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"Science of Reward Circuitry: Addiction and the Impact of the NADA Protocol"

Summary of Paper presented at Annual NADA-UK Conference: 'Pointing in the Right Direction'. 11th November 2006, Marriott Hotel, Liverpool.

Dr. Stuyt has 16 years experience in addiction psychiatry, including six years as Medical Director of the Circle Program – a treatment programme for dual diagnosis cases in Colarado, USA, which includes acupuncture. Her presentation focused on three areas: the workings of the brain; the biological basis of drug addiction in the brain; and the role of acupuncture in the treatment of addiction and dual diagnosis (comorbidity) – including an assessment of the effectiveness of the Circle Program.

The brain

The mind is a process that regulates the flow of energy and information in the brain (somatic and psychological treatments can shift the direction of energy). The mind emerges from the interaction of neurobiological processes in the brain and environmental events (physical and social). The brain and mind have a two-way relationship. Though the brain determines the mind (eg. brain damage), the mind also shapes the brain – the flow of information can actually change the function and structure of the brain. The various kinds of psychological function/process - notably perception, cognition, memory, affect, and motivation – are based in different parts of the brain, and are mediated by specific neurotransmitters.

The nervous system is comprised of two parts: the central nervous system (brain and spinal cord), and the peripheral nervous system (somatic and autonomic systems). The primary function of the CNS is information processing; while the primary function of the PNS is relaying information between the brain and body (sense organs, muscles, glands and organs). The brain is comprised of 100 billion neurons, with an average of 10,000 connections each. There are over 80 neurotransmitters (NTs) serving as chemical messengers between brain cells. They can be organised into four main groups:
(1) monoamines – notably dopamine (boosted by all dependence-causing drugs), along with noradrenaline (boosted by stimulants) and serotonin (boosted by hallucinogens);
(2) amino acids – notably GABA and glutamate – modified by alcohol, sedatives, etc.
(3) peptides – notably endorphins and the opioid peptides – simulated by opiates;
(4) endocannabinoids – notably anandamide and 2AG – affected by THC (in cannabis).
Other notable NTs include acetylcholine (affected by nicotine), adenosine (affected by caffeine), and gaseous NTs (eg. nitric oxide).

Neurons have two types of connecting fibre: axons to transmit NTs into the synapse (the gap between cells), and dendrites to pick up NTs from the synapse. A brain cell is activated when a neurotransmitter makes contact with receptors on the cell surface (NTs typically have several sub-types of receptor on the post-synaptic neuron). Drugs modify levels of NTs in various ways - notably by (a) affecting synthesis, storage, release, or reuptake (recycling) on the pre-synaptic neuron, (b) by affecting reception on the post-synaptic neuron, or (c) by affecting excretion (metabolisation) of NTs.

Siegel has suggested a 'hand' model of brain structure and components:
* Spinal cord (wrist) – relays signals between brain and body
* Brain stem (palm) – fundamental processes of alertness, hunger, thirst, survival
* Limbic system/amygdala (thumb) – regulation of fear, hippocampus, hypothalamus, & NA
* Cortex – perception of body (back of hand); motor action & planning, thinking (front)
* Prefrontal cortex (fingers) – executive functioning.

An integrated middle prefrontal cortex (MPC) is responsible for nine functions: regulating body (autonomic nervous system), attuning communication, balancing emotions (eg. calming volatile states), response flexibility (pausing before action), empathy (mapping others' minds), self-knowing awareness (ability to connect past, present and future), freedom from fear, intuition (gut feelings), and morality.

The brain is also divided into two hemispheres. Left hemisphere processes are linear, logical, language-based and literal; while right-hemisphere processes are visuo-spatial, holistic, and non-verbal (including eye-contact, facial expressions, tone of voice, posture, gestures, and timing and intensity of responses). The right hemisphere is also involved in autobiographical memory, empathy, body awareness and the stress response. The two hemispheres communicate through the corpus callosum (CC). When the two hemispheres of the brain are integrated and balanced, the person can achieve a coherent narrative, i.e. a linear telling of a sequence of events, which helps make sense of what happens to you. It also permits implicit memories to be integrated into explicit form. The brain requires both horizontal and vertical integration (VI). Horizontal integration involves understanding the meaning of words in the left hemisphere, combined with a 'call for neural response', i.e. sending information across CC to right hemisphere. It also allows us to put feelings into words, to bring feelings into conscious awareness, to balance left and right hemisphere biases, to mediate mindfulness (eg. theme emergence), and to tell our personal story. Vertical integration incorporates bodily sensations coming into the right hemisphere, the 'checker system' (amygdala, basal ganglia and brain stem), and dialogue between the cortex and sub-cortical areas.

