OK, here's the recently-mentioned and awaited results in full detail. This is an "alpha pre-release", references not included and I hadn't planned on posting this at all except it's kinda started to spread on its own.

Bottom line: all dissociatives carry a real risk of permanent brain damage. Dissociatives include ketamine, DXM, PCP, dizocilpine, and nitrous oxide (tho it may not be nearly so dangerous due to very short duration of action). Individual susceptibility varies *greatly*, so if you've snorted enough K to tranq an entire pet shelter and downed A. H. Robins' entire year's production of Robo and are still OK, this *doesn't* mean that everyone else can do the same thing. I've spoken with numerous people who *have* suffered permanent impairment from heavy dissociative use. This document explains the process by which it occurs, and how to minimize or prevent it. I take NO RESPONSIBILITY for any errors; if you're old enough to do drugs, you're old enough to take responsibility for your own fuckups.

I don't get on Usenet much, so don't expect rapid response. If you have a question, ask RFG or email me; I have a real job that takes up almost all of my time these days. Most general questions about DXM are answered in the FAQ; ketamine probably has an FAQ somewhere too. (Note that ketamine is probably *slightly* better for you than DXM *in theory*, but the hydrobromide in DXM HBr may make it about even. It's still too early to know).

This is Your Brain on Dissociatives:
The Bad News is Finally In

Version 0.1 (pre-release)

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11/28/1998

(hint: for the down-and-dirty, see section ii.)

Contents:

i. Introduction To This Document

This is a fairly detailed file which covers a type of brain damage known as NMDA Antagonist Neurotoxicity or Olney's Lesions (after the researcher who discovered it). It also covers other risks of using dissociatives, and how to minimize them. If you currently use, have used, or plan to use, any dissociative (drug which blocks NMDA receptors or which is a dissociative anaesthetic), then you should read this document. This includes ketamine, PCP, dextromethorphan, and nitrous oxide; see Section iv. below for more information.

ii. Summary of Findings

Several years ago, JW Olney discovered that dizocilpine (MK-801), a chemical being tested to prevent brain damage from strokes, actually caused damage to specific areas of the brain in rats. Since this time, numerous other drugs in the same class (the

dissociatives) have been tested, and they all share this problem. As some of you might know, I have spent a great deal of time trying to make sure that the Internet community, and the larger world, has detailed information about this complex, difficult-to-use, and often dangerous class of drugs. I first learned of Olney's lesions a few years ago, but it has taken me much time to review all the evidence, compare drug dosage within and across species, speak to heavy dissociative users, and so on. I am now ready to state my conclusions and make some recommendations, which are as follows (explained in detail in the full document).

- Dissociatives definitely cause brain damage if used heavily. One sub-anaesthetic "line dose" of ketamine, an equivalent dose of PCP, or a third plateau DXM dose, is probably at least as damaging to your brain as a few day "bender" on hard liquor, and possibly more so because it affects specific areas of the brain.
- The risk of brain damage is worse the longer you stay high at any given time; constant moderate-dose use is probably just as damaging as a brief, high-dose use.
- Reaching the anaesthetic level is exceedingly hard on your brain.
- Ketamine is probably the least harmful, PCP the most, and DXM somewhere in the middle, but this is a rough guesstimate. Nitrous oxide is brief acting, but it too may be dangerous; it is also known to damage both central and peripheral nerves by depleting vitamin B12.

Some people may be more susceptible to Olney's lesions than others. There is, to my knowledge, NO way of knowing how susceptible you are.

In addition to brain damage, these drugs can also trigger psychosis, limbic seizures, temporal lability, depression, and other neurological and psychological diseases much more frequently than other types of drugs. The dissociatives can be highly addictive to a minority of users. In comparison, the marijuana and the serotonergic psychedelics (LSD, psilocybin mushrooms, peyote, DMT) are many times safer.

People who have used dissociatives heavily have shown clear evidence of brain damage. This is not necessarily conclusive, since the people who become addicted to them might have underlying conditions (specifically, temporal lobe complex partial seizures) which could be responsible for some of the damage. Nonetheless, I can't ignore the fact that most everyone who uses dissociatives both frequently and heavily ends up with some sort of neurological or psychological problem, ranging from impaired memory to a schizophrenia-like syndrome. Many of the impairments

correspond exactly to the areas of the brain damaged in lab animals.

If you will not abstain from using dissociatives, there are several steps you can take to protect your brain, ranging from limiting frequency and dosage to taking nutrients and neuroprotective drugs. You can also use alternative methods (ranging from safer drugs to meditation) to reach the same places that dissociatives take you.

iii. Why am I Telling You This: My Background

If you know me, you probably know me from the Dextromethorphan FAQ which covers the dissociative drug dextromethorphan (DXM) in considerable detail. I've been studying the brain for several years now, concentrating specifically on memory and congition, the limbic areas, and neuropharmacological agents that affect NDMA receptors. I've tried to keep everything I write down-to-earth while still supporting it with medical fact, and I've also tried to be as honest as possible. Sometimes this means speaking the truth, even when the truth happens to conflict with the "official version" given by those who participate in the War on Drugs.

