Are You Morally Modified?: The Moral Effects of Widely Used Pharmaceuticals

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Are You Morally Modified? *The Moral Effects of Widely Used Pharmaceuticals*

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Abstract: A number of concerns have been raised about the possible future use of pharmaceuticals designed to enhance cognitive, affective, and motivational processes, particularly where the aim is to produce morally better decisions or behavior. In this article, we draw attention to what is arguably a more worrying possibility: that pharmaceuticals currently in widespread therapeutic use are already having unintended effects on these processes, and thus on moral decision making and morally significant behavior. We review current evidence on the moral effects of three widely used drugs or drug types: (i) propranolol, (ii) selective serotonin reuptake inhibitors, and (iii) drugs that effect oxytocin physiology. This evidence suggests that the alterations to moral decision making and behavior caused by these agents may have important and difficult-to-evaluate consequences, at least at the population level. We argue that the moral effects of these and other widely used pharmaceuticals warrant further empirical research and ethical analysis.

Keywords: moral psychology, moral enhancement, moral decision making, moral judgment, oxytocin, propranolol, selective serotonin reuptake inhibitors

The prospect of the development of pharmaceuticals designed specifically to enhance normal cognitive, affective, and motivational processes has alarmed a number of thinkers. They have worried that these pharmaceuticals may be used to enhance human beings in ways that are unacceptable because they conflict with the appropriate attitude we ought to take toward our nature, because they raise significant social justice concerns, because they may have serious side effects, and for other reasons (Fukuyama 2002; Kass 2003; Sandel 2007). Pharmaceuticals designed to *morally* enhance aspects of human psychology or behavior—for example, by producing morally better dispositions, motives, decisions, or behavior—have come in for especially strident criticism (Harris and Chan 2010; Harris 2011, 2012; Sparrow, 2014).[1] Although debates about neuroenhancement in general, and moral enhancement in particular, are important, we believe that there is a more urgent issue confronting us today. Whereas the pharmaceuticals that have attracted the most interest are still at the experimental stage, or are used only by a relatively small number of people (in psychiatric contexts, or in a few cases off-label, with the aim of enhancing cognition), there are a number of pharmaceuticals already being used on a large scale that affect human cognition and emotion. Analyzing how these

pharmaceuticals might alter our psychology, and especially our *moral psychology*, is therefore a pressing task, yet it is a task on which surprising little effort has been expended.

In this article, we review some of the available data on a number of pharmaceuticals currently in use and demonstrate that these pharmaceuticals alter either moral decision making or morally significant behavior. We understand moral decision making as the process of forming judgments about how agents (the decision-maker or other people) ought, morally, to act. We understand morally significant behavior, which we henceforth often refer to simply as 'moral behavior,' as human behavior that is guided by, conforms with, or violates moral *norms* in some significant way. It is beyond the scope of this paper to try to offer a precise definition of 'morality.' But on any plausible understanding of morality, it will centrally include norms concerned with benefiting and harming other agents. We focus herein on this core part of the moral domain.

As we shall see, most of the pharmaceutical effects identified to date are relatively small, but they may nevertheless be large enough that there will be real-world situations in which they cause agents to make decisions or engage in behavior that they would not otherwise have made or engaged in. Moreover, collectively the influence of small changes over large numbers of people may be very substantial. We hope that the demonstration that these pharmaceuticals influence important elements of moral decision making and behavior will motivate others to engage in the scientific and normative work of further exploring these effects, investigating other drugs for similar effects, and examining the ethics of using drugs that have these effects. Given that literally millions of doses of cognition- and affect-altering drugs are consumed annually, empirical and philosophical analysis of their moral effects is an urgent task.

Pharmaceuticals in Current Use

In this section, we review some of the available data on how widely prescribed pharmaceuticals might influence psychological processes, especially the processes involved in moral decision making. It must be stressed that the pharmaceuticals upon which we focus in this section are not the only drugs currently being used that may have effects on moral decision making. Other pharmaceuticals, and especially those that have been investigated as general cognitive enhancers, might also have been included. Examples of such enhancers include modafinil, atomoxetine, and methylphenidate. Atomoxetine and methylphenidate, both of which are indicated for attention deficit hyperactivity disorder (ADHD), are prescribed extremely widely: the U.S. Drug Enforcement Administration (2011) reports around 15 million prescriptions for methylphenidate annually. Improving impulse control in attention deficit hyperactivity disorder has significant effects on moral behavior, among other things, reducing risk of harm to others. Pramipexole, and some other dopamine agonists used to treat parkinsonism, are further examples of drugs with morally important behavioral effects. These drugs are well-known to produce pathological gambling and hypersexuality in some people, as well as, more rarely, to induce extreme paraphilias (Bostwick et al. 2009; Wolters et al. 2008). In one case, a man using pramipexole was acquitted in a case involving downloading of child porn because the court felt that this behavior was uncharacteristic and had been induced by the drug (Irvine 2008).