Treatment of drug addicts and PTSD cases (see below) should take into account which 'side' each patient tends towards – very few will be of the integrated hemisphere type. Therapies should be aimed at achieving hemispheric integration: 'integration creates harmony'. The 'START Healing from Trauma' programme is based on the following steps: seek safety and support (S), talk about your trauma with a supportive person (T), use altruism to move beyond your trauma (A), re-visit, re-live, research and re-write the trauma scene/event/story (R), and transform yourself from victim to survivor, as well as transforming society to make it a better place (T).

Addiction and the brain: dopamine and the Reward Pathway

The Reward Pathway (RP) underlies the experience of pleasure linked to food, sex, and people, and so reinforces the behaviours of eating, procreating and interacting. The RP links brain cells in the prefrontal cortex, the nucleus accumbens (NA) and the ventral tegmental area (VTA) of the limbic system. Dopamine (DA) is the primary NT of the RP (though endorphins – the brain's endogenous morphine NTs – also play a role in the RP). DA release leads to neuronal plasticity that may underlie incentive learning and memory – and so also determines cravings and tolerance. With repeated drug use and increasing concentrations of DA in the NA, there is an increase in cAMP which activates CREB (camp response element binding protein). CREB binds to a specific set of genes that code for proteins that dampen the

RP. This leads to the same dose of a drug becoming less rewarding, i.e. tolerance [for a good overview, see Nestler & Malenka, 2004, 'The Addicted Brain', *Scientific American*, 290(2), 50-56].

For natural rewards like food or sex, DA is acutely released in a pulse fashion, whereas drugs of abuse (addictive drugs) raise DA levels in a sustained fashion (flooding the synapse). DA levels are raised much more by drugs of abuse, though are unaffected by drugs which do not cause dependence (eg. LSD). For instance, opiates and nicotine raise DA levels by 2 to 2.5 times the levels produced by food or sex; cocaine produces a fourfold increase - while speedballing (cocaine and heroin together) and methamphetamine each produce a tenfold increase. Some drugs (eg. cocaine) work directly on DA and the NA, whereas others (eg. nicotine) work indirectly through the effects of other NTs (eg. acetylcholine).

Addiction/dependence results from repeated drug use, and is based on three components - craving, tolerance and withdrawals – which lead to compulsive, drug-seeking/taking behaviour. In short, taking drugs of abuse is a reinforcing behaviour, and leads to loss of control in limiting intake. Genes and biology play a key role in vulnerability to addiction. For instance, the number of dopamine D2 receptors has been found to be significantly lower in cocaine, alcohol and heroin addicts. However, it is difficult to determine whether addicts started off this way, or whether their DA receptors were reduced by abusing drugs.

Research shows that different drugs have a different propensity for addiction. Of four notable drugs of addiction, the percentage of those ever using a drug who become addicted is highest for tobacco (32%), followed by heroin (23%), cocaine (17%), and alcohol (15%).
Volkow et al. injected subjects with the stimulant methylphenidate (Ritalin), and found that subjects with low levels of dopamine D2 receptors reported the effect as pleasant, while those with high levels of D2 receptors reported the effect as unpleasant. Lewin et al. (2000) found that rats exposed to nicotine as adolescents self-administered more nicotine than rats exposed to nicotine as adults. In addition, rats exposed to methylphenidate during adolescence were more likely to self-administer cocaine as adults. Morgan et al. (2002) assessed the impact of cocaine injection on four groups of rats, based on two variables: personality (dominant versus submissive), and housing (group versus individual). It was found that submissive group-housed rats 'liked' cocaine the most, while dominant group-housed rats 'liked' cocaine the least.

