

*“Anything green that grew out of the mould
Was an excellent herb to our fathers of old...”*

“Our Fathers of Old,” Rudyard Kipling

10. THE ANTIPARKINSON'S DRUGS

THE WAYS IN WHICH THE DRUGS AND POTIONS WORK

Now it's time to jump from generalities about dopamine to some specifics about the pharmacological actions of the individual anti-PD drugs. It was often difficult for my patients to understand how a perfectly legal drug could be addictive, and so I devised the following instruction method: based on the particular mechanism of action of each of the anti-PD drugs, I sorted these drugs and correlated them with well known addictive drugs that used the same mechanism. All my patients knew that cocaine, nicotine, and methamphetamine were addictive. By showing the relationship between the mechanisms of these street drugs and their parkinson's drugs, my patients started to understand why they couldn't reduce their medication without going into an addiction-like tailspin.

Most of the antiparkinson's drugs have “cousins,” drugs that are well known to the person on the street, that use similar, though usually milder, mechanisms to elevate dopamine. Others have different mechanisms from their related illegal (street) addictive drugs but similar overall effects on the brain during use and withdrawal.

And so, here is a brief look at some of the dopamine-enhancing street drugs, their mechanisms of dopamine enhancement, and a comparison with some of the anti-parkinson medications that have similar mechanisms. This is brief because each of these drugs will be discussed in greater detail in the appendices.

Dopamine Agonists – Nicotine

Dopamine agonists have been used in the treatment of PD since the 1980's. Some of the more popular agonist PD drugs are Mirapex, Permax (also known as Pergolide), bromocriptine (Parlodel), Requip, and Cabergolene. These drugs are cousins of nicotine. Nicotine is, of course, a much milder and much less addictive chemical than any of the antiparkinson's drugs. After all, nicotine is not strong enough to allow initiation of movement in a person who can no longer move. Nicotine, in the small amounts delivered via tobacco, merely lifts dopamine levels for a short while. The amounts are not great enough to counter symptoms of Parkinson's disease. However, the gentle nicotine molecule works in the exact same way as the anti-PD meds listed above – it can assume the role of a dopamine molecule on a brain's dopamine receptor, tricking the receptor nerve into firing off as if dopamine, and not nicotine, was in the receptor slot. When the dopamine agonist takes on the job of a dopamine molecule, the remaining dopamines are freed to do their work elsewhere, so the net dopamine activity in the brain occurs at higher than usual levels – whatever “usual” happens to be.

Are the dopamine agonists addictive? Yes, indisputably. Cigarettes are internationally recognized as addictive. Nearly everyone knows that it can be very difficult to quit smoking. Nicotine provides a brief, mild feeling of well-being, but very

quickly after taking up the smoking habit, a user finds that he is irritable and irascible if he doesn't get his regular smoke. Nicotine is addictive because it is a dopamine agonist.

Word play

People who forgot to learn Latin, this author included, often misunderstand the word agonist at first. We imagine that “agonist” means “works against.” Well, that's wrong. An ***antagonist*** is something that works against something. Note the prefix “ant” (as in anti) in the word *antagonist*. Agonist is a completely different word!

The word agonist comes from the Greek “agon,” meaning contest. Agonistikos¹ means “fit to compete.” So “agonist” means, in a dopamine context, a chemical that competes with dopamine for the little dopamine receptor sites. A dopamine-receiving nerve doesn't care whether it is actually dopamine or some imposter molecule that is hooked up at the receptor site – once the receptor is filled with something, either a dopamine or a dopamine agonist, the nerve can work.

Actually, it would have been a boon if the person who named this class of drugs had used a more correct word instead of agonist. Agonist implies competition and suggests that if the agonist gets to the receptor, it is the winner, and dopamine is therefore, somehow, the loser. This is not the way it works. A dopamine agonist works like a look-alike drug. It is not exactly dopamine, but many receptors cannot tell it apart from a dopamine, and so it is allowed to stimulate a dopamine receptor, working hand in hand with dopamine to help push a nerve over the threshold. A more appropriate name for the agonists would have been “dopamine teammates,” or “dopamine substitutes.”