It has also not gone unnoticed that drugs employed in psychiatry to reduce the risks of harm have an important moral dimension. For example, Spence (2008) notes that "the antipsychotics and mood stabilizers taken by those with major psychoses, the anticraving, substitute and deterrent medications taken by those with addictions (especially disulfiram, given the serious consequences of any subsequent relapse), the antipsychotics accepted by those with personality disorders to reduce their impulsivity and aggression, the antilibidinal medicines accepted by sex offenders" may "enhance morality." Finally, anxiolytics—drugs used to treat disorders involving excessive anxiety—may also have morally significant effects, given that anxiety can cloud decision making, including moral decision making.

The moral effects of the drugs just surveyed are rather straightforward and unsurprising. However, the influence on moral decision making and behavior of drugs influencing general cognition and emotion can be more subtle and less predictable. In what follows, we therefore focus on pharmaceuticals that are widely used but whose moral effects would have been rather more difficult to foresee.

Although none of the pharmaceuticals on which we focus were designed primarily to influence moral decision making and behavior, some were designed to alter other psychological states. We discuss, for instance, antidepressants that are prescribed for the alleviation of clinical depression. Others are, however, prescribed typically for the treatment of somatic problems, but may also have important effects on psychological processes. We begin with an example of this sort.

Propranolol

Propranolol is β-blocker widely prescribed for the treatment of hypertension. Although it is no longer a first-line treatment, tens of millions of people have taken it over the past four decades. It continues to be used for hypertension, angina, migraine, and other conditions. Propranolol is also used to reduce performance anxiety, for instance by musicians. It is a drug with a wide range of neural effects, but one of its main actions is to block the effects of adrenaline and noradrenaline (epinephrine and norepinephrine) on the β_1- and β_2-adrenoceptors; hence the name 'β-blocker.'[2]

Propranolol has recently been investigated as a treatment or prophylactic for posttraumatic stress disorder (PTSD). PTSD, according to one widely accepted theory, arises from the overconsolidation of traumatic memories. The experience of traumatic events causes the release of endogenous adrenaline, which plays a role in memory consolidation. This process is probably an adaptation, because it would typically have been highly advantageous to our ancestors to have a powerful memory of traumatic events—this memory might motivate the avoidance of cues that predict a repetition of the trauma. In PTSD, however, these same mechanisms lead to recurrent and disruptive, and probably maladaptive, distress. The mechanisms for memory consolidation must strike a fine balance. When they are working well, they cause us to recall the traumatic event with an appropriate degree of vividness, but they can misfire by causing the emotional impact of the memory to be so great that recall itself is retraumatizing. When this occurs, a vicious cycle may begin, with recall of the traumatic memory in response to cues causing the release of adrenaline and the consequent deeper consolidation of the memory (Pitman and Delahanty 2005). The memory may also come to be cued by an ever wider range of environmental stimuli.

If this account of the etiology of PTSD is correct, it might be possible to treat the disorder, or even better, to prevent its occurrence, by blocking the effects of adrenaline on memory consolidation. There is evidence that the administration of β-blockers affects memory consolidation in this way (Cahill et al. 1994; McGaugh 2000). Administration of propranolol, either in the immediate aftermath of a traumatic event, or at times of possible memory reconsolidation, might therefore help to alleviate the symptoms of PTSD by preventing overconsolidation of memory. Building on this hypothesis, Roger Pitman and colleagues (Pitman et al. 2002; Pitman and Delahanty 2005) have produced evidence suggesting that PTSD may be preventable by β-blocker administration.

There are a number of ethical issues raised by this research, which have not escaped attention. If PTSD involves the overconsolidation of memory, the use of propranolol might cause the opposite problem: *under*consolidation. Memory is central to identity in the narrative or psychological sense: we understand our lives in ways that center around an ongoing narrative. For this reason, erasing or even substantially weakening the memory of genuinely significant events threatens to leave us with a distorted understanding of our own lives and of our relations to the world. For this reason, philosophers have worried that the use of propranolol to treat PTSD may threaten goods we have reason to value. For instance, Hurley (2007) worries that erasing trauma blocks our epistemic access to the meaning of traumatic events, and Evers (2007) suggests that propranolol might promote what she calls mendacity: even if users recall what happened, because they have been inoculated against

the emotional effects of trauma, they will live as though the traumatizing events had not occurred.