I'm in favor of drug reform, and I don't try to hide that fact. I think the current policy is wrong-headed, and I think that psychedelic drugs in particular should be available to people who want to use them with respect and who can take responsibility for their actions. With some psychedelics, there is extensive evidence showing that careful use is less harmful than many currently legal drugs, and many societies have successfully integrated psychedelic use into their culture.

However, I also have to admit when there's a danger out there that people should be made aware of. Even now that the dangers of DXM are better known, I still stand by my decision to publish the FAQ, because I still think that people make better decisions about risks when they have information than when information is kept from them (and they learn about drugs by hearsay). Telling the truth means telling the whole truth, the good along with the bad.

Sometimes there's bad news. This is one of those times. Please read and think carefully, and take good care of your body and brain.

iv. The Dissociative Drugs

The term "dissociative" derives from "dissociative anaesthetic", a class of anaesthetics which produce unresponsiveness to stimuli by dissociating various elements of the mind (in simple terms, they knock you out by putting you 'out of your body'). Consciousness, memory, perception, and motor activity are all dissociatied from each other. The dissociative anaesthetics all block the N-methyl-D-aspartate (NMDA) neuroreceptor, though many act on other receptors like sigma. I prefer "dissociative" to "dissociative anaesthetic" when discussing these drugs, for two reasons: first, most recreational use occurs below the anaesthetic level; second, some drugs in this category are not, and probably never will be, marketed as anaesthetics.

Dissociatives are not frequently used as anaesthetics in humans because of what are known as "emergence effects", various odd effects that can happen when people come out of anaesthesia. All anaesthetics can produce these effects, but with the dissociatives it is much more common and much more severe. Dissociative anaesthetics (ketamine and tiletamine) are used in veterinary practice, since animals don't often complain about out-of-body experiences. Ketamine is also used in burn trauma and in children (who don't get the psychedelic effects of the dissociatives, and are not susceptible to dissociative brain damage).

The psychedelic effects of the dissociatives are difficult to explain. They are nothing whatsoever like LSD or related drugs (mescaline, DMT, mushrooms, etc.) but they are clearly psychedelic. For years I've struggled to understand the dissociatives, and the best way I can explain the difference between dissociatives and traditional serotonergic psychedelics is this:

Serotonergic psychedelics are Eros, and dissociatives are Thanatos. The serotonergics are Birth, they are sensory overload, focus on the details, awareness of the external universe. The dissociatives are Death, sensory shutdown, focus on the archetypes, awareness of the internal universe. Serotonergics are the "Ana" side of Chaos, dissociatives the "Kata" side of Chaos (Chaos being the essential driving energy behind reality, if you will).

Ultimately, they can both take you to the same place -- mystical union, ego-loss, or just plain "trippin' balls" depending on your point of view -- but they take you by different routes. I like to think of both routes as complementary ... but only if they don't hurt you in the process of getting there!

A recent study confirms that nitrous oxide is a dissociative anaesthetic. YOU HAVE BEEN WARNED! Nitrous oxide also depletes vitamin B-12, incidentally.

These are some dissociative drugs you might encounter:

- Street Drugs:
  - Ketamine (K, Special-K, Vitamin-K), in injection bottles or as powder
  - Dextromethorphan (DXM), in capsules or as powder
  - PCP (Angel Dust, Embalming Fluid, etc.), powder, liquid, or on smoking material
- Over-The-Counter and Quasi-Legal Drugs:
  - Dextromethorphan (DXM), available in cough syrups and pills
  - Nitrous Oxide ("Whippets" and iSi whipped cream chargers)
- Prescription Drugs:
  - Ketamine (veterinary and human anaesthetic)
  - Tiletamine (veterinary anaesthetic)
  - Memantine and amantadine
- Research Drugs:
  - Dizocilpine maleate (MK-801)

I. Onley's Lesions (NMDA Antagonist Neurotoxicity)

(this is excerpted largely from the DXM FAQ's "Side Effects" section)

When NMDA antagonists were first studied they seemed like a dream come true: here were drugs which could block from part to all of the damage from strokes, head injury, hypoxia, polio, and a variety of other conditions. However, it seems that nature never gives something for nothing, and here too there was another side to the coin.

The dream ended when Olney et al. demonstrated that animals given high doses of dizocilpine (MK-801), a new dissociative used in research, showed curious vacuoles (essentially, tiny holes) in their brains. Specifically, the vacuoles showed up in the posterior cingulate cortex and retrosplenial cortex (see I.1 for an explanation of what these parts of the brain do). Further research showed that other indicators of damage were present, such as proliferation of microglia, secretion of a protein called HSP70 (Heat-Shock Protein 70), and expression of certain genes.

Since then, Onley's lesions, also known as NMDA Antagonist Neurotoxicity or NAN, have been discovered with ketamine, PCP, and dextrorphan (the metabolite of DXM), as well as a bunch of dissociative drugs you won't find outside of a research lab. PCP causes additional damage to the cerebellum and other areas, by the way.

