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ORIGINAL PAPER

# Drug-Induced Impulse Control Disorders: A Prospectus for Neuroethical Analysis

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**Abstract** There is growing evidence that dopamine replacement therapy (DRT) used to treat Parkinson's Disease can cause compulsive behaviours and impulse control disorders (ICDs), such as pathological gambling, compulsive buying and hypersexuality. Like more familiar drug-based forms of addiction, these iatrogenic disorders can cause significant harm and distress for sufferers and their families. In some cases, people treated with DRT have lost their homes and businesses, or have been prosecuted for criminal sexual behaviours. In this article we first examine the evidence that these disorders are caused by DRT. If it is accepted that DRT cause compulsive or addictive behaviours in a significant minority of individuals, then the following ethical and clinical questions arise: Under what circumstances is it ethical to prescribe a medication that may induce harmful compulsive behaviours? Are individuals treated with DRT morally responsible and hence culpable for harmful or criminal behaviour related to their medication? We conclude with some observations of the relevance of DRT-induced ICDs for our understanding of addiction and identify some promising directions for future research and ethical analysis.

**Keywords** Addiction · Neuroethics · Dopamine agonists · Parkinson's Disease · Impulse control disorders · Moral responsibility

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## Introduction

A small but significant proportion of individuals with Parkinson's Disease (PD) treated with dopamine replacement therapy (DRT) develop compulsive behaviours or *impulse control disorders* (ICDs), such as pathological gambling, compulsive buying and hypersexuality. Like more familiar drug-based forms of addiction, these iatrogenic disorders can cause significant harm and distress for sufferers and their families, adversely affect social functioning and lead to marriage and family break-up and unemployment [1]. Some affected individuals have reportedly lost hundreds of thousands of dollars, their homes and businesses as a result of pathological gambling and compulsive buying [2, 3]. Others have developed a compulsive interest in sex and spent large amounts of time viewing pornography, interacting on adult

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websites and engaging in sexual acts that, in some cases, have resulted in criminal prosecution [4–6].

DRT has been successfully used to treat PD for over three decades. The emergence of compulsive behaviours in patients receiving them has only become widely recognised in the last few years. Given that the uses of dopaminergic drugs are likely to expand in the future, it is essential to examine the ethical and clinical issues raised by their use. The aims of this paper are as follows. First, we describe the phenomena of DRT-induced ICDs. Second, we briefly examine the evidence that these disorders are caused by DRT. Third, we highlight some of the key ethical issues raised by these disorders. Research in this area is only in its infancy, and as we will show, there are many empirical questions that remain to be answered before ethical conclusions can be drawn. At this early stage of research, our intention is to draw attention to this clinically and ethically important issue. Fourth, we conclude with some observations of the relevance of DRT-induced ICDs for our understanding of addiction and identify some promising directions for future research and ethical analysis.

## Behavioural Phenomena Associated with DRT

Parkinson's Disease is a neurodegenerative disorder characterised by stereotypical motor disturbances, such as slowness in the execution of motor movements, rigidity and tremor [7]. These impairments are primarily the result of a loss of dopaminergic neurons in the basal ganglia that control movement [8], although serotonergic, cholinergic and noradrenergic systems are also implicated. Patients with PD also display non-motor symptoms that include depression and impaired executive function [9]. These cognitive and affective changes are thought to be due to the loss of dopaminergic neurons in the ventral tegmental area that project to the limbic system, including the amygdala, hippocampus and prefrontal cortex, all of which are involved in emotional expression and memory [8].

The motor symptoms of PD are commonly treated with long-term DRT. This involves using either the dopamine precursor, levodopa, or synthetic dopamine agonists that mimic the effects of dopamine, such as pramipexole, ropinirole and pergolide. These drugs have been shown to reduce the severity of the motor symptoms of PD [9], and may also improve the affective and cognitive symptoms of the disorder [10].

DRT is also associated with significant cognitive and behavioural changes [11, 12], including ICDs [13], hallucinations and paranoia [14]. ICDs are characterised by "the failure to resist an impulse, drive, or temptation to perform an act that is harmful to the person or to others" [15]. Initial case reports and retrospective reviews of patient's records of DRT-induced ICDs have been confirmed in large systematic studies [16–18]. ICDs reported after DRT treatment include: pathological gambling [19], compulsive buying [20, 21], hypersexuality [22], intermittent explosive disorder (IED) [23], internet or computer addiction [24], and compulsive eating [25].

