

The 10 most important things known about addiction

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ABSTRACT

If you were asked: 'What are the most important things we know about addiction?' what would you say? This paper brings together a body of knowledge across multiple domains and arranged as a list of 10 things known about addiction, as a response to such a question. The 10 things are: (1) addiction is fundamentally about compulsive behaviour; (2) compulsive drug seeking is initiated outside of consciousness; (3) addiction is about 50% heritable and complexity abounds; (4) most people with addictions who present for help have other psychiatric problems as well; (5) addiction is a chronic relapsing disorder in the majority of people who present for help; (6) different psychotherapies appear to produce similar treatment outcomes; (7) 'come back when you're motivated' is no longer an acceptable therapeutic response; (8) the more individualized and broad-based the treatment a person with addiction receives, the better the outcome; (9) epiphanies are hard to manufacture; and (10) change takes time. The paper concludes with a call for unity between warring factions in the field to use the knowledge already known more effectively for the betterment of *tangata whaiora* (patients) suffering from addictive disorders.

Keywords Addiction, comorbidity, compulsion, entheogens, knowledge, lifestyle change, motivational interviewing.

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Everything of importance has been said before by somebody who did not discover it (Alfred North Whitehead, 1861–1947)

The most important things in life aren't things (Anthony J. D'Angelo, 1972–present).

INTRODUCTION

Enthusiastic young colleagues new to the addiction treatment field not infrequently ask a question something like this: 'What are the most important things I need to know about addiction and how to treat it that I can read about over the next month or two?'. This paper documents a list of 10 things about addiction that have emerged over the last three or four decades that form an overview of the most important things known about addiction that I think would be useful for new colleagues to get to grips with quickly as they embark on their career in addiction treatment. It may also be useful for established colleagues to compare with their own list in the ongoing process of freshening up clinical practice and as a prelude to considering the most fruitful areas to research that will bring

about the greatest treatment improvements for addicted people. This summary is not intended to be an exhaustive catalogue of addiction treatment knowledge. It focuses upon addiction treatment in dedicated addiction treatment settings and is naturally biased towards the work of key figures in the international field who have had a significant influence on the thinking of our group at the National Addiction Centre (NAC) Aotearoa, New Zealand. If you were limited to listing the 10 most important things known about addiction, would your list be similar to what follows?

I. ADDICTION IS FUNDAMENTALLY ABOUT COMPULSIVE BEHAVIOUR

A key element to understanding addiction, often lost on the public and even lost at times on health professional colleagues, is the way in which an individual's behaviour associated with various addictive objects (alcohol, other drugs, electronic gambling machines, pornographic websites, hedonic food, etc.) becomes increasingly compulsive [1–4]. Although not understood fully at a neurobiological level, the normal flexibility of human behaviour

guided by neocortical ‘higher power’ [5] appears to become increasingly eroded towards a dehumanized state of compulsive behaviour, the ‘sticky’ repertoire of habitual behaviour that constitutes the addictive life-style, mediated by a ‘compulsive circuit’ (nucleus accumbens, ventral pallidum, thalamus and orbitofrontal cortex) [6]. Thirty years ago the diagnostic concept of addiction (dependence) in the DSM-III [7] was focused around neuroadaptation to drugs—evidence of acquired tolerance and/or withdrawal symptoms. This traditional American concept was reviewed in DSM-III-R [8] to one much closer to an earlier-described UK concept [9], focused upon a behavioural syndrome including dyscontrol, salience and neuroadaptation, but also compulsive behaviour evidenced by the addicted person continuing to use drugs despite knowledge of negative medical and psychological consequences. A challenge for the future is to understand the development of compulsivity at a neurochemical level not only for drugs, but for the range of emerging behavioural addictions and, moreover, how to measure addiction compulsivity more accurately. Instruments such as the Obsessive Compulsive Drinking Scale [10] are a good starting point, but ultimately an instrument needs to be compatible with advancing neurobiological aspects as well as the psychobehavioural characteristics of compulsive behaviour.