You may ask, since dopamine agonists work just the same as dopamine, why not use dopamine? Good question. Here's why: dopamine is a naturally occurring compound. The dopamine receptors in your brain are designed to attach quickly to dopamine, and the dopamine reuptake transporters are designed to remove the dopamine efficiently. But the dopamine agonist drugs, especially the ones that are completely synthetic, not derived from naturally occurring compounds, are complete foreigners to your brain. Your brain doesn't have a clue as to what to do with a synthetic dopamine agonist. These agonists are not a perfect fit into the dopamine slots on the receptor nerves, but eventually, enough of them can wiggle into the dopamine slots that your brain nerves go over the action threshold.

Then, after the agonists are in position, it is a tad difficult for your body to get rid of them: their free end doesn't match up with the dopamine reuptake transporters. Once the agonist has wedged itself into a slot intended for dopamine, it can stay there for a while.

Well, actually your brain has lots of defense mechanisms for getting rid of chemicals that it doesn't want, such as alcohol, cocaine, and dopamine agonists. But these mechanisms are much slower and clumsier than the elegant and lightening fast dopamine transporters. Consequently, the agonist drugs produce a much more gradual On, and a much more gradual off. The dopamine agonists are used instead of or in addition to levodopa because they can activate a dopamine receptor almost as well as dopamine, but your brain has a harder time getting rid of them.

¹ *Webster's New World Dictionary.*

NADH – straight nicotine

Some PDerS in very early stage PD find that NADH, a pill form of nicotine available at health food stores, can provide enough dopamine so that they do not need the stronger drugs for a little while. Sometimes even humble nicotine, a drug much more mild than the mind-altering¹ antiparkinson's dopamine agonists, can provide a newly diagnosed PDer a small dopamine boost adequate to obtain the threshold for movement.

Cigarettes are hard to quit. The PD agonists are much, much harder to quit. This example of the relationship between nicotine and the antiparkinson's dopamine agonists may be helpful in understanding just how addictive the Parkinson's meds are. If you are taking Permax, Mirapex, Requip, or bromocriptine, remember: they work the same way as cigarettes, only much more so.

MAO inhibitors – Methamphetamine/amphetamine

Selegeline hydrochloride (referred to during its research days as both deprenyl and L-deprenyl hydrochloride) has many patent names: Eldepryl, Atapryl, Carbox, Selegeline, and Selpak. I will use the most common name, Eldepryl, when referring to this drug. Once in the body, this antiparkinson's drug rapidly breaks up into its active ingredients: amphetamine, methamphetamine, and other less understood compounds.

Eldepryl was promoted in its first antiparkinson's release in the mid nineteen nineties as “possibly preventing further degeneration of substantia nigra cells.” This sort of hype is pure routine. Once the FDA approves a drug, there is no legal reason that an advertising campaign can't say something utterly hypothetical about it, such as “possibly prevents further degeneration.” For example, it is perfectly legal to say that “possibly spinach prevents further Parkinson's degeneration,” or even “possibly chocolate-dipped macaroons.”

It is also legal to say that a drug possibly increases sex appeal. We see this perfectly legal but highly unlikely implication of sex appeal increase in ads for soft drinks and cars. This is all legal and above board. As long as the word “possible” is used, no illegality has been perpetrated.

Although it has been shown now through experience that this drug does absolutely nothing to slow the onslaught of accelerating PD, and in fact causes a special type of brain damage, the brief flash of advertising hype did its job – for several years people were asking for this hot new drug. Many doctors who got in the habit of prescribing this drug continue to do so.

