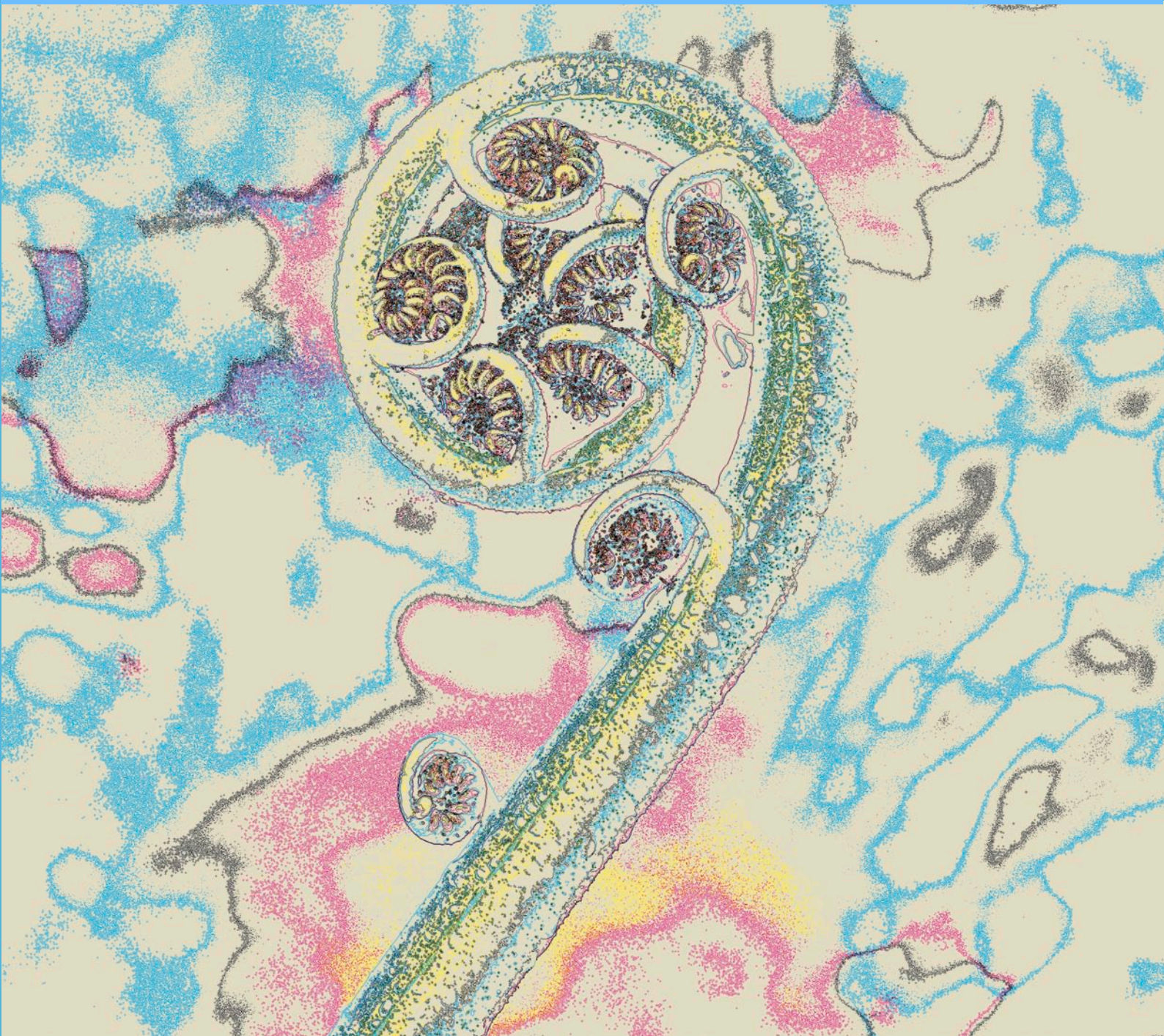# Matua Raki

National Addiction Workforce Development

What's new in Interventions and Treatment for Problematic use of Methamphetamine and Other Amphetamine-Type Stimulants (ATS)

2013

Overview

Interventions and Treatment for Problematic Use of Methamphetamine and Amphetamine-Type Stimulants (ATS) 2010 was commissioned by the Ministry of Health as part of the Tackling Methamphetamine Action Plan in response to the Cabinet Briefing paper 2009 and published by Matua Raki in 2010.

