Chapter 3
The Assessment of Executive Functions: A New Neuropsychological Tool for Addiction

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3.1 Neurocognitive Deficits in Addiction

Given the severity and pervasiveness of the neurophysiological anomalies that result from the repeated consumption of substances or the systematic implementation of dysfunctional behaviours, it is not surprising that addiction pictures are often connoted by neurocognitive deficits especially affecting higher cognition, as documented by numerous studies focused in the use of different types of psychoactive substances and behavioural addiction profile (Antons et al., 2020; Brand et al., 2019; Fernández-Serrano et al., 2011; Yücel et al., 2007).

In particular, as we have shown in Chap. 1, alterations of the mesocorticolimbic dopaminergic circuits and of the corticostriatal glutamatergic circuits in prefrontal regions compromise various executive functions such as inhibitory control, attribution of salience to stimuli, decision-making and goal-oriented behaviour, flexibility in selecting and initiating an action, inverted learning, and error tracking (Antons et al., 2020; Bechara, 2005; Koob & Volkow, 2016), making it more difficult to decide to stop using the substance of abuse or enacting dysfunctional behaviours, as well as to persist in this decision. The ability to develop conscious decision-making strategies and the efficiency of metacognition also appear to be partially compromised, as happens in pathologies that involve similar deficits in neural circuits that foster decision-making processes (Angioletti et al., 2019, 2020; Balconi et al., 2018). Structural and functional alterations, then, contribute to the exacerbation of

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states of malaise, worsen conditions of psycho-physical frailty, and aggravate the severity of the general clinical picture.

As for the cognitive domain, the functions that show the greatest vulnerability are attention regulation, memory, executive functions (EF)—in particular inhibitory control, working memory, decision making, cognitive flexibility, and strategic orientation of cognitive resources—and emotion regulation skills (Antons et al., 2020; Gould, 2010). Furthermore, while the impairment of the "addiction circuit"—which includes parts of the reward, learning, and memory circuits and cortical structures involved in decision-making and inhibitory control—entails a set of generalized deficits transversal to different addiction pictures, it was shown that specific functions and cognitive processes may be more or less compromised depending on the substance of abuse and other parameters such as the duration of abstinence (Fernández-Serrano et al., 2011).

Specifically, notwithstanding the variability in clinical observations and inconsistencies in empirical findings, the most consolidated data suggest that persistent use of psychostimulants (cocaine and MDMA) affects, in particular, cognitive flexibility, working memory, inhibitory control and impulsivity, and regulation of affects, whereas the systematic use of opioids mainly affects decision-making processes and the efficiency of attention regulation, besides—again—working memory and cognitive flexibility, on decision-making abilities and on the efficiency of divided attention.

Conversely, currently available literature exploring cognitive deficits associated to behavioural addiction mostly highlight a shared impairment of inhibitory and executive control (attention regulation, inhibition, decision making, working memory) that, starting from cue-reactivity and altered sensitivity to specific stimuli of interest, affect the generalized ability of impulse control (Antons et al., 2020; Brand et al., 2019; Ioannidis et al., 2019; van Timmeren et al., 2018). Yet, it has to be acknowledged that such literature is still in its first moves and, though promising, had just began to systematically explore potential differences in the profile of neurocognitive and neurobiological alterations that pair with different categories of behavioural addiction (e.g. problematic internet use, gaming disorder, pathological gambling, compulsive buying disorder).

Despite the methodological efforts, it seems clear that the identification of the relationships between models of abuse, addiction-related neurofunctional alterations, and specific patterns of impairment of neurocognitive functions, with particular reference to EF, continues to be a complex and almost unsolved problem, likely due to the multiplicity of factors that affect those relationships. That underlines the clinical and methodological need for new assessment tools capable of detecting, qualifying, and quantifying the alteration of higher cognitive functions in patients who have developed addiction, in order to rapidly sketch an effective definition of their cognitive profile and of specific deficits and impairments.