Deprenyl is a slightly modified (liquid) version of Selegeline that is not legal in this country but which is available via mail order from overseas. The sales reps for Deprenyl insist that the special addition of a hydrogen atom here and there on the molecule make it safe and non-addictive. Considering it only works against Parkinson's because it increases dopamine levels, and it is the propensity to increase dopamine that

¹ The dopamine agonists used in treating Parkinson's are all strong enough to cause hallucinations and alter mental function. For example, the plant compound from which Permax was derived is historically famous for its mind-altering properties. During the Middle Ages, people who ingested this compound (a toxin given off by Ergot, a fungus that grows on rye) were considered to be divinely touched. St. Vitus's dance was the name given to the unrestrainable movement (dyskinesia) and appearance of ecstasy in those who inadvertently ate moldy rye. Cigarettes are not able to incite this level of bliss or movement.

determines whether or not a drug is addictive, this claim of “safe and non-addictive” is clearly misleading.

This drug works for PDers the same way it works for kids who take methamphetamine in order to party all night without stopping – it causes dopamine vesicles unrestrictedly to pour their dopamines out into the brain, where they slosh around stimulating everything in sight.¹

Originally, the MAO inhibitors were thought to work because they slow down MAO. MAO is the enzyme that breaks up dopamine. This drug’s apparent effect of allowing PDers to initiate movement was assumed to be occurring via this mechanism, in which MAO was tied up, and dopamine was allowed to last longer. However, with the finding that this product breaks up into amphetamine and methamphetamine, the guess as to this drug’s action has changed. It is now suggested by the manufacturer that this drug’s action is only in part affected by a decrease in dopamine breakdown. In the addictive drug research community, it is currently thought that the drug works by overstimulating the vesicles – a known function of methamphetamine.

Of course, when it comes to actually knowing what is causing what, all bets are off: western science is still, to a large extent, guesswork.

¹ The information presented by the drug company on this drug suggests that the drug works by slowing the reuptake of dopamine. This turns out to be only a guess, as newer research indicates that possibly this drug works by stimulating the vesicles, rather than by slowing reuptake. It doesn’t really matter for the user or the doctor, but I thought you might enjoy knowing that a drug company does not need to know the mechanisms of the drugs they are selling. They only need to guess at what the pharmacodynamics might be. What they do need to prove, in the USA, is that the drugs are not fatal in the short term.

I find it appalling that most people assume that, if a drug is on the market, it has been proven to be “safe,” without bothering to find out what is meant by “safe.” The FDA seal of approval imparts a rosy aura in the minds of most American consumers, despite regular exposés and lawsuits that reveal that approved drugs are often, in fact, dangerous.

In *Prozac Backlash* you can learn that Prozac was found to be safe to use on mice or rats only if the animals were simultaneously given sedatives. Without the sedatives, the animals appeared to go berserk. However, because the Prozac did not harm the animals when accompanied by sedatives, the drug was approved. No mention is ever made in the prescribing literature available to doctors that explains that this drug may only be safe over the long run if given in combination with sedatives.

As for the dosing, Prozac was found to be safest when used at a very low level. Only in extreme cases should the drug be slowly boosted up to a higher level. In general (because they are often taught this in med school), many MDs feel that their patients are, for the most part, too stupid to take drugs that must be built up slowly over the long term. Neither are most MDs able or willing to work closely enough with a patient to determine whether or not a lower dose or a higher dose is appropriate. Therefore, when Prozac was first introduced with the sliding scale dosage instructions and pills of many finely graded dosages, it was not at all popular with prescribing physicians.

The manufacturers, throwing caution and moral guidance to the winds, rereleased the drug at only two dosage levels: high and highest. The safest level, the lowest dosage, is no longer even available. However, now that prescribing doctors do not have to worry about patient compliance, they happily prescribe this very dangerous, brain-altering drug to a population that wants happiness and wants it immediately.

This footnote has come a long way from pointing out that the original guess at what makes Eldepryl work has been changed. Please forgive me.

