

Bibliography¹²

Scientific Papers

[1]

Adamson, Simon J., J. Douglas Sellman, Ann Futterman-Collier, Terry Huriwai, Daryle Deering, Fraser Todd, and Paul Robertson. 2000. A profile of alcohol and drug clients in New Zealand: results from the 1998 national telephone survey. *New Zealand Medical Journal* 13:414-416.

Provides profiles of clients seeking treatment for drug or alcohol problems, based on a survey of randomly selected treatment workers. Of 291 clients, the primary problem of 45% was alcohol, of 27% was cannabis, and of 17% was opiates. Only 5.5% had problems with other drugs, including combinations of drugs. Maori were over-represented, and more likely to have problems with cannabis. Pacific Islanders and Asians were under-represented. Women were 40% of the sample, an over-representation as women make up around 30% of people with substance disorders. Women may be more likely to seek help, and Asians and Pacific Islanders less likely.

[2]

Austin, Helen, and Erik Monasterio. 2004. Acute psychosis following ingestion of 'Rapture'. *Australasian Psychiatry* 12 (4):406-408.

Describes a brief psychotic episode following the ingesture of the social tonic Rapture. A twenty-year-old man with no history of psychiatric problems took four tablets of Rapture, along with small quantities of cannabis and nitrous oxide. Twelve hours later, he developed an acute psychiatric episode, including delusions of persecution and auditory and visual hallucinations. Believing his life was in danger, he attempted to alert the authorities by setting fire to his flat, then jumped out of the (second floor) window. He was admitted to a psychiatric ward, treated with benzodiazepines, and recovered within 48 hours. The very low level of cannabis he consumed makes it unlikely that this drug had anything to do with his condition.

The background to social tonics in New Zealand is described. The chemistry of BZP is also described - the drug is derived from the pepper plant (explaining the 'herbal' label) but can also be produced synthetically. It is absorbed through the gastrointestinal tract - some is degraded and the rest is excreted in urine. There is no human therapeutic application for BZP or TMFPP.

¹² Throughout the bibliography, text in italics is used to represent commentary on the source document, where it may be unclear whether opinions cited are mine, or those of the author of the source document. Where italics are not used, the views expressed are those of the author of the source document, except where it is obvious from the context that they are mine.

BZP abuse was first reported in the USA in 1996, and the drug has been classified as a Schedule 1 controlled substance. However, a literature review showed no systematic research or case reports on the use of these substances. Anecdotal evidence suggests possible psychiatric symptoms following their use.

This article provides the first scientific evidence that these drugs might pose short-term psychiatric risks.

[3]

Batenburg, Marijke. 2001. The agony and the intimacy of 'ecstasy'. *New Zealand Doctor*, 23 May 2001, 27.

A therapist reports that more of her patients have been using ecstasy. The drug has effects on both mental performance, though users don't notice that they are performing poorly, and mood. Direct questioning of patients as to whether they use ecstasy is recommended. If a patient is abusing ecstasy, referral to a specialist psychologist is recommended, and is cheaper than the cost of the drugs.

Batenburg asks why, as intimacy is a fundamental human need, do many people choose or need drugs to obtain it? Supporting people to develop intimacy without drugs might be the challenge of this decade for therapists, she suggests.

The article is let down by some inaccuracies - the suggestion that ecstasy is similar to marijuana at lower doses, and that GHB is the liquid form of the drug. (Though nicknamed 'liquid ecstasy', GHB is a completely different substance, with different effects).

[4]

Black, Steve, Sally Casswell, and A. Wyllie. 1993. *Drugs in New Zealand: a survey, 1990*. Revised edition. Auckland, N.Z.: Alcohol & Public Health Research Unit.

Several thousand people were interviewed via telephone in Auckland and Bay of Plenty. Alcohol and tobacco were the most commonly used drugs, but many (43%) had tried cannabis. Few people used any other drug. Ecstasy had less than a 1% lifetime use rate, and stimulants had a 5% rate. Lifetime use rates were similar to Australia, but lower than in the USA (other than for hallucinogens).

The majority of people thought that penalties for using or selling drugs were too lax.

The researchers suggested a possible under-reporting of the more socially unacceptable drugs. Youth, ethnic minorities, and lower socio-economic groups were under-represented in the survey.

This research is obviously not necessarily generalisable to the rest of the country (Auckland, as the largest city, and Bay of Plenty, as a rural area where marijuana could be grown easily, would possibly have higher rates of use than the rest of the country). However, it does provide good baseline data on rates of drug use in New Zealand, at that time.

