morning depression ratings across medication and withdrawal phases.

The data on this single case are suggestive that a subset of cases showing adverse reactions to SSRIs may in fact benefit from significantly smaller doses currently considered sub-therapeutic. While placebo effects are unlikely to account for such sustained therapeutic effects in a patient with a long history of depression, they cannot be ruled out. Further testing of this idea is warranted using more robust designs and monitoring of blood levels to check relationships between dosage, circulating levels and therapeutic effects. If found to be reliable, the results would extend the lower range of doses available to achieve the optimal balance between efficacy, tolerability, and acceptability in the acute treatment of major depression [4].

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