There are various behavioural & brain theories of drug dependence (DD):
* withdrawal avoidance – DD is conditioned (Wilkler)
* hedonic theory – DD is dopamine-related (Wise & Bozarth)
* hedonic set point – DD is based on reward system dysregulation requiring more drug to produce same high, making it less likely that natural rewards will be experienced as pleasurable – can explain tolerance and anhedonia, but not compulsivity (Koob et al.)
* Learning theories – incentive sensitisation, wanting and liking are distinct neural systems – DA regarded not as a reward signal per se, but as a learning signal (Robinson & Berridge 1990)

Addiction shuts down the prefrontal cortex, causing it to go 'off line'. The learning processes underlying drug addiction are based in three parts of the brain, the first two of which produce behaviour unconsciously, and the third consciously (White 1996):
(1) amygdala-NA (incentive) – promotes approach to & interaction with drug-related cues;
(2) caudate-putamen (habit) – promotes repetition of behaviours performed in the presence of drug-related stimuli;

(3) hippocampus (declarative): promotes focusing of cognitive processes on drug-related situations.

Memory, based in the hippocampus, consists of implicit memory (starts in womb) and explicit memory (develops from 18 months of age). Implicit memory is concerned with four primary domains of experience: emotion, perception, motor action and body memory. Explicit memory involves storing or retrieving factual or episodic information – when you pay attention to something, you put the information in explicit memory. If the hippocampus is shut off during a traumatic experience, the brain can activate an implicit memory but not an explicit memory. The hippocampus can be turned off for short periods of time by a massive cortisol surge (stress), or by diverting attention (dissociation). Drugs of abuse can shut off painful sensations of implicit memory intrusion. Chronic use of drugs of abuse can decrease hippocampal volume (shrink it), and decrease neurogenesis. Research shows that an increase in adverse events during childhood increases the odds ratios for obesity (x2), smoking (x2), IV drug use (x10) – as well as physical diseases like asthma and heart disease.

Neuro-imaging studies demonstrate a decrease in hippocampal volume and amygdala volume in post-traumatic stress disorder (PTSD), borderline personality disorder (BPD), and DID. Stressful events result in the following cycle of brain events: (1) release of corticotropin-releasing factor (CRF) from the hypothalamus, which (2) stimulates release of adrenocortico-tropic hormone (ACTH) from pituitary gland, which (3) triggers release of cortisol from the adrenal glands, and then (4) cortisol travels back to hypothalamus and inhibits release of CRF and ACTH – though if the stress is ongoing, the cycle continues. Opioid peptides (notably endorphins), and opioid drugs, can inhibit the release of CRF, and thus reduce stressful emotions (Kreek & Koob 1998). But opioid withdrawal results in the release of stress hormones/NTs, producing a hypersensitivity to stress. Cocaine similarly increases sensitivity to stress.

Glutamate, the brain's most common NT, permits communication between different parts of the brain – for instance, the amygdala, hippocampus and prefrontal cortex talk to the RP via glutamate. Changes in sensitivity to glutamate enhance release of DA from VTA to NA, promoting release of CREB and delta fos B (DFB). This strengthens pathways that link memories of drug use with reward (long-term potentiation/LTP). LTP primes cells to react more strongly, releasing DA more abundantly in response to future exposure. A single exposure to cocaine can establish LTP in mice. All drugs of abuse trigger the same change. LTP is based on an increase in the ratio of AMPA to NMDA (two types of glutamate receptor). In mice, stress alone can induce increased AMPA-NMDA ratios in VTA cells within 24 hours – which are similar to changes induced by drugs of abuse. This suggests a priming mechanism, i.e. people who have experienced stress are more vulnerable to addiction. For instance, Saal et al. (2003) found that both addictive drugs and stress increase the sensitivity of DA cells in mice.

Drugs of abuse are potent negative regulators of adult neurogenesis in the hippocampus. Chronic administration of opiates, THC or alcohol decrease hippocampal function, reducing the ability of the adult brain to adapt to new information. Stress is also associated with hippocampal neuronal damage, hippocampal volume reduction on MRI, and memory deficits in humans with PTSD. A cortisol surge can shut down the hippocampus – which is why people often forget what happened during a stressful event, and why people exposed to chronic stress (or addictive drugs) have a shrunken hippocampus. The effect of addictive drugs and stress (decreasing neurogenesis in the hippocampus) arguably provide a

biochemical explanation for denial. That is, they can explain why someone continues to use drugs or stays in an abusive relationship despite the negative consequences.