For a long time, nobody knew whether Olney's lesions applied to human beings or not, or at what dosage they applied. The amount of ketamine used to knock out a rat, for example, is obviously different than the amount used for humans; it's also not the same dosage in mg/kg (milligrams per kilogram) either. And different effects of drugs "scale" differently too.

However, several things have happened recently which have led me to conclude that Olney's lesions apply to humans at recreational doses. First, I've received reports from many hundreds of users of DXM, some of whom have used it heavily and been clearly harmed. Second, more recent studies have shown that damage occurs to lab animals' brains even at lower doses (including ordinary anaesthetic doses of ketamine and dizocilpine!). Third, reports of ketamine-related brain damage have started to show up. Finally, the type of impairment people are reporting coincides exactly with the areas of the brain damaged in lab animals.

If you think you might be suffering from Olney's lesions, DON'T PANIC. You may just have depleted neurotransmitters, or induced long-term (but reversible) changes to neuroreceptor function. If you feel you are impaired, STOP USING NOW, and stay clean for several months before you get worried. Many people have told me that their "brain damage" cleared up after a few months.

IMPORTANT NOTE: Olney's lesions are WORSE in female animals than males, probably because females have different limbic connections. This may apply to humans.

I.1. Areas of the Brain Involved

Nobody's totally sure exactly what most parts of the brain do, but there is some evidence which may indicate possible functions for the posterior cingulate and retrosplenial cortex. Although modern science's understanding is far from complete,

and mine is considerably worse than that, I'll try to put together the published results into a coherent whole.

The posterior cingulate cortex is the posterior (rear) part of the cingulate cortex, a section of the cerebral cortex interconnected with the limbic areas. The front part of the cingulate cortex is called, appropriately enough, the anterior cingulate cortex (you expected "fore" and "aft" maybe?). Like most areas of the brain, the boundaries of the cingulate cortex are somewhat indistinct. There are differences between the posterior and anterior cingulate cortex (beyond the obvious one of location); notably, the anterior cingulate cortex has fewer pyramidal neurons than the posterior cingulate, and in the anterior cingulate these neurons have more complex connections. This entire area may relay information between the hippocampus (and other limbic systems) and other areas of the brain.

There is a lot of disconnected research that points towards possible purposes for the posterior cingulate cortex. It may be one of the components of verbal and auditory memory, multisensory perception, visuospatial cognition and/or evaluation of emotional behaviour. The right hemisphere posterior cingulate is activated in comprehension of metaphors, and the left in associative learning. Story comprehension seems to use the posterior cingulate. In late Alzheimer's disease the posterior cingulate may be subject to atrophy. It is activated during anxiety and in OCD (Obsessive-Compulsive Disorder), and may be overactive in bipolar disorder; it is deactivated during phobic fear.

It has been suggested that the cingulate cortex in general may be involved in evaluating (posterior) and acting on (anterior) one's own behaviour and spatial orientation. This is, in my opinion, the most comprehensive view of the existing research. To put it simply, the job of the posterior cingulate cortex might be to evaluate and consider where you are and what you're doing. Since dissociatives tend to interfere with the ability to evaluate one's own behaviour, it may be that the posterior cingulate is a part of a self-evaluation system.

An interesting aside here, many people who really like dissociatives have told me they find them so attractive because they help to take away a near-constant self-consciousness, an almost self-absorbing embarassment or "inner critic". While I don't think any one part of the brain can be the "home" of anything so complex, I am willing to accept that the posterior cingulate may be a major contributor to self-evaluation gone haywire. The good news is, there are healthier ways of getting beyond this

problem; see III.4 below.

Another paper analyzed the network properties of the posterior cingulate, and suggested that neural output from the hippocampus that was in sync with the theta rhythm would pass through the posterior cingulate cortex in preference to other routes. What makes this so interesting is that the flanging or strobing effects of DXM and other dissociatives seem to occur at theta rhythm, which may be a consequence of their effects on the posterior cingulate.

There was considerably less information published on the retrosplenial cortex. One paper found that it was activated during the encoding of novel situations. Another suggests that the circuitry between the retrosplenial cortex and hippocampus is an important path by which the hippocampus affects learning, memory, and emotional behaviour. Numerous papers suggest it has a role in visual processing (interestingly, some dissociative users report problems getting their eyes to track right after heavy binges). My totally unfounded hunch is that the retrosplenial cortex may be involved in converting the two-dimensional data that appears on the retina into a three-dimensional space, and the "third person perspective" some get on dissociatives may be related to retrosplenial cortex disruption.

To sum up: these are the skills which damage to these areas might impair:

- Memory, especially language-related (e.g., finding words)
- Understanding metaphors
- Evaluating, and possibly controlling, your own behaviour
- Multi-sensory thinking
- Learning in new situations
- Certain aspects of visual perception

With increasing doses, damage spreads beyond the posterior cingulate and retrosplenial cortex into other areas of the brain including the hippocampus and olfactory areas. Damage to the olfactory tubercule would, obviously, impair one's sense of smell. Damage to the limbic system itself could have wide-ranging consequences including:

- Autobiographical memory
- Declarative memory (as opposed to remembering skills)
- Place-memory (learning and remembering your way around)
- Coupling of emotions to experience

I.2. How and Why Olney's Lesions Happen (probably)

The mechanism for Olney's damage is still being sorted out, and is somewhat perplexing, since NMDA antagonists generally protect neural tissue from damage rather than causing it. Trying to tie everything together is a little like trying to solve a crime with only circumstantial evidence; there are clues, but nobody's been able to watch the criminal in action. Here is what current research seems to indicate, pieced together into a coherent whole. A simplified explanation is given below.