[5]

Bushnell, John, Helen Carter, and Philippa Howden-Chapman. [1994]. *A review of the epidemiology of substance use disorders in New Zealand, Research Report; 2*. [Wellington, N.Z.]: Health Services Research Centre.

Reviews research on the nature and number of substance use disorders reported in New Zealand. A key source of the material is the study by Black and Casswell (1993) [4]. Also reports results from a 1989 study in Christchurch, which found a lifetime prevalence of amphetamine use of 2.7%, with 0.7% of subjects reporting problems with amphetamine abuse/dependence. This study deliberately targeted people with mental disorders, so it is not a random sample of the population as a whole. The other information in the report is general, referring only to 'drug addiction' or 'drug abuse', without consideration of the type of drug abused.

The report predicted that the number of drug users and abusers would stay more or less the same - that there is a core number of users which is unlikely to increase or decrease much.

This was a reasonable prediction, but the authors did not take into account the possibility of locally-manufactured drugs overcoming the geographic isolation that has seen New Zealand maintain a relatively low rate of drug use. With the benefit of hindsight, we see that the market for illicit drugs other than cannabis is larger than was then thought.

[6]

Caldwell, Jane. 2003. CPP: Co-Morbidities in mental health. *Pharmacy Today*, August 2003.

The NZHPA Mental Health Special Interest Group (SIG) held a seminar on methamphetamine use in Auckland. Janie Sheridan (Auckland University) reviewed the history of methamphetamine. It is not widely used in the UK because other stimulants are widely available. Users may binge for several days, or alternatively use methamphetamine just at parties (for example). In contrast, media reporting implies that all users binge.

Sheridan discusses the neurochemistry and positive and negative effects of methamphetamine and the rapid rise in tolerance which regular users experience.

Possible treatment for addiction is discussed, along with specifics of methamphetamine psychosis, by psychiatric consultant Dr Angela Ryan. Ryan points to a lack of clinical data, but some anecdotal evidence of successful treatments.

[7]

Cheung, Vivian, Jean-Louise Nguyen, and Polly Ho Yi Yeung. 2004. *Alcohol and drugs in New Zealand: an Asian perspective: a background paper, ALAC Occasional Paper: 22*. Wellington: ALAC.

<http://www.alac.org.nz/InpowerFiles%5CPublications%5CCategorisedDocument.Document1.2952.7a4c171f-c525-4903-8ebf-d25104831703.pdf> [accessed 14 May 2005].

Reviews the experience of Asian New Zealanders in relation to drugs and drug use. The paper is a literature review of New Zealand and overseas research, aiming to identify factors associated

with an increased risk of drug abuse in New Zealand Asians. It proposes reasons for such abuse (such as post-migration issues), and discusses cultural perspectives on alcohol and drug use (for example, the belief that alcohol and some drugs are therapeutic).

The report is written at a very general level. It does note that Asian students are becoming involved as importers of the precursor ingredients for methamphetamine, and apparently offering their houses as clearing houses for importation. This is the only mention of methamphetamine in the article. There is a small mention of ecstasy, pointing out that some of the biggest hauls of ecstasy seized in this country have been imported by Asians.

[8]

Dacey, Brendon, and Helen Moewaka Barnes. 2000. *Te ao taru kino = Drug use among Māori, 1998*. [Auckland, N.Z.]: Whariki Māori Health Research Group, Alcohol & Public Health Research Unit. <http://www.aphru.ac.nz/whariki/publications/Te%20Ao%20Taru%20Kino.htm> [accessed 5 May 2005].

Reports Maori usage of drugs. There is very little information on the drugs of interest to this study. Usage rates (lifetime and last-12-month) are reported for hallucinogens (15%, 7%) and lifetime usage rates are reported for stimulants (7%). These are not broken down.

Illegal drugs (other than marijuana) were reported to be the drugs of most concern for the community. Most people felt that penalties and levels of law enforcement for selling drugs, or using drugs other than marijuana, were too light. Some felt that penalties for using marijuana were too heavy.

[9]

Daniela, Evangelene, K. Brennan, D. Gittings, Lincoln Hely, and Susan Schenk¹³. 2004. Effect of SCH 23390 on (+/-)-3,4-methylenedioxymethamphetamine hyperactivity and self-administration in rats. *Pharmacology, Biochemistry and Behavior* 77 (4):745-50.