Some patients treated with DRT appear to use their medication in a compulsive way that resembles the behaviour of persons with a drug addiction [26]. They consume increasing amounts of DRT, often far in excess of that necessary to treat their motor symptoms, and they persist in doing so despite experiencing adverse consequences, such as DRT-induced dyskinesias: involuntary, jerky and irregular, dance-like movements. An abrupt cessation or reduction in DRT dose can also produce withdrawal symptoms [26]. This pattern of symptoms is commonly referred to as *dopamine dysregulation syndrome (DDS)* [27], but has also been described as "levodopa addiction" [27] and "DRT addiction" [8].[1]

## Is There a Causal Relationship Between DRT and ICDs?

There is considerable evidence for a causal relationship between DRT and ICDs when we use the standard epidemiological criteria—strength of an association, consistency of the relationship, biological gradient, specificity and biological plausibility, and

[1] Research suggests that ICDs are most strongly associated with dopamine agonist use, whereas DDS and punding are found primarily with levodopa use. This is an unresolved issue in the literature: there are a small percentage of PD patients treated only with levodopa who develop ICDs [28], while some treated with DAs develop addiction-like use of their medication, including a DA withdrawal syndrome [29]. Such a debate is beyond the scope of this analysis. However, readers should keep in mind that the majority of cases of ICDs in medicated PD patients involve DA use. For simplicity, we use DRT to refer to any dopaminergic treatment of PD.

coherence [30]. Evidence for each of these criteria comes from: (1) an increased prevalence of ICDs in DRT-treated PD patients; (2) the incidence of ICD temporally following DRT use; (3) a DRT dose dependent effect; (4) an identifiable subpopulation who are more likely to develop an ICD following DRT use; and (5) a plausible neurobiological explanation of how DRT might induce ICDs.

1. *The prevalence of ICDs in PD patients and in the general population*

The overall incidence of ICDs in PD patients is estimated to be between 6 and 14% depending on the method of diagnosis [1, 28, 31]. In PD patients taking a dopamine agonist such as pramipexole, this proportion may be as high as 17% [28]. It is more difficult to assess whether the rates of ICDs in patients treated with DRT are higher than in the community because there is as yet no agreed method of classifying ICDs and very few epidemiological studies have been conducted on the prevalence of different types of ICDs in large representative community samples [32, 33]. Pathological gambling is the best studied ICD in PD. The estimated lifetime prevalence of pathological gambling in the general population is less than 0.5% [34], compared with 2–6% of PD patients [15, 28, 31, 35], and up to 7.2% of those taking dopamine agonists [36]. On these estimates, rates of pathological gambling appear to be several times higher in PD patients treated with DRT than in the general population. A recent case-control study estimated that PD patients treated with DRT are over 25 times more likely to develop an ICD than healthy controls [35]. It is less clear whether the rates of other ICD disorders are also elevated in PD patients receiving DRT compared to the general population.

The high prevalence of ICDs in PD patients treated with DRT is unlikely to be attributable to the neuropathology of their PD. Firstly, PD patients are generally middle aged and older and usually have lower levels of impulsive and sensation seeking traits usually associated with addiction [37]. They are also less likely to use alcohol, caffeine and tobacco [38]. The observed increases in ICD behaviour in a population that otherwise exhibit lower rates of ICD and other addictive behaviours provides further weight to the argument that DRT is causally related to the appearance of ICDs in PD [13]. Secondly, ICDs have been observed in patients treated with DRT for other unrelated conditions, such as restless legs syndrome (RLS) [39–41], fibromyalgia [42], and prolactinoma [43].

2. *Temporal order*

The onset and resolution of ICDs in PD patients is closely related to their use of DRT. The onset of ICD often occurs after the initiation of DRT or after a significant increase in dose [19, 31, 44]. In the majority of cases, the ICD quickly resolves after either a reduction in dose or the cessation of DRT [21, 31, 45].