Methamphetamine

What is known about methamphetamine? This drug is not as well known as cigarettes to the man on the street, but it is well known in drug abuse circles, where it has various names including “speed” and “meth.” It is related to Ecstasy. It is easy and cheap to make. Narcotics police are constantly busting “Meth” labs, but new labs spring up to take their place like mushrooms after the rain. Meth is a powerful, mind-altering drug. Methamphetamine, like its sister amphetamine, causes release of dopamine and norepinephrine from their storage sacs. Meth is a *very* powerful stimulant.¹ Meth makes a person feel unnaturally fast, capable, strong, and tireless. This drug is highly addictive and causes permanent brain lesions.

This group of drugs, the MAO inhibitors, is specifically prohibited from being used in conjunction with levodopa type drugs. From what I have seen, this prohibition is widely ignored. Drug reps (salesmen) seem to be completely unaware of this contraindication, and they promote the MAO inhibitors as a nice adjunct drug for L-dopa. Dr. Leslie (Rose and Becky’s doctor) had many of his PD patients taking Sinemet together with Eldepryl.

Anticholinergics – Psychedelics

Next, let’s consider the most commonly used anticholinergic drug, Artane, also known as Trihex. This class of drugs is falling out of favor with neurologists, possibly because they have been out for so long that the patents have expired and so the salesmen aren’t pushing them, but also because they aren’t as gratifying as the dopamine-enhancing drugs.

Anticholinergics work against the neurotransmitter acetylcholine (ACh). They work by blocking the receptor sites (the hookup sites) where acetylcholine is supposed to land on a muscle-stimulating nerve and trigger a “go” signal.

These drugs are mainly effective in reducing the restlessness and anxiety that is found in PD. Unless a patient has tremor or extreme anxiety, anticholinergics should not be used. When ACh is suppressed, the muscles can’t move as fast, so motor function is slowed considerably. Also, the thinking processes are slowed as brain function, including anxiety, is reduced. Considering that most PDers already have a slowdown of motor function, it is counter-productive to use a drug that further slows the brain. This is why the anti-ACh’s should probably only be used for patients whose tremor or anxiety is a greater problem than slowness and rigidity.

You might not be surprised to find out that this drug is often incorrectly prescribed to treat slowness and rigidity, even though this drug specifically and intentionally causes slowness. That is because in many doctor’s books, this drug is listed as being used against Parkinson's disease without reference to *which* symptoms of Parkinson's disease it addresses.

Most neurologists – I am not making this up – have no idea that the various PD drugs have distinct functions and that certain drugs are best suited for specific symptoms. Most MDs will try any drug in the “antiparkinson’s” category on their PD patients without regard to which PD symptoms are dominant. I have seen anticholinergic drugs,

¹ *A Primer of Drug Action*, p. 31.

which cause sleepiness and confusion and muscle weakness, being prescribed for people whose main complaints are fatigue, loss of balance and muscle weakness.

Belladonna

Scopolamine, the street drug most closely related to the anticholinergic anti-parkinson drugs, is becoming passé – just like the similar PD drug. The psychedelic drug scopolamine, an anticholinergic, is derived from the belladonna plant. Scopolamine is also found in the Datura plant, in jimsonweed (locoweed) and other plants. It has been used for centuries both as a poison and as a hallucinogen. Ever since the advent of LSD and the increased availability of psychedelic mushrooms in the 1960's, the scopolamines are no longer in fashion. Considering that these drugs were very often deadly, in addition to being psychedelic, it is just as well that they are falling out of favor.

The anticholinergics are not addictive in the same way as dopamine-enhancing drugs. However, the body does accommodate to them. Daily use of Artane, which suppresses acetylcholine, will cause the body to set in motion steps to *increase* the manufacture of ACh, in an attempt to override the effects of the drug. Then, if a person stops taking the drug, the excess acetylcholine causes insomnia, edginess, severe anxiety, and twitchiness for several weeks or more.