Although these worries about the use of propranolol to treat or prevent PTSD are important, it is more urgent to respond to the ways in which propranolol is *already* affecting cognition. Because it has been used on a large scale for decades, we ought to expect it to have had effects on the cognition of ordinary people in multiple ways. These effects, we suggest, are likely to involve psychological processes beyond those involved in memory.

Propranolol is known to have an effect on the memory of some of those people taking it, even for somatic conditions like hypertension. In addition, there is evidence of some relatively subtle effects on the judgments of subjects taking propranolol at the dosages prescribed for the treatment of PTSD. Corwin et al. (1990) tested subjects taking propranolol on a short-term memory task, where the task was to judge whether or not an item on a list shown to subjects had appeared on an earlier list. They found that normal subjects on propranolol were significantly more likely than controls to say that a word was not on the earlier list, thus exhibiting a form of aversion to risk that is known as 'conservative bias.' This result has been replicated independently (Callaway et al. 1991).

This conservative bias may affect the behavior of agents in the real world: there are many situations in which correctly or incorrectly reidentifying a person, an object, or a situation may be important morally. Most obviously, a conservative bias in memory might lead witnesses in legal cases to be less likely to identify a defendant as the perpetrator. Whether this is a good or bad effect depends on many factors. Given the frailties of eyewitness testimony, it may be that a conservative bias is actually a good thing, in many cases, leading to fewer wrongful convictions; at least, that is a permissible conclusion from the fact that studies of convictions later overturned on the basis of incontrovertible DNA evidence reveals that in fully 90% of cases the defendant was convicted at least in part on the basis of eyewitness testimony (Gazzaniga 2005).

Recall of information is not moral judgment; rather, it is upstream of moral judgment. That is, it is an input that feeds into moral judgment. However, it is not therefore any less significant; moral decision-making processes can only work on the information which is fed into them. There is, however, reason to suspect that propranolol might directly influence the very processing underlying moral decision making.

A number of researchers believe that emotions and even "gut reactions" play an essential role in causing or constituting many moral judgments. That is, we often judge whether an action is right or wrong, permissible or impermissible, by reference to how it makes us feel. If we feel unease when contemplating an action, we judge it wrong, whereas positively valenced feeling causes us to judge it right or at least permissible. Evidence for this hypothesis comes from several sources. For example, several studies have suggested that unconscious disgust responses can influence whether some act is perceived as morally wrong (Haidt 2001). Wheatley and Haidt (2004) tested the hypothesis directly by manipulating subjects' disgust response utilizing post-hypnotic suggestion. Subjects who felt a pang of disgust when reading about moral transgressions rated them as significantly worse than controls. These results might be understood within the framework of the somatic marker hypothesis, according to which somatic states—or neural representations of somatic states—influence explicit responses (Damasio 1996). On this hypothesis, our experience of somatic states orients us toward relevant stimuli and shapes our decisions.

Propranolol acts to block the transmission of a neural signal by blocking adrenergic receptors in the amygdala, a limbic brain region strongly linked with associative learning and emotion processing (Pitman and Delahanty 2005), and one of the three key brain regions proposed to mediate somatic markers (Bechara et al. 2003). Given that the stress hormones (adrenaline and noradrenaline) blocked by propranolol also play a causal role in producing the gut reactions that seem to guide moral judgment, it can be predicted that moral judgments will differ in subjects under its influence. We might expect, for example, that moral judgments that are typically triggered by strong emotional responses would be blunted in

users of propranolol. This might make propranolol users less vulnerable to the biasing influence of morally irrelevant emotional influences, but might also diminish the influence of affective responses that, on some views, play a key part in our moral sensibility.[3]

There is yet a further important way in which propranolol could influence morally significant behavior. Negative attitudes toward people who are different in ethnic origin, nationality, religion, gender, and so forth remain a central source of conflict. Although explicit prejudice is now somewhat less common in developed countries, there is extensive evidence that biases against members of such 'outgroups' continue to operate at an implicit, unconscious level, even in educated individuals who, at the conscious level, would passionately reject such prejudice (Greenwald et al. 1998; Nosek et al., 2007). Such implicit bias can influence behavior in subtle but important ways—for example, by leading to avoidance behavior or by making a black person or woman seem to be a weaker candidate for some post, independent of objective criteria.

