The neuropsychologist working in addiction: What to know? Ten questions and answers

Antonio Verdejo García, PhD

Monash Institute of Cognitive and Clinical Neurosciences, Monash University
Turning Point Alcohol and Drug Centre

ABSTRACT

Substance addiction is characterized by problems in controlling drug use, significant interference with other meaningful activities, and persistent use despite growing negative consequences. Psychoactive drugs have a strong impact on brain function and related consequences on thinking, emotion and behavior, and hence social and occupational functioning. Thus, this is an area of interest for neuropsychologists in terms of characterizing deficits, functional impact, and strategies for recovery or compensation. The aim of this review is to go over some of the fundamental questions and challenges that neuropsychologists working in this field often face. I approach this goal in the form of ten key questions and their corresponding answers, which are based on existing research and personal experience in the field. Questions and answers cover some of the fundamental aspects of drug-related neuropharmacological and behavioral effects, the neuropsychological assessment in the context of addiction, and the approaches to retraining and rehabilitation of deficits. I conclude by presenting a vision of the future for neuropsychological practice in the context of the addiction clinic.
Substance use disorders, or substance addictions, are characterized by problems in controlling drug use, significant interference with other meaningful activities and persistent use despite growing negative consequences. Substance addictions are associated with significant medical and psychosocial harms and are a major contributor to the global burden of disease. Psychoactive drugs, including alcohol, cannabis, stimulants and opioids, have a strong impact on brain function and related consequences on thinking, emotion and behavior, and hence social and occupational functioning. Thus, substance addiction is an area of interest for neuropsychologists in terms of characterizing deficits, functional impact, and strategies for recovery or compensation. Moreover, the fact that there is diminished control and continued use despite negative consequences reflects alterations in executive control and decision-making, which seem to be at the core of the disorder. Therefore, it is not surprising that substance addiction has become a fruitful area for neuropsychological research and practice, with growing scientific interest and implementation in research clinics and addiction treatment centers. The aim of this review is to go over some of the fundamental questions and challenges that neuropsychologists working in this field have to face. I have done this in the form of ten key questions and their corresponding answers, which are based on existing research and personal experience in the field.

Do people with addiction have cognitive deficits?

Yes. This seems like an obvious answer, but some researchers have challenged it. The controversy may lie in the confusion between drug use and addiction. Many people use drugs experimentally and/or recreationally, and most won’t have cognitive deficits unless drug use escalates and related problems arise. But addiction typically involves heavy drug use, difficulty to stop, and significant interference with daily life activities that keep our cognitive systems up to speed (e.g., studies, work, social relationships). We, and others, have shown that heavier drug use is dose-relatedly associated with poorer cognitive performance among people with different types of addiction. Moreover, recent research has shown that people who meet cannabis addiction criteria have greater reductions in the brain’s gray matter than heavy cannabis users who do not meet these criteria. This finding suggests that suffering addiction symptoms is linked to additional cognitive burden. Overall, there is compelling evidence from well-controlled studies and meta-analyses demonstrating that people with addiction typically have cognitive deficits, although similar to the ones observed in other populations with mental health problems, such as depression, bipolar or psychosis-related disorders.

Why?

Drugs of abuse produce supraphysiological stimulation (and hence dysregulation) of neurotransmitter systems that are pivotal for cognitive functioning. One of the most researched mechanisms is the neuroadaptation of dopaminergic cortico-limbic circuits. Stimulant drugs such as cocaine or methamphetamine induce both transient and long-term neuroadaptations in striatal dopamine receptors. Alcohol, cannabis and opioids also affect dopamine via indirect pathways. Such neuroadaptations end up affecting the functioning of frontal-striatal systems, including those involved in executive functions, emotion regulation and decision-making. But dopamine is only part of the story; stimulants have strong neuregulatory effects on glutamate, noradrenaline and serotonin, alcohol on glutamate and GABA, and cannabis on the balance of several neurotransmitter systems that use negative feedback mechanisms linked to endocannabinoid modulators. Moreover, most drugs mobilize second messenger systems that result in maladaptive changes in gene expression and neurotrophic cascades. In addition to the well-known direct neuropharmacological effects...
of drugs, addiction (and its mental health strain) is associated with alterations in stress and pain systems, which have a considerable impact on attention, memory and executive functions. Some drugs such as opioids do not have powerful neurotoxic effects, but they can impact cognitive function via dysregulation of stress and emotional systems. Altogether, there is compelling evidence that shows that drugs of abuse induce significant changes in brain function that are meaningfully associated with deterioration of cognitive systems involved in attention, memory, executive functions, emotion regulation and decision-making.

