

Psychoactive Drugs in Plastic Surgery

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Background: Psychoactive drug use is on the rise in the United States, with plastic surgery patients a potentially susceptible group. This study aimed to determine the incidence of cosmetic and reconstructive patients in our practice taking psychoactive drugs and to compare those values with the national average. Furthermore, we discuss the patient safety concerns when patients withhold their medical history information over the course of their treatment.

Methods: Urban private plastic practice patients who underwent surgery in a closed practice from 2009 to 2016 were divided into cosmetic and reconstructive cohorts. Review for drug use was medical scripts, history, and Surescripts drug reporting. Extracted information includes age, race, procedure, psychoactive medications, and whether or not they stated a mental health diagnosis on their medical history forms. Only patients with complete records were included.

Results: A total of 830 patients were included in statistical analysis. Due to minimal cohort number, 70 men were excluded, as there were no comparative national data. Our analysis found that 33.6% cosmetic patients and 46.3% reconstructive patients used at least one psychoactive drug.

Conclusion: There is a statistically significant difference between psychoactive drug use at our practice compared with the general population and a significantly larger percentage of reconstructive patients taking drugs compared with the cosmetic cohort. (*Plast Reconstr Surg Glob Open* 2017;5:e1282; doi: 10.1097/GOX.0000000000001282; Published online 28 March 2017.)

There is a precipitous increase in the number of patients on psychoactive drugs, which we define here as chemical substances that alter perception, mood, and thoughts of those who take them. This includes antidepressants, stimulants, anxiolytics, mood stabilizers, and antipsychotic medications. A report by Medco found that the number of American women taking psychoactive drugs has increased from 21% in 2001 to 26% in 2010.¹ The influence of these drugs in plastic surgery has recently come to the fore.² This is a significant issue, as a plastic surgeon often must decide if a patient would benefit more from surgery or from therapy.³ In our urban, private plastic surgery practice, we have found an explosion in the number of patients taking psychoactive drugs, prompt-

ing us to investigate potential risks for surgical patients, such as bleeding or anesthetic interactions, and the risks of temporarily stopping the medications perioperatively. These are important drugs to be reported to the anesthesiologist or the surgeon supervising the anesthesiologist to avoid harmful interactions. Given the current prevalence of psychoactive drug usage among plastic surgery patients, this article aims to explore the following issues:

What is the prevalence of psychoactive drug use in practice and is there a difference between cosmetic and reconstructive patients? Is there a difference between plastic surgery patients and the general population in psychoactive drug use? The experimental hypothesis that there is a statistical difference was tested against the null hypothesis that plastic surgery patients do not differ from the general population for psychoactive drug use and reconstructive plastic surgery patients have similar drug use to cosmetic surgery patients.

METHODS

We conducted a review of 830 urban private plastic practice patients who underwent surgery performed by a single board-certified plastic surgeon. Patients who had multiple staged surgeries were counted only once. Seventy

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men were excluded from the cosmetic cohort due to minimal cohort number and no comparative national data. The data collected were divided into 2 groups: 1 of 405 female cosmetic surgery patients from 2013 to 2016 comparable with a group of 322 reconstructive breast patients from 2009 to 2016 (Table 1). Reconstructive patients were defined as any patient undergoing breast reconstruction regardless if they had any cosmetic surgery procedures included in the duration of their treatment. The groups were analyzed for age, race, procedure, psychoactive medications, and whether or not they stated a mental health diagnosis on their medical history forms. To avoid patient-reporting bias objective, Surescripts, a pharmacy database, and outside records were reviewed.

We further divided the 2 groups into binary categories by positive or negative psychoactive drug use. Positive use was defined as any psychoactive medication found on their medical history or Surescripts history during the period of time in which they were treated as a patient at our practice. A Student's *t* test was conducted to determine the statistical significance of sample data as compared with population data from national averages. The *t* test was further divided into categorical classes of each class of psychotropic drugs: antidepressants, stimulants, anxiolytics and antipsychotics, and mood stabilizers, and further tested for statistical significance using a *t* test at an alpha 0.5.

