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NEUROPSYCHOLOGY AND DRUG ADDICTION

Gloria García Fernández, Olaya García Rodríguez and Roberto Secades Villa
Addictive Behaviors Research Group, Psychology Faculty, University of Oviedo

In this paper we describe the main neuropsychological factors related to the onset and maintenance of drug-use behaviours, together with the neuropsychological alterations related to drug-dependence and their clinical implications. Drug addiction has been related to alterations in executive control and decision-making, and to changes in reinforcer choice and preference. In turn, these alterations have an impact on psychosocial functioning, on the course of the addictive process and on patients' outcomes when receiving formal treatment. Thus, a neuropsychological approach can help overcome some limitations of current models of treatment for drug-use disorders.
Key words: *Drug addiction, Neuropsychological functioning, Executive functions, Clinical implications.*

En el presente trabajo se resumen los principales factores neuropsicológicos relacionados con el inicio y el mantenimiento de las conductas de uso de drogas, se describen las alteraciones neuropsicológicas asociadas a la dependencia, y se discuten sus posibles implicaciones clínicas. La adicción a drogas se ha relacionado con alteraciones en las funciones ejecutivas y en la toma de decisiones, y con cambios en la preferencia y en la elección de reforzadores. A su vez, estas alteraciones tienen repercusión en el funcionamiento psicosocial, en el curso del proceso adictivo y en la evolución de los pacientes en los programas de tratamiento. De este modo, el enfoque neuropsicológico puede ayudar a superar algunas limitaciones de los modelos actuales del tratamiento de los trastornos asociados al uso de sustancias.
Palabras clave: *Adicción a drogas, Funcionamiento neuropsicológico, Funciones ejecutivas, Implicaciones clínicas.*

According to the latest Annual Report from the European Monitoring Centre for Drugs and Drug Addiction (EMCDDA, 2010), there is a high level of demand for treatment related to the use of illegal drugs in the European Union; indeed, it is estimated that a million people received such treatment in the EU in 2007. Drug abuse is a particularly complex problem, since it is modulated by highly diverse factors and associated with the presence of medical, family, social, work-related, economic, legal and psychological problems. So far, a robust theoretical and empirical framework has been developed in relation to addictive behaviours and their treatment, together with increasingly sensitive, specific and refined assessment instruments and ever more effective forms of intervention (Secades & Fernández, 2003). However, in spite of the undoubted progress in knowledge of and treatment for substance-use disorders, there are still many unanswered questions in relation to the explanation of their development and, above all, their effective treatment.

In recent years, new research lines have contributed to the explanation of these types of problem and have guided intervention initiatives. In particular, neuropsychology has provided a wealth of knowledge about the phenomenon of addictive behaviors that has yet to be transferred to the field of clinical practice. In this line, a recently published consensus document on the neuroscientific approach to addictions (Sociedad Española de Toxicomanías, 2009) outlined an explanatory framework for addictions and their therapeutic treatment from a neuropsychological perspective.

Numerous clinical, neuroanatomical and neuropsychological studies have explored the potential effects of the use of different drugs on the brain (for a review, see Garavan & Stout, 2005). The specific type of cognitive abilities preserved and affected in persons addicted to different substances and with different patterns of use (including variables relating to severity of addiction, age at first use, types of substance used, etc.) has been the focus of interest in numerous studies. Likewise, research has looked at the role of neuropsychological alterations as a vulnerability factor or as the direct consequence – and a maintaining factor – in drug use. Moreover, studies in this field have explored the influence of neuropsychological alterations not only on the assessment and prevention of substance-use disorders, but also on the success of their treatment.

The neuropsychological perspective offers potential applications for overcoming some of the limitations of

Correspondence: Gloria García Fernández. *Facultad de Psicología. Universidad de Oviedo. Plaza Feijoo s/n. 33003 Oviedo. España. E-mail: garciagloria.uo@uniovi.es*

current approaches to the treatment of addictions. The incorporation of these neuropsychological findings in clinical practice can contribute substantially to improving our understanding of the onset and maintenance of substance abuse, to its assessment and to the design of effective clinical intervention. Thus, the objectives of the present work are to describe substance-use disorders from a neuropsychological perspective, to summarize the principal findings of neuropsychological research on addictions from recent years, and finally, to discuss the possible implications of this research line for clinical practice.