3.2 Tools for Assessing EF in Addiction

In most of the cases and clinical contexts, cognitive and executive deficits shown by patients who present to psychiatric emergency or addiction assistance/treatment services are typically assessed via basic screening tools or short assessment batteries such as the Mini Mental State Examination (MMSE; Folstein et al., 1975), the Neurobehavioral Cognitive Status Exam (NCSE; Marcotte et al., 1997), the Brief Assessment of Cognition in Schizophrenia (BACS; Keefe et al., 2004), the Montreal Cognitive Assessment (MoCA; Nasreddine et al., 2005), the Neuropsychological Assessment Battery – Screening Module (NAB-SM; Grohman & Fals-Stewart, 2004), and the Addenbrooke's Cognitive Examination – Revised (ACE-R; Mioshi et al., 2006).

Given the advantage of short administration and correction times (from 30 to 45 min) and the possibility to quickly outline global functioning profile, short cognitive batteries are commonly preferred to exhaustive neuropsychological assessment procedures. Again, further alternatives are neuropsychological screening tools focused on frontal functions or originally devised to assess dysexecutive syndrome in neurology patients, such as the Frontal Assessment Battery (Cunha et al., 2010; D'Onofrio et al., 2018; Dubois et al., 2000; Floris et al., 2012).

Neurology patients suffering from frontal lesions or dysfunctions, indeed, show behavioural disorders—such as impulsivity, altered self-awareness, and vulnerability to rewards—and cognitive impairments shown even by people who developed addiction – namely, difficulties in attention regulation, processing speed, and episodic memory. However, these and other tools built to detect executive deficits in the case of clinical pictures other than addiction (e.g. neurodegenerative disorders, schizophrenia, multiple sclerosis, HIV-associated dementia, etc.), may not be optimal when used to screen different clinical populations. This becomes even more relevant when the target population, as in the case of people presenting substance-related or behavioural addiction, differ from the original validation cohorts in terms of personal features other than the primary diagnostic profile, such as the age range. Yet, some brief assessment tools have been tested for feasibility and usability even in cases of substance use disorder and showed an interesting potential – namely, the NAB-SM (Cannizzaro et al., 2014; Grohman & Fals-Stewart, 2004) and the MoCA (Bruijnen et al., 2019; Copersino et al., 2009).

The Screening Module of the Neuropsychological Assessment Battery (NAB-SM) allows for a relatively brief assessment of five core cognitive domains: attention, language, memory, visual-spatial skills, and EF, providing also an overall functioning index. The NAB-SM has been validated as a screening tool in subjects with substance use disorder (Copersino et al., 2009; Grohman & Fals-Stewart, 2004) and, specifically, with people presenting cocaine addiction (Cannizzaro et al., 2014). Still, this tool might be overly broad, thus providing information on cognitive functions that are not at the core of addiction-related neurocognitive disorders, while lacking focused investigation of functions that are typically affected by addiction, such as inhibitory control.

The focus on EF is more peculiar of another screening tool that has been borrowed by neurology to psychiatric practice and tested with people showing substance use disorder (Bruijnen et al., 2019; Copersino et al., 2009): the Montreal Cognitive Assessment battery. The MoCA includes specific subtests for verbal memory, visuospatial skills, verbal and non-verbal EF, attention, working memory, language, and temporal-spatial orientation. Yet, it has to be acknowledged that memory and orientation subtests have a considerable weight compared to those that evaluate EF, therefore the sensitivity of the MoCA and its ability to identify profiles with prevalent executive deficits may not be optimal. Furthermore, from a qualitative point of view, it might be suggested that the subtests used to assess set-shifting and attention regulation skills are presumably too simple for the typical population of subjects who present to care and assistance services due to addiction.

3.3 Why a New Neuropsychological Battery for Screening of EF in Addiction

Available evidence and, especially, clinical practice, however, point out the inadequacy of the assessment or screening methods for EF currently used in the care and assistance services. In addition, in line with prevalence estimates, common field experience highlights that, in most cases that present themselves independently to assistance services seeking treatment for addiction disorders, the severity of neurocognitive disorders is mild and that peculiar deficits are not adequately detectable and quantifiable via general screening tools that were originally conceived for the evaluation of global cognitive impairment in neurological patients or cognitive decline in old age. Indeed, while those tools have shown good validity and accuracy for the detection of serious impairments, it was suggested that they are not fully apt for the identification and quantification of milder executive deficits (Bruijnen et al., 2019; Copersino et al., 2009), which, nevertheless, can have a significant impact on everyday activities and personal autonomy (e.g. by increasing the amount of cognitive resources required by routine activities due to the enlarged need for constant conscious monitoring).