H0cosm = Cosmetic Patients Psychoactive Drug Use = General Population Psychoactive Drug Use
 Hacosm = Cosmetic Patients Psychoactive Drug Use (not =) General Population Psychoactive Drug Use
 H0recon = Reconstructive Patients Psychoactive Drug Use = General Population Psychoactive Drug Use
 Harecon = Reconstructive Patients Psychoactive Drug Use (not =) General Population Psychoactive Drug Use

RESULTS

Sample testing showed that 33.6% of cosmetic surgery patients are on psychoactive drugs compared with the 26% national expected average.¹ Using the national data available, the 7.6% difference between the cosmetic patient sample (*n* = 405) and national population data is statistically significant (*P* = 0.0006); thus, we reject the null hypothesis. The difference between cosmetic surgery patients' psychoactive drug usage and that of the national population was statistically significant, with 95% certainty (Table 2).

Reconstructive patients showed a stronger correlation with 46.27% of the sample patients on psychoactive drugs, compared with the 26% national average. These results were significant (*P* = 0.0001). We reject the null hypothesis. It was concluded with 95% certainty that there is a difference between reconstructive surgery patient's psychoactive drug usage and national population psychoactive drug usage. Female breast cancer patients aged 18–70 years show greater than a 20% difference between the expected and actual percentage of drug usage within this sample subgroup, providing evidence for the psychoactive drug phenomenon.

Statistically significant results were found for both the usage of anxiolytics in reconstructive surgery patients and the usage of stimulants in cosmetic surgery patients, compared with the America's State of Mind report.¹ It was found that 31.06% of the sample population took anxiolytic drugs, whereas the national average is 11%. It was concluded that there is a notable difference between reconstructive surgery patient's antianxiety drug usage and national population antianxiety drug usage. Additionally, it was found that 7.41% of the cosmetic cohort took stimulant drugs, whereas the national average for adult women is 1.9%.

Finally, the data collected from our cosmetic and reconstructive surgery patients showed a high percentage of patients prescribed more than one psychoactive drug. The data from each group, 10.62% of cosmetic surgery patients and 14.91% of reconstructive surgery patients were compared against the national average of 3.1% of the population who take more than 1 psychoactive drug. The finding was statistically significant for both reconstructive and cosmetic surgery patients.

DISCUSSION

The use of psychoactive drugs in patients in general is on the rise, with more than a quarter of the current population taking them.¹ Each class of drugs has its own particular set of risks and considerations for patient safety, particularly during surgery and anesthesia. The benefits of discontinuing a patient's psychotropic drug must be weighed against the physical effects of withdrawal or discontinuation syndrome, in which a patient relapses into a condition that they had up until that point controlled with medication. Those taking psychotropic medications may require more narcotics or anesthesia, and they may be at risk for hazardous drug interactions.

The main classes of psychoactive agents are:

1. Antidepressants
2. Antipsychotics
3. Anxiolytics
4. Stimulants
5. Mood stabilizers

Antidepressants

Antidepressants are among the most widely prescribed drugs in the world; the rate of antidepressant use in the United States has increased nearly 400% from 1988–1994 through 2005–2008.⁴ Antidepressants are divided into three categories: tricyclic antidepressants (TCAs), selective serotonin reuptake inhibitors (SSRIs), and monoamine oxidase inhibitors (MAOIs). Each class of antidepressant works by a different mechanism and has different risks and implications for anesthesia, including drug interactions. Withdrawing a TCA or SSRI may precipitate a relapse of the condition for which it is being used and is to be avoided.⁵

Selective serotonin reuptake inhibitors are considered to have a low-risk safety profile but are not devoid of adverse effects. SSRIs can increase peripheral serotonin in the body by interfering with platelet uptake, especially when taken in combination with tramadol, meperidine,

Table 1. Summary of Psychoactive Drug Categories and Their Effects and Interactions in Surgery⁵⁻⁷