Recent research suggests that nicotine has negative effects on memory and cognition. Nicotine self-administration in rats profoundly decreases neurogenesis, and increases neuron death in the hippocampus (Abrous et al. 2002). A steeper decline in IQ has been observed in smokers compared with non-smokers between 11 and 64 years of age (Whalley et al. 2005). Adolescent smokers show impairment of memory and cognition (Jacobson et al. 2005). Brain recovery in abstinent alcoholics is affected by chronic smoking (Meyerhoff et al. 2006). Chronic smoking is associated with increased brain atrophy in people over 50 years old. Active smoking is associated with diminished neurocognitive performance, including executive functions (Razari et al. 2004), general intellectual abilities (Deary et al. 2003), memory (Hill et al. 2003, Schinka et al. 2003), and psychomotor speed and cognitive flexibility (Kalmijn et al. 2002).

Treatment can help promote neurogenesis (1) by providing the brain (especially the hippocampus) with an opportunity to heal and regenerate – improving the patients' ability to adapt to new information when in treatment; (2) by providing a safe environment – removing the patient from chronic stress/drug abuse; (3) by providing an environment free of addictive drugs – ideally, including tobacco. Gage (2000) concluded that treatment provides an enriched environment which promotes physical activity and learning. Also, medications can help in various ways, including SSRIs and Lithium. For instance, paroxetine increased verbal declarative memory and hippocampal volume in PTSD cases (Vermetten et al. 2003).

Additional treatment modalities include: medications approved for treating drug dependence (notably: acamprosate, naltrexone, disulfiram); EMDR; thought field therapy; cognitive behavioural therapy; interpersonal neurobiology (bringing MPC back 'online'); and auricular acupuncture.

How does acupuncture work?

The theory for analgesia (Lee et al. 2004) states that, in acupuncture, the stimulus travels from insertion point to spinal cord – promoting release of enkephalin and dynorphin (opioid peptides) – attenuating pain transmission. The stimulus then travels up the spinal cord, releasing enkephalin in the midbrain, and stimulating the descending pain inhibition pathway. Upon reaching the hypothalamus, the stimulus prompts accuate nucleus and pituitary to release beta-endorphin (pain inhibition) and ACTH (anti-inflammatory effect). This explanation is supported by the findings that (1) opioid antagonists (naloxone, naltrexone) block or inhibit acupuncture analgesia; (2) following acupuncture, cerebrospinal fluid endorphins increase and brain endorphins decrease; and (3) when the circulation of one animal is crossed with another receiving acupuncture, both experience analgesia - and naltrexone reverses the effect in both animals.

The journey of the stimulus from the insertion point to the spinal cord involves interstitial connective tissue in neuromodulation (Langevin et al. 2002). Acupuncture may produce changes in the connective tissue milieu surrounding sensory afferent nerve fibres. These connective tissue changes may be long lasting – explaining the prolonged therapeutic effects of acupuncture. Langevin & Yandow (2002) have proposed a model of the physiological effects seen in acupuncture. This covers such concepts as acupuncture meridians and points; needle grasp; qi and the de qi sensation; convergence of connective tissue plains; tissue

winding and/or contraction of fibroblasts around needle; and stimulation of connective tissue sensory mechanoreceptors.

Acupuncture has also been shown to modulate the brain's limbic system. Hui et al. (2000) conducted a study of normal subjects, comparing needle stimulation with tactile stimulation of the LI4 point. Signal decreases were observed in many parts of the brain with needle stimulation, but not tactile stimulation. This supports the use of acupuncture in treating such mental disorders as anxiety, depression and substance abuse (including cravings and withdrawals). Indeed, research has shown that drugs of abuse induce signal increases in the same regions. Bonta (2002) hypothesised that acupuncture may amplify the interaction between neuropeptides and cytokines. Stuyt believes that the key question, beyond the endorphin concept, is: "does winding of the connective tissues by the needle release cytokines from immune cells (i.e. interleukin-4, interleukin-10) that modulate the inflammatory process and interact with neuropeptides (i.e. endorphin) through meridian channels of liquid crystalline collagen fibres of the connective tissue".

