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Attempting to discontinue antipsychotic medication: Withdrawal methods, relapse and success

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ABSTRACT

Few studies explore subjective experiences of attempting to discontinue antipsychotic medication, the withdrawal methods people use, or how their efforts affect their outcomes. People who take antipsychotics for off-label purposes are poorly represented in the literature. This study investigates experiences of attempting to discontinue antipsychotics in a cross-sectional sample and explores potential associations between withdrawal methods, relapse, and success. An anonymous online survey was completed by 105 adults who had taken antipsychotics for any reason and had attempted discontinuation at least once. A mixed methods approach was used to interpret the responses. Just over half (55.2%) described successfully stopping for varying lengths of time. Half (50.5%) reported no current use. People across diagnostic groups reported unwanted withdrawal effects, but these were not universal. Withdrawing gradually across more than one month was positively associated, and relapse was negatively associated with both self-defined successful discontinuation and no current use. Gradual withdrawal was negatively associated with relapse during withdrawal. We conclude it is possible to successfully discontinue antipsychotic medication, relapse during withdrawal presents a major obstacle to successfully stopping AMs, and people who withdraw gradually across more than one month may be more likely to stop and to avoid relapse during withdrawal.

1. Introduction

Antipsychotic medication (AM) is commonly used by people diagnosed with schizophrenia spectrum disorders and bipolar disorder to manage symptoms of psychosis and mania (Castle et al., 2002; Fountoulakis et al., 2012). They are also commonly prescribed to people with a range of other off-label conditions including depression, dysthymia, obsessive-compulsive disorder, other anxiety disorders, or specific symptoms like insomnia or agitation, often at lower doses or alongside other psychiatric medications, despite limited evidence to support these practices (Maher et al., 2011; Monasterio and McKean, 2011; Carton et al., 2015; Walton et al., 2008; Albert et al., 2016; Vanbronkhorst et al., 2018). Most of the existing AM research focuses exclusively on people diagnosed with psychotic disorders (Landolt et al., 2016; Wunderink et al., 2013; Jung et al., 2016; Wils et al., 2017) and little is known about whether the experiences and outcomes of this group represents the experiences of those who take AMs for other reasons.

It is well-documented that people taking AMs to manage psychosis often attempt to discontinue (Cooper et al., 2005; Moritz et al., 2009). AMs are often accompanied by serious adverse effects (Carrick et al., 2004; Waterreus et al., 2012), and do not effectively reduce psychotic symptoms or prevent relapse for everyone (Leucht et al., 2009). People frequently make independent changes to their prescribed medication regimes to manage the impact of adverse effects (Bülow et al., 2016) and reports of discontinuation rates around 60%−80% are common among samples with schizophrenia spectrum diagnoses (Lieberman et al., 2005; Cooper et al., 2005). A similar pattern of adverse effects, variable levels of effectiveness, and high rates of discontinuation also appears among people who take AMs for bipolar disorder (Sajatovic et al., 2006; Greene et al., 2018; Djebbi et al., 2012) depression, anxiety disorders, OCD, and post-traumatic stress disorder (PTSD: Painter et al., 2017; Albert et al., 2016), leading some researchers to conclude that attempted discontinuation should be considered the norm across different groups (Moritz et al., 2009).

Research has suggested people who experience psychosis and stop taking AMs show better functional outcomes and lower relapse rates in the long-term relative to those who maintain continuous use (Harrow et al., 2012; Landolt et al., 2016; Wunderink et al., 2013; Wils et al., 2017; Jung et al., 2016). These more favourable results do not appear to

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emerge until four years after discontinuation and prior to this point groups with psychosis and bipolar disorder who stop taking AMs show higher rates of relapse than those who persist (Harrow et al., 2012). Such findings have led some researchers to argue that "long-term 'maintenance' treatment with antipsychotics is based on hope rather than evidence" and encourage prescribers to reduce this practice (Murray et al., 2016, p. 362).

People taking AMs for bipolar disorder and other off-label purposes are poorly represented in the discontinuation literature, but several studies suggest they show a similar pattern of improved recovery outcomes following discontinuation of AMs. One longitudinal study compared participants with diagnoses of depression or bipolar with psychotic features to those with schizophrenia or schizoaffective disorder diagnoses and found improved remission and relapse rates for those who stopped AMs in both groups, with significantly more favourable outcomes for those with psychotic mood disorders than those with schizophrenia spectrum disorders (Harrow et al., 2012). An earlier AM discontinuation study among people with bipolar disorder diagnoses found that continued use of antipsychotics after achieving remission from an episode of acute mania was detrimental due to increased depressive symptoms (Zarate and Tohen, 2004). Other studies have found improved recovery outcomes for those who discontinue AMs following off-label use for non-psychotic depression (Mortimer et al., 2003) and challenging behaviour associated with intellectual disabilities (Ramerman et al., 2018).