This update has been prepared to review the content of the guidelines and current developments in the treatment of problematic methamphetamine and amphetamine-type stimulant (ATS) use. The content of the update is based on a literature search of current best practice and emerging developments in the treatment field.

Summary

From a review of the recent research and treatment literature related to the use of methamphetamine and ATS it appears that the information and recommendations contained within Interventions and Treatment for Problematic Use of Methamphetamine and Amphetamine-Type Stimulants (ATS) are still relevant and current. Specifically the current literature confirms that:

- no pharmacotherapy has been consistently identified as being effective in helping people to reduce and or stop use of ATS

- no pharmacotherapy has been identified as being particularly useful to help with withdrawal management

- the stepped care model for treatment remains appropriate as an intervention pathway, ie:

    » Brief Interventions

    » Contingency Management

    » Combined Motivational Interviewing and Cognitive Behavioural Therapy

    » Matrix Model

    » Treatment of co-existing problems

    » Residential addiction treatment

This update to the original guidelines contains a summary of new information about the impact of methamphetamine and ATS use and an introduction to promising pharmacotherapy and treatment options that may emerge as significant adjuncts to current best practice.

Contents

Current trends in methamphetamine and ATS use in Aotearoa New Zealand

The 2011/12 New Zealand Health Survey shows a prevalence rate of methamphetamine use over the past 12 months of 0.9 per cent for the population between 16 and 64 years old, with males being 2.6 times more likely to use methamphetamine than females. In comparison, data from 2007 suggests that 2.2 per cent of the population had used methamphetamine in the previous 12 months [1].

Hospital admissions throughout New Zealand related to methamphetamine use appear to have been relatively stable over time with 203 people admitted to hospital in 2009, 234 in 2010 and 229 in 2011 (ibid). The main reasons people were hospitalised for methamphetamine use were psychotic disorders or other mental health and behavioural disorders.

Accurate nationwide data about the number of people seeking treatment for problematic methamphetamine and ATS use is currently unavailable due to inconsistent data collection. Although flawed, information collected by the Ministry of Health shows a general increase in the number of people attending mental health and addiction services with a diagnosis of ATS abuse or dependence. Between 2008/09 and 2011/12 the number of people with a primary diagnosis of ATS abuse or dependence doubled [2]. Significant numbers of people have also been identified as having ATS use as a secondary issue when attending mental health and addiction services. Internationally it has been noted that "5% of reported drug clients" entering treatment in Europe in 2009 described ATS as their primary problematic substance [3].

Figure 1: Number of people attending mental health and addiction services with a primary or secondary diagnosis of harmful or dependent use of ATS: 2008/09-2012/13
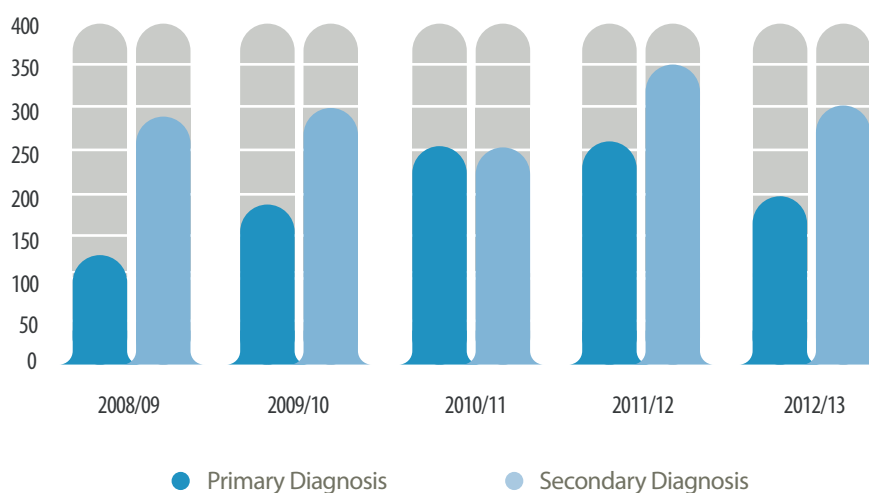
Source: Ministry of Health: PRIMHD October 2013