The Circle Program is a 20-bed, 90-day, inpatient treatment program for men and women, aged 16 to 65, who have failed all other treatments for dual diagnosis (Axis I Mental Illness and Substance Dependence Diagnoses). The program is abstinence-based – including exclusion of tobacco smoking. It is a voluntary program, though about 75% are court ordered to treatment. The program components include: very intense cognitive/behavioural program; 40 hours of group work weekly (17 different groups); homework assignments; many rules (including reporting violations by self and peers); and a Level System (staff determine levels - stages of change – weekly, based on objective measures such as progress made on homework, group attendance, and documented rule violations. The four Levels are: precontemplation (minimal compliance, not ready to make changes); contemplation (increasing but inconsistent compliance, thinking about change); action (decision to change, actively changing behaviour); and ownership (consistently demonstrating change and appropriate behaviour).

The groups are based on four treatment cornerstones: relapse prevention, behavioural change, education, and origin of issues. Relapse prevention involves learning to manage cravings and stress that lead to relapse, by retraining the brain - including: resolutions (cue exposure response prevention), re-entry (recovery plan), recreational therapy, support groups (eg. AA, DTR), relaxation techniques, thought field therapy, and auricular acupuncture (voluntary). Behavioural change includes the HOPE group (gift system, teaching tools, and peer coordinators), and strategies for self-improvement and change (thinking reports, and addressing criminal thoughts and behaviours). The educational groups include recovery education (how different drugs and therapies work), management of mental illness symptoms, discovery (grief and loss, inner child), and talks with the doctor. The origin of issues groups include parenting, spirituality, and men and women's process and anger groups.

In the three years between January 2001 and December 2003, 440 patients were treated, and 246 (56%) successfully completed the program. The mean length of stay was 86 days (+/– 13) for successful completers, and 38 days (+/– 23) for unsuccessful patients. Variables that did not predict successful completion included gender, race and primary psychiatric diagnosis. Variables that influenced completion rates included: tobacco use (74% of non-users versus 54% of tobacco users completed successfully); primary drug of choice (cocaine dependent people were less likely to succeed than other drug dependent people); Axis II diagnoses (those with Axis II diagnoses were less likely to succeed than those without them);

and age (successful completers were older than non-completers). Overall, 367 (83%) of the patients participated in auricular acupuncture. Among these, 61% successfully completed, compared with 32% of those who did get acupuncture. Among patients receiving acupuncture, successful completers participated in significantly more needling sessions (223, compared with 144 among non-completers).

The Circle Program Protocol states that if patients voluntarily choose to receive acupuncture, they are encouraged to have five daily sessions a week for the first two weeks. After the first four weeks they are encouraged to attend three days a week, then two days a week for the remainder of their stay (so that they can participate in the other groups held at the same time). At the start of each session all patients fill out the Acupuncture Treatment Record – assessing their present symptom severity. Needles are placed in each ear in five points – liver, lungs, kidney, nervous system and a fifth point for relaxation (the Spirit Gate, or Shen Men). Lights are turned down, soft relaxation music is played, and the patients are asked not to talk. A staff nurse remains in the room the entire session, and then removes the needles after 45 minutes. Patients are not allowed to leave the room until all needles have been accounted for.

Statistical comparisons were made of 75 patients receiving acupuncture with 21 controls. It was found that, compared with controls, acupuncture patients exhibited significant improvements in anger symptoms, concentration, sleep problems, pain symptoms, and energy levels. Variables that did not predict use of acupuncture included gender, race, primary drug, primary psychiatric diagnosis, Axis II diagnosis, age, and tobacco use. Compared with those who did not receive acupuncture, significantly more patients receiving acupuncture moved up through the level system – 87% graduated on ownership level, 93% on action level, 92% on contemplation level, and 73% on precontemplation level. Also, patients' intentions toward using tobacco after discharge also predicted successful completion rates – 41% of those planning to smoke successfully completed the program, compared with 80% of those who planned to remain non-smokers. Also, significantly more patients completed successfully if they had eight or more acupuncture sessions – whether they were planning to restart smoking on discharge (57% versus 24%) or whether they were planning to remain non-smokers (90% versus 69%). In other research, schizophrenic patients have reported that acupuncture helped reduce 'the voices'; while research on hyperactive children has found that acupuncture helps them to calm down, keep still, and concentrate better.

Conclusions. Stuyt concluded that there have been no negative experiences associated with auricular acupuncture in dual diagnosis treatment, and that its use improves treatment retention and participation. The simple, respectful and confident touch of an ADS hand on the patient's ear or shoulder without any other agenda can be very supportive, calming and healing. Acudetox is nurturing and allows other aspects of treatment programs to be more harsh and confrontative.