2. COMPULSIVE DRUG SEEKING IS INITIATED OUTSIDE OF CONSCIOUSNESS

Addictive behaviour appears to involve processes outside of the sufferer’s personal consciousness by which cues are registered and acted upon by evolutionary primitive regions of the brain before consciousness occurs. The nucleus accumbens, a key limbic structure in these primitive regions, puts drug-seeking behaviour into motion [11], and so ‘decision making’ can be said to occur without conscious initiation. This putative process challenges the traditional view that people exercise their ‘free will’ to use drugs [12]. ‘Free won’t’ [13], presumably involving healthy orbitofrontal functioning [14], is half a second behind the ‘decision’, given the half-second delay required to ‘crank up’ consciousness in the human brain in response to cues [15]. However, the consequences of the usual disconnected human state of living consciously half a second behind what has already been ‘decided’ is exaggerated in people with addiction, because the initiation of drug-seeking behaviour is engaging a well-worn pattern of learned compulsive behaviour, overriding the ability to alter course when anticipated negative consequences are finally realized. The optimally functioning human brain with all its pre-existent imperfections [16] is compromised further by addiction.

3. ADDICTION IS ABOUT 50% HERITABLE AND COMPLEXITY ABOUNDS

Thirty years ago, alcoholism was demonstrated to be a strongly familial disorder [17]. With this foundation, a large literature including twin, half-sibling and adoption studies demonstrated subsequently that alcohol dependence is a genetically influenced disorder for both men and women, with heritability estimates ranging from 40 to 60% [18,19]. The development of animal models has strengthened the concept of addiction as a genetically influenced disorder [20]. Further, heritability estimates for other drug addictions have been reported subsequently from 0.4 for hallucinogens to 0.7 for cocaine and alcohol just above 0.5 [21], and the concept of addiction as a ‘complex genetic disease’ [22], involving multiple interacting genetic and environmental factors, has become the dominant paradigm.

However, 30 years ago environmental influences seemed almost impossibly complex in the aetiology of addiction, given the multitude of potential factors from intrauterine experience through to early life trauma and deprivation, family disadvantage, peer influences in adolescence, as well as societal attitudes and public policy. In contrast, at the turn of the century with the mapping of the human genome, molecular genetics seemed bold, clear and hopeful, with great promise that the genetic base to many diseases, including addictions, would be unravelled swiftly and a new era of genetically based treatments ushered in. The early tridimensional structure of personality [23], highlighting behavioural activation, inhibition and maintenance, respectively, pointed to the possibility of there being perhaps three key genetic influences in the common familial factors associated with addictions [24] that are temperamentally based. However, the dream of rapid resolution of the genetics of addiction has not been realized, and the hope of a handful of primary genes has been expanded to ‘hundreds’ with compounding genetic complexity, including multiple linked genes, multiple functional variants and epigenetic processes [25,26]. The latter have been instrumental in the collapsing of the Sir Francis Galton (1822–1911)-inspired ‘nature versus nurture’ debate into a new interactive model of ‘nature via nurture’ [27]. Genes and environment are no longer viewed as separate entities, but interconnected intimately as a continuum in the mysterious dance of life.

4. MOST PEOPLE WITH ADDICTIONS WHO PRESENT FOR HELP HAVE OTHER PSYCHIATRIC PROBLEMS AS WELL

It is somewhat unusual to encounter a person presenting to out-patient addiction services with addiction problems

alone. In New Zealand the extent of co-occurrence of current Axis I psychiatric disorder in out-patient community services at 74% makes psychiatric comorbidity the rule, rather than the exception [28], the three most common disorders being social phobia, major depression and post-traumatic stress disorder. This is the same order of prevalence rate found in other systematic studies of patients presenting to addiction services in Scandinavia and the United Kingdom, where 75–85% of those presenting with alcohol problems and 75–90% of those presenting with drug problems other than alcohol were found to have current psychiatric problems [29,30].

In contrast to this, the three major randomized controlled trials of our field over the past 30 years, Project MATCH [31], the UK Alcohol Treatment Trial (UKATT) [32] and the Combined Pharmacotherapies and Behavioral Intervention (COMBINE) Study [33], all operated with exclusion criteria that would have excluded many people with psychiatric disorder who are the ‘bread and butter’ of routine addiction treatment services: people with significant multiple drug problems, those with psychiatric disorders that can benefit from medication, including psychotic disorders, and people whose accommodation and general life functioning is brittle. There is therefore a credibility gap between the findings of the most important (and most expensive) studies in the field and the challenges of real-life addiction treatment work [34]. A priority for future clinical addiction research must be for inclusion/exclusion criteria to be formulated which will yield more valid research samples, particularly in terms of co-existing psychiatric disorder.