	Classes	Discontinue	Withdrawal Symptoms	Effects/Interactions
Antidepressants	SSRI	No	Yes	Serotonergics (other antidepressants, opioids, CNS stimulants), e.g., tramadol, meperidine (Demerol) or dextromethorphan increases peripheral serotonin and can precipitate a serotonin syndrome Increased risk of bleeding due to their interference with platelet function and a decrease in platelet serotonin storage P450 enzyme inhibition slows drug metabolism, elevating other plasma drug concentrations, e.g., midazolam Type 1 antiarrhythmics (Na ⁺ channel blockers) may cause cardiovascular depressant effects Anticholinergic effects
	TCA	Yes, gradually	Yes	Sympathomimetics (epinephrine, norepinephrine, dopamine) can precipitate a hypertensive crisis Seizures with enflurane Tramadol can result in seizures and a serotonergic crisis P450 enzyme inhibition slows drug metabolism elevating other plasma drug concentrations like midazolam Muscarinic, histaminergic, and alpha-adrenergic blocking effect Renal toxicity Decreased cardiac conduction Anticholinergic effects
	MAOI	Yes, gradually	Yes	Epinephrine can result in severe hypertension Serotonergics (meperidine or dextromethorphan) can precipitate a serotonin syndrome Increased risk of bleeding
	Wellbutrin	No	Yes	Intravenous methylene blue increases blood serotonin levels Reversible MAOIs (linezolid) can precipitate a serotonin syndrome Increased risk of bleeding Hypertensive reactions
	SNRI	No	Yes	Serotonergics (other antidepressants, opioids, CNS stimulants), e.g., meperidine (Demerol) or dextromethorphan can precipitate a serotonin syndrome
Antipsychotics	First generation (typical)	No	Yes	ACE inhibitors (lisinopril, enalapril, and captopril) may increase hypotensive side effects Antacids interfere with absorption of antipsychotics Sudden death related to a prolongation of the QTc interval Thioridazine, pimozide, sertindole, droperidol, and haloperidol all have been documented to cause torsade de pointes Extrapyramidal symptoms Cardiac conduction changes Cholinergic, alpha adrenergic, histaminergic blocking effect Desflurane has been reported to cause seizures Drugs with an antidopaminergic effect (antiemetics, choline, TCAs, melatonin) could exacerbate potential for side effects of the drug
	Atypical	No	Yes	Agranulocytosis
Anxiolytics	Benzo	No	Yes	Sedative
Stimulants	Non-benzo	No	Yes	Sedative, potential narcotics
	Amphetamine salts	No	Yes	Increased heart rate Increased systolic blood pressure Weight loss Depletion of catecholamine receptor storage causing sympathetic response to hypotension
	Methylphenidate	No	Yes	Anesthetic agent action Increased heart rate Increased systolic blood pressure Weight loss
Mood stabilizer	Lithium	Yes, day of	No	NSAIDs and ACE inhibitors (lisinopril, enalapril, captopril) may increase blood levels of lithium and cause toxic effects Diuretics (hydrochlorothiazide) Prolongation of neuromuscular blocking drugs (pancuronium and succinylcholine) Reduction in anesthetic agent requirements Cardiac conduction

ACE, angiotensin-converting enzyme; CNS, central nervous system; NSAIDs, nonsteroidal anti-inflammatory drugs; SNRI, Serotonin-norepinephrine reuptake inhibitor.

and pentazocine. Serotonin syndrome is marked by an increase in blood pressure, rapid heart rate, and agitation, and has also been exhibited to be a risk to patients who take MAOIs, which impair serotonin metabolism.^{5,8} Other

risks to patients taking SSRIs include an increased risk of bleeding due to their interference with platelet function and a decrease in platelet serotonin storage.^{5,9} One study showed a 4-fold greater risk of breast hematoma needing

Table 2. A summary of the Statistical Data Collected from Private Practice Cosmetic and Reconstructive Patients Regarding Taking Psychoactive Drugs

	Drug Category					Total (no overlap)	No. Patients on >1 Drug	Sample Size (n)
	Antidepressants	Antipsychotics	Anxiolytics	Stimulants	Mood Stabilizers			
Cosmetic	72	5	54	30	4	136	43	405
Reconstructive	80	0	100	7	0	149	48	322
Cosmetic	18%	1.2%	13%	7.4%	0.99%	33.58%	10.62%	405
Reconstructive	25%	0.0%	31%	2.2%	0.00%	46.27%	14.91%	322
Baseline national data	21% [1]		11% [1]	1.9% [1]		26% [1]	3.1%	

intervention in cosmetic breast surgery patients who used SSRIs compared with those who did not.¹⁰