1. Dissociatives activate neurons in the posterior cingulate cortex (PC) and retrosplenial cortex (RC). These overactive neurons pass along their excitation to "downstream" areas such as the hippocampus and olfactory areas. There are two theories on why the PC and RC neurons get overexcited in the first place; either one, both, or neither could be true. One theory is that NMDA receptors are found on inhibitory GABA interneurons, and that when these receptors are blocked, these interneurons secrete less GABA, and thus excitatory pyramidal neurons that normally receive a lot of GABA inhibition are overexcited. The other theory is that the PC and RC are less affected by NMDA blockade than the hippocampus (and related areas), and that these formations serve as feedback to the hippocampus and surrounding networks. As these limbic networks are inhibited, the PC and RC increase their output to compensate, resulting in overactivity.
2. The overactive cells begin to heat up, use up their energy supply generate toxic waste products, and/or let in too many calcium ions.
3. Regardless of the mechanism, or whether the mechanism is none of the above, the overactivity seems to cause intracellular organelles (notably mitochondria and endoplasmic reticulum) to malfunction.
4. The mitochondria probably lose their proton gradient and allow their innards to spill into the surrounding cell material, where they cause all sorts of trouble, possibly including forming free radicals which cause further damage to the cell. Another possibility is that the free radicals come first, and they cause damage to the mitochondria and other organelles. Mitochondrial damage can occur within 15 minutes of the drug dose, the endoplasmic reticulum is damaged 30 minutes, and in both cases gets worse as time progresses. The free radicals, basically, destroy everything in the cell like a rampant two-year-old on a spending spree through Toys-R-Us.
5. The cell responds to this damage with a protein called HSP70. This "heat shock"

protein is made and activated when something (such as overheating, thus the name "heat shock protein" or HSP) is causing a cell to malfunction so badly as to be in danger of self-destructing, and its job is to turn the cell off until repairs can be made. Hopefully, the cell will get a lot of rest (about 24 hours) until it goes back to normal. At this point the problem is still reversible and the brain cells have not been permanently damaged.

6. If the cell continues to be overexcited, it eventually burns out completely as the increased temperature, disrupted ion gradient, hypoxia, calcium ions, free radicals, and/or buildup of waste products kill it. At this point, surrounding support cells called microglia are activated and come in and eat the cell (probably under the theory that if an infectious organism caused the cell death, it'd better be destroyed before the infection can spread).

To put it bluntly, taking excessive doses of dissociatives make certain parts of your brain fry like the proverbial egg-on-the-frying-pan in the "This is Your Brain on Drugs" commercial.

I.3. Lab Critters vs Humans (or, Yes, it can happen to you!)

As I stated above, there are several reasons why I now believe that Olney's lesions can, and do, happen to humans.

First, the animal data. Ketamine is normally used as an anaesthetic in a mixture with another drug called xylaxine, an alpha-2 adrenergic agonist sedative. When used alone, it takes about 40mg/kg to knock out a rat. The same dosage will also induce HSP70, the protein that shuts down damaged neurons; twice this dosage will actually kill cells. Note that this is from just one dose; if you give a rat multiple doses, or extend the dosage too long, the damage will be much worse. A prolonged, lower dose of dissociatives may be just as dangerous as a single higher dose!

If humans respond like rats do, this means that taking a single anaesthetic dose of ketamine will put an enormous amount of stress on the neurons in your posterior cingulate and retrosplenial cortices. (Recreational doses are, of course, less than anaesthetic doses, but not by enough; it may take a dose five times lower before the danger is gone). This stress will cause the neurons to shut down in order to make repairs; if they can't make repairs, or if they are damaged again too quickly (i.e., from too-frequent use of ketamine), they will die. Ketamine is used as an example; any

dissociative will cause the same sort of damage.

Then there's also the issue of people's experiences. Since publishing the DXM FAQ, I've heard from dozens of people who have used dissociatives (mostly DXM, but also ketamine and PCP) and had lasting impairment. Most of these people were very heavy users (daily use of PCP, ketamine, or high-plateau DXM), but a few weren't. One person I heard from recently used DXM for less than a year, taking it twice a week at most, in doses of 600mg to 1500mg (once at 2000mg). This particular individual complained of impaired memory and difficulty understanding metaphors which has lasted over a year.