Several studies have suggested that implicit prejudice involves a strong emotional component. For example, Phelps et al. (2000) found increased amygdala activity when White participants viewed faces of unknown Black people, a finding confirmed by other studies (Amodio 2003; Lieberman et al. 2005). These findings suggest that implicit bias might involve immediate fear-like reactions, mediated by activity in the amygdala. Because propranolol has been shown to play a role in emotional memory and emotional perception (Cahill et al. 1994; Harmer et al. 2001), and to reduce amygdala responses to both facial expressions and visual emotional stimuli (Hurlemann et al. 2010; van Stegeren et al. 2005), one might expect that propranolol would blunt implicit bias. Our own research provides strong support for this hypothesis. We found that a single, 40-mg dose of propranolol led to a significant reduction in implicit racial bias, as measured by a standard test, compared with placebo (Terbeck et al. 2012). Because this is only a first study, it would be premature to draw general conclusions, and further research is needed to confirm that this effect can also be observed in chronic users of propranolol (and perhaps other β-blockers) outside the laboratory. However, to the extent that this hypothesis is further confirmed, propranolol would provide a paradigmatic example of a widely used drug that turns out to have important and utterly unexpected effects on behavior that are highly significant from a moral point of view.

Selective Serotonin Reuptake Inhibitors

Whereas propranolol is typically prescribed for the treatment of somatic medical conditions, selective serotonin reuptake inhibitors (SSRIs) are prescribed for the treatment of depression and a wide range of anxiety disorders. SSRIs block the reuptake of serotonin in the presynaptic nerve terminal, thereby increasing its activity at the synapse. Some of these drugs also have similar effects on other neurotransmitters, including noradrenaline and dopamine (Bymaster et al. 2002). They are used to alleviate depressed mood and excessive anxiety, but have also been shown to have effects on moral behavior. For example, in rare cases, they seem to have extreme morally *negative* effects on behavior. It has been claimed, for example, that the SSRI paroxetine has played a role in triggering violent acts such as murder in some users.[4]

Other findings show that at least some SSRIs can produce more subtle changes in social behavior in healthy volunteers. For example, some SSRIs seem to make subjects more cooperative and less critical of others (Knutson et al. 1998). They also seem to increase social affiliative behavior (Tse and Bond 2002, 2003). Tse and Bond (2002) had subjects play the Dictator game—a game in which a 'dictator' decides how a certain sum of money is to be divided between the dictator and another participant—and found that subjects administered the SSRI citalopram divided the sum more fairly than controls. Conversely, depletion of tryptophan—a serotonin precursor—leads to lower rates of cooperation in the Prisoner's dilemma game (Wood et al. 2006). The effect was only evident for subjects with depleted tryptophan in the first round of interaction, suggesting that adequate serotonin is needed only for establishing a cooperative pattern

of response, not for maintaining it.

Further experiments suggest that SSRIs also influence other fairness-related behavior. In the Ultimatum game, one player, the proposer, decides how a sum of money shall be split between the proposer and another player. The second player can either accept the offer and take the amount the proposer has offered, or reject it, in which case neither player gets anything. Normal subjects typically reject offers they regard as unfair, despite the fact that rejection decreases their payoff (in a one-shot game), although what is regarded as unfair can differ from culture to culture (Oosterbeek et al. 2004). Crockett et al. (2008) found that depletion of tryptophan led to increased rates of rejection of unfair offers relative to controls. This suggests that SSRIs may have the contrary effect, thereby making subjects easier to exploit by modulating their assessment of what counts as unfair.

More recent work has been taken to suggest that potentiating serotonin increases aversion to directly causing harm to others (Crockett et al. 2010). Because rejecting an unfair offer harms the proposer in the ultimatum game, researchers have suggested that increased levels of serotonin lead to high rates of acceptance of unfairness by making takers more averse to harming others. Evidence for this claim comes from studies of the effect of citalopram on subjects' judgments in moral dilemmas where saving the lives of several people requires seriously harming another person (Foot 1978; Thomson 1971). In the standard dilemma of this type, a trolley is hurtling down a railway line toward five people on the track. You can prevent the trolley from hitting and killing the five people, but only by diverting the trolley onto a side track where one person is standing. If you divert the trolley, the five will live, but the one will die. If you do not, the five will die. Administration of citalopram decreased subjects' willingness to choose that one person be harmed to save several, but only in so-called 'personal' moral scenarios where the harm was direct and emotionally salient (e.g., because it involved directly pushing a person onto a track in front of a trolley, rather than merely pushing a lever). Interestingly, further analysis revealed that this effect was driven by an increase in harm aversion only in subjects who were already highly empathetic before administration of the drug.