**Which cognitive domains are affected?**

Drugs of abuse predominantly affect executive functions, decision-making and emotion regulation. They also have negative effects on attention and memory, although in aspects that are at least partly related to executive control, such as memory coding, strategic retrieval, and sustained and selective attention. An interesting point is the specific effects of different drugs. Systematic review and meta-analytic research has shown that addiction to stimulants such as cocaine and methamphetamine are linked to deficits in working memory, response inhibition, cognitive flexibility and decision-making. Opioid addiction is associated with deficits in verbal episodic and working memory as well as fluency and decision-making. Alcohol addiction relates to cognitive deficits across the board, spanning from basic abilities such as speed and language to attention and memory and more complex executive functions and decision-making. Cannabis addiction, however, is linked to specific alterations in episodic memory although they can be short-lived. MDMA (ecstasy) users also show discrete alterations of memory processes. Most populations with addiction problems have deficits in emotion processing and regulation as well as social cognition and interaction problems. The severity of cognitive deficits also differs as a function of the principal drug of choice. Deficits are typically of medium/large effect size in people with alcohol and stimulant addictions, whereas they are of small to medium effect size in the case of opioid and cannabis addictions. All of these patterns are aggravated in the context of polysubstance use, and thus people addicted to multiple substances show additive cognitive alterations. Altogether, the domains of memory, executive functions, decision-making and social cognition are typically impaired, with medium effect size deficits, among people with addiction. Alcohol and stimulants such as cocaine and methamphetamine are linked to broader and more severe alterations, whereas opioids, cannabis and MDMA users have more specific alterations in decision-making and memory processes.

**Why should we worry?**

We should worry for at least three reasons. First, cognitive deficits can contribute to continuation and escalation of drug use in active users. Drugs can temporarily boost executive functions and emotion processing, and thus people with cognitive deficits can be inclined to increase drug use to improve cognition and related outcomes (i.e., productivity, wellbeing). Second, cognitive deficits interfere with treatment efficacy. Addiction treatment involves cognitively-demanding psychotherapies, and longitudinal research has shown that people with poorer cognitive functioning are less likely to adhere to these interventions and more likely to dropout prematurely. Third, there is a strong relationship between cognitive deficits and the risk of drug relapse. People with greater impulsivity and poorer decision-making skills are significantly more likely to relapse after treatment discharge. Moreover, (dis)inhibition and impulsive decision-making also contribute to poorer recovery of quality of life. In this regard, cognitive deficits can critically contribute to the chronic nature of addiction.

**Do cognitive deficits recover with abstinence?**

Cognitive deficits do improve with continuous abstinence, but it takes a long time, and we still do not know if recovery is complete. Longitudinal research among people with cocaine and methamphetamine addiction have shown that six to twelve months of sobriety are associated with
significant recovery of cognitive deficits, such that performance becomes very similar to that of healthy controls\textsuperscript{49,50}. In people with alcohol addiction, over one year of sobriety is associated with normalization of most cognitive functions, with visual-motor skills being the most lingering deficits\textsuperscript{16,51}. Therefore, we can confidently say that long-term abstinence pays off. But we also know that it is uncommon for people with addiction problems to completely abstain for such a long time. Unfortunately, cognitive recovery is not so apparent among people who reduce (but maintain) alcohol and drug use\textsuperscript{50,52}. Another important consideration is that there are very few longitudinal studies, and some of them have not assessed some of the cognitive domains that are most critical for addiction, such as impulse control or decision-making\textsuperscript{46}. Moreover, we need to consider that even normative recovery of cognitive functions might not be enough for some individuals, since (i) baseline cognitive skills failed to prevent onset of drug use in origin, and (ii) state-related fluctuations in mood and/or stress levels can return cognitive processes to a risky status\textsuperscript{53}. Altogether, available research suggests that abstinence periods of over six months result in meaningful recovery of cognitive deficits among people with addiction, but additional support is needed to get more people over that line, and more comprehensive longitudinal studies are needed to determine if such recovery is complete.