Cocaine – L-dopa

Cocaine's pharmacodynamics are different from those of L-dopa, but many of the effects on the brain during usage and withdrawal are quite similar. They are both fairly non-specific with regard to the activity region: L-dopa washes over the entire brain, and cocaine inhibits dopamine reuptake enzymes over a large area. The net result of both is similar: an increase in dopamine effectiveness spread over most of the brain. Did you know that L-dopa is beginning to be used on the street for its high? It is used both by everyday folks looking for a lift and by a few savvy doctors who enjoy the energy boost. Cocaine is often mixed with inert or toxic fillers, and pharmaceutical L-dopa or carbidopa/levodopa is fairly pure and the amounts are more reliable. (Presumably, the amounts are more reliable. However, some patients who have tried the brand name and the generic versions of Sinemet say that there is quite a difference between the various brands. Other patients say there is no difference at all.)

Cocaine

Cocaine works differently than the dopamine-releasing drugs (methamphetamines) or the dopamine helper drugs (agonists). Cocaine, as described earlier, works by blocking the reuptake of dopamine after it has finished its dopamine job at the nerve work site. The net result of cocaine use is that dopamine molecules that should ordinarily only stay hooked up for a few seconds get to stay in their position for a bit longer than they should. This frees up the other dopamines that are floating around, waiting their turn to be used.

Cocaine is a highly addictive, dopaminergic drug.¹ Both cocaine and L-dopa are mild anesthetics. People with cocaine addictions and those who are in cocaine withdrawal have characteristic, well-studied behaviors. These patterns of denial, paranoia, and deceit

¹ R. M. Julien, MD, PhD, *A Primer of Drug Action, A Guide to the Actions, Uses, and Side Effects of Psychoactive Drugs*, W.H. Freeman and Co., New York, NY, 1999, p. 126.

from cocaine abuse are so similar to the patterns that develop in abusers of L-dopa that I consider L-dopa to be more comparable to cocaine than any of the other drugs that elevate dopamine levels.

Street cousin summary

In summary, the most common anti-PD drugs, the agonists, MAO inhibitors, anticholinergics, and L-dopa have strong similarities to their street cousins: nicotine, methamphetamine, psychedelics and cocaine. Except for the cholinergics, these street drugs are highly addictive. They are all addictive in slightly different ways, and they all have different mechanisms for increasing dopamine, but every increase in dopamine will be met by the brain with addictive counter-forces that semipermanently reduce the ability of the brain to ever again go over the brain's internal plimsoll¹ line for dopamine. Even though the street drugs are illegal and the PD drugs are legal, your brain can't tell the difference. If you go over the brain's Safety Limit, you have gone over the line, and you will have to pay the price. Your brain may never be the same.

MEDICATIONS NOT RELATED TO STREET DRUGS

There are also drugs that do not have a parallel on the street that are used in the treatment of PD. While they may not be technically addictive, most of them cause changes in the brain that lead to accommodations. This means that there will be a backlash if you stop taking them. A mere backlash might only last for a few months, compared to the true, dopamine-based addictions which can create changes that may well be lifelong.

The Antihistamines

Some people take mild antihistamines such as diphenhydramine (Benadryl, Tylenol PM, and others) to help with the insomnia of Parkinson's disease. These drugs are sold over-the-counter, but they have a strong effect on the central nervous system and should not be taken for more than two weeks, as it clearly says on the box. They are accommodative. They have a strong rebound effect when they are stopped. Rebound means that your previous symptoms may return with a vengeance when you stop taking the drug. For example, if you had insomnia before you started taking these pills and you took the pills for too long, then, when you stop taking the pills, your insomnia might be far worse than it was before you started taking the pills.