Harm aversion is often morally praiseworthy and can lead to better moral decisions and behavior—indeed, both psychopaths and normal individuals who have psychopathic tendencies tend to be less averse to harming other individuals in the 'personal' moral scenarios described (Bartels and Pizarro 2011; Koenigs et al. 2011). It is to be expected that a reduced aversion to harming others will often have highly antisocial effects. In some circumstances, however, it may nevertheless be desirable for people to be willing to inflict harms on others (or at least accepting of the need to do so). Punishment for the violation of social and legal norms involves the infliction of harms on unwilling victims; such punishment is plausibly needed for the maintenance of fair institutions and social trust. Too many individuals strongly averse to inflicting direct harms on others may lead to suboptimal results, especially when these individuals exercise power within the justice system. A refusal to cooperate with those who would take advantage of weakness and vulnerability is arguably also a virtuous disposition, inasmuch as it is likely to play a role in ensuring that cooperative behavior is rewarded and thereby encouraged. Refusal to cooperate is also desirable when the aim of the cooperative behavior is immoral. For example, cooperation within the Nazi regime was clearly not desirable. Whether SSRIs cause morally better or morally worse behavior depends on many factors, including the preexisting dispositions of subjects who take them, and the range of cooperative or conflictual interactions into which they are likely to enter. For example, we would not want judges and jurors to be extremely averse to imposing harm, but we might value different dispositions in social workers and doctors.

It is not yet clear whether the effects of SSRIs on moral decision making and behavior are on the whole positive or negative. This is a matter for further research and debate. Our aim here has rather been to point out that it is becoming increasingly clear that SSRIs, a form of medication currently used by millions of individuals, *do* have such effects.[5]

Oxytocin

The hormone and neurotransmitter oxytocin is best known for its somatic effects—it facilitates birth and breastfeeding in humans and other mammals—but it also influences morally significant behavior. For example, in nonhuman mammals oxytocin seems to mediate pair bonding, maternal care, and other prosocial behaviors (Insel and Fernald 2004), and recent studies suggest that it plays a role in mediating trust, cooperation, empathy, and generosity in humans.

Oxytocin is produced naturally in the brain's hypothalamus and released into both the brain and bloodstream. It is also sometimes administered in obstetric settings, for example, to induce labor. The effects of medical oxytocin administration are unlikely to be significant, however; unless it is administered via nasal spray, little of the hormone crosses into the brain. Much more significant is the fact that several other drugs—including widely used ones—are thought to affect the release or metabolism of the hormone. For example, use of the combined oral contraceptive pill, currently used by more than 100 million women worldwide, has been associated with increased baseline oxytocin levels and is thought to increase oxytocin secretion (Stock et al. 1994). Similarly, glucocorticoids, widely used to treat asthma and other disorders of inflammation, are thought to modulate both the release and activity of oxytocin (Liberzon, and Young 1997; Link et al. 1993). A recent study found that, compared with placebo, administration of the glucocorticoid cortisol increases plasma oxytocin levels in some women (Tops et al. 2007). Meanwhile, the anxiety-reducing drug buspirone has been shown to increase oxytocin levels in rats (Bagdy and Kalogeras 1993).

What morally significant effects might drugs that influence oxytocin activity be expected to have? Experiments involving intranasal administration of oxytocin may give us some idea. One possibility is that they might increase levels of trusting behavior. Kosfeld et al. (2005) investigated the relationship between oxytocin and trust in a simple game of cooperation. Research subjects were divided into pairs and the first member of the pair (the 'investor') was asked to choose an amount of money to give to the second member (the 'trustee'), knowing that the second member will receive three times the amount of money given. The second member then chooses an amount of money to return to the first member. The initial payment can thus be viewed as a signal of trust, whereas the return payment can be interpreted as an indication of trustworthiness. A greater level of trust signaled by the investor increases the total amount of money to be allocated between the two players, but the investor benefits from this only to the extent that the trustee is trustworthy. Before playing the game, participants were randomized to receive a nasal spray containing either oxyotocin or placebo. Investors administered oxytocin exhibited significantly more trusting behavior—that is, they entrusted the trustee with a significantly greater amount of money (Kosfeld et al. 2005).

If oxytocin administered by nasal spray can induce more trusting behavior, we might expect that drugs inducing greater endogenous oxytocin release (or reduced breakdown) would have similar effects. The desirability of such an effect is difficult to assess. Whether trusting others benefits an individual depends on how trustworthy those others are: trusting the untrustworthy typically results in exploitation, whereas failing to trust those who *are* trustworthy can prevent mutually beneficial forms of cooperation. What is important, from the point of view of individual self-interest, is that our trust mirrors others' trustworthiness. There is some evidence that high levels of oxytocin may lead to levels of trust that are excessive by this standard: Baumgartner et al. (2008) found that oxytocin inhibits the attenuation of trust after repeated betrayal. On the other hand, oxytocin itself may help to increase trustworthiness, as well as trust. In a similar game to that used by Kosfeld et al., Zak et al. (2004) found that receipt of a signal of trust by the trustee is associated with a spike in oxytocin levels and that the degree of trustworthiness exhibited by the trustee is correlated positively and significantly with oxytocin level. Thus, in a population with universally elevated oxytocin levels, increased trust may be matched by increased trustworthiness.