MDMA-produced hyperactivity was reduced by pre-treatment with SCH 23390. This suggests that hyperactivity has a dopaminergic basis. Results suggest that use and abuse of MDMA is related to dopaminergic mechanisms. The researchers cite other research showing that subjective feelings of well-being produced by ecstasy are reduced by pre-treatment with dopamine blockers.

The research is interesting, but would seem to have little practical relevance in the debate over ecstasy. It doesn't change our knowledge of the effects of ecstasy, it analyses the reasons for those effects.

[10]

Dragunow, M., Barbara Logan, and Richard Laverty¹⁴. 1991. 3,4-Methylenedioxymethamphetamine induces Fos-like proteins in rat basal ganglia: reversal with MK 801. *European Journal of Pharmacology* 206 (3):255-8.

Shows that injections of MDMA to rats leads to an accumulation of c-fos protein (Fos)¹⁵. This is inhibited by MK 801, but not by fluoxetine. This action involves activation of NMDA receptors. The implications of these results are not discussed.

[11]

Ellis, Paul, and Peter Schimmel. 1989. Ecstasy abuse. *New Zealand Medical Journal* 102 (871):358.

The case of an "agitated and distressed" woman who presented at Wellington Hospital experiencing mood swings and depression. She made frequent references to ecstasy and exhibited signs of paranoia and delusion. She was admitted and given medication, but killed herself days later.

Drug tests showed no evidence of ecstasy in her bloodstream, but the medication she had been given could have masked it.

The diagnosis that she was abusing ecstasy is somewhat problematic - her references to it could have been delusions. Nevertheless, this is the first published reference to ecstasy in New Zealand.

[12]

Field, Adrian, and Sally Casswell. 1999. *Drugs in New Zealand: national survey, 1998*. [Auckland, N.Z.]: Alcohol & Public Health Research Unit.

A national survey of the drug usage of 5475 people aged between 15 and 45. Alcohol, tobacco and marijuana were the most frequently used drugs, with 50% having tried marijuana, though few used it frequently. 3% of the group had tried ecstasy, 1% had used it in the last year. 9% of the population had used stimulants, 3% had used in the last year. These results are reported to be similar to usage rates in the UK, Australia and the USA.

Later research [24] shows that, while the prevalence of use in New Zealand may be comparable to those countries, the frequency and volume of use is much lower.

Public opinion was generally that the penalties for sale and possession of drugs are too lenient.

Usage rates were higher in Northland, and in urban areas, especially Auckland.

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¹⁵ Substances such as Fos and MK801 will not be described in this bibliography. The assumption is that readers who have an interest in the technical aspects of research described here will already understand what they are.

[13]

Hattaway, Vivienne. 2002. Ecstasy and methamphetamine: what do they do and how do they work? *New Zealand Pharmacy* 22 (9):17-19.

An informative, highly technical review of the effects of ecstasy and methamphetamine, including details of neurotoxicity caused by the drugs, and the risk of serotonin syndrome. Describes possible neuroprotective measures, and when and how these might work.

Describes how knowledge of these measures has reached rave/dance culture. Advises chemists that the purchase of neuroprotectors, such as 5-HTP, tryptophan and anti-oxidants might be considered a predictor of possible ecstasy or amphetamine use.

Health risks of ecstasy are reviewed (for a medically-trained audience), and the history and neurochemistry of the drug are briefly discussed.

[14]

Inter-Agency Committee on Drugs. [1999]. *Resource document relating to National Drug Policy: identification of outcome indicators*. [Wellington, N.Z.?]: [Inter-Agency Committee on Drugs]. [Title from cover.]

A report designed to accompany the National Drug Policy (NDP) [59]. It sets out indicators that can be used to measure progress against the outcomes listed in the National Drug Policy. As with the NDP, much of this document relates to the reduction of alcohol, tobacco and cannabis-related harm.

Only a few indicators related to stimulants are given. These include reducing the number of people who have ever used, or are currently using, stimulants or hallucinogens, the amount of drug-related crime, and the amount of drugs being imported into the country.

Measures for these indicators have been developed in some cases - for the number of drug users, the *Drugs in New Zealand* surveys [4, 12]. For other indicators, developing appropriate measures is harder - Customs are working on a measure of drug importations, but Police state that arrest data is not a suitable measure for drug-related crime.

It's interesting to note how little research there is on drug use, and the drug economy, in New Zealand - especially with relation to illicit drugs other than cannabis.

[15]

Laverty, Richard, and Barbara J. Logan. 1989. Ecstasy abuse. *New Zealand Medical Journal* 102 (874):451.