3. *A dose dependent effect*

The relationship between DRT dose and ICD is difficult to establish due to the changes in dopaminergic medication dose and type that most individuals with PD undergo as they are stabilised in treatment and as their disease progresses [1, 46]. Early studies suggested that the likelihood of ICDs occurring in individuals with PD was related to DRT dose (both DA and levodopa) and the duration of its use. However, more recent studies have not been able to replicate this finding. A recent study of over 3,000 PD patients did not find an association with the dose of DA (the drug most strongly associated with ICDs) but did for levodopa (a drug less likely to cause ICD) [28]. More research is required to resolve this issue. What is certain is that ICDs emerge in response to increases in an individual's medication. It may be that there are susceptible individuals who develop an ICD in response to increasing doses of DRT, but that this finding is masked when averaging across populations.

4. *An identifiable sub-population who are more likely to develop an ICD*

Certain individuals with PD are at greater risk of developing an ICD following DRT. This includes those: with a younger age of PD onset; taking dopamine agonists; or with a personal or family history of ICDs, alcoholism or tobacco use [21, 28, 47].

5. *Neurobiological plausibility*

The development of ICDs and compulsive medication use in those treated with long-term DRT is consistent with the neurobiology of drug addiction, particularly addiction to psychostimulant drugs [48, 49]. Both behavioural and drug addictions appear to involve sensitisation of the dopaminergic reward pathway in the forebrain. This lends plausibility to the hypothesis that chronic use of dopaminergic medications could produce compulsive behaviours (see [13]).

## The Ethical Implications of DRT-induced ICDs

### Ethical Issues in the Clinical Use of DRT

The risk of developing ICDs and DDS when taking DRT medications poses an important but largely under-recognised issue for clinicians and patients. The majority of PD patients experience significant relief from the debilitating motor symptoms of their disease, but somewhere between 6 to 14% will develop an impulse control disorder. Clinicians and patients need to carefully balance the benefits of DRT against the potential harms of ICDs.

Dopamine agonists and levodopa have also been trialled in the treatment of a range of other disorders including: RLS [50], prolactinoma [43], fibromyalgia [42], ovarian hyperstimulation syndrome [51], psychostimulant addiction [52], disorders of consciousness (e.g. persistent vegetative, minimally conscious states) [53] and traumatic brain injury [54], and erectile dysfunction [55]. DRT has also been suggested as a possible treatment of depression [56] and bipolar disorder [57]. It is easier to justify the use DRT to treat neurodegenerative disorders such as PD where the course of the disease is known and the prognosis without medication is poor. A stronger justification and more careful monitoring is warranted for the long-term use of DRT in disorders that are less severe, have an uncertain pathophysiology and may resolve with time or with other treatments. The use of dopamine agonists to treat children with RLS [58], for example, should be avoided [59].

Patients with PD and other neurodegenerative disorders are a vulnerable population who may be desperate for relief of their symptoms. Given that DRT has been used for many years and is a well-established first line treatment of PD, newly diagnosed PD patients may be unaware of or sceptical about possible side-effects that are only now beginning to be understood. It may also be difficult for such patients to appreciate the harm and distress that these ICDs can cause when the prospect of relief from major motor symptoms is foremost in their minds.

For these reasons it is important that PD patients are fully informed of the risks and benefits of DRT and of alternative treatments such as deep brain stimulation. They also need to be informed about therapeutic options to treat an ICD should one develop. Given the risk that ICDs pose to families, this process should also involve family members where possible. Education of patients and families will be important, including measures to reduce the harm caused by ICDs, such as transferring financial control to a family member [1]. It is important that clinicians identify patients who may be vulnerable to developing an ICD by asking about personal and family history of ICD, alcohol and drug abuse. Diagnostic tools are being developed for this process [18, 60].

### Moral Responsibility, Agency and Authenticity in DRT-induced ICD Behaviour

If individuals with PD develop iatrogenic ICDs that arguably would not have occurred in the absence of DRT, can they be held responsible for their behaviour related to their medication use? This is an issue that has already been considered by the courts.