Even if elevated oxytocin levels do lead to *too much trust* from an individual point of view, whether they lead to *socially harmful* levels of

trust is a further matter. Being too trusting for one's own good may have social benefits. For example, if untrustworthy people are repeatedly trusted, they may become less inclined to betray others' trust.[6] On the other hand, high rates of indiscriminate trust in a population might *increase* untrustworthiness by removing any incentive to demonstrate trustworthiness to benefit from continued trust in the future.

The ethical picture is further complicated by the fact that oxytocin's effects on trusting and other 'prosocial' behavior toward others seem to be sensitive to the group membership of those others. De Dreu et al. (2011) presented participants who had been randomized to receive either oxytocin or placebo via nasal spray with 'personal' moral scenarios, such as the trolley dilemmas described, in which one individual could be sacrificed to save a greater number of others. Participants administered oxytocin were significantly more likely to sacrifice a different race individual to save a group of race unspecified others than they were to sacrifice a same race individual in the same circumstances. Among participants administered placebo, the likelihood of sacrificing an individual did not depend on the racial group of the individual. The bias toward in-group members in the oxytocin group seemed to be driven by a greater reluctance to sacrifice same race individuals, because the likelihood of sacrificing different race individuals was the same for the oxytocin group as for controls. This suggests that the prosocial effects of oxytocin may be limited to in-group members.

Further experiments by De Dreu's group indicate that oxytocin can also *reduce* prosocial behavior toward out-group members where this helps one's in-group. Administration of oxytocin to subjects before their participating in a group-based financial game induced 'tend and defend' reactions: it increased trust and cooperation within groups, but also increased noncooperation with (although not aggression against) members of other groups when this helped to protect one's in-group (De Dreu et al. 2010).

This work suggests that the so-called 'prosocial' effects of oxytocin might be more aptly characterized as 'pro–in-group' effects, because the hormone can in fact induce antisocial behavior when this conduces to the interests of one's in-group. Increased bonding within a family might be beneficial, and might help with the moral development of children. However, in-group favoritism, although seemingly benign, may also drive many of contemporary society's greatest evils, such as genocide and terrorism, as well as more mundane but pervasive problems like class and race differences in wealth, health, and political power. Given this fact, and assuming that the effects of oxytocin are replicable and robust, it seems doubtful whether drugs that increase oxytocin levels would have ethically desirable effects on behavior, even if they motivate more prosocial behavior within groups. Again, however, this is likely to be context dependent. For example, in circumstances where an individual regards humanity as a whole as her in-group, the effects of elevated oxytocin levels may be less problematic than where 'in-group' is understood in narrower ways. It should be stressed that how agents draw the lines between in-group and out-group seems to be sensitive to context. Laham (2009) found that subjects were more likely to classify others as out-group members when using an exclusion mindset—that is, when deciding which subjects to exclude from the moral circle—than when using an inclusion mindset. This suggests that the social and political environment will influence whether subjects classify others as belonging to their in-group or not, and that therefore assessments of the ethical impact of oxytocin will have to take this environment into consideration (Table 1).

Discussion and Proposals

The evidence reviewed is a small slice of the data available on the ways in which pharmaceuticals modulate moral decision making, as well as the upstream influences on such decision making and its downstream implementation. In some cases, the effects on cognition and behavior seem to be rather small. However, where drugs are used widely even small moral effects on individuals should not be ignored, because they might aggregate to have a serious impact. Many of the most serious challenges currently facing humanity—climate change, pollution, global poverty, and war—can all, arguably, be attributed to widespread but