5. ADDICTION IS A CHRONIC RELAPSING DISORDER IN THE MAJORITY OF PEOPLE WHO PRESENT FOR HELP

Abstinence as the basis for recovery from severe alcohol problems is now a well-established treatment strategy, buttressed by the seminal *Addiction* editorial in 1995 which drew upon 25 years of moderation research in alcoholism [35]. However, although up to about a third of people with alcohol dependence will achieve abstinence following treatment in the short to medium term [36–38], continuous ongoing abstinence from alcohol in those with alcohol addiction, or indeed abstinence from other drugs in other drug addiction, is relatively unusual in the long term. In fact, fewer than 10% of people with drug addiction (alcohol dependence/opioid dependence) will have continuous abstinence following treatment when followed long term [39]. The majority of people with addiction experience a chronic relapsing course of their illness, although many experience significant periods of stability and improvement along the way.

Addiction as a ‘chronic relapsing disorder’ has been consolidated by an illustrative comparison of drug dependence with three chronic medical illnesses: Type 2 diabetes, hypertension and asthma [40]. Similar rates of symptom recurrence and relapse are found between these three traditional medical diseases and addiction, as well as similar rates of treatment adherence, especially in the area of life-style change where fewer than 30% of patients with the three diseases are found to adhere to prescribed diet and/or behavioural changes aimed at improving health. The place of addiction as just one of a range of contemporary life-style-based diseases is well established conceptually and phenomenologically, but the expression of positive humanitarian attitudes towards people with addiction compared with sufferers of other chronic medical diseases remains low. Miraculous (long-term continuous abstinence) cures are still an expected standard for people entering addiction treatment, not only by many of the public but by pockets of professionals working in the field as well. Unrealistic expectations are likely to inhibit people initially presenting for help, but more importantly put them off re-presenting when a recurrence has occurred.

6. DIFFERENT PSYCHOTHERAPIES APPEAR TO PRODUCE SIMILAR TREATMENT OUTCOMES

Prior to the beginning of a new era of anti-craving pharmacotherapies [41,42], treatment of addiction was dominated by psychosocial methods of intervention. A truly intriguing two decades of research on psychological treatment for addiction have now passed, focused upon alcohol dependence and featuring four main psychotherapies: cognitive-behavioural therapy (CBT), 12-Step facilitation therapy (TSF), motivational enhancement therapy (MET) and social and behavioural network therapy (SBNT). Project MATCH, ‘the largest, statistically most powerful, psychotherapy trial ever conducted’, led the way with 1726 people randomized to receive CBT, TSF or MET. In terms of main treatment effects, no significant differences were found between these quite disparate therapies in terms of the two primary alcohol outcome measures [31]. Two subsequent studies have proved very instructive. A UK initiative undertook an equally ambitious treatment outcome trial in alcohol dependence comparing MET and SBNT in 742 participants. Similar main effects findings were obtained—no significant differences in treatment outcome despite quite disparate psychological methods being applied [32]. Here in New Zealand the same MET being used in both Project MATCH and UKATT was tested against two control conditions: a placebo psychotherapy consisting of ‘non-directive reflective listening’ (NDRL) and a no-therapy

group [43]. Against expectations NDRL and no-therapy were found to be similar in effectiveness but both less effective than MET.

However, all these studies either excluded many patients with co-existing psychiatric disorders or focused upon less severe cases, reinforcing the need for more real-life psychotherapy research [34]. Nevertheless, Jim Orford is right about the need for a radical shift in the way in which psychological treatments for addiction are being conceptualized [44] in order to progress beyond simply further contributions to the pool of important negative findings; and Jerome Frank (1909–2005) can still be heard beyond the grave that successful outcomes from disparate psychotherapeutic modalities involve a range of common factors: ‘First we need to gain a better understanding of the interactions between patients, therapists, therapeutic settings and therapeutic rationale that arouse patients’ hopes, provide them with success experiences, arouse them emotionally and offer alternative solutions to their problems’ [45]. Demonstrating the qualities of being a good friend such as being flexible, honest and trustworthy and being interested and warm, as well as having therapeutic skills including exploration, reflection, making accurate interpretations, facilitating expression of affect and being affirming, are the basis for developing strong therapeutic alliances [46]. Strong therapeutic alliances are in turn strong predictors of engagement and retention of patients in treatment, including those with psychiatric co-morbidities [47], remembering inherent differences between men and women in terms of utilitarian and empathic needs, respectively [48].