This pattern of contact with services over the past few years is also reflected in data provided by the Alcohol Drug Helpline. The Alcohol Drug Helpline reports that between July and September 2013 they had 314 people make contact with the Helpline about methamphetamine use. Significantly 226 of these calls were from family and whānau members concerned about someone else's methamphetamine use. This is consistent with an on-going pattern of family and whānau members being more likely to seek help for someone's methamphetamine use than the person themselves. Of the 88 people who contacted the Helpline on their own behalf between July and September of 2013 19 'self' callers and 24 'concerned other' callers chose to take up the support of the specialist meth help team at the Helpline.

Figure 2: Family/whānau and self-referral to Alcohol Drug Helpline July 2010-September 2013
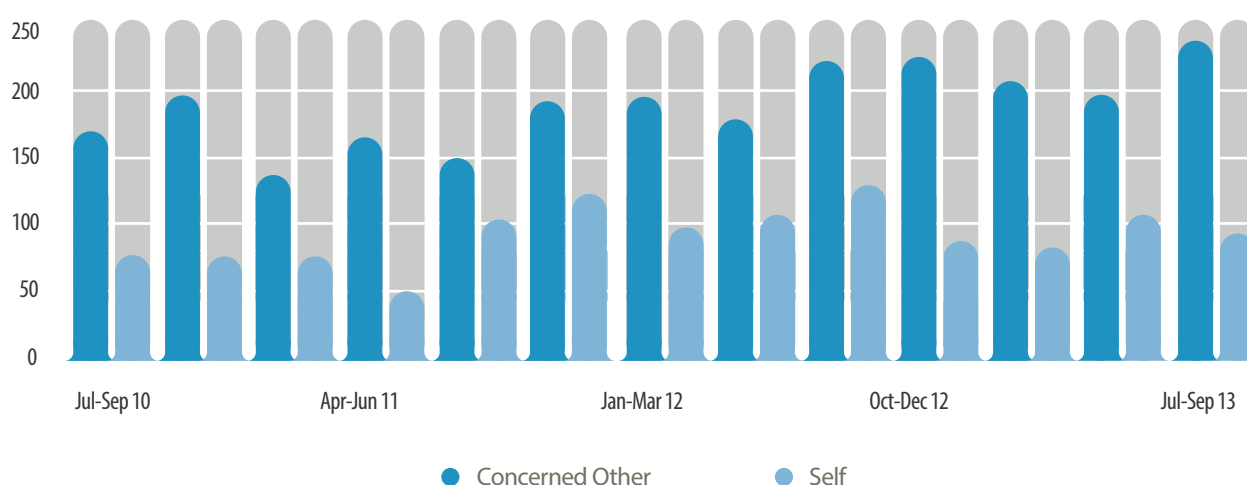
Source: Robert Oborn, Alcohol Drug Helpline Quarterly Report, October 2013

Predictors and potential risks associated with methamphetamine and ATS use

The development of ATS use disorders is associated with a history of:

- alcohol use disorder (79%)

- cannabis use disorder (73%)

- family histories of substance use (32%), mood disorders (41%) and psychosis (20%)

- imprisonment, homelessness or hospitalisation for substance use or mental health problems (20%) [4].

Risks associated with use of ATS as a young person include:

- an increase in the prevalence of depressive symptoms in the year following first use independent of any evidence of a predisposition to a mood disorder [5]

- a greater risk of early onset psychosis in schizophrenia [6].