Responds to [11]. Reports that the authors are investigating the effects of MDMA, including attempting to develop tests for the drug. They ask that doctors let them know if they have patients who are using the drug, and attempt to obtain a sample of the drug, so that Laverty and Logan can analyse the contents. The intention is to determine the chemical nature of drugs that are being

sold as ecstasy, to determine whether they are truly MDMA or if they are some other substance.

[16]

Laverty, Richard, and Barbara J. Logan¹⁶. 1990. Protection by MK801 and other drugs of methylenedioxymethamphetamine (MDMA) neurotoxicity in rats and mice. *European Journal of Pharmacology* 183:451-2.

Builds on previous research by the authors, which showed that high doses of ecstasy could cause depletion of serotonin and dopamine in rats and mice respectively. This research shows that the neurotoxicity can be blocked by pre-treatment with MK 801. Pre-treatment with fluoxetine (Prozac) was shown to have no effect.

This research has important implications. An often-cited health risk of ecstasy use is the potential of neurotoxic brain damage. This research shows that neurotoxicity can be prevented by taking another drug before or simultaneously with the ecstasy. This is a point that is almost never made by critics of ecstasy - the argument is that, since it can potentially be harmful, its use should be avoided completely.

The suggestion that fluoxetine does not prevent neurotoxicity is also important, as it is widely believed by ecstasy users that it does so.

[17]

Lee, J. W. Y¹⁷. 1994. Catatonic stupor after "ecstasy". *British Medical Journal* 308:717-718.
<http://bmj.bmjournals.com/cgi/content/full/308/6930/717/b> [accessed 8 May 2005].

Responds to a case study published in the *British Medical Journal*. Says that two ecstasy users should not have been diagnosed as suffering from 'catatonic stupor', as they did not meet clinical criteria for that diagnosis. Mutism might be an appropriate diagnosis.

[18]

Logan, Barbara J¹⁸., Richard Laverty, William D. Sanderson, and Yet Ben Yee. 1988. Differences between rats and mice in MDMA (methylenedioxymethamphetamine) neurotoxicity. *European Journal of Pharmacology* 152 (3):227-34.

Ecstasy causes different forms of neurotoxicity to rats and mice. Neurotoxicity is dose dependent - single doses caused only temporary falls in serotonin, dopamine and noradrenalin levels, which returned to normal within 24 hours.

Multiple doses within a short period caused a large fall in serotonin levels, which persisted for at least 7 days. Increasing the dose again produced a fall of serotonin levels for 14 days, and a "profound" fall in dopamine levels. Specific effects varied between species, and can not

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necessarily be generalised to humans.

This study has practical applications, because it suggests that single doses (even relatively high ones) of MDMA are not likely to cause neurotoxicity. The problem occurs when multiple doses are taken in short spaces of time. If these effects are generalisable to humans, then the potential neurotoxicity caused by ecstasy can be minimised.

[19]

Logan, Barbara, and Richard Laverty. 1989. MK801 blocks the dopaminergic neurotoxicity of MDMA in mice. *Proceedings of the University of Otago Medical School* 67:51-52.

Ecstasy neurotoxicity may be caused by over-activation of amino acid receptors. The NMDA receptor is one such receptor. MK 801, taken prior to methamphetamine, reduces the neurotoxicity caused by that drug. This study shows that MDMA neurotoxicity is also reduced by pre-loading with MK 801. Other research shows that this protective mechanism does not work in rats. This is because MDMA neurotoxicity takes different forms in rats and mice – in the former it is related to serotonin, in the latter, to dopamine.

A noteworthy feature of the research is the very high doses of MDMA the mice received – 50mg/kg of body weight, repeated three times in the space of 30 hours. Such doses approach the LD 50 of MDMA.

[20]

Russell, Bruce R., and Richard Laverty¹⁹. 2000. Correlation between 5-HT Content and Uptake Site Density following (S)-MDMA and Dexfenfluramine-induced Depletion, and with Neuroprotection by the Glycine Site-specific NMDA Antagonist ACEA 1021. *Annals of the New York Academy of Sciences* 914:208-214.

http://www.annalsnyas.org/cgi/content/abstract/914/1/208?maxtoshow=&HITS=&hits=&RESULTFORMAT=1&andorexacttitle=and&titleabstract=ecstasy+MDMA+amphetamine+BZP+&andorexacttitleabs=or&fulltext=zealand&andorexactfulltext=and&searchid=1110687204897_19867&stored_search=&FIRSTINDEX=0&sortspec=relevance&fdate=1/1/1988&resourcetype=1

[accessed 20 April 2005].