7. ‘COME BACK WHEN YOU’RE MOTIVATED’ IS NO LONGER AN ACCEPTABLE THERAPEUTIC RESPONSE

Although never adopted formally as an appropriate therapeutic response to those who are struggling with their compulsive behaviour or, more likely, have not yet reached ‘square one’ in the change process, the rejecting comment ‘come back when you’re motivated’ (and/or ‘when you’ve reached rock bottom’) has had its fair share of circulation in treatment services. However, times have changed and there is no more influential contemporary champion of the importance of beginning treatment where the patient is, rather than where the therapist expects them to be, than Bill Miller; through the development of motivational interviewing (MI) [49], incorporating the Prochaska & DiClemente stages of change model [50,51] and, of course, sitting on the shoulders of the client-centred approach of Carl Rogers [52]. MI has brought about a seismic shift in the basic approach to helping people with addiction problems over the past few

decades, from noisy confrontation strategies to quiet listening approaches, particularly in the United States where confrontational models were expressed most intensely. During this time addiction treatment and motivational interviewing have become as synonymous with each other as addiction treatment and 12-Step programmes and MI has now been studied in many dozens of randomized controlled trials across a broad range of human problems [53,54]. The starting-point for therapeutic work is engagement through an empathic and respectful human relationship, which takes into account the person’s readiness for change. Clinicians will vary in their inherent capacity for seeing the world through their patients’ eyes; nevertheless, the experience and expression of empathy has been shown to be a learnable skill [55].

Parallel to these methods of strengthening internal motivation through a therapeutic relationship has been a growing awareness that a variety of external social pressures can also be invaluable in assisting people to engage in treatment and change their addictive behaviour [56]. However, addiction treatment is no different from any other health disorder intervention in terms of the importance of maintaining high standards of human rights, particularly related to informed consent for treatment [57].

Addiction treatment expertise must be applicable to the most severe and complicated of the people who present for help or the addiction treatment speciality will be viewed as hollow and lacking credibility. Effective models must be applicable to those with co-existing addiction and mental health disorders as much as they are to more mild and uncomplicated addiction problems. The work of Osher & Koefed [58] stands out in this regard, with a model that combines pragmatically internal and external methods of engagement, persuasion and relapse prevention in assisting people with complex problems.

8. THE MORE INDIVIDUALIZED AND BROAD-BASED THE TREATMENT A PERSON WITH ADDICTION RECEIVES, THE BETTER THE OUTCOME

Not confined to the addiction treatment field are various inter-professional group struggles regarding the nature of the problems that people present with and how best to intervene with these problems. A common example is whether a person’s difficulties should be considered via a categorical diagnosis versus an individualized formulation. Like many other such conceptual conflicts this is a false dichotomy, as both can contribute usefully to a full understanding of a person presenting with addiction-related problems in order to inform a comprehensive treatment plan. A service engaged in such conceptual

conflicts, or lacking in broad-based clinical expertise, can be limited severely in the assistance people with addiction can receive from such a service.

The new pharmacotherapy era of anti-craving medications brings the power of a nomothetic 'medical' approach to addiction treatment involving making diagnoses and instituting treatment for them, thus adding to the range of drug substitution treatments, which remain the most effective specific interventions for people with opioid dependence [59] or nicotine dependence [60,61]. However, this should never replace the vital ideographic approach of tuning into the uniqueness of each individual and fashioning a plan together, which addresses individual needs. Often practical solutions to social problems are required in the plan including accommodation, legal and vocational problems as well as addressing specific medical, psychiatric and family issues. The more a treatment plan addresses the individualized broad-based needs of a person the more effective it is [62,63], and clinical case management is an effective way of ensuring that patients receive such assistances [64].

9. EPIPHANIES ARE HARD TO MANUFACTURE

One of the most fascinating aspects of working in the addiction treatment field is the occasional dramatic recovery experience a person with addiction has that is often independent of the treatment in which the person is or has been engaged. Bill Wilson's 'white flash' experience of God in the midst of detoxification despair, following which he is said to have never taken another drink of alcohol [65], not only transformed his life but has had a profoundly positive effect on the whole of our field, with the advent of Alcoholics Anonymous as a prototypical self-help group and the development of the 12-Step programme as a spiritual path to recovery. However, dramatic life-changing experiences are hard to manufacture.

Lysergic acid diethylamide (LSD) was used extensively in Europe and the United States during the 1950s and 1960s [66], and systematic research in the late 1960s showed that those treated with LSD had significantly better treatment outcomes than those in control conditions during the first 3 months of treatment [67–69]. Psilocybin may be a useful hallucinogen to research further, with addicted people as another therapeutic 'entheogen' [70] following the demonstration of its significant impact on increasing meaningfulness in life in non-addicted subjects [71]. The US-led religious-based 'War on Drugs', however, is an impediment to rational thinking and serious research and development of new epiphany generating technologies such as this. It is note-

worthy that ketamine psychotherapy research from St Petersburg [72] has contributed to keeping this line of addiction treatment research alive. Where could we be today if the LSD research of the 1950s and 1960s had continued unabated in the United States, with its great National Institute on Drug Abuse (NIDA) and National Institute on Drug Abuse and Alcoholism (NIAAA) resources?