Mirtazapine

There is a powerful new "antihistamine," mirtazapine (Remeron), which has recently been approved for Parkinson's tremor. I have heard of this drug being described by neurologists as merely a strong type of antihistamine. This is a highly misleading

¹ Plimsoll was the British engineer who first started painting a line around the hull of a boat that indicated when the boat was safely loaded. If a boat was so heavily loaded that the Plimsoll line was under water, no longer visible, then the boat was too heavy to go safely to sea.

description. One of the actions of mirtazapine is to block histamine receptors, making it hard for histamines (the chemicals that cause sneezing and runny nose) to hook up. The major function of this drug, however, is that of SSRI/norepinephrine reuptake blocker. Most SSRI reuptake blockers can be addictive and they can cause tardive dyskinesia. Mirtazapine has been primarily used, not as an antihistamine, but as an antipsychotic, a sedating/heavily pacifying drug.

However, this drug caught the attention of the Parkinson's researchers due to its apparent ability to reduce tremor. The researchers figured that the tremor reduction was due to the histamine-blocking effect of this drug, which also causes extreme drowsiness. *The drowsiness induced by this drug leaves a person suspended in that "just falling asleep" state.* Because tremor ceases when sleep begins, this drug is able to decrease tremor. By keeping a person right at the edge of falling asleep, the tremor is subdued.

This drug was approved for tremor in late 1999, and it is not safe for anyone who must drive a car or perform any activity requiring alertness. The tremor rebounds with vigor as soon as the drug wears off.

The fact that it is also an antipsychotic was not known to any of the people I have met who were taking this drug. Also, because of its serotonin/norepinephrine enhancing properties, it is also, inadvertently, a dopamine enhancer and therefore addictive.

I have not known anyone who was able to continue taking this drug for very long. After repeatedly falling asleep while driving, my patients decided that the drug was not worth the benefit. After discontinuing (stopping) even a short course of the drug, there was a rebound effect: tremor was much worse for a month or more.

Amantadine

Amantadine, also known as Symmetrel, was first used as an anti-viral drug and appears to work by boosting adrenaline. The mechanism of this drug is unknown, and so it is impossible to make a comparison with street drugs. In Appendix 2, you will read some case studies that demonstrate how quickly the brain accommodates to this drug even though its pattern for withdrawal follows a slightly different timeframe than the dopaminergic drugs. This drug is considered to be very mild by some doctors. Why that is, I can't imagine, after watching so many people trying to stop this drug and failing. Typically, all benefit from this drug has ceased (due to accommodation) within three months, and after that it has powerful rebound side effects if discontinued.

Digestion Inhibitors

Comptan and Tasmar do not elevate dopamine directly. They work by shutting down the body's digestive process so that more L-dopa can make its way unmolested up to the brain. These drugs do not in and of themselves cause addiction. They simply gum up the digestion, often causing liver and/or kidney damage. These drugs are usually not used until a person is having On-Offs. The thinking behind these drugs is that advancing Parkinson's is the reason for the levodopa "failures." By eliminating digestive enzymes, thus insuring that the L-dopa gets delivered to the brain in extra-large quantities, they can increase the payload (and the damaging effects) of a given dose of L-dopa.

Curiously, these drugs are given by doctors as a “safer” alternative to increasing levodopa dose. However, this completely uninformed approach fails to recognize that these drugs only work by increasing the effective payload of levodopa – the very thing the doctor is trying to avoid. If a doctor has determined that what the patient needs is more dopamine in the brain, it makes more sense to take more levodopa than to take a toxic drug that shuts down gastrointestinal function.

True, with these digestion inhibitors, a person can continue to take the same number of levodopa pills that he was taking before and get more levodopa into the brain, but at what cost? So many people died in the first three months that Tasmar was on the market that they changed the prescribing recommendation: in the USA a person should have biweekly liver scans if he wants to use this drug. Canada has banned the drug. And at the brain end, the dopamine effect from taking the Tasmar was exactly the same as if the patient took a slightly higher dose of levodopa. Then again, Tasmar is recently patented and the patent for Sinemet has recently expired, but I do not like to think that this is significant.

NEW PRODUCTS

I get several emails a month asking me about exciting new “non-addictive” products or “harmless supplements” that help Parkinson's disease. I also hear regularly from patients telling me either that these exciting new (and usually expensive) products don't work in the long term, or else that they have turned out to be addictive after all.