Table 1. Possible Moral Effects of Some Widely Used Pharmaceuticals

Drug (Class)	Main Current Use(s)	Possible Morally Significant Effects
Alcohol	Recreational	Impulsivity Hostility Reduced social inhibition Impaired ability to drive
Amphetamines	Recreational Enhancement of attention and alertness Treatment of ADHD, narcolepsy	Increased or reduced activity Increased or reduced restlessness Reduced distractibility Excitation Hostility and aggression Paranoid behavior Drug-seeking behavior owing to addiction
Anti-psychotics	Treatment of psychotic disorders such as schizophrenia	Prevention of paranoid, disorganized behavior and lack of motivation associated with psychosis Restlessness
Atomoxetine (SNRI)	Treatment of ADHD	Reduced classroom rule violation Reduced impulsivity Obsessive behavior Psychosis and mania and associated behaviors
Benzodiazepines	Treatment of anxiety disorders, insomnia, seizures Recreational	Reduced anxiety Aggression Impulsivity Reduced motivation (chronic use) Reduced attention Drug-seeking behavior owing to addiction
Cannabinoids	Recreational Treatment of nausea from chemotherapy, AIDS-related anorexia	Reduced attention Reduced inhibitions Impaired driving ability Impaired short-term and working memory Impaired learning Panic reactions, paranoia and psychosis Illusions of increased insight

Table 1. Continued.

Citalopram (SSRI)	Treatment of major depression and anxiety disorders	Increased motivation due to treatment of depression Reduced anxiety Triggering violence Increased cooperation Reduced criticism of others Fairer distribution of resources Reduced rejection of unfair offers Increased aversion to harming others (in highly empathetic individuals)
Cocaine	Recreational Local anesthesia	Drug-seeking behavior due to addiction Increased friendliness Increased activity Disruption of fear conditioning Increased confidence Irritability, anxiety, agitation and suspicion (in withdrawal)
Combined oral contraceptive pill	Contraception Treatment of polycystic ovary syndrome, endometriosis, painful menstruation, acne	Reduced motivation due to depression: May increase oxytocin secretion, which may cause Increased trust Increased trustworthiness Increased cooperation within in-group Reduced cooperation with out-groups
Disulfiram	Treatment for alcohol abuse	Reduced alcohol use
Glucocorticoids	Treatment for asthma, adrenal insufficiency, autoimmune conditions	Improved concentration and vigilance Memory impairment Improved memory (especially for emotionally arousing events) Mood change and psychosis May increase oxytocin secretion, which may cause Increased trust Increased cooperation within in-group Reduced cooperation with out-groups
L-Dopa	Treatment of parkinsonism	Excitement Confusion Psychosis Agitation and anxiety
Lithium	Treatment of bipolar disorder	Reduced paranoia, grandiosity and risk-taking due to treatment of mania Increased motivation due to prevention of depression

Methylphenidate	Treatment of ADHD, narcolepsy	Increased attention Improved working memory Psychosis Confusion Irritability Effects on dopamine-based reward system
Modafinil	Cognitive enhancement Treatment of narcolepsy, shift work sleep disorder, excessive daytime sleepiness	Increased alertness and attention Improved working memory Anxiety Aggression Effects on dopamine-based reward system
Opiates	Pain relief Anesthesia Treatment of cough, diarrhea, irritable bowel syndrome, opiate addiction Recreational	Confusion and mental clouding Restlessness Excitement Drug-seeking behavior due to addiction
Pramipexole	Treatment of parkinsonism	Pathological gambling Hypersexuality Paraphilias (e.g., pedophilia) Compulsive behaviors (e.g., compulsive shopping and cross dressing)
Propranolol (β-blocker)	Treatment of hypertension, angina, migraine, arrhythmias, myocardial infarction Reduction of anxiety	Reduced memory consolidation Reduced emotional effect of psychological trauma Conservative bias (reduced risk taking) in memory tasks Effects on fear and disgust reactions and thus on moral judgment and implicit bias against outgroup members

Abbreviations: ADHD, attention deficit hyperactivity disorder; SNRI, selective norepinephrine reuptake inhibitor; SSRI, selective serotonin reuptake inhibitor.

relatively minor moral failings. Small changes in the degree to which large segments of the population are concerned about the long-term future, are inclined toward out-group aggression, or are altruistic toward spatially and temporally distant strangers might massively aggravate or mitigate these problems. Similarly, small differences in trust or out-group aversion could have large effects on the results of elections where candidates differ in their ethnic group or perceived trustworthiness. The possibility of such aggregation makes the scientific and ethical assessment of the moral effects of widely used drugs, such as contraceptives, painkillers, antidepressants, and medications used to lower blood pressure or cholesterol, a matter of great practical importance. There is a need to determine what the moral effects of these drugs are, and whether they are desirable ethically.

Existing evidence suggests an ethically mixed picture: in some ways, pharmaceuticals can produce morally better decisions and behavior—for instance, by increasing prosociality—and, in other ways, the very same pharmaceuticals can cause a moral decrement in decisions and behavior. Whether using a particular pharmaceutical induces morally better or worse decisions and behavior depends, crucially, on the individual's preexisting dispositions and the circumstances in which they act, as well as on what the drug is used for and the effect of any underlying condition on moral decision making and behavior.