Recovery from addiction involves a re-orientation from self-deception to the pursuit of higher ideals [5]. New meaning and hope in life is required, a spiritual experience, which for some is best described as 'finding God'. Research into ways of assisting people more effectively and predictably re-orientate their lives is needed urgently to fill a gaping hole between current treatment methods and people's world-views and personal sense of purpose and meaning. Transformation of people with addiction through re-connection with their ethnic and indigenous worlds is at an early phase of scientific investigation, being led by work in New Zealand [73].

10. CHANGE TAKES TIME

Having an epiphany, which re-orientates a person's view of themselves and their place in the universe, is one thing; consolidating these new insights into ongoing real-life behaviour is another. Recovery from addiction is not so much a matter of changing one's mind but changing one's brain. Gene expression as a result of therapeutic experiences (formal and informal) must result in enough protein synthesis so that new behaviour in response to internal and external cues begins to trump old styles of response. This is a variable process rather than a discrete event [74], which can be likened to a career [75]. The key thing is that it takes time—months to years rather than days to weeks [76,77]. Recovery involves a person making substantial changes to their 'whole pattern of living' [39]. It is therefore useful to think of recovery in terms of life-style change, and for those accessing treatment services this involves clinical management giving way to self-management across four phases, as follows:

- 1 Treatment (picking up the pieces of a failed life-style);
- 2 Rehabilitation (assembling a new life-style);
- 3 Aftercare (practising the new life-style); and
- 4 Self-management (living the new life-style) [78].

One of the keys to achieving recovery from compulsive behaviour is having the patience to practice new behaviour for a long period of time [79]. Addicted people with temperaments featuring low persistence [80] will benefit from persevering therapists who can join in the process, genuinely valuing small improvements along the way and continuing despite disappointments.

SUMMARY AND CONCLUSIONS

These 10 things represent a broad sweep of addiction knowledge spanning from molecules to meaning in life, which have emerged over the past 40 years or so. Addiction involves a genetically influenced set of behaviours that become increasingly compulsive with repetition, although consciousness is not particularly required for the learning to take place. Most people who present for help have multiple problems, the majority of whom subsequently run a chronic relapsing course of their addiction problems. Various psychological treatments appear to produce similar results, but the more individualized and broad-based the whole input, the better the outcomes will be. Empathic listening is central to the beginning of the change process but consolidated life-style change takes time, even in those who recover from addiction following a seemingly miraculous life-changing experience.

It is clear that contemporary addiction treatment workers are faced with a challenge to think and develop skills across a range of domains, but sadly the international addiction treatment field continues to be held back by ongoing battles between different camps. Professional rivalries and mutual disrespect between various groups, such as between researchers and clinicians, physicians and psychologists, neuroscientists and social scientists, residential workers and community workers, practitioners and managers, impede progress. We all need to work harder at rising above those reptilian aspects in our human nature that tie us into territorial protection and a competitive stance in order that all the available knowledge can be used more effectively for the benefit of our *tangata whaiora* (clients).

Declaration of interest

None.