#### *Personal Responsibility*

Should PD patients who developed iatrogenic ICDs be held personally responsible for the adverse consequences of their behaviour, such as the large financial costs or losses incurred as a result of pathological gambling or compulsive shopping? Class action suits in Australia and the US have been brought against pharmaceutical companies that manufacture the dopamine agonists, pramipexole, ropinirole, pergolide and cabergoline. Claimants argue that their pathological gambling, compulsive shopping and hypersexuality were induced by these drugs [4]. A successful case against the pharmaceutical companies depends upon the courts accepting that: (1) these behaviours were caused by DRT; and (2) the company was aware of and failed to warn physicians and patients of the possible side-effects. Success in this litigation (assuming for argument that prior knowledge by the company can be proven) would indicate that courts do not hold individuals responsible for their behaviour and its harmful consequences when the behaviour can reasonably be attributed to medication prescribed to treat a serious medical disorder.

Proving such a claim will require evidence that the chronic use of DRT significantly impaired their decision-making processes or made engaging in these behaviours irresistible. Evidence that DRT increases the incidence of ICDs may not suffice to demonstrate that DRT impairs decision-making sufficiently to

abrogate personal responsibility, but it does provide some evidential support for such a claim. Further study of the neurocognitive impairments induced by DRT may assist in answering these difficult questions.

### *Criminal Responsibility*

The criminal responsibility of individuals who committed offences while receiving DRT has recently been the subject of several court cases [5, 6]. In England, a 58 year old headmaster, who was tried for child pornography offences, was acquitted after the judge ruled that his behaviour was the result of his taking DRT for PD. The man argued that the DRT he had been prescribed for PD "turned him into a paedophile" [5].

According to a news report [5], the headmaster was found with over 8,000 pieces of child pornography on his computer. All but one image had been downloaded after the man was treated with DRT. At the centre of this case was the question of whether DRT caused this criminal behaviour, effectively compelling the individual to commit the offence, or simply unmasked a latent tendency? Did the presence of a single piece of child pornography prior to initiation of DRT establish a latent tendency that DRT unmasked? It is important to note that in the overwhelming majority of cases we have reviewed, the behaviour resolved following cessation of DRT [31].

Answers to these questions may be informed by large scale prospective studies that carefully examine people's behaviour for the presence of premorbid conditions or traits both before and after DRT. Empiricism alone, however, will not resolve the question of the legal and moral responsibility of individuals who commit criminal offences while on DRT. While there is considerable evidence that DRT can cause hypersexuality [22], it is not clear that it specifically causes sexual interest in young children. Science can help to ascertain how a drug may impact upon the brain to motivate behaviour or impair decision making, but judgements about moral and legal responsibility for these behaviours require interdisciplinary analyses by scientists, philosophers, ethicists and legal academics. Whether we believe that the judge's assessment in this case was correct, it shows that the question of moral and legal responsibility in DRT-induced ICDs will need to be addressed by the courts.

### *Authenticity and Self Understanding*

The reports that DRT can produce new forms of behaviour, or intensify manifestations of pre-existing behaviours, raises the question of *authenticity*: are these individuals' actions and choices expressions of their "true selves" or own intentions? Are their actions consistent with their sense of themselves, or are the behaviours induced by dopaminergic stimulation of their reward pathways?

Defining authenticity is a challenging task. Is authenticity simply consistency with one's previous behaviour, consistency with one's stated intentions, or does it require identification with a particular desire or choice of action? In drug-based addictions, a distinction is often made between the desire to consume a drug (a first order desire) and a reflective decision to abstain from drug use to avoid the harm that such use causes (a second order desire) [61]. The first order desire to consume drugs over-rides the second order wish to avoid harm to self or others. It is often argued that an addicted individual is acting authentically only when they act according to their second order desires [61, 62], although this interpretation is open to debate [63]. Implicit in this argument is the assumption that only decisions to avoid known harm can be authentic. However, people can and do choose actions that risk significant harm (e.g. mountain climbing). Authenticity does not require that a decision should be free from harm. A similar argument is likely to be made in the case of DRT-induced ICDs, and will be open to similar criticisms.

In many cases of DRT-induced ICDs, the behaviours are so harmful and aversive that individuals take significant steps to avoid them, such as reducing their DRT medication potentially worsening their PD symptoms, or trying other more invasive forms of treatment such as deep brain stimulation. In such cases, it could be argued that these behaviours do not represent authentic choices that the affected person identifies with or wishes to pursue.