Many of the peculiar effects of dissociatives seem to correspond with their effects in animals (including damage). DXM users often report that their upper-plateau trips rapidly lose the interesting effects, perhaps because the cells that are going haywire (and making the whole temporal lobes function unusually, thus the effects) are burning out. After frequent use, a lot of DXM users and some ketamine users have reported strange "jolts" or "shocks" when moving their eyes, and sharply impaired visual tracking is characteristic of high dose use; this may be related to the retrosplenial cortex, which encodes eye position (among other things). Impaired recognition of metaphor, impaired language skills, and memory problems are all frequent consequences of excessive dissociative use (in most people these problems fade with time).

There seems to be a lot of unpredictability here. Some people can use dissociatives heavily and not suffer; others suffer after using more moderately. Unfortunately, you don't know how susceptible you are until it's too late. Sure, the chance may be one in a hundred, but if you're that one, it's not terribly comforting to know that the other ninety-nine percent are doing fine.

I.4. Best and Worst Case Scenarios

There's still a lot of unknowns here. Nobody has ever seen Olney's lesions in a human brain. It could be that this damage only occurs very rarely, to people with underlying neurological disorders, and that most people who experience impairment are simply suffering from neurotransmitter depletion, receptor reregulation, or some sort of learned phenomenon (similar perhaps to the flashbacks a small percentage of LSD

users get). That's the best case scenario.

The worst case? Everyone using dissociatives may be doing permanent damage to their temporal and perhaps frontal lobes. This damage would be cumulative, adding up over each experience, with heavy or extended doses doing especially heavy damage. Unfortunately, you may not know there's anything wrong at first. Neural networks are a lot like holograms, in that you can remove or damage part of them and the built-in redundancy will keep things working more or less properly (perhaps with a bit less flexibility). Once you get to a certain threshold, however, it gets rapidly worse. Think about it like a curve ball; from the batter's perspective, the ball goes in a straight line and then suddenly darts away, even though it's really making a steady arc.

The damage you do now may not even show up until you are much older. There are many causes of neuron loss; mild head injuries, high blood pressure, unnoticed infections, maybe even the passage of time. The neurons that were overstressed may be forever weakened. You may find, thirty or forty years from now, that you've developed severe memory problems. I realize that sounds like a long time off, but believe me, the years pass a lot faster than you'd think.

The reality probably lies somewhere in the middle. After all, there are a lot of potential causes of brain damage. If activities were regulated on their potential to damage the brain, marijuana would be legal and alcohol would be banned, and boxers would get life in prison. And there are a lot of steps you can take to minimize the damage and improve your chances. I can't make decisions for you, and I wouldn't try to either; all I can do is point out all the risks. Climbing mountains is risky too, but I wouldn't suggest that nobody should do it.

II. Other Complications of Dissociative Use>

Just in case you didn't already know, there are a lot of other problems you can run into from using dissociatives. I don't intend to try and "preach" here, but a lot of people know very little about the drugs they take. There are some drugs, like marijuana, mushrooms, and LSD, which are very forgiving of ignorance. The dissociatives are not forgiving. I don't necessarily agree with the distinction between "hard" and "soft" drugs, but dissociatives probably lie on the borderline between the two. Not nearly as addictive as cocaine or heroin (or nicotine for that matter), but far more dangerous and

difficult to use safely than the serotonergic psychedelics and marijuana.

Here are some of the major dangers of dissociative use. At the end of this section are the dangers of specific dissociatives -- DXM, ketamine, PCP, and nitrous oxide.

II.1. Limbic Seizures and "Temporal Lobe Lability"

Simply put, if you are epileptic (diagnosed or not) or are susceptible to seizures, you should absolutely avoid dissociatives. They can induce seizure-like brain activity even in normal individuals, and there are several documented cases of people with underlying seizure disorders who suffered severe brain damage from using dissociatives.

There's also the possibility that dissociative use may induce seizures even in normal individuals. EEG activity suggests this, and many of the more extraordinary effects of dissociatives -- religious visions, for example -- are reminiscent of temporal lobe seizures. But I have yet to hear any solid evidence, and I'm skeptical.

A more reasonable phenomenon sometimes goes by the name "temporal lobe lability", and refers to a cluster of symptoms which are similar to those experienced by temporal lobe epileptics, without the involvement of actual epilepsy. Some of the more common symptoms include hearing voices (especially in white noise or static), visual disturbances, frequent deja vu or jamais vu, intense and fluid emotions, somatic hallucinations (electric shocks, "crawling skin"), delusions of reference (events seem to have unusual meaning), sensed presences, and spiritual experiences (within the current mythology this can appear as alien encounters). By the way, this refers to symptoms experienced while sober, not while intoxicated.

It's not clear (to me) whether this represents a real phenomenon or whether it's a product of cultural factors, but I'm inclined to believe the former. The phenomenon is more frequent and intense in women and left-handers, which implicates the temporal lobe or limbic areas (thus the name). Michael Persinger has published papers on the subject, suggesting it may be an undiagnosed seizure disorder, but I think Persinger sees limbic seizures hiding behind every tree.

Whatever the nature of temporal lobe lability, quite a few long-term dissociative users

have told me these specific symptoms tend to become more frequent over time. Most seem to view it as an annoyance more than anything else. I have a personal hypothesis on this subject, but it's rather complex and detailed; essentially, I think its a learned phenomenon, not a neurological one. The counterpoint view is that it is neurological, and may represent a gradual loss of inhibitory GABAergic neurons or glial cells (this would be bad).