Reports on neurotoxicity and possible neuroprotective mechanisms for MDMA in rats. Uses two measures of serotonin depletion in each animal, rather than just one, and demonstrates that both measures were closely correlated. The measures were serotonin content in specific brain regions, and serotonin uptake site density. ACEA 1021 protects against neurotoxicity, though via a different process than MK 801.

These results are significant because they show that there are ways of protecting the brain from potential damage caused by ecstasy.

[21]

Russell, Bruce R., and Richard Lavery²⁰. 2001. The effect of (R)-HA966 or ACEA 1021 on dexfenfluramine or (S)-MDMA-induced changes in temperature, activity, and neurotoxicity. *Pharmacology, Biochemistry and Behavior* 68 (3):565-574.

Shows that ACEA 1021 prevented MDMA-induced neurotoxicity in some parts of the brain, and partially prevented it in other parts of the brain. Suggests that this may be due to ACEA 1021 preventing MDMA-induced hyperthermia.

[22]

Schenk, Susan, D. Gittings, M. Johnstone, and Evangelene Daniela²¹. 2003. Development, maintenance and temporal pattern of self-administration maintained by ecstasy (MDMA) in rats. *Psychopharmacology (Berl)*. 169 (1):21-7.

Laboratory rats who have been trained to self-administer cocaine were quicker to learn to administer MDMA than drug naive rats. A high response rate was observed in the first hour, followed by a decline to a steady rate. Self-administration was extinguished by substituting a salt solution for the MDMA, but reinstated when MDMA was reintroduced.

The authors claim that these results indicate that MDMA has a high addictive potential.

However, when used by humans, MDMA usage tends, eventually, to be self-limiting - taking multiple doses of the drug does not increase the effect or maintain the 'high'. It is not possible to binge on MDMA for days. There is anecdotal evidence that users spend a period of perhaps 6 months to 2 years using MDMA heavily, and then voluntarily cease or greatly reduce their use, with no major ill effects. So the study may not have identified true addictive potential.

[23]

Wilkins, Chris, Sally Casswell, Krishna Bhatta, and Megan Pledger. 2002. *Drug use in New Zealand: national surveys comparison 1998 & 2001*. [Auckland, N.Z.]: Alcohol & Public Health Research Unit. <http://www.aphru.ac.nz/projects/drugs%202001%20TC.htm> [accessed 5 May 2005].

Compares the results of the 1998 and 2001 National Drug Surveys. Each survey interviewed a random sample of 5,500 people aged between 15 and 45 nationwide. Alcohol and tobacco were the most widely used drugs. Around half the population (50% and 52% in 1998 and 2001 respectively) had tried cannabis.

More respondents had tried ecstasy (3% in 1998, 5.4% in 2001) and had used it in the past year (1.5% in 1998, 3.4% in 2001). Use of stimulants (amphetamine/methamphetamine) also increased, from 7.6% to 11% for lifetime use and from 2.9% to 5% for current use. Prevalence of use of other drugs was stable.

20 University of Otago.

21 Victoria University of Wellington.

Multiple drug use was common, but this primarily involved use of marijuana and the various legal drugs. 'Other' drugs (that is, illegal drugs other than marijuana) were considered to pose the biggest problems to New Zealand, though there was a decrease in the number of people stating this from 1998 to 2001. Most people believed that penalties for supply of illegal drugs were too lenient.

[24]

Wilkins, Chris, James Reilly, Emily Rose, Debashish Roy, Megan Pledger, and Arier Lee. 2004. *The socio-economic impact of amphetamine type stimulants in New Zealand: final report*. Auckland [N.Z.]: SHORE.

One of the key pieces of research in this field, aiming to provide police with better data than they would obtain from arrest or treatment records. It reviews the prevalence, financial value, health risks, and links to crime of amphetamine-type stimulants (ATS), including methamphetamine, crystal methamphetamine and ecstasy. The study found 1 in 10 18-29 year olds had used the drugs in the last year. The dollar value of the amphetamine industry (\$168.3 million) is equal to that of the cannabis industry, meaning that the illicit drug economy in New Zealand has doubled in value in the last 10 years, with most proceeds going to gangs.