Tricyclic antidepressants prevent presynaptic reuptake of norepinephrine and serotonin. This class of antidepressant has risks of more severe drug interactions. First, a reaction between TCAs and tramadol could result in seizures and a serotonergic crisis. Next, an anesthesiologist should be aware of the possibility of a hypertensive crisis from an interaction between indirectly acting sympathomimetic contained in local anesthetic solutions and TCAs.⁵ Finally, and most importantly, the contractile force of the heart has been found to be decreased by increasing levels of TCAs.^{7,11} This can result in hypotension, slowing of sodium channel electrical conduction and result in dysrhythmias.⁷

Monoamine oxidase inhibitors are an older class of antidepressant drug. They can be either reversible or irreversible and function by inhibiting the breakdown of norepinephrine and serotonin. Like other antidepressants, MAOIs carry risks of precipitating a serotonergic crisis of hypertension, agitation, rigidity, convulsions, and hyperthermia when given with meperidine.^{5,12} The combination of MAOIs with sympathomimetics has also been shown to cause hypertensive crises.⁷

Antipsychotics:

There are two classes of drugs used to treat psychotic disorders: typical and atypical. Typical antipsychotics block dopamine, histamine, alpha1-adrenergic, and cholinergic receptors. Atypical antipsychotics may block subtypes of the dopaminergic receptor family and affect the serotonin-2A receptor with reduced extrapyramidal side effects.⁵ Both classes of drugs are significant to a patient’s clinical team because of the high rate of patient relapse if the drug is discontinued. Anesthesiologists should be aware of the complication of sudden death related to a prolongation of the QTc interval and torsades des pointes, a malignant ventricular arrhythmia that is associated with syncope and sudden death.⁶ Thioridazine, pimozide, sertindole, droperidol, and haloperidol all have been documented to cause torsade de pointes and sudden death, but even those antipsychotics without specific documented evidence of these complications have the potential for these serious adverse events.¹³ Therefore, these medications that prolong the QT interval should be avoided and there should be careful cardiac monitoring in patients using these drugs.¹⁴ Other notable reactions include the

concurrent use of an antipsychotic with desflurane, which has been reported to cause seizures, and the use of antipsychotics with drugs producing an antidopaminergic effect like other antiemetics, choline, the TCA antidepressants, and a drug as innocuous as melatonin, which could exacerbate the potential for side effects of the drug.^{5,15}

Anxiolytics

Benzodiazepines are the common drugs used to treat short-term anxiety symptoms and come with little surgical risk to the patient. Medco data show that the rate of usage in middle-aged women (11%) is nearly double the usage in the similar age range for men (5.7%).¹ Antianxiety medications, although sedatives, come with the potential of withdrawal symptoms in patients who have fasted for a prolonged period, like when waiting to undergo surgery, so physicians should be cognizant of possible signs of withdrawal in those patients.⁵

Stimulants

Stimulants are being prescribed in increasing frequency for medical conditions such as attention-deficit hyperactivity disorder (ADHD) in both children and adults. The rates of use of these amphetamine and methylphenidate drugs have skyrocketed in recent years, particularly in the age–sex group of women ages 20–44. From 2001 to 2010, this group showed a spike of 264% in ADHD medication usage.¹ The adult use may reflect the perceived benefit of the side effects not seen as much in the pediatric population, specifically appetite suppression. These drugs, and other closely related sympathomimetic amines have been used for weight loss and have been banned by the FDA due to a significantly increased risk of stroke in users.¹⁶ Stimulants in particular have had multiple unforeseen cardiac effects as the use of amphetamines increases cardiac rate and blood pressure, putting long-term users at increased risk for a cardiac event.

Chronic use of amphetamines causes a depletion of catecholamine receptor storage, which is thought to cause reduced physiologic and sympathetic response to hypotension.¹⁷ Chronic use also leads to tolerance, which could manifest emotionally as depression and fatigue, or physiologically as a diminished pressor response to ephedrine and a diminished anesthetic requirement.^{17,18} Different formulas for ADHD medication could lead to increased anesthesia requirements. Drugs derived from both methylphenidate and mixed amphetamine salts have short acting

and extended-release formulations. A study compared the effect of food on extended-release formulations and found that a large meal affected the drug concentration of the extended-release capsules depending on the drug. Blood amphetamine concentrations were lower when subjects had eaten breakfast, compared with blood methylphenidate concentrations, which stayed constant and were unaffected by the meal.¹⁹ This could be a factor to consider for surgery as a patient fasting preoperatively could lead to increased blood amphetamine concentrations.