In New Zealand, as in many other developed countries, government legislation upholds service-users' human right to informed choice, including the choice to stop taking medication, and details specific conditions that must be met to compel someone to continue treatment without their consent (Ministry of Health, 1992; The Health and Disability Commissioner, 1996). However, there is reason for caution when contemplating discontinuation and the choice to stop medication or consent to continuing use is not as straight forward as it may first seem. Discontinuation can entail a range of somatic, emotional, and cognitive withdrawal effects, and psychotic or manic relapse during the withdrawal period is common among those with schizophrenia spectrum and bipolar diagnoses (Salomon and Hamilton, 2013; Gilbert et al., 1995; Harrow et al., 2012; Moncrieff, 2013; Boonstra et al., 2011; Gilbert et al., 1995; Harrow et al., 2012; Buchanan et al., 1992; Moncrieff, 2006a). Little is known of whether psychotic or manic symptoms emerge during withdrawal following off-label use, but it may be common for the symptoms that were the original treatment targets to reappear during or following withdrawal of off-label AMs (Moncrieff, 2006b). In one study of 18 people with OCD who discontinued AM while continuing with an antidepressant, 83.3% reported a relapse of OCD symptoms, most within eight weeks of discontinuation (Maina et al., 2003).

It is difficult to determine whether relapse of psychosis or other symptoms proximal to discontinuation represents a withdrawal syndrome, the re-emergence of a chronic mental-health problem, or both. Some researchers hypothesise that relapse of psychosis following withdrawal is the result of neurological adjustments to the dopamine blockade, which produce a subsequent surge of excitation when the AM is withdrawn (Steiner et al., 1990; Chouinard, 1991; Moncrieff, 2006a). They note AMs also act on a range of neurotransmitter systems which appear to be associated with other physical, cognitive and emotional withdrawal effects (Moncrieff, 2013).

Gradual withdrawal is recommended to curb and potentially prevent withdrawal effects, regardless of diagnosis, but there is little available research regarding whether or how people implement this advice. Some writers advocate for reductions of no more than 10% of the previous dose (Breggin, 2013; Hall, 2012), but most of the clinical withdrawal studies have employed relatively swift tapering protocols in comparison. All of the clinical studies of withdrawal among people who experience psychosis conducted up to 1995 tapered people off their medication within 60 days, the vast majority within 30 days or less (Gilbert et al., 1995). More recent trials have used longer withdrawal protocols and appear to show improved outcomes, both in terms of success and safety (Nishikawa et al., 2007), but only two discontinuation studies have tested whether the reduction period is associated with the outcomes of attempts to stop taking AMs. One meta-analysis found an increased risk of early relapse for those who withdrew abruptly compared to those who reduced gradually over three weeks or more (Viguera et al., 1997), while a more recent meta-analysis using the same definitions found no significant difference (Leucht et al., 2012). To our knowledge, none of the withdrawal studies have explored whether gradual withdrawal is associated with successful discontinuation.

A small handful of studies represent the only existing information about how people attempt to withdraw from AMs (Roe et al., 2009; Salomon and Hamilton, 2013; Salomon et al., 2014; Geyt et al., 2016). Two small interview studies investigating the decision-making process found people with psychosis or bipolar disorder highlight the importance of 'weaving a safety net' of coping skills and supportive alliances (Geyt et al., 2016; Roe et al., 2009). One larger survey study explored withdrawal methods and effects alongside people's personal efforts to manage and their chosen withdrawal methods (Salomon and Hamilton, 2013; Salomon et al., 2014). Among the sample of 88 people who had taken AMs for any reason, 54.7% stopped without consulting their prescriber, 40.9% withdrew abruptly, 27.3% withdrew in under a month, and 22.7% withdrew in one to six months, 78% experienced withdrawal effects, and 21% were no longer taking AMs (Salomon et al., 2014). It was not specified how many of the participants had been taking AMs for psychosis, bipolar disorder or off-label purposes. Again none of these studies explored what characterises the efforts and outcomes of those who succeed in their attempts to stop taking AMs. However, when considered in conjunction with the longitudinal research and studies exploring psychiatric medication withdrawal in general they suggest that discontinuation is "a legitimate choice that requires and justifies appropriate support" (Katz et al., 2018, p.1).

The problem is that there is little clarity about what the appropriate support needs to be. Several guidelines have been put forth (e.g. Breggin, 2013; Hall, 2012; Gupta et al., 2018; Reeve et al., 2014), but these are based on scarce data and none are considered widely accepted as best practice at this point in time. It remains unknown whether there is an association between gradual withdrawal methods, withdrawal effects and successful outcomes, or how experiences might differ across groups with different diagnoses. Such information is important for everyone who attempts discontinuation, regardless of their diagnosis, and for the people they turn to for support, including clinicians and personal networks. Research exploring how people manage their attempts to discontinue and what affects their outcomes may help guide people who wish to stop AMs and their support systems towards strategies that will minimise the costs and maximise their chances of success. A mixed-methods exploratory study was designed in an attempt to address these issues.

2. Methods

This mixed-methods investigation aimed to describe the discontinuation experiences of people who take or have taken AMs for different purposes, and to explore the possible associations between withdrawal methods, withdrawal effects, and success. This article draws on the results of questions concerning attempted discontinuation of AMs in The Experiences of Antipsychotic Medication Survey. The anonymous survey was available for online completion in 2014. Ethical approval for the study was granted by the University of Auckland Human Participants Ethics Committee.