Regarding health issues, many users reported pre-existing mental health problems, but use of methamphetamine increased their psychological problems (anxiety, mood swings, paranoia, depression, suicidal thoughts and attempts). Over half of frequent users reported harm to friendships, health, energy and vitality. 13% of frequent users reported suicide attempts after ceasing use. On the other hand, 50% of users reported no problems, and that they could easily stop or go without. 20% of drug treatment patients cited methamphetamine as their main problem. Polydrug use and bingeing were common among frequent users.

Ecstasy users also reported harmful effects - around 30% said they had experienced negative effects, mainly on their energy and vitality. Other effects (such as on health, outlook on life, social life, and finances) were all much lower - unsurprising, given the very low doses taken by New Zealand users.

Frequency of use in New Zealand far lower than in other countries. For example, 60% of ecstasy users had used only 1 or 2 times in the past year - only 2% used weekly. So though 3% of the population had used ecstasy in the past year, only a fraction were regular users. Additionally, doses were very small - 60% took 1 pill per session, but 25% took only half a pill.

By comparison, in the UK, multiple pills per session are common, with 3 or 4 being common, and 8 or 10 not unheard of²².

5% of the population had used methamphetamine in the past year, but 54% of those only used 1-2 times in that year, 19% more than once a month, and only 0.2% daily. Ice use showed a similar profile, although there was a hard core of 2% using several times a day.

22 This figure confirmed by discussion with British ecstasy users on the Bluelight bulletin board <http://www.bluelight.nu>

Polydrug use is high, but basically consists of alcohol, cannabis, tobacco and one other drug - few users are bingeing on multiple classes of drug.

Around 20% of arrestees had used methamphetamine in the month before they were arrested - 9% just before they committed the offence. They indicated drug use was a factor in their offending, making them angry. Arguably, this could be seen as criminals attempting to shift the blame for their behaviour from themselves to an external source.

Frequent users were also likely to sell or manufacture methamphetamine, so focusing attention, whether the criminal justice system or the health system, on frequent users would lead to an impact on the overall drug economy. Most users did not buy from tinny houses (only 5%, as opposed to 50% of cannabis sales), and methamphetamine dealers were much more likely to only sell to people they knew.

The demographics of drug use are changing, with the possibility that different socio-economic groups, Maori, Pacific Islanders, and teenagers are becoming more likely to use methamphetamine.

Smoking, snorting and injection were the most common methods of taking methamphetamine. Users reported that it was very easy or easy to get (though this is of course a circular question - if someone can't obtain a drug they can't be a user of it). On the other hand, pharmacy medications containing methamphetamine precursors are becoming harder to obtain.

Police claimed that various gangs were prominently involved in manufacture - with the Triads, Black Power, Mongrel Mob and Tribesmen the key players.

ATS users were mainly European or Maori - use was low in the Pacific Island and Asian communities.

This is a very important piece of research. It provides a factual analysis of the scope of the problem in New Zealand, and refutes both those who claim that New Zealanders' use of amphetamine-type substances is high by global standards, and those who claim that such drugs are basically harmless.

[25]

Zheng, Yiwen, and Richard Laverty²³. 1998. Role of brain nitric oxide in (+/-)3,4-methylenedioxymethamphetamine (MDMA)-induced neurotoxicity in rats. *Brain Research* 795 (1-2):257-263.

Investigates the mechanisms by which ecstasy may cause neurotoxicity. Begins by reviewing the evidence that shows that damage occurs (all of which is based on animal research), and then reports the results of a study into neurotoxicity, using rats as subjects.

23 University of Otago.

Results show that a single high dose of MDMA caused significant decreases in brain serotonin levels, which according to the investigators indicates long-term damage to serotonin terminals. The authors report that results suggest that brain nitric oxide may play a role in the damage caused by ecstasy use, at least in some parts of the brain.

It's worth noting that the dosage given to the rats was far in excess of what any human would take as a single dose.

[26]

Zheng, Yiwen, Bruce Russell, David Schmierer, and Richard Lavery²⁴. 1997. The effects of aminorex and related compounds on brain monoamines and metabolites in CBA mice. *Journal of Pharmacy and Pharmacology* 49 (1):89-96.

Reports the results of a study comparing the neurotoxic effects of ecstasy, fenfluramine, and aminorex. MDMA is only a tangential part of this study, being used as a control condition. Researchers were comparing the effects of aminorex with the known effects of the other amphetamine-type substances. In accordance with much previous research, MDMA was found to reduce brain concentrations of dopamine and serotonin. However, as MDMA affects neurochemistry differently in different parts of the brain, and when different species are studied, the researchers conclude that the mechanisms are complicated and require more study.

24 University of Otago.