DRUG ADDICTION FROM A NEUROPSYCHOLOGICAL PERSPECTIVE

Drug addiction is characterized by the abusive and persistent use of substances despite the negative consequences for the individual, and an apparent loss of control over behaviour. As reflected in the DSM-IV-TR (2000) diagnostic criteria, people with drug addiction continue to use the substance even though they are aware of the problems it appears to cause; moreover, they show persistent desire or make fruitless attempts to control or cease their use. These clinical characteristics indicate, from the neuropsychological point of view, possible alterations in the mechanisms that regulate decision-making and inhibitory control. In this regard, neuropsychological and neuroimaging studies carried out with substance users have indicated alterations in the functioning of the frontal lobe and associated cognitive functions, which play a key role in inhibitory control and decision-making (Yucel & Lubman, 2007).

Currently, there are different theories and explanatory models from a neuropsychological perspective in relation to the onset and maintenance of drug-use behaviour (for a critical review, see Robinson and Berridge, 2003, or the consensus document from the Spanish Society for the Study of Drug Addiction; Sociedad Española de Toxicomanías, 2009). What they all have in common is the idea that drug use triggers neuropsychological and neuroanatomical changes, which in turn lead to neuroadaptation in cognitive, motivational, behavioural and emotional functions, and this eventually influences the everyday psychosocial functioning and quality of life of persons dependent on substances. These altered functions have to do with attention capacity, concentration, integration, information processing and execution of action plans. Furthermore, these modifications would act as maintaining variables within a broader, idiographic biopsychosocial model of addiction.

Various neuroscientific models of addictions have been generated, which have been related to different underlying mechanisms and factors to explain the origin and maintenance of addictions. These theories have attempted to associate the behavioural expressions observed in addictions with the neurobiological substrates that support them.

On the one hand, classical models have stressed the short-term reinforcing power of substances and the role of tolerance, dependence and avoidance of withdrawal syndrome in the long-term maintenance of use (Koob & Le Moal, 2001). On the other hand, the alterations caused by drugs in systems that regulate learning and memory influence the structures that regulate classical conditioning and the acquisition of habits, making it easier for drug use to be triggered automatically following exposure to signals associated with drugs (Everitt, Dickinson, & Robbins, 2001). Thirdly, the motivational system and the sensitization of the brain's reward system are altered by substance use, so that the motivational value of the drug becomes larger than that of any other natural reinforcer and becomes fixed, ceasing to be dependent on the needs of the organism (Robinson & Berridge, 2000).

Furthermore, drug use has been associated with alterations in the fronto-cortical systems responsible for the executive functions, which play an important role in decision-making and in the inhibitory control of behaviour, leading to impaired judgement and facilitating impulsiveness (Bolla et al., 2004). The executive functions constitute a set of higher organizational and integrational skills that have been associated neuroanatomically with different neural circuits which converge in the pre-frontal lobes of the cortex. They are involved in anticipation and goal-setting, planning, inhibition of inappropriate responses, selection of appropriate behaviours and their temporal and spatial organization, cognitive flexibility in the monitoring of strategies, supervision of behaviours according to motivational and affective states, and decision-making (Verdejo-García, López-Torrecillas, Orozco, & Pérez-García, 2004).

From the neuroanatomical point of view, different functional circuits have been described within the prefrontal cortex involved in the executive functions (Stuss & Alexander, 2000). On the one hand is the dorsolateral circuit, related to purely cognitive activities, such as those of working memory, selective attention, concept formation

or cognitive flexibility. On the other hand is the ventromedial circuit, which is associated with the processing of emotional signals that guide our decision-making toward ethical and prosocial alternatives. Dorsolateral circuit activity has been linked to performance in classic executive function tasks, such as the Stroop test (Golden, 1993). In contrast, the development of neuropsychological tests for the assessment of decision-making processes involving the ventromedial circuit has been much more recent, a relevant example being the Gambling Task (GT) (Bechara et al., 2001).

Thus, there are neurobiological theories that explain substance addiction as the result of damage and decompensation between the motivational system and the executive system due to the effects of drug use. On the one hand, the motivational system, responsible for evaluating the motivational relevance of reinforcers, makes an exaggerated appraisal of the properties of drugs and undervalues those of other natural reinforcers (such as food, sex, social relations), and on the other, the executive system, charged with inhibiting inappropriate behaviours, is affected by the substance use itself, making it impossible to inhibit the drug-use behaviour.