Cognitive Problems

A debate continues in the literature over the nature of the impact of methamphetamine and other ATS use on cognitive functioning and what that means for people in terms of day to day functioning. There does seem to be general agreement that people with an established ATS use disorder are more likely to have deficits in:

- executive functioning
- learning
- verbal fluency
- working memory.

This may be reflected in:

- greater disinhibition
- aggression
- slower reaction times
- higher rates of errors on cognitive testing [7,8].

These effects are apparently more pronounced when people are exposed to ATS related cues [9]. Prospective memory (an aspect of memory related to making decisions to do something at a particular point of time in the future) impairment is particularly related to executive dysfunction and earlier age of first ATS use. As a consequence people with an ATS use disorder may have difficulties learning cognitive strategies that are promoted in Cognitive Behaviour Therapy approaches or recalling when and or how to use them [10].

 A 2010 study [11] investigating the possible impact of ATS use disorders on day to day functioning observed that people were cognitively impaired in areas that correlated to:

- comprehension
- finance
- transportation
- communication
- medication management.

It has also been suggested that the impact of ATS on verbal episodic memory (where people may be less able to store and recall new visual information) could have a significant impact on ability to drive, work or use a computer in unfamiliar situations [12].

The exact causes of the cognitive changes due to ATS use have been theorised as due in part to the action of ATS at the 'blood brain barrier' increasing permeability and allowing toxins such as bacteria and viruses to cause neuroinflammation. ATS use also has an impact on central and peripheral immune systems adding to neuroinflammation and neuronal damage that can persist for at least two years in people who have abstained from ATS use following a severe ATS use disorder [13].

Physical changes to the structure of the brain of people with ATS use disorders include reduced volume in the frontal, parietal and occipital regions of the cortex [14].

It is possible that some of the cognitive impairments that are attributed to ATS use predate ATS use. This is suggested in a study of siblings of people with an ATS use disorder who appeared to have similar impairments in executive functioning and slower reaction times, despite no history of ATS use disorders[15]. The implication of this is that people with these pre-existing cognitive impairments may have a greater attraction to ATS use, possibly to compensate for the impairments. This cannot be verified, however, as there have been few studies that have a baseline of cognitive functioning prior to ATS use for comparison. It has also been observed that the significance of the effects of ATS on cognitive functioning may be overstated as the majority of the deficits noted in the literature fall within normal ranges of functioning [16].

Co-existing substance use, physical and mental health problems

People who have an ATS disorder appear to have a greater risk of:

- premature death (compared with people with cannabis, cocaine and alcohol use disorders) [17]

- poor quality of life (especially if female, European, educated, married, a poly substance user, intravenous user, or having co-existing mental and/or physical health problems) [18]

- having a past or current mental health disorder (largely accounted for by mood disorders, anxiety disorders and anti-social personality disorder) which is associated with higher rates of ATS use and impairment [19]

- aggressive and violent behaviour, especially in young males [20]

- having psychotic symptoms, especially with high levels of ATS use and or alcohol and or cannabis use at the same time [21]

- neurochemical changes and a reduction in amygdala and hippocampal volume similar to those observed in people with schizophrenia, as there appears to be genes common to the susceptibility to experience an ATS induced psychosis and schizophrenia and these genes probably lower the threshold for becoming psychotic [22, 23]

- neurochemical levels and brain functioning changes similar to those observed in Parkinson's Disease with an apparent higher risk of developing symptoms of Parkinson's Disease [24]

- poorer treatment outcomes and physical and mental health problems if an anxiety disorder is present at the commencement of treatment [25]

- poorer treatment outcomes and greater use of health services and higher levels of functional impairment if bulimia nervosa is present at the commencement of treatment [26].

Treatment

Pharmacotherapy

Medications that have been used in trials to treat ATS use disorders and help maintain abstinence include:

- methylphenidate
- naltrexone
- bupropion
- mirtazapine
- sertraline
- modafinil
- dextroamphetamine
- ondansetron
- risperidone
- aripiprazole
- baclofen
- gabapentin
- flumazenil
- topiramate.