### What factors – other than drug use – impact cognitive performance in addiction?

People with addiction problems are likely to have lower education and socioeconomic levels than the general population or the populations typically assessed by neuropsychologists. Probably as a result, they also tend to show lower IQ levels, which can have a significant influence on their cognitive performance and particularly on executive function performance\textsuperscript{54}. In addition, the prevalence of child trauma and neurodevelopmental disorders such as attention-deficit/hyperactivity disorder (ADHD) is greater in people with addiction than in the general population\textsuperscript{55}. Proxys of childhood trauma have been associated with poorer performance in tests of executive function among people with cocaine addiction\textsuperscript{56}. Similarly, the comorbidity between cocaine addiction and ADHD is associated with greater general cognitive deficits\textsuperscript{57}. People with addiction are also more likely to suffer other mental health problems, including depression, bipolar disorder, psychosis-related disorders and personality disorders\textsuperscript{58,59}. Comorbidity with psychosis is associated with additive deficits in a broad range of functions including speed, attention, memory and executive functions\textsuperscript{50}. We and others have shown that the comorbidity with personality disorders is associated with cumulative deficits in working memory and response inhibition, as well as greater brain and behavioural alterations in emotion regulation compared to non-comorbid patients\textsuperscript{51,52}. Although not many studies have examined cognition in the context of comorbidity with depression and bipolar disorders, available evidence suggest cumulative alterations in the executive function components of response inhibition and cognitive flexibility\textsuperscript{54}. Finally, it is important to consider the presence of other medical comorbidities, such as HIV, hepatitis or alcoholism-related dementias, which have unique neuropsychological profiles associated with impairment of executive functions, episodic and working memory, processing speed and motor skills\textsuperscript{55}.

### How should we approach assessment?

The main challenges for neuropsychological assessment in the context of addiction are: controlling the effects of recent drug use; making an adequate estimation of premorbid characteristics versus addiction-related problems; achieving a good sampling/coverage of the most relevant cognitive domains; selecting appropriate tests for the population and the purpose of the assessment; and considering ecological validity\textsuperscript{17}. With regard to recent drug use, we should be mindful about the cognitive-enhancing effects of certain drugs such as cocaine and amphetamines, as well as the cognitive-dampening effects of acute alcohol, cannabis or benzodiazepine intake. To make sure we are capturing long-term rather than acute effects, assessments should be scheduled at least 48 hours after last use, and ideally after two weeks...
(to rule out residual withdrawal effects). To discriminate between premorbid versus addiction related alterations, the interview should focus on some of the well-known antecedents of drug using behavior, including socioeconomic disadvantage, history of trauma, ADHD and psychosis-related and personality disorders (which precede or overlap with onset of drug use). Moreover, the assessment protocol needs to incorporate measures of IQ and lifetime drug use, to scrutinize the relationship between general intelligence and severity of drug use measures and cognitive performance. In terms of coverage, the assessment should focus on measuring episodic and working memory, sustained and selective attention, the different domains of executive function including fluency, response inhibition, cognitive flexibility and decision-making, and social cognition. Special emphasis should be placed on different aspects of impulsivity and decision-making, including reflection/planning, delay discounting, risk taking and effort-based decision-making, since they will be directly relevant to clinical outcomes. Test selection needs to prioritize complex over simple tasks (e.g., California over Hopkins verbal learning test; Probabilistic over deterministic reversal learning tasks of flexibility), since deficits are not gross and will only be apparent in difficult tasks. Finally, in a still emerging field, it is important to demonstrate that the conclusions of our assessment will be relevant to explain difficulties in daily life. Therefore, we should prioritize ecologically valid tests, both in terms of predictive validity and similarity to real-life, relevant situations.