An agent already high in empathy, for instance, will probably exhibit increased aversion to causing harm under the influence of SSRIs. Whether this is likely, in turn, to result in morally desirable behavior depends on the circumstances in which the agent then finds herself. If an agent is likely to find herself in a situation in which the enforcement of norms by way of punishment is important socially, we may wish to discourage medically unnecessary SSRI use. When antidepressants are indicated medically, in circumstances like these, we may wish to encourage, or even require, that the agent uses alternative antidepressants (although it is possible that many of these may have similar, or similarly problematic, effects, particularly because many other antidepressants also affect serotonin reuptake). It is even possible to envisage circumstances in which we may have to contemplate preventing an agent from using medically indicated antidepressants, because the costs might be too great for others.

The costs and benefits of propranolol are similarly context dependent. We need to compare the cognitive capacities and dispositions of the agent before propranolol use to those she exhibits under its influence, and also to consider the range of circumstances in which she is likely to be required to make moral decisions. Whether propranolol use is advisable or obligatory, permissible or impermissible, depends on a range of factors, some of them extremely hard to assess.[7]

Similar thoughts apply to drugs that increase levels of oxytocin. Whether use of such drugs is desirable, from a moral point of view, may depend on factors such as how trusting or cooperative an individual is to begin with, how trustworthy others are, how sharply in-group/out-group distinctions are drawn, and how effects on individuals might aggregate if these drugs are widely used. Because the moral consequences of the use of pharmaceuticals are so context dependent, where the context includes the political and social factors that influence how agents circumscribe their in-group, assessing the permissibility of their use requires detailed knowledge of agents and their circumstances, including the number of agents who might take the drug, as well as a great deal of further research into the properties and effects of widely used pharmaceuticals. As the case of the trait dependency of the effects of SSRIs indicates, this research must be fine grained: we need to know not only the average effects of pharmaceuticals, but also how they interact with preexisting dispositions of agents and the underlying condition for which they are being used. We lack sufficient knowledge of these factors with regard to an enormous number of widely used pharmaceuticals. Investigating their effects ought to be an urgent priority, given that they may sometimes have significant consequences for moral decision making and behavior. Moreover, this investigation cannot be limited to psychopharmaceuticals, because a range of pharmaceuticals prescribed for somatic conditions also have effects on the brain and mind. Many chemicals involved in the

regulation of somatic processes are also involved in the regulation of neural processes: serotonin, for instance, is involved in cardiovascular regulation, respiration, and sleep–wake cycles as well as appetite, pain sensitivity, and reward learning (Churchland 2011, 98).

Matters are further complicated by the fact that individuals with different moral outlooks might interpret the moral effects of various pharmaceuticals in different ways—for example, the effects of emotions or of group affiliation in moral decision making will be seen as biases on some views but as positive influences on others. A complete assessment of the influence of pharmaceuticals on moral decision making would thus require not only further scientific research, but also important ethical input.

The investigation of the effects of those pharmaceuticals currently touted as cognitive enhancements is an important task. However, it is far more pressing that we investigate the effects of pharmaceuticals currently being used on a large scale. These pharmaceuticals may already be influencing the shape of our societies, for better or for worse. We need urgently to discover how they influence moral decision-making and behavior so that we avoid the worst dangers they pose for us, and perhaps harness them to better ends.

Notes

1. Two of the authors have responded to some of these criticisms elsewhere (Douglas 2011; Persson and Savulescu 2013). See also Spence (2008), Faust (2008), Walker (2009), and DeGrazia (2014).

2. Although we focus here on propranolol, it is plausible that much of what we say may also apply to some of the newer β-blockers that are replacing propranolol as the first line of treatment for hypertension.

3. Our own research confirms this hypothesis: we found that propranolol can significantly alter moral decision making in the context of 'personal' moral dilemmas (Terbeck et al. 2013).

4. See:http://www.healyprozac.com/academicstalking/Post%2019%20-%20Cowen%20Review%20of%20Panorama%20Secrets%20of%20Seroxat.htm

5. John Harris (2011, 2012) has argued that the effects of SSRIs on moral decision making are, on the whole, negative. Whether or not this is right (and we are yet to be persuaded), the important point is that these effects are not merely hypothetical speculations in philosophical debates about 'moral enhancement,' but actual and very widespread, in ways we cannot yet quantify.

6. However, see Schotter and Sopher (2006), who found that trustworthiness increases trust in others but not the reverse.

7. Even if a reduction in implicit negative bias against outgroups is thought to be an unqualifiedly positive effect, the reduction in fear that accompanies it might, in many contexts, lead to rather more negative consequences.

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