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References

1. Kenny P. J. Brain reward systems and compulsive drug use. *Trends Pharmacol Sci* 2007; **28**: 135–41.
2. Hyman S. E., Malenka R. C., Nestler E. J. Neural mechanisms of addiction: the role of reward-related learning and memory. *Annu Rev Neurosci* 2006; **29**: 565–98.
3. Everitt B. J., Robbins T. W. Neural systems of reinforcement for drug addiction: from actions to habits to compulsion. *Nat Neurosci* 2005; **8**: 1481–9.
4. Lubman D. I., Yucel M., Pantelis C. Addiction, a condition of compulsive behaviour? Neuroimaging and neuropsychological evidence of inhibitory dysregulation. *Addiction* 2004; **99**: 1491–502.
5. Sellman J. D., Baker M. P., Adamson S. J., Geering L. G. Future of God in recovery from drug addiction. *Aust NZ J Psychiatry* 2007; **41**: 800–8.
6. Koob G. The neurobiology of addiction: a neuroadaptational view relevant for diagnosis. *Addiction* 2006; **101**: 23–30.
7. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders*, 3rd edn. Washington, DC: American Psychiatric Association; 1980.
8. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders*, 3rd edn, revised. Washington, DC: American Psychiatric Association; 1987.
9. Edwards G., Gross M. M. Alcohol dependence: provisional description of a clinical syndrome. *BMJ* 1976; **1**: 1058–61.
10. Anton R. F., Moak D. H., Latham P. The Obsessive Compulsive Drinking Scale: a self-rated instrument for the quantification of thoughts about alcohol and drinking behaviour. *Alcohol Clin Exp Res* 1995; **19**: 92–9.
11. Hammer R. P. Neural circuitry and signaling in psychiatry. Chapter 4. In: Kaplan G. B., Hammer R. P., editors. *Brain Circuitry and Signaling in Psychiatry*. Washington, DC: American Psychiatric Publishing, 2002, p. 99–124.
12. Burns K., Bechara A. Decision making and free will: a neuroscience perspective. *Behav Sci Law* 2007; **25**: 263–80.
13. Obhi S., Haggard P. Free will and free won't. *New Sci* 2004; **92**: 358–65.
14. Schoenbaum G., Shaham Y. The role of orbitofrontal cortex in drug addiction: a review of preclinical studies. *Biol Psychiatry* 2008; **63**: 256–62.
15. Libet B., Gleason C. A., Wright E. W., Pearl D. K. Time of conscious intention to act in relation to onset of cerebral activity (readiness-potential): the unconscious initiation of a freely voluntary act. *Brain* 1983; **106**: 623–42.
16. Kluge M. G. *The Haphazard Construction of the Human Mind*. London: Faber and Faber; 2008.
17. Cotton N. The familial incidence of alcoholism. *J Stud Alcohol* 1979; **40**: 89–116.
18. Prescott C. A., Aggen S. H., Kendler K. S. Sex differences in the sources of genetic liability to alcohol abuse and dependence in a population-based sample of US twins. *Alcohol Clin Exp Res* 1999; **23**: 1136–44.
19. Hesselbrock M. N., Hesselbrock V. M., Epstein E. E. Theories of etiology of alcohol and other drug use disorders. Chapter 3. In: McCrady B. S., Epstein E. E., editors. *Addictions: A Comprehensive Guidebook*. New York/Oxford: Oxford University Press; 1999, p. 50–72.
20. Li T. K., Lumeng L., Doolittle D. P. Selective breeding for alcohol preference and associated responses. *Behav Genet* 1993; **23**: 163–70.