There are cases, however, in which DRT induces behaviour that individuals claim are authentic. For example, one male who became fascinated with anal sex following DRT claimed that he had these desires prior to DRT treatment but was too embarrassed to act on them [64]. The medication allowed him to "realise these desires". His interest in these sexual behaviours stopped following a change in his medication, and he

later expressed regret at his behaviour. Similar experiences have been expressed by users of other drugs that affect the dopaminergic system. Singh [65] interviewed adolescents treated for ADHD with Ritalin (a drug which also increases dopaminergic stimulation) and their parents, and found that the attribution of authenticity to various actions depended on whether the behaviour was seen as positive or negative. For example, a child's bad behaviour was often attributed to a failure to take their medication, whereas success on the sporting field was more likely to be attributed to the child [65, 66]. This reflects a common human characteristic documented by social psychologists to take personal credit for our successes and blame circumstances for our failures. There has been no attempt as yet to examine whether DRT patients believe that these changes in behaviour are authentic expressions of who they are or simple neurochemical reflexes.

### *The Neuropsychology of DRT and Drug Addiction*

If we accept that DRT is a contributory cause of ICDs in people who would not have otherwise behaved in this way, we still need to establish how DRT affects their decisions, and whether these effects are sufficient to absolve individuals of responsibility for their behaviour. Are affected individuals compelled to act in ways that they would not have otherwise? To what degree is DRT unmasking a latent tendency by exacerbating existing personality traits (e.g. impulsivity) or undermining the person's cognitive capacity to resist pre-existing urges? If individuals are compelled to do things that they would not otherwise do, it is hard to see how they could be held legally or morally responsible for behaviour while receiving DRT. Even if we accept that pre-existing traits play a contributory role, there is good reason to question culpability. It may still be unreasonable to hold people responsible for latent desires that they would have otherwise resisted, particularly when their capacity to resist these impulses is restored by ceasing DRT.

To better understand the moral and legal relevance of the effects of DRT on decision-making and behaviour we need to answer the following sorts of questions: What part of the decision-making process is affected, and to what extent? Does DRT impair the capacity to comprehend or reasonably assess the costs and benefits of one's actions (i.e. impairing cognitive capacity)? Does DRT increase the salience of various rewarding activities, making impulses harder to resist (that is, impairing volitional capacity)? Or does DRT decrease an individual's concern about the adverse consequences of a decision?

It may be useful to compare issues of moral and legal responsibility in DRT-induced ICDs with other disorders for which claims of criminal exculpation have been made (e.g. sleep disorders, automatism, mania and psychosis) (e.g. see [67]). Such analyses will need to consider the relevance of differences between these cases and DRT-induced disorders. For example, in some cases behaviours emerge as a result of *not* adhering to medication (e.g. in persons with psychoses). There are important neurocognitive differences as well; some of these conditions involve disorders of consciousness rather than disorders of volition.

Moral responsibility in the case of drug addiction may prove a more useful comparison [13]. The chronic use of DRT can lead to compulsive drug seeking and taking (or DDS) that would be defined as addiction or drug dependence in psychiatric diagnostic systems [26]. DRT and addictive drugs such as cocaine also have similar impacts upon the reward circuitry of the brain [13, 48]. Research of DRT-induced ICDs and DDS has shown that rewarding activities increase the release of striatal dopamine in individuals with an ICD or DDS and sensitises the dopaminergic reward pathway [68]. This is thought to represent the increased salience of the activity in which they engage [13]. Persons with an ICD also have an impaired ability to learn from negative experiences while taking their DRT medication [68]. Similar changes are also found in persons suffering from drug addiction [69].

Legal judgements that long-term DRT use can absolve an individual for criminal responsibility, as in the case of the British headmaster [5], contrast with court decisions on the responsibility of addicted persons for behaviour arising from their chronic use of drugs (e.g. alcohol, amphetamines, cannabis, and cocaine), which also involves impaired executive function and impulse control. Addicted persons are generally held to be responsible for their actions while under the influence of these substances including crimes committed to finance their drug use (e.g. drug dealing, robbery or property crime). Courts may take their addiction into account when setting a penalty by diverting addicted offenders into treatment if they plead guilty.