Another contemporary neurobiological model applied to drug-use behaviour is the somatic marker model (Verdejo-García & Bechara, 2009), in which addiction is explained as the result of decision processes that are maladaptive for persons with substance-use problems. Drug-taking affects the motivational and emotional systems responsible for the generation of emotional markers (vegetative, muscular, neuroendocrine or neurophysiological changes) which govern decision-making. With these systems altered, the person is more likely to choose responses based on desire and urgency to use drugs (which works as a maladjusted emotional marker for decision-making) and biased toward such use (immediate reinforcement) as against its potential negative consequences (delayed punishment).

In sum, chronic drug use seems to produce alterations in brain circuits involved in processes of reward, motivation and learning, executive functions and decision-making mechanisms, changes which in turn appear to play an important role in the maintenance of addiction.

NEUROPSYCHOLOGICAL ALTERATIONS ASSOCIATED WITH DRUG USE

The use of opiates, cannabis, alcohol, solvents and psychostimulants has been associated with neuropsychological alterations in numerous studies, which have focused on the specific assessment of the executive functions. A recent work on the theoretical and methodological aspects of neuropsychology and drug dependence (Verdejo-García & Bechara, 2009) includes a review of the principal neuropsychological findings related to the residual effects of the chronic use of different drugs. In the case of addiction to heroin and opiates, the residual effects of their use appear to affect executive processes of flexibility, planning and inhibition, impulsiveness and decision-making. Moreover, alterations in processing speed, attention, visuo-spatial processes and working memory are commonly observed. Depending on time of abstinence, some of these deteriorations in attention and flexibility appear to be reversible.

Cannabis has been widely and consistently associated with temporal alterations in processing speed, attention, memory executive control and decision-making in the hours and days following use. However, recent studies comparing task performance of cannabis users at different time points during periods of abstinence indicate that in the majority of cases these alterations can be reversed during abstinence. The most resistant deterioration seems to occur in memory; moreover, alterations in executive performance appear to be more stable among users with more severe addiction and whose onset of use was earlier.

The neuropsychological alterations linked to alcohol use have been the subject of considerable research in recent decades, its results suggesting that abusive drinking is associated with a wide range of stable alterations in information processing, psychomotor skills, visuo-perceptual organization, memory and executive control. For this reason, it is considered important to evaluate alterations in memory and executive functions in those dependent on alcohol.

As far as cocaine addiction is concerned, the majority of studies indicate the presence of alterations in aspects such as attention, memory, psychomotor skills and executive functions (response inhibition, flexibility and decision-making). In a review of studies carried out between 1987 and 2002 on the neuropsychological effects of cocaine use (Jonanovski & Zakzanis, 2005), the largest effect size and agreement was found for alterations in attention and executive functions.

In this line, a study by our Addictive Behaviors Research

Group at the University of Oviedo explored the neuropsychological performance of 50 cocaine addicts at the start of a treatment programme, compared to a control group of 22 individuals matched for age, sex and years of education. The results ruled out the presence of a generalized neuropsychological deficit in the cocaine-dependent group, suggesting specific and subtle alterations in partial aspects of the executive functions. In particular, the clinical group showed poorer performance in tasks related to information processing and response inhibition, as well as a tendency for less mental flexibility (García Fernández, García-Rodríguez, Secades-Villa, Álvarez Carriles, & Sánchez Hervás, 2008).

Moreover, in a follow-up study (García Fernández, García Rodríguez, Secades Villa, Fernández Hermida, & Sánchez Hervás, 2010), the authors explored the neuropsychological evolution of a group of patients who completed 12 months of treatment, with the aim of assessing the course of their executive functioning and considering possible clinical implications. In the majority of cases patients' scores on the tests of neuropsychological performance were better after 12 months of treatment than at baseline, but not in all the tasks. Neuropsychological performance in tasks related to attention and fluency improved, it remained stable in tasks related to inhibitory control and it worsened in tasks of mental flexibility. Thus, it would seem that deficits in some components of the executive functions – specifically mental flexibility and inhibitory control – remain stable and are more robust and less malleable, whilst alterations in attention and processing speed appear to be reversible or more amenable to change.