21. Goldman D., Oroszi G., Ducci F. The genetics of addictions: uncovering the genes. *Nat Rev Genet* 2005; **6**: 521–32.
22. Edenberg H. J., Kranzler H. R. The contribution of genetics to addiction therapy approaches. *Pharmacol Ther* 2005; **108**: 86–93.
23. Cloninger C. R. Neurogenetic adaptive mechanisms in alcoholism. *Science* 1987; **236**: 410–6.
24. Bierut L. J., Dinwiddie S. H., Begleiter H., Crowe R. R., Hesselbrock V., Nurnberger J. I. *et al.* Familial transmission of substance dependence: alcohol, marijuana, cocaine and habitual smoking. *Arch Gen Psychiatry* 1998; **55**: 982–8.
25. Kruglyak L. The road to genome-wide association studies. *Nat Rev* 2008; **9**: 314–8.
26. Ducci F., Goldman D. Genetic approaches to addiction: genes and alcohol. *Addiction* 2008; **103**: 1414–28.
27. Ridley M. *Nature via Nurture: Genes, Experience and What Makes Us Human*. New York: HarperCollins; 2003.
28. Adamson S. J., Todd F. C., Sellman J. D., Huriwai T., Porter J. Co-existing psychiatric disorders in a New Zealand outpatient alcohol and other drug clinical population. *Aust NZ J Psychiatry* 2006; **40**: 164–70.
29. Tomasson K., Vaglum T. A nationwide representative sample of treatment-seeking alcoholics: a study of psychiatric comorbidity. *Acta Psychiatr Scand* 1995; **92**: 378–85.
30. Weaver T., Madden P., Charles V., Stimson G., Renton A., Tyrer P. *et al.* Comorbidity of substance misuse and mental illness in community mental health and substance misuse services. *Br J Psychiatry* 2003; **183**: 304–13.
31. Project MATCH Research Group. Matching alcoholism treatments to client heterogeneity: project MATCH Post-treatment drinking outcomes. *J Stud Alcohol* 1997; **58**: 7–29.
32. UKATT Research Team Effectiveness of treatment for alcohol problems: findings of the randomised UK alcohol treatment trial (UKATT). *Br Med J* 2005; **331**: 541–6.
33. Anton R. F., O'Malley S. S., Ciraulo D. A., Cisler R. A., Couper D., Donovan D. M. *et al.* for the COMBINE Study Research Group. Combined pharmacotherapies and behavioural interventions for alcohol dependence: the COMBINE Study: a randomized controlled trial. *JAMA* 2006; **295**: 2003–17.
34. Humphreys K., Weingardt K. R., Horst D., Joshi A. A., Finney J. W. Prevalence and predictors of research participant eligibility criteria in alcohol treatment outcome studies, 1970–98. *Addiction* 2005; **100**: 1249–57.
35. Sobell M. B., Sobell L. C. Controlled drinking after 25 years: how important was the great debate? *Addiction* 1995; **90**: 1149–53.
36. Armor D., Polich J., Stambul H. *Alcoholism and treatment*. New York: John Wiley; 1978.
37. Edwards G., Orford J., Egert S., Guthrie A., Hawker C., Hensman M. *et al.* A controlled trial of treatment and advice. *J Stud Alcohol* 1977; **38**: 1004–31.
38. Sellman J. D., Joyce P. R. Does depression predict relapse in the six months following treatment for men with alcohol dependence? *Aust NZ J Psychiatry* 1996; **30**: 573–8.
39. Vaillant G. E. What can long-term follow-up teach us about relapse and prevention of relapse in addiction? *Br J Addict* 1988; **83**: 1147–57.
40. McLellan A. T., Lew D. C., O'Brien C. P., Kleber H. D. Drug dependence, a chronic medical illness: implications for treatment, insurance and outcomes evaluation. *JAMA* 2000; **284**: 1689–95.
41. Volpicelli J. R., Alterman A. I., Hayashida M., O'Brien C. P. Naltrexone in the treatment of alcohol dependence. *Arch Gen Psychiatry* 1992; **49**: 876–80.
42. O'Malley S. S., Jaffe A. J., Chang G., Schottenfeld R. S., Meyer R. E., Rounsaville B. Naltrexone and coping skills therapy for alcohol dependence: a controlled study. *Arch Gen Psychiatry* 1992; **49**: 881–7.
43. Sellman J. D., Sullivan P., Dore G. M., Adamson S. J., MacEwan I. A randomized controlled trial of motivational enhancement therapy (MET) for alcohol dependence. *J Stud Alcohol* 2001; **62**: 389–96.
44. Orford J. Asking the right questions in the right way: the need for a shift in research on psychological treatments for addiction. *Addiction* 2008; **103**: 875–85.
45. Frank J. D. Common features of psychotherapy. *Aust NZ J Psychiatry* 1972; **6**: 34–40.
46. Ackerman S. J., Hilsenroth M. J. A review of therapist characteristics and techniques positively impacting the therapeutic alliance. *Clin Psychol Rev* 2003; **23**: 1–33.
47. Meier P. S., Barrowclough C., Donmall M. C. The role of the therapeutic alliance in the treatment of substance misuse: a critical review of the literature. *Addiction* 2005; **100**: 304–16.
48. Fiorentine R., Nakashima J., Anglin M. D. Client engagement in drug treatment. *J Subst Abuse Treat* 1999; **17**: 199–206.
49. Miller W. R., Rollnick S. *Motivational Interviewing: Preparing People to Change*. New York: Guilford Press; 2002.
50. Prochaska J. O., DiClemente C. C. Stages and processes of self-change of smoking: toward an integrative model of change. *J Consult Clin Psychol* 1983; **51**: 390–5.
51. DiClemente C. C., Velasquez M. M. Motivational interviewing and the stages of change. Chapter 15. In: Miller W. R., Rollnick S., editors. *Motivational Interviewing: Preparing People to Change*. New York: Guilford Press; 2002, p. 201–16.
52. Rogers C. *Client-Centered Therapy: Its Current Practice, Implications and Theory*. Boston: Houghton Mifflin; 1951.
53. Burke B. L., Arkowitz H., Menchola M. The efficacy of motivational interviewing: a meta-analysis of controlled clinical trials. *J Consult Clin Psychol* 2003; **71**: 843–61.
54. Hettema J., Steele J., Miller W. R. Motivational interviewing. *Annu Rev Clin Psychol* 2005; **1**: 91–111.
55. Miller W. R., Yahne C. E., Moyers T. B., Martinez J., Pirritano M. A randomized trial of methods to help clinicians learn motivational interviewing. *J Consult Clin Psychol* 2004; **72**: 1050–62.
56. Wild T. C., Roberts A. B., Cooper E. L. Compulsory substance abuse treatment: an overview of recent findings and issues. *Eur Addict Res* 2002; **8**: 84–93.
57. Wild T. C. Social control and coercion in addiction treatment: towards evidence-based policy and practice. *Addiction* 2006; **101**: 40–9.
58. Osher F. C., Kofoed L. L. Treatment of patients with psychiatric and psychoactive substance abuse disorders. *Hosp Commun Psychiatry* 1989; **40**: 1025–30.
59. Ward J., Hall W., Mattick R. P. Role of maintenance treatment in opioid dependence. *Lancet* 1999; **353**: 221–6.
60. Nides M. Update on pharmacologic options for smoking cessation treatment. *Am J Med* 2008; **121**: S20–31.
61. Stead L. E., Perera R., Bullen C., Mant D., Lancaster T. Nicotine replacement therapy for smoking cessation. *Cochrane Database Syst Rev* 2008; **1**: CD000146.
62. McLellan A. T., Arndt I. O., Metzger D. S., Woody G. E., O'Brien C. P. The effects of psychosocial services in substance abuse treatment. *JAMA* 1993; **269**: 1953–9.