Mood Stabilizers

Lithium is a mood stabilizer used to treat manic depression. It affects the flow of sodium through nerve and muscle cells and stabilizes manic episodes. It is known that lithium interacts with neuromuscular-blocking agents, including pancuronium and succinylcholine, and increases the duration of these drugs, making their reversibility more difficult.²⁰ As a result, it would require that those certain anesthetic agents are reduced. Additionally, non-steroidal anti-inflammatory drugs combined with lithium can cause toxic plasma levels as they reduce the excretion of lithium by the kidneys.²¹ It is the general anesthesia recommendation that lithium use is discontinued at least 24 hours before surgery.

In our practice, the incidence of psychoactive drug use in our female cosmetic patients is 33.6% and 46.3% in female breast reconstruction patients. Our data exhibit a high rate of psychoactive drug use in comparison with the general patient population. The number of American women taking psychoactive drugs has increased from 21% in 2001 to 26% in 2010.¹ Moreover, a study by the CDC showed that women are 2.5 times as likely to take antidepressants as men, with the largest age–sex group being women aged 40–59.⁴ Although antidepressant use is on the rise, one study evaluating the prevalence of antidepressant use among breast cancer patients showed that its use has increased from <1% before 1993 to 1.8% from 1993 to 1996, to 8% from 1997 to 2002; clearly these data are out of touch with our findings in 2016.^{10,22} In our practice, the percent use of antidepressants in the reconstructive patients is statistically significantly higher than our cosmetic surgery patients. The high incidence in breast cancer patients could be a result of an increased prescription of antidepressants over time of treatment as depression associates with the disease. Out of the population of breast cancer patients at our practice, 24.8% are taking antidepressants. However, we are unable to identify how many patients were on these drugs before their diagnosis of breast cancers as they presented to our practice only after their diagnosis. Because breast cancer patients may change medications often and undergo repeated surgery, they should update their medical history frequently. As the incidence of Axis I disorders (such as schizophrenia) is unlikely to have changed in recent times, antipsychotics are expected to be the most constant and smallest group. It is the other categories that are in the ascension. Notably, stimulant use has increased among our patients in the last few years. Cosmetic surgery patients are 3 times more likely to be taking amphetamine salts than reconstructive

patients. These are typically younger patients that are representative of the spike in ADHD medication prescription.

We have found from collecting data on psychotropic drug use that a patient's medical history alone will often not disclose a patient's entire medical or drug history. SureScripts, an online portal that lists the medications a patient has filled from their pharmacies over a period of 4 years, has identified underlying medical problems, including psychological or anxiety issues, that patients have not disclosed. Recent studies in psychological issues among plastic surgery patients found 70% of cosmetic patients had Axis II disorders, and 19.5% had Axis I disorders, based on the diagnostic criteria from the *Diagnostic and Statistical Manual of Mental Disorders, third edition, revised [DSM-III-R]*.²³ These results align with previous studies throughout the 1960s, which employed clinical interviews to analyze psychiatric disturbance.²³ One could have anticipated that cosmetic surgery patients use more psychoactive drugs than the general population. However, one may not have anticipated that the psychoactive drug usage of reconstructive patients exceeds both the usage of the general population and the usage of cosmetic surgery patients.

CONCLUSION

Use of psychoactive drugs is endemic in the US population. Plastic surgery patients as a subgroup are even more likely to be on psychoactive medications, with 33.6% cosmetic patients versus 46.3% reconstructive patients. This study shows that plastic surgery patients are more likely to be on psychoactive medications than the general population. Significantly more reconstructive patients (46.3%) took psychoactive medications than did cosmetic patients (33.6%), and the cosmetic patient is more likely to be on a stimulant than and the reconstructive patient on an antidepressant. However, by the end of their treatment, reconstruction patients are more likely to be on medications than cosmetic surgery patients, which have implications for staged surgery. A patient's drug history forms need to be appropriately updated as care progresses as the patient may now be on a psychoactive agent when in surgical care. Modern plastic surgery training with its focus on procedures and products under emphasizes the medical and psychological issues. Training in psychiatry and psychoactive drugs should be incorporated as more of our patients present on them.

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