II.2. Psychosis and Schizophrenia

There is always a risk of psychotic breaks whenever you use psychedelics; intense experiences have a way of doing that. I don't believe that the serotonergic psychedelics (LSD, mescaline, DMT, psilocybin, etc.) can turn normal individuals psychotic; instead, I suspect that people with an underlying mental condition may find the drug experience triggers an outbreak of the disease. This isn't good, of course, but keep in mind that any intense experience can do this; if we want to protect such people from outbreaks of mental illness, we'd be best off by outlawing divorce, marriage, and having children. A followup study of people who used LSD in the 1960's showed no evidence of more frequent mental illness, and among native Ayahuasca-using cultures, those who used the drug were just as stable and sane as those who didn't.

The dissociatives may be a different story, however. I don't yet have complete statistical data here, but it seems thus far that psychotic breaks and schizophrenia-like symptoms (both positive and negative, unlike LSD-induced breaks) are far more frequent with heavy or regular dissociative use than any other type of psychedelic. I base this opinion on having communicated with hundreds of current and former users of DXM and a smaller number of ketamine and PCP users; it seems that the duration of intoxication is the crucial element here (and that DXM is the worst offender, possibly because of greater activity at sigma receptors and longer duration). About 5% of regular users of DXM in my sample have experienced some form of psychotic reaction that lasts well beyond the drug effects (usually a few weeks, rarely requiring hospitalization). It's worth noting that PCP's negative stereotypes come from these (rare) reactions.

II.3. Other Problems

All dissociatives are extremely toxic to developing fetuses and they should never be used during pregnancy (this probably includes cough-suppressant doses of DXM, by the way). Severe brain damage and mental retardation may result.

Dissociatives are addictive. Regular use depletes neurotransmitters, and heavy use (or addiction) will usually leave you depressed, anxious, and mentally impaired. Alcoholics are at higher risk of dissociative addiction, as are people with anxiety problems, social phobias, and mood disorders. My opinion is that the addiction is psychological and may be largely a response to the withdrawal symptoms.

Many dissociatives have a heavy "body load". DXM is the worst offender here, for details see The DXM FAQ (briefly, there's potential for hypertension or hypotension, and rarely, cardiovascular and liver damage). Some sources claim that breathing may be suppressed or slowed down too much at high doses; others say this doesn't happen. My personal feeling is that near-anaesthetic doses are risky if you are already at risk for hypoxia (e.g., you smoke a lot of cigarettes).

Dissociatives impair judgement and coordination so driving is a definite no-no. You are also prone to self-injury, and won't feel it until the drug wears off, so avoid overexertion. For unknown reasons some people seem to be attracted to water, and drownings have happened on ketamine and DXM; remember, you can't breathe water no matter how much you may think you can. Generally speaking, always keep in mind that you're somewhat "out of your body", and that no matter what you think you can do, you still have to consider whether your body can do it.

There's literally dozens of problems that people have reported from dissociative use, some of the uglier ones include bad allergic reactions, peripheral neuropathy, impotence, tinnitus (persistent ringing in your ears), and "acting like a narcissistic, self-absorbed wacko" (to quote one former ketamine user).

III. How to Minimize the Risks

Okay, that's the bad news. The good news is, there are ways to protect yourself and alternatives to dissociatives that may work for you. I'm going to go over some of the

more general ones, as well as some especially risky things you should avoid.

III.1. Abstainance and Limiting Use

Obviously the best thing to do is not use dissociatives. Duh. And the best way to avoid hitting the ground at terminal velocity is to avoid skydiving, the best way not to get pregnant is to avoid sex, and so on. A lot of people in this country (USA) have problems taking responsibility for the risks they take, so I'd better mention it.

If you won't quit, at least make sure you don't overdo it. The things to consider are frequency, duration, and dose. An analogy would be driving a car with a broken radiator. The longer or harder (heavier dose) you drive it, the more the engine heats up, and the longer you have to wait to let it cool off. If you drive it too long, too hard, or too frequently, you'll ruin your engine. I don't have any definite recommendations here, just try to keep use to a minimum (once a week at most).

After each dose you should wait at least two days before taking another dose; that is the minimum time it takes for neural activity in lab animals to return to normal. Dosing again within this time may be especially hard on your brain cells. If you do decide to take an extended dose, it's probably a good idea to wait a long time before dosing again. With DXM, for maximum safety I recommend one week per plateau between uses (and at least a month if not two between the extremely-dangerous "plateau sigma" trips). With ketamine, two weeks between uses would be the approximate equivalent. I'm not going to speculate on PCP because of its additional toxicity to other areas of the brain. Because nitrous oxide is so short-acting, I have no recommendations other than "use as little as possible" (not usually a problem, since it tends to deplete one's wallet of cash before depleting one's brain of neurons).