There are several probable differences in attitudes towards DRT-induced ICDs and drug addiction that

may explain differences in the attribution of moral responsibility. One major explanation may well be that affected persons in these two categories have very different reasons for taking the drugs that have impaired their cognitive ability and capacity to exercise personal responsibility. Drug users typically "choose" to use drugs in order to experience their euphoric and other desired effects on cognition and emotions. PD patients who develop DRT-induced ICDs, by contrast, have taken drugs on medical advice to relieve severe impairments arising from a neurological disorder. They are accordingly not seen as morally responsible for their drug use or the behavioural disorders. This is not likely to be the case for a person who becomes addicted to "recreational" drugs. Deeper analyses of the reasons for these contrasting moral attitudes towards the different origins of these forms of impulsive behaviour may prove illuminating.

## Implications for Behavioural Addictions

Behavioural forms of addiction are compulsive behaviours that closely resemble the features of drug addiction, namely, difficulty controlling use and persistence despite harms arising from the behaviour. The list of behaviours in which people can purportedly addictively engage in now includes (in addition to those described previously): internet and gaming [70], prolonged grief [71], reckless driving [72], and love [73]. There has been considerable debate whether these putative disorders are "real" disorders in the same way that pathological gambling and drug addiction are. The apparent ability for DRT to produce ICDs that resemble forms of behavioural addiction, may be seen as adding weight to the dubious claim that all compulsive behaviours are in fact "real" brain disorders and not simply excuses for bad behaviour [74–76].

An emerging understanding of the neurobiological basis of DRT-induced ICDs may reveal the extent to which similar neurobiological mechanisms are implicated in behavioural and drug-based forms of addiction (i.e. dopaminergic reward pathway) [13, 48]. This neurobiological understanding may also assist in the development of more effective therapeutic interventions, whether they be pharmacological, psychological or social, or some combination of these. However, as we have argued elsewhere, a neurobiologically reductive understanding of addiction may have significant adverse ethical and public policy consequences [77–79].

1. Libertarian critics (e.g. [80]) argue that the inclusion of more behaviours under the rubric of "addiction" simply provides an excuse for behaviour that harms others. It may encourage some to abdicate responsibility for their behaviour or for taking steps to change it.
2. The broadening of the use of behavioural addiction may also impact upon the clinical utility of the term. Will an expansion of the use of the category of addiction "banalise" the concept of addiction so that it ceases to have any clinical meaning or utility? Will this trivialise the concept of addiction and adversely affect the way in which we treat people with arguably more serious forms of addiction?
3. The fact that behavioural addictions may involve neuropsychological changes that impair choice, does not necessarily mean that affected individuals warrant a DSM diagnosis. There are important social implications of our use of psychiatric labels. Psychiatric labels can stigmatise and medicalise normal behaviour, and may also increase the unnecessary use of psychopharmaceuticals or other medical interventions that can have significant side-effects.
4. Psychiatric diagnoses may provide a great benefit to a subset of individuals who suffer enormous hardship as a result of their illness, by leading to targeted and effective treatment of their symptoms. However, expanding the category of addictions as a brain disease may also be used to justify the coercive use of invasive medical interventions to "cure" addiction. In China for example, children have been detained in military hospitals and "treated" for internet addiction with electroconvulsive therapy based on the claim that internet addiction is a "brain disease" [81, 82].
5. Medicalisation of these behaviours as psychiatric disorders may focus attention on medical solutions to treat the individual [83]. It may distract us from considering the social factors that facilitate addictive behaviours (e.g. the ready availability of drugs and opportunities to gamble, advertising and promotion of legal drug use, poverty, and lack of education). It may also undervalue

effective social policies for preventing addiction (e.g. restrictions on alcohol and junk food advertising and decreasing ready access to poker machines and online gambling).

Some proponents of neurobiological explanations of addiction argue that their public acceptance will reduce stigma and lead to better treatment of all types of addiction [84, 85]. The history of the treatment of drug addiction and other psychiatric disorders suggests that we should be sceptical about both these claims [86]. Neuroscience has yet to increase the use of treatment, and in the case of other psychiatric disorders, decrease stigma and discrimination [87].