I will list just a few of the currently popular ones.

Glutathione

This one has gotten lots of publicity from MDs who offer expensive shots of this drug. Patients who have reported to me after taking it say that they sometimes feel powered up by it but no more than if they ate several candy bars at one sitting. As soon as they stop taking the shots, they go into a slump for several weeks to several months, and then they find themselves right where they were before or a little worse.

NADH / nicotine patches / cigarettes

NADH is nicotine in a pill form. Regardless of delivery system (pills or patches, or the old fashioned chaw and cigarettes), nicotine is a powerful acetylcholine agonist, as well as a dopamine agonist. Nicotine, being an agonist for both of these movement-related neurotransmitters, can assist in imparting movement. It does nothing to deter the progress of Parkinson's disease, but it can help mask the symptoms, just as all dopamine-enhancing drugs do.

Do you think nicotine is addictive? Ha ha ha. Of course it is. So why is nicotine, in any form, legal? Nicotine is a naturally occurring compound. It requires an act of congress to make a natural substance illegal. There are powerful political reasons that nicotine has not been made illegal, plus our country's disastrous experience with alcohol prohibition.

NADH is sold as a supplement at your local health food store. NADH does not need FDA approval to be legal; since nicotine is a naturally occurring substance, it does not need to be tested and proven safe, nor can it be patented. You will find companies

trying to get around this limitation on patents by adding a hydrogen atom onto the molecule, thereby creating a patentable product (the hydrogen breaks off as soon as it hits the stomach and you have plain old nicotine again). This “enhanced” product can then be hyped and sold for much more money than plain old nicotine plant extract, which would be dirt-cheap. The patented forms are much pricier and are usually the only forms carried by health or vitamin stores.

There are side effects of nicotine that can make this form of PD treatment unpleasant: because nicotine enhances acetylcholine as well as dopamine, some people feel more edgy and restless when using nicotine. Others find it mildly beneficial.

OLD PRODUCTS

Macuna, fava beans

Macuna is in the same legal category as nicotine: found in nature, therefore unpatentable and legal until decided otherwise. It has a high L-dopa level. This herb occurs naturally, and therefore it is perfectly legal to sell it over the counter. It can be found in Ayurvedic herb stores. In India it is used as a brain and sex stimulant – similar to cocaine, but milder. Taking this herb can elevate brain dopamine levels quite high, thus its use in Parkinson's disease is explained. It is highly addictive under certain conditions. Despite the fact that it is natural and an “herbal” product, I repeat: it can be addictive.

I have seen several patients using this herb. Two were never able to reduce their daily amounts despite being clearly stoned even to the point of glazed eyes and illogical thought. One Macuna user visited the clinic just once. His wife told us that she pleaded with him constantly to stop taking so much Macuna because he was so strange all the time. He just laughed at her and told her she didn't understand. When we told him that Macuna was addictive, he laughed again and said that we didn't understand and that he could take as much as he wanted because he had Parkinson's disease.

Lance

Lance was a real fighter and survivor. He had survived polio as a child and was determined to survive PD as well. He was able to get off this herb. Lance took Macuna three times a day. His blood dopamine levels were measured in a lab test and his blood numbers were 10 times (!) higher than normal.

When I met Lance he seemed overmedicated. His eyes were unnaturally bright and his twitching seemed more like ticcing than like true tremor. Also, he seemed over-quick in initiating movements, and he bragged that, despite his Parkinson's, he worked out at the gym and ran miles every day, manifesting no symptoms of Parkinson's. I asked him what drugs he was taking and he said none. The next time I saw him he seemed even more overmedicated. He assured me again that he didn't like drugs and wouldn't take them. The third time I saw him I asked him again. Exasperated, he explained that he wouldn't take drugs because he didn't trust them and he didn't need them. He never took anything but herbal supplements. I asked about his supplements. He was taking Macuna and Deprenyl together: levodopa and an MAO inhibitor, together. Together, these two drugs are much more dangerous than either one on its own, and fatal interactions have

occurred in some patients. The makers of L-dopa state that it should not be used with MAO inhibitors.