III.2. GABAergic Sedatives and Other Drugs

If you aren't going to abstain, the best thing you can do to protect your brain when you take a dissociative may be to take another drug which will keep the susceptible brain cells from becoming overactive, or help them resist the stress. There are several

possible options, however keep in mind that I am only going to report what has helped in animal tests, and what some have suggested may help in humans. I do not recommend that you take these drugs, of course; that decision is up to you and your doctor. I'm only offering you the knowledge that's available from medical science.

Sedative drugs which act upon the GABA receptor are proven to prevent Olney's lesions in lab animals. They almost certainly work in humans too, and their use in conjunction with nitrous oxide may be what keeps the anaesthetic from being more dangerous to brain cells. Of the various types of GABAergic sedatives -- benzodiazepines and barbiturates, chiefly -- the benzodiazepines are by far the safest; barbiturates are extremely dangerous. Unfortunately, benzodiazpines are also prescription drugs in the USA and some other countries, so if you live in such a country, you must see your doctor to obtain benzodiazepines legally. Benzodiazepines are the minor tranquilizers, including Valium, Librium, Klonopin, etc. (chemically they go by names ending in -pam, e.g., diazepam, clonazepam, etc.). A very low dose is all that is needed to protect lab animals, so a single dose may be enough for humans (but this is unknown).

Note that the major tranquilizers (antipsychotics) are an entirely different class of drugs, and you do not want to take them with dissociatives. They protect some brain cells, but make the damage far worse for others. They also lower the seizure threshold, making it more likely you may experience seizures from dissociatives.

GHB, gamma-hydroxybutyrate, is a sedative drug but its interaction with dissociatives is unknown. Some research suggests it may also lower the seizure threshold. There is another class of sedatives which activate the alpha-2 adrenergic receptor (xylaxine is one), but research is inconclusive and you should probably avoid them.

Alcohol is partially a GABA blocker, and may be effective, but this is unproven. Alcohol also blocks the NMDA receptor and has some qualities of dissociatives; it hasn't been shown to cause Olney's lesions in animals (though keep in mind that it is toxic to the brain and liver, especially in higher doses). Most people say that drinking more than one or two drinks can make them violently ill while on dissociatives. I personally don't think alcohol is a good choice.

There are some problems with using GABAergics, though. The biggest danger is respiratory depression. All sedatives will suppress breathing to some degree, and mixing a sedative and a dissociative could be very dangerous, especially when you

approach the anaesthetic level. Also, some people find that the more interesting effects of dissociatives are blocked when they take a sedative, possibly because it is the unusual limbic activity that creates such unusual effects on consciousness. Finally, keep in mind that all GABAergic sedatives are addictive, and should never be used for long periods of time because withdrawal can be very dangerous. Remember, in many areas these are prescription drugs and you must see your doctor to get an actual recommendation and a prescription.

You can also try to prevent damage by increasing the resilience of your brain cells. There are several different vitamins and nutrients which may help, may do nothing, or may even hurt; I'm going to mention some which physicians and researchers have mentioned. Coenzyme Q10 may offer some protection by preventing mitochondria from running out of energy. Antioxidants (vitamin C, vitamin E, and several natural products) may help to curb the free-radical reaction thought to be involved. A few people have suggested Ginko biloba which may increase cerebral metabolism (and help bring nutrients to cells and clear out waste products); on the other hand, it may also affect brain activity more directly, and the results are unknown (it could make things worse). And of course a multivitamin (an ordinary dose, not megadoses!) probably wouldn't hurt, since many people don't eat as well as they should.

Finally, there may be drugs which specifically protect against Olney's lesions. Curiously, in animal tests, LSD is one such drug (because of its affinity for a particular neuroreceptor, incidentally it's probably not the neuroreceptor involved in its psychedelic effects). However, LSD is also illegal so of course you shouldn't take it. Furthermore, combining LSD and dissociatives may produce overpowering effects which many find very unpleasant.

Nitrous oxide specifically depletes vitamin B12, so a supplement may be a good idea. Vitamin B12 doesn't absorb well, but there are sublingual forms available which may absorb better.

III.3. Health Issues

Always stay healthy! The very best thing you can do to protect yourself, short of abstinance, may be to keep yourself in good physical health so your brain can heal itself before permanent damage occurs. This means eat right, exercise, and don't smoke

cigarettes. You want to keep your blood pressure low, because high blood pressure makes Olney's lesions much worse (but taking drugs to lower blood pressure probably won't help; high blood pressure may be more a symptom than a cause). Exercise and not smoking will improve oxygen flow to the brain, and help limit and clear out free radicals.

III.4. Safer Alternatives to Dissociatives

No matter what altered state you are looking for, there are usually alternative ways to find it. Sometimes they can be easy, sometimes it may take more effort, but this effort usually pays off.

If you find yourself using dissociatives to self-medicate -- to make yourself feel better, to block out anxiety or social phobia, or for other such reasons -- then you might be best off consulting a psychiatrist. You may have an underlying problem which is treatable, either by therapy or safer drugs or both. Many areas have low-cost mental health services available. Barring that, you may wish to try natural products like St. John's Wort for depression and Kava Kava for anxiety; they can be surprisingly effective (not to mention cheaper than commercial drugs). It should be obvious, but if you have social anxiety problems, cutting down on caffeine can help. For a major problem, though, natural products may not be strong enough, and you should always see a professional. Keep in mind that antidepressants alone can trigger manic reactions if you have bipolar disorder.