A study of DRT-induced compulsive behaviour may also improve our understanding of the neurobiology of addiction [13]. There has been considerable disagreement in the literature about whether dopamine is the critical neurotransmitter in addiction, with sceptical researchers highlighting the important role of other neurotransmitters systems such as opioids, glutamate, serotonin and norepinephrine [88], and dopaminergic-independent pathways to addiction [89]. The ability of DRT to induce addiction and impulsive behaviour would seem to support a central role for dopamine. The fact that these disorders occur in a population at a lower pre-existing risk of addiction is also important. There are a number of other questions in addiction research that DRT-induced behavioural addictions may help researchers to answer: By what mechanism does dopamine influence learning and reward? Are there pre-existing abnormalities in the dopamine system that make some more vulnerable to developing an addiction? The prevalence of other psychiatric disorders, social and educational disadvantage, and poly-substance use among drug abusing populations often makes it difficult to determine what is a cause and what is a consequence of drug use. DRT-induced ICDs may help scientists to answer some of these questions.

## Directions for Future Research

There are many interesting empirical questions in DRT-induced ICDs that remain to be answered. These include: what is the comparative prevalence of these disorders in the DRT-treated population and the general population; and to what extent impulsive or compulsive behaviours pre-date DRT treatment or are aggravated by it. Answers to these questions will require large prospective studies that explicitly assess patients' personal and family history of these disorders and other well known risk factors for addictive behaviours. Studies so far have largely looked retrospectively at premorbid conditions in ways that are unlikely to pick up all ICD and related behaviours because of patients' reluctance to report them.

While there is growing evidence of the association between DRT and ICDs, the specific neurobiological mechanisms that explain this association also remain uncertain. Neuroscience research on persons with DRT-induced ICDs is needed to better elucidate the type and extent of the DRT-related impairments in decision-making. Do these drugs decrease impulse inhibition, increase the salience of certain activities or increase sensitivity to their rewarding effects? Research suggests that DRT may stimulate mesolimbic circuitry related to engagement in motivated behaviours that have been implicated in ICDs [90]. One interesting puzzle is why DRT is more likely to increase compulsive behaviours rather than the use of alcohol or tobacco [38]? The growing understanding of the neurobiology of addictive behaviour may help us to understand how DRT may cause ICDs in a significant minority of those that take them long-term [1]. There has been no attempt to-date to identify how those who suffer from DRT-induced ICDs and DDS view the impact of DRT on their behaviour. Do they think that their emergent behaviour is an authentic expression of who they are, is it consistent with their true desires, or do they believe that it is a result of their medication? What is their opinion on how DRT affects their ability to control their own behaviour? Do they feel like they are being controlled by the medication? One may expect answers to these questions will vary with the severity of compulsive behaviour, and how harmful or aversive it is. It would therefore be interesting to conduct these studies in a range of patients affected by DRT, as well as with families, carers and doctors.

Finally, DRT-induced ICDs warrant closer examination by ethicists, philosophers of mind, and legal academics. Multidisciplinary research is needed to tease out issues such as: the impact of DRT treatment on autonomy; the moral relevance of this impairment

to legal and moral responsibility; and the agency and authenticity of behaviour arising from DRT treatment. An important legal question that needs to be answered is whether a person's criminal behaviour can be exculpated by their being on DRT at the time of the offence.

## Conclusions

DRT probably can induce ICDs in patients with PD as indicated by: elevated rates of these disorders in PD patients taking DRT; the fact that this is a patient group at lower than usual risk of these disorders; the close temporal relationship of these disorders to DRT (their onset after initiation or dose increase and their remission after cessation); and the biological plausibility of DRT producing these effects.

These disorders raise interesting ethical issues that warrant closer analysis. These include most immediately the clinical ethical issues in: weighing the risk of these disorders against the undoubted benefits of DRT in treating the debilitating symptoms of PD; ensuring informed consent to use these drugs in PD and other conditions for which they are now being prescribed. They also include the more challenging issues of patients' legal and moral responsibility for behaviours that harm themselves (e.g. problem gambling) or others. Ethicists, philosophers and legal academics interested in the issue of moral responsibility in addiction may find it useful to explore the implications that these disorders have for our understanding of more familiar forms of drug-based and behavioural addictions.

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