Are cognitive training and rehabilitation programs effective in amending cognitive deficits and improving clinical outcomes?

Yes, but only when they are targeted and tailored to the specific deficits of the population. At least three cognitive training/rehabilitation strategies have been shown to be effective in restoring cognitive deficits and/or improving clinical outcomes in patients with addiction. Approach Bias Modification, which uses computerized training to tame approach biases towards alcohol cues and promote approach biases towards non-alcoholic beverages (e.g., juices, sodas), has shown to reduce relapse rates in numerous studies. However, it is unclear if the training can be successfully generalized to other forms of substance addiction, since most drugs (unlike alcohol) do not have straightforward alternative rewarding stimuli. Computerized Working Memory Training has been shown to reduce alcohol use in problem drinkers, illicit drug use in methadone maintenance patients and impulsivity levels in people with methamphetamine addiction (but see). Using a more holistic, compensatory-based approach, Goal Management Training (GMT), which was originally designed for executive dysfunction in neurological patients, has also obtained very promising results. GMT can decrease impulsivity and improve planning and decision-making in patients with polysubstance use and patients with methamphetamine addiction and HIV. Altogether, there is growing, promising evidence on the efficacy of cognitive training and rehabilitation as an adjunctive strategy for the treatment of addiction, but there is also a need for better-controlled trials and examination of moderators and mediators of training/rehabilitation effects.

When and how can rehabilitation be applied?

We have shown that Approach Bias Modification is feasible and effective as early as during the detoxification phase once acute withdrawal symptoms are medically controlled. In fact, it is possible that cognitive training during detoxification can take advantage of the neuroplasticity processes that accompany early abstinence. The application of more intensive cognitive rehabilitation strategies, such as Goal Management Training, requires more time and engagement from participants, and hence it can be better suited for dishabituation after acute and residual withdrawal effects have subsided. Therefore, it is theoretically plausible to link up both approaches, using computerized cognitive training to strengthen prerequisite cognitive processes during the early detoxification stage (e.g., attention, working memory), and then capitalize on such improvements to facilitate delivery of Goal Management Training or other intensive interventions to consolidate meta-cognitive strate-
gies and apply them to real-life scenarios. Future studies will need to assess the validity of this concept and the potential efficacy of the combination. Another promising approach is overlapping cognitive training/rehabilitation interventions with other non-neuropsychological therapies that can synergize their effects. For example, we have applied Goal Management Training in combination with mindfulness, using the latter to smooth the transition between identification of impulses and the development of a goal-focused meta-cognitive approach. Cognitive training interventions can also benefit from the neuroplasticity changes that can be achieved via physical exercise training. For example, a recent study has shown that eight weeks of aerobic exercise training increased the availability of dopaminergic receptors in the striatum. However, more research is needed to establish what is the right blend, timing and intensity of these combined interventions.

What is the future of the neuropsychologist in addiction?

The future should bring greater and improved utilization of neuropsychologists in addiction treatment centers. After two decades of solid research on the characterization of deficits, the addiction clinic should embrace this knowledge, and neuropsychologists need to be ready to implement it. There are several models to achieve this goal. One is embedding a neuropsychology service in existing addition treatment centers, taking advantage of a pre-existing structure and a comprehensive duty of care. Another possibility is creating specialized addiction-neuropsychology clinics, which then use other complementary external services. The future will also bring more consensus and evidence-based practice on neuropsychological assessments and interventions tailored to populations with substance addictions. The format of assessments and interventions will probably change. Assessments will become more portable and engaging using digital technology. Additionally, interventions will likely be more sophisticated, with greater personalization and dynamic adjustments as a function of therapeutic progress. The essence remains, however, that addiction is inherently a disorder of executive control and decision-making, and thus will necessitate better assessment and intervention tools to profile and amend executive and decision-making deficits.

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