Despite some promising trials the consensus appears to be that none of these medications consistently reduce the use of ATS in people with an ATS use disorder [27, 28] including a recent trial of methylphenidate in Aotearoa New Zealand [29].

The future

Medications currently being considered for potential therapeutic effects include naltrexone implants [30] and oxytocin [31], which has been observed to reduce the effects of methamphetamine in rats.

Vaccines to combat addiction have been considered a possible approach to help people who wish to stop using substances (and stay stopped). These vaccines work by antibodies attaching themselves to substances to make their molecules too large to cross the blood brain barrier. Vaccines against cocaine and methamphetamine have been developed and are currently undergoing clinical testing for safety[32]. Anti-methamphetamine monoclonal antibodies could theoretically be taken once every two to four weeks to reduce or prevent the effects of methamphetamine and have been demonstrated to reduce methamphetamine effects and self-administered use in rats [33].

Modafinil, while not particularly effective in terms of reducing methamphetamine use, does appear to have some positive cognitive benefits, including improving working memory [34], and also reduces daytime sleepiness in people who have stopped ATS use. It has been suggested that there is a correlation between the acute withdrawal effects of excessive sleepiness and 'craving' for ATS and modafinil may help to reduce this aspect of 'craving' in early treatment [35]. A trial of a combination of gabapentin and flumazenil also appeared to reduce 'craving' and subsequent methamphetamine use [36].

Medications that have been recently trialled to treat cognitive deficits associated with ATS use disorder include:

- ibudilast (an anti-inflammatory)

- minocycline (a broad spectrum antibiotic)

- RTL551 (a neuroantigen peptide construct).

All these medications have anti-inflammatory properties that are theorised to address some acute and protracted neuroinflammatory effects of ATS. In mice, ibudilast reduced the acute and chronic effects of ATS on activity levels [37]. Minocyline has been shown to improve deficits in the ability to recognize new objects and RTL551 has been observed to improve learning, memory and CNS inflammation in rodents that have been exposed to ATS over time [38].

Treatment services

People with ATS use disorders appear to be most likely to access treatment services when they are either reducing levels or frequency of ATS use. Half of the people who use ATS problematically are unlikely to access treatment services very often if at all. A quarter will use for less than five years before engaging in treatment while the other quarter will use for over five years [39].

Detoxification by itself apparently has little impact on later ATS use patterns, but residential treatment has been associated with reductions in later ATS use. In one study about a third of people who attended residential treatment abstained from ATS use for at least three months after treatment, though after three years this figure had reduced to 6 per cent remaining abstinent [40].

Abstinence, or near abstinence at the beginning of treatment, appears to be a reasonable predictor of treatment outcomes, with people who have few if any ATS-positive urine drug screens in the first days of treatment being more likely to finish treatment [41]. Sustained abstinence during treatment, as measured by urine drug screening, has also been observed to be the strongest predictor of abstinence at follow up[42].

An adapted treatment programme which involved people attending group and individual sessions with a 12-step focus and introducing them to peers from a 12-step programme (eg Narcotics Anonymous), STAGE-12, has recently been shown to be effective in supporting people to remain abstinent. However, those people who did not become abstinent during treatment used more ATS during the eight weeks of treatment than people receiving treatment as usual [43].

A 'stepped care' approach to intervention has been demonstrated to be effective to ensure treatment is targeted appropriately [44]. Recent studies have also demonstrated that Brief Interventions appear to be effective as interventions with problematic ATS use. Brief modified Motivational Enhancement Therapy (MET) appeared to be effective with young people to promote readiness to change ATS use behaviours [45] and the Brief Intervention associated with ASSIST[46] appeared to be particularly effective for changing ATS use [47]. Telephone based treatment has also been shown to be effective in the short term with some people responding better to directive and others to non-directive interventions [48].

In terms of treatment for ATS use disorders and retaining people in treatment, the combination of Cognitive Behavioural Therapy with Contingency Management remains the most effective intervention according to research findings. In addition this combination is of benefit when used in combination with pharmacotherapy [49, 50].

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