I told him that he was, in fact, taking powerful drugs, whether or not they came in a pill form or as ground up leaves. He refused to believe me. I asked him if he could stop taking either one of his “supplements.” He assured me that stopping would not be a problem, that they were sort of like vitamins: helpful, but not crucial for activities of daily living.

It took Lance eight months to get off the Macuna, during which time he felt all the usual symptoms of drug withdrawal. As he always put it, “*I’m still reducing the Macuna, but it’s killing me, it’s just killing me.*”

He is now off the Macuna and still working to slowly get off of Deprenyl. For more than a year he has been going through agonies. “*It’s killing me, just killing me.*”

Another Macuna case study

A patient who visited our clinic had taken a Macuna extract that contained 10% levodopa. She took 1000 mg/day for two weeks. (This would be equivalent to 25 mg/day of carbidopa-levodopa. Without a buffer such as carbidopa, levodopa is only about 25% as effective: one must take four times as much levodopa as they would carbidopa-levodopa, to get the same effect as Sinemet.) When she tried to double the dose, as instructed, she felt more rigid, and resumed it at the lower dose. She took the Macuna at this level for nearly four months before she stopped abruptly. Three months after stopping she had not noticed any traumatic reduction or withdrawal side effects. Her Parkinson’s symptoms worsened; for example, she became more rigid. However, she did not experience the reduction symptoms of nausea, insomnia, paranoia, or longing for Macuna. She had not yet recovered from Parkinson’s, and she was taking less than the “small amount” that is listed for levodopa in chapter 17.

Vicia fava, Fava beans

Fava beans (*Vicia fava*) also contain L-dopa. However, a very large amount of daily fava beans is required to give the same effect as the buffered carbidopa/levodopa. A few people with mild Parkinson’s find that they benefit from this food. You can find articles about it on the Internet. Most people do not get enough benefit from this food to overcome their Parkinson’s symptoms. If they do, they run the same risks as a person who is taking L-dopa. The brain does not differentiate between L-dopa from a veggie and L-dopa from a vial.

On the other hand, dopamine levels are subject to the placebo effect. If by taking fava beans you can feel better about yourself than you would if you were taking a drug, then by all means, do so. Possibly the positive attitude will help you increase dopamine levels naturally. Attitudinally-produced dopamine never goes over the Safety Limit.

The safe new discoveries

As you have learned, short of the placebo response, there is almost no way to pharmaceutically or herbally increase dopamine without quickly setting in motion an addiction response. Whether the dopamine level is raised through the mechanism of 1) taking the place of dopamine on the dopamine receptor sites (agonists), 2) increasing

dopamine release from vesicles (methamphetamines), 3) increasing dopamine derivatives (such as serotonin and norepinephrine) so that the dopamine supply backs up, 4) slowing the reuptake of dopamine (cocaine), or simply 5) inserting dopamine precursor (levodopa) into the brain, the final result will be that dopamine levels will temporarily go up. This rise in dopamine will trigger an addiction process. After that process has been initiated, the native dopamine levels will be permanently or semipermanently lowered.

Because addiction-lowered dopamine levels can cause slow movement, rigidity, poor balance, and tremor – in other words, parkinsonism – it is clear that any drug for treating Parkinson's disease that works by enhancing dopamine may eventually create parkinsonism.

As I was writing this chapter, I got an email from someone asking about a hot new form of a Deprenyl-like supplement for Parkinson's disease that is sold over the counter and which has “all the addictive parts removed, and only the effective, dopamine-stimulating parts remaining.” He wanted to know what I thought.

Here's what I think: if a drug elevates dopamine, then it is addictive. How dumb do they think we are? Pretty dumb, evidently.