63. Platt J. J. Vocational rehabilitation of drug abusers. *Psychol Bull* 1995; **117**: 416–33.
64. McLellan A. T., Hagan T. A., Levine M., Meyers K., Gould F., Bencivengo M. *et al.* Does clinical case management improve outpatient addiction treatment? *Drug Alcohol Depend* 1999; **55**: 91–103.
65. White W. L. Transformational change: a historical review. *J Clin Psychol* 2004; **60**: 461–70.
66. Dobkin de Rios M., Grob C. S., Baker J. R. Hallucinogens and redemption. *Journal of Psychoact Drugs* 2002; **34**: 239–48.
67. Johnson F. G. LSD in the treatment of alcoholism. *Am J Psychiatry* 1969; **126**: 481–7.
68. Pahnke W. N., Kurland A. A., Unger S., Savage C., Grof S. The experimental use of psychedelic (LSD) psychotherapy. *JAMA* 1970; **212**: 1856–63.
69. Soskin R. A. Personality and attitude change after two alcoholism treatment programs: comparative contributions of lysergide and human relations training. *Q J Stud Alcohol* 1970; **31**: 920–31.
70. Ruck C., Bigwood J., Staples D., Ott J., Wasson R. G. Entheogens. *J Psychedelic Drugs* 1979; **11**: 145–6.
71. Griffiths R. R., Richards W. A., McCann U., Jesse R. Psilocybin can occasion mystical-type experiences having substantial and sustained personal meaning and spiritual significance. *Psychopharmacology* 2006; **187**: 268–83.
72. Krupitsky E., Burakov A., Romanova T. Ketamine psychotherapy for heroin addiction. *J Subst Abuse Treat* 2002; **23**: 273–83.
73. Huriwai T., Sellman J. D., Sullivan P., Potiki T. Optimal treatment for Maori with alcohol and drug problems: an investigation of the importance of cultural factors in treatment. *Subst Use Misuse* 2000; **35**: 281–300.
74. Gossop M., Marsden J., Stewart D. The UK National Treatment Outcome Research Study and its implications. *Drug Alcohol Rev* 2000; **19**: 5–7.
75. Anglin M. D., Hser Y., Grella C. E. Drug addiction and treatment careers among clients in the Drug Abuse Treatment Outcome Study (DATOS). *Psychol Addict Behav* 1997; **11**: 308–23.
76. Simpson D. D., Joe G. W., Brown B. S. Treatment retention and follow-up outcomes in the Drug Abuse Treatment Outcome Study (DATOS). *Psychol Addict Behav* 1997; **11**: 294–307.
77. Gossop M., Marsden J., Stewart D., Kidd T. The National Treatment Outcome Research Study (NTORS): 4–5-year follow-up results. *Addiction* 2003; **98**: 291–303.
78. Sellman J. D. Drug addiction and the meaning of life. Keynote address, International Addiction Summit, Melbourne, July 2008.
79. Sellman J. D. *Real Weight Loss: A Practical Guide To Changing Your Lifestyle and Achieving Long-Term Weight Loss*. Nelson: Craig Potton Publishing; 2008.
80. Cloninger C. R. A psychobiological model of temperament and character. *Arch Gen Psychiatry* 1993; **50**: 975–90.