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"Acupuncture's Role in Addiction – The Evidence Base"

Summary of Paper presented at Annual NADA-UK Conference: 'Pointing in the Right Direction'. 11th November 2006, Marriott Hotel, Liverpool.

Dr. Rotchford has been practising acupuncture for treatment of addiction as part of his medical practice for 25 years, and is a founding member of the American Academy of Medical Acupuncture. His presentation aimed to examine the scientific evidence base on acupuncture's effectiveness in treating addiction to drugs or alcohol, based on a review of over 300 relevant references, including 69 since 2004.

The presentation began with some general observations about the nature of scientific research, and its relevance to understanding the value of acupuncture in helping drug addicts. In addition to deductive and inductive reasoning, used for testing hypotheses (verification), science involves a third, neglected, type of reasoning: abductive reasoning. This refers to the process involved in generating and selecting worthwhile hypotheses. Abductive reasoning is used in scientific discovery, medical diagnoses and legal arguments. To the primary evaluative question 'does it work?', abductive reasoning responds not yes or no, but 'it depends'. This broader perspective on scientific reasoning was employed in evaluating the evidence base on acupuncture and addiction.

Evidence-based medicine (EBM) emerged in 1992, and was defined as "rejection of authority and experience-based medicine in favour of systematic observation" (Guyatt 1992). EBM fits well with increasing reliance on official guidelines to shape and evaluate clinical practice. Scientific research is an extension of the Western philosophical tradition of reasoning and formulating arguments. The belief that this approach is useful to evaluating acupuncture is based on many assumptions – for example, that thinking is required for knowing, that the reductionist approach leads to truth, that animate and inanimate objects adhere to the same laws. Indeed, a major neglected distinction in medicine is between the Hippocratic and Aesculapian traditions (mechanistic versus non-mechanistic explanation). And there are many cultural biases in how we assess the relevant scientific evidence (eg. does it help, is it safe?).

Acupuncture is contextual and synergistic – so is EBM the best approach to understanding and assessing its value? The relevant question to ask is: does acupuncture research improve health outcomes for addicts undergoing acupuncture treatment? There are no studies which properly answer this question – that is, what helps practitioners to enhance their acupuncture practice and produce better health outcomes? Eisenberg's Survey Study only prompted more research; and clinical trials neither ask nor answer the question. The assumption that acupuncture research does lead to improved health outcomes derives from beliefs associated with pharmaceutical and surgical interventions. Acupuncture practitioners should ask themselves a number of questions: How many patients can I think of who were helped because of the findings of research on acupuncture? Do I provide acupuncture because of acupuncture research? Should we all practice acupuncture in the same way? Is it easy to trust acupuncture research?

There is a need for common-sense here – for instance, are things that are not easy to objectively define or precisely replicate suitable to scientific research? Indeed, acupuncture emphasises subjective experience (eg. pain perception), and involves non-linear and

contextual relations. Non-specific factors are important in explaining the effect of acupuncture. Acupuncture and oriental medicine developed without the input of modern research.

There also needs to be an assessment of the risks and benefits of acupuncture research. What are the benefits? They include improving health outcomes (determining optimal therapies for given conditions); marketing (to increase demand by patients, and promote third-party reimbursement); fear (the need to know why, and the ability to predict and/or prognosticate; creating jobs, and improving professional ethics. What are the possible risks/costs of acupuncture research? They include huge financial costs and human effort for little or no health outcome returns; communication of inappropriate expectations and attitudes about health (eg. acupuncture treats only the symptoms of chemical dependency, and/or promotes healing); a possible negative marketing effect; research protocols leading to interference with good clinical training; and the inappropriate standardisation of acupuncture practices (see Greenwood 2002).

Acupuncture research has covered several types of drug dependence, but is typically inconclusive and of limited relevancy to clinical practice. Regarding research on smoking cessation, the Cochrane Collaborative Database (2002) concluded that there is no consistent evidence that acupuncture, acupressure, laser therapy or electro-stimulation are effective for smoking cessation – but various methodological problems preclude firm conclusions. The Cochrane Database Systematic Review (2006) reported that there is currently no evidence that auricular acupuncture is effective for the treatment of cocaine dependence, though research to date is inconclusive. Two recent reviews of the literature covering all forms of drug dependence (Margolin 2003, and British Columbia Office of Health Technology 2002) concluded that, based on randomised control trials, there is inadequate evidence to confirm acupuncture's effectiveness in treating drug addiction. However, based on all evidence sources - notably observational data, expert opinion, and risk/benefit analysis – acupuncture as an adjunctive therapy is helpful in the treatment of addiction to four drugs (nicotine, cocaine, opiates and alcohol), as well as the treatment of comorbid conditions.