If you like the introspective, self-exploratory aspects of these drugs, then consider meditation. It takes awhile to get good at it, and until you do it can seem rather silly, but it really does work if you stick with it. Transcendental Meditation was suggested to me as an alternative for some of the more interesting altered states induced by dissociatives, and though I know little about it, there are published papers which seem to support this idea.

If you're just looking to get high, or for a party drug, then there may be far safer drugs available to you. If you live in an area where marijuana (cannabis) is legal, that is the best alternative; not only is it non-toxic to the brain (recent research shows it actually protects brain cells), it's also impossible to overdose, unlike dissociatives. Unfortunately, marijuana is illegal in most places so you're out of luck there. Alcohol

is a poor alternative; it is addictive and causes brain damage. Numerous psychedelics exist in nature which may be legal in your area, though of course most of them are very different than dissociatives.

There is one natural psychedelic which may be the very best alternative for those interested in the visionary and self-exploratory aspects of dissociatives. It is not, however, a party drug. This is Salvia divinorum, the "Diviner's Sage", a member of the mint family. It can take numerous tries before the drug has any effect, and set and setting are extremely important. There is a wealth of information available about Salvia divinorum at . Be careful with fortified Salvia products, as large doses of Salvia can be extremely disorienting. If at first you get no response, keep trying; if you approach this plant with patience and respect, the quid method (chewing the leaves for sublingual absorption) can be quite rewarding. Incidentally, it is not known whether Salvia is toxic to the brain or otherwise dangerous, though indigenous people have used it for many years without ill effect.

III.5. What to Avoid Like the Plague

There are a number of drugs and conditions which you should absolutely avoid if taking dissociatives, because they may seriously increase the risk of brain damage or health problems. Here is a partial list of some of the more common ones. This doesn't include the various things which can increase the risk of adverse psychological problems or bad trips; such a list would probably be rather large.

- Drugs which may make Olney's Lesions worse:
  - Yohimbine and yohimbe (and other alpha-2 antagonists) may dramatically increase the brain damage! These should be avoided at all costs.
  - Major tranquilizers (antipsychotics) may specifically increase damage to certain areas
  - Anticholinergic deliriants (atropine, scopolamine, and anti-nausea drugs) may increase damage to the hippocampus. This may include antihistamine-anticholinergics including the DXM-antihistamine preparation Coricidin!
- Drugs which lower the seizure threshold, and may increase the risk of seizures (this is a very incomplete list):
  - Antibiotics of certain classes, notably ofloxacin (which can be extremely neurotoxic on its own)

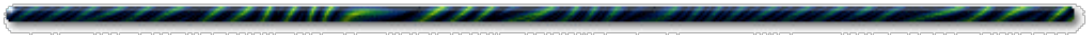
    - Anticholinergics
    - Antipsychotics
    - Bupropion, sold as the antidepressant Wellbutrin and as the "stop smoking" pill Zyban
    - Caffeine (in large doses; otherwise probably low risk)
    - GHB and 1,4-butanediol (possibly)
    - Various unusual drugs, e.g., Absinthe
- Drugs which suppress respiration, when high doses of dissociatives are taken:
    - Tranquilizers (benzodiazepine sedative-hypnotics) in high doses
    - Barbiturates and methaqualone (Quaaludes)
    - Alcohol in moderate to heavy doses
    - GHB and 1,4-butanediol (possibly)
- All monoamine oxidase inhibitors (MAOIs) including herbal MAOIs such as Syrian Rue
- Concurrent use of too many serotonergic drugs such as selective serotonin reuptake inhibitors (SSRIs) and tricyclics, MDMA (ecstasy), tryptophan and 5-hydroxytrypophan (5-HTP), due to risk of serotonin syndrome.
- Poor physical condition, which can increase risk of hypertension and Olney's Lesions
- Large doses of sugars (like drinking cough syrup) which may increase free radical damage.

IV. Conclusions

Remember that the risks from dissociatives, though manageable, are also very real. The everyday drug-ignorant person likely has a belief in "acid casualties", people who were driven insane by too much tripping in the 1960's. And there undoubtedly are people who took LSD and lost touch with reality, just as there are people who have lost touch with reality subsequent to any number of activities (one study found watching too many late night movies to be especially significant, probably because certain mental illnesses cause insomnia). But more than one formal study of LSD users has shown that the drug hasn't made its users any crazier than everyone else.

But anyone who has had firsthand contact with enough dissociative users will eventually run across the casualties, those people who find themselves addicted to

a drug which is driving them deeper and deeper into the abyss. Like I said, the risks are manageable, but taking risks means taking responsibility. I've already heard of far too many people who rolled the dice and lost their sanity, their loved ones, their emotions and memory, even their lifes. Let's try to keep this sort of thing to a minimum.



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