Previous studies assessing impulsiveness in tasks associated with delayed reinforcement under the delay-discounting paradigm show that substance use is related to lower capacity for delaying reinforcement and greater impulsiveness (Reynolds, 2006). In a recent experiment, the performance of cocaine addicts in a delay-discounting task was compared with that of a control group of non-users (García Fernández et al., 2010). The task involved choosing hypothetically between receiving different amounts of money immediately or higher-value rewards after a time delay. The results indicated that cocaine users tended to select immediate rewards over delayed but higher-value rewards. Moreover, delayed reinforcers lost value more quickly in the cocaine-dependent group than in the control group.

NEUROPSYCHOLOGY, CLINICAL PSYCHOLOGY AND DRUG ADDICTION

The contributions of neuropsychology to clinical psychology can help to improve knowledge about drug addiction, its assessment and its treatment. Recent studies have begun highlighting the utility of neuropsychological assessment in the clinical evaluation of patients, in the selection and adaptation of treatment, and even for improving the understanding of core clinical characteristics in addictive disorders.

First of all, the neuropsychological evaluation of people seeking treatment for drug use can constitute a substantial prognostic factor. The deterioration of cognitive functions has been associated, in the context of drug-dependence rehabilitation, with lower percentages of treatment completion and higher relapse rates. Several studies have stressed the importance of neuropsychological state for retention rates on treatment programmes. The inclusion of neuropsychological aspects as additional tools in pre-treatment assessment may help the identification of those patients at greater risk of dropout or relapse – which would facilitate the selection and adaptation of treatment for each case in particular – as well as the identification of risk factors associated with poorer prognosis.

Secondly, the neuropsychological profile of patients can indicate the most appropriate therapeutic lines for the intervention. Executive alterations may have considerable negative impact on the course and outcomes of treatments for drug dependence. As mentioned earlier, the pharmacological targets of drugs are a diverse set of brain structures involved in attention, information acquisition and processing, decision-making and response inhibition. Paradoxically, the treatments of choice in addictions use strategies that require adequate functioning of these cognitive elements (for using, say, the development of coping strategies, training in problem-solving or the active search for alternative activities incompatible with substance use).

The relevance of this aspect increases as these treatment programmes become more cognitively demanding, bearing in mind that drug-dependent individuals can have considerable difficulties for becoming aware of their own deficit, understanding and following complex instructions, inhibiting impulsive responses, planning their daily activities and making everyday decisions (Tirapu, Landa, & Lorea, 2003). Some authors stress how such difficulties can lead to frustration and premature treatment dropout (Aharonovich, Nunes, & Hasin, 2003). Time

adjustments in programme content in relation to potential recovery of the deficits or direct intervention through cognitive rehabilitation strategies could help to optimize current therapeutic interventions in the field of drug dependence. Specifically, to address attentional and information processing deficits it would be necessary to adapt assessment and treatment sessions in particular ways: using different media or materials, adjusting the duration and frequency of sessions, introducing breaks, providing feedback and asking patients more often about their progress.

As regards alterations in decision-making and inhibitory control in addictive disorders, it would be useful for treatment initiatives to intervene actively on these key aspects. In the work by Lorea, Tirapu, Landa and López-Goñi (2005), the authors point out how these patients show more difficulties for foreseeing risk situations and planning self-control strategies, as well as more problems to resist stimuli associated with drug use and inhibit automatic responses. Therefore, it would be appropriate to use therapeutic paradigms focused on work with aspects of prefrontal cortex functioning, as well as adapting such paradigms, by increasing, for example, the use of role-playing for practicing sequences of behaviours alternative to drug use and helping to make them automatic. The same above-cited work reviews three models of intervention in drug dependence: the motivational interview, relapse prevention and skills training, and relates their possible effects to neuropsychological functioning. Such intervention models would help to improve decision-making, exploring the pros and cons of drug use (improving the ventromedial circuit), to reduce the likelihood of relapse through work on skills for rejecting drugs, and to manage craving by improving inhibitory control (dorsolateral circuit).