Other evidence supporting the usefulness of acupuncture in treating addiction includes: neurological research showing that acupuncture stimulates endorphins, and produces changes in brain blood flow and metabolism (confirmed by PET scans and functional MRIs); evidence of areas of reduced skin resistance consistent with acupuncture theories; and animal research showing that acupuncture affects the autonomic and immune systems, has pain modulating effects, and modifies areas of the brain involved in drug dependence. Also, people like it and are willing to pay for it ($27 billion in USA in 1997).

Four clinical metrics inform our conscious clinical reasoning about the best treatment for each patient: effectiveness, efficacy, therapeutic morbidity; and costs to patient. Research in acupuncture may help illuminate these clinical metrics. Rotchford stated that he chose to promote acupuncture research "primarily because I believe in the value of acupuncture". Research promotes acupuncture because (1) in our Western medical culture, the acceptability of an intervention is largely defined by its capacity to accurately predict associated desirable outcomes (efficacy and effectiveness); (2) population-based evaluations, which require clinical research, will continue to dominate as long as governments and third parties continue as the purchasers of healthcare; and (3) ethical considerations.

There are several ways in which clinical acupuncture research presents specific challenges when compared with allopathic medical clinical research: non-specificity/objectivity of diagnoses; non-specificity of interventions (dosing and style issues, needling techniques); lack of clinical relevancy; possible need to individualise/contextualise intervention; practitioner skill and competency; significant differences between research protocols and standard clinical practice; and difficulty with blind surgical procedures, particularly with non-specific needling effects.

The priorities for future research on acupuncture and drug dependence should be: better definition of terms; emphasis on the subjective over the objective; establishing priority of effectiveness over efficacy; improving methodology of basic research (eg. dosing issues, surrogate markers of effect); and recognising the place of different schools/styles (including justifying more invasive interventions, and the place for adjunctive modalities).

Conclusions. Overall, the evidence to date suggests that acupuncture is effective, but not that it is efficacious – though, as noted above, hard evidence is clearly lacking. A variety of reasons underlie the lack of hard evidence: defining acupuncture is problematic/ controversial (eg. is it a surgical procedure?); there are a lack of established standards for adequate intervention; there may be an enhancement of the placebo effect; the mechanism of action remains unknown; it is not suitable for mechanistic evaluation (subjective, contextual); there is a lack of financial incentives to do costly research; standard clinical research in the area of drug dependence is difficult; and various methodological issues (inadequate sample sizes, confounding variables, etc.).

To sum up, there are ten main reasons for using acupuncture in addiction therapy:
(1) it stimulates endogenous opiates (the currency of our natural reward system);
(2) it implies and reinforces an internal locus of control (by stimulating internal self-regulating mechanisms);
(3) it honours the disease model through a physical intervention;
(4) through symptom reduction, it can facilitate a therapeutic relationship (it encourages follow-up and treatment retention);
(5) it acknowledges feelings as positive sources of energy that are to be explored and appropriately managed for good health (eg. supports emotional awarness);
(6) it stimulates blood flow and metabolic activity in brain areas involved in addiction;
(7) it may evoke the relaxation response which counters the arousal that occurs in association with drug withdrawal;
(8) it introduces a sense of mystery into the healing process, and addresses the illusions of control that are prevalent in addictive disorders (possibly stimulating spiritual growth);
(9) it is relatively cheap and quite safe; and
(10) extensive operational data and clinical trials confirm various uses of acupuncture.

Whereas the effects of drugs on the brain are like a canon going off, the effects of acupuncture are more subtle, and so require careful research and observation to be assessed. Drug dependency is a chronically relapsing condition. The best predictor of a favourable treatment outcome is time in treatment – which, among many other things, facilitates the teaching of new ways of feeling good rather than using drugs. Future research should focus on ‘is it effective?’ – not ‘is it efficacious?’