Furthermore, treatment programmes may benefit from the use of Contingency Management (CM) procedures, which use immediate reinforcers alternative to substance use. This type of technique would help treatment participants to attain initial abstinence, but moreover, the use of reinforcers of various types (sporting, cultural and social activities, credits for goods or services, etc.) would facilitate intervention on the exaggerated value of reinforcers associated with drug use and patients' maladaptive preference for them.

Also, and with regard to the prevention of drug use, the most recent studies attempt to determine whether these neuropsychological alterations are the cause or consequence of drug taking, and in the case of these deficits being previous (vulnerability factor), to analyze the implications for the design of programmes for the prevention of substance abuse disorder. Whilst there is empirical evidence for the presence of neuropsychological alterations, it is still not clear whether such alterations precede addiction or are a direct consequence of it. In some cases, these alterations have been related to clinical variables of addiction, such as years consuming the drug or pattern of use, suggesting that they are indeed a consequence of the drug taking. However, cross-sectional research cannot determine whether the alterations found are a result of drug use or are related to vulnerability, or whether there is a combination of these aspects at work. According to some longitudinal studies, such as that by Tarter et al. (2003), capacity for response inhibition, measured with the Stroop test, a temperament questionnaire and a behaviour questionnaire for 16-year-olds, predicts with 85% success the presence of drug-use problems at age 19.

It is likewise important to take into account neuropsychological development during adolescence. Numerous recent studies suggest that the adolescent brain may be more vulnerable to the neurotoxic effects of psychoactive drugs, due to the unique and critical neurodevelopmental processes that take place in this age group. Some authors, such as Yucel and Lubman (2007), argue that people who begin using drugs at an early age, before the brain has matured, may be more vulnerable to neuropsychological and neurobiological alterations, as well as to the development of addiction disorders or other psychological disorders. Early prevention would involve delaying as long as possible the age at onset of drug use, as well as fostering the development of the executive functions in children and adolescents belonging to high-risk groups, or who have begun using drugs sporadically.

CONCLUSIONS AND FUTURE RESEARCH LINES

Drug addiction has been consistently associated with changes in executive functioning, in the attribution of the relative value of reinforcers, and in decision-making. Furthermore, these changes in turn influence psychosocial functioning, the course of addiction and, finally, the success of treatment, so that the neuropsychological approach could help to improve current explanatory models and treatment programmes for disorders related to substance use.

In any case, it is difficult to draw firm conclusions from the considerable number of studies carried out in this research field. First of all, due to certain methodological limitations in the majority of studies to date. In particular, the great disparity between the types of neuropsychological assessment employed is a problem that makes it hard to generalize the results. In this regard, it would be useful to replicate studies with the same neuropsychological tests in different groups of addicted patients, with a view to being able to carry out meta-analyses and to study the relation between neuropsychological deficits and clinical variables of interest.

In addition, it should be borne in mind that the executive functions are highly complex, being responsible for the coordination and integration of multiple cognitive, motivational and affective processes and representations. In consequence, there are discrepancies in the classification and definition of these functions and their components, leading some authors to argue that this term has become a kind of "conceptual umbrella", and that there is a need to integrate the different models to aid our understanding of executive processes, their components and their subcomponents. Accompanying this conceptual confusion in relation to the executive functions are the limitations regarding their measurement – differences of opinion over which aspects are to be measured and the ecological validity, sensitivity and specificity of the neuropsychological tests. It would therefore be advantageous to employ neuropsychological instruments that are sensitive to the alterations, and work towards closer correspondence between tests and neuropsychological functions.

Other common methodological limitations that make it difficult to come to definitive conclusions are the variability in duration of abstinence at the time of applying the tests, or the frequent use of other substances, which precludes the "pure" study of the effects of one drug in particular. There is thus a need for studies in which participants have been abstinent for a similar period, and which use periodical neuropsychological assessments to identify the way deficits develop over time.

Finally, we should stress the need for studies that explore the long-term executive functioning of persons addicted to different substances. It is important to continue research on the potential reversibility of neuropsychological alterations, the variables that can mediate their recovery, and their therapeutic implications. Moreover, it would be advantageous to carry out studies which, while controlling abstinence, compare the neuropsychological evolution of addicts to different substances on different treatment programmes, with a view to exploring the differential efficacy of the programmes, as well as the effects of abstinence, of treatment, or of both on neuropsychological performance. There is likewise a need to explore in depth the role of impulsiveness in drug addiction and in interventions which address it.

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