During the diagnostic process (including a clinical interview with the patient and his family), it is therefore important to be able to effectively discriminate the nature of executive deficits and to identify risk factors and critical needs in the earliest stages. This would allow defining the most appropriate therapeutic plan for the patient, possibly planning a parallel cognitive rehabilitation phase. Such impairments or executive dysfunctions could, in fact, compromise the recovery programs and, above all, the patient's autonomy and sense of efficacy in the activities of daily life.

The neurocognitive assessment of executive dysfunctions associated with addiction pictures represents an element of the diagnostic process that is as fundamental as it is currently underrepresented in the routine general assessment practice in drug assistance/treatment services. The lack of suitable tools for the neurocognitive assessment of executive dysfunctions associated with addiction pictures and specific training of clinical staff has largely contributed to that scenario.

We have, therefore, designed and tested a novel brief neurocognitive screening battery to meet those clinical, methodological, and practical needs. In designing and developing such novel tool, we started from practice and field experience by mapping cognitive assessment procedures and neuropsychological assessment tools that were most commonly used in drug assistance/treatment services, with a focus on the national context. Such field observations were then integrated with the critical analysis of the national and international literature on the subject, with particular focus on neuropsychological tests used for the evaluation of executive deficits associated with addiction. Those first steps provided valuable information that guided the subsequent phase of review of existing measures and design of novel tests included in the battery. The first version of the new screening battery underwent, then, pilot testing with a clinical cohort ($N = 30$ patients diagnosed with substance use disorder) to assess its efficiency and usability. Finally, taking into account the observations that emerged during conception phases and, above all, from pilot testing, the final version of the battery was created and subjected to validation with both control and clinical normative samples.

The neurocognitive battery—named Battery for Executive Functions in Addiction (BFE-A)—consists of seven subtests and includes measures dedicated to short- and long-term verbal memory, working memory, cognitive flexibility (with both verbal and non-verbal materials), focused attention, attention regulation and suppression of interference and inhibitory control (see Fig. 3.1). The BFE-A allows for outlining a general profile of the alterations of EF associated with addiction pictures. In addition, the calculation of specific performance indicators for the individual subtests allows to compare inter-test performance, as well as to identify strong and weak points in individual profiles, providing relevant information for planning targeted diagnostic investigations or personalized empowerment/rehabilitation interventions that take into account the patient's potential and specific needs.

The structure of the BFE-A includes both digitized neuropsychological tests and computerized neurocognitive tasks. The choice to implement such different methods for assessment originates from methodological and clinical reasons. Digitized

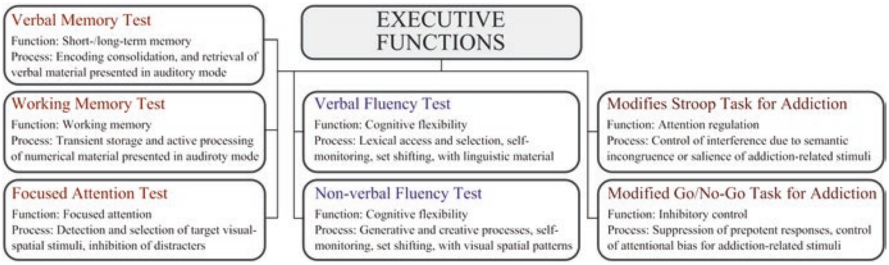

Fig. 3.1 Global structure of the Battery for Executive Functions in Addiction (BFE-A) with a focus on specific subtests and their functional correlates

testing and computerized performance measures, in particular, are characterized by a high level of control over the procedures of administration and execution of the test, and by remarkable precision in the presentation of stimuli. These peculiar properties are particularly useful in assessing moderate or mild cognitive impairment and increase the sensitivity of the assessment, thus allowing for a finer-grained picture of examinee's difficulties and residual abilities. Such greater sensitivity and discriminating capacity, even in case of milder impairment, becomes peculiarly relevant when applied to screen attention regulation skills and the efficiency of interference inhibition and cognitive control mechanisms. The consequences on behaviour and everyday life of minor alterations of those essential executive skills may, in fact, be hidden by compensation mechanisms, making them more difficult to identify via traditional cognitive tests.

3.4 Potential Applications: Salience and Innovativeness of the BFE-A

In its entirety, the above-presented BFE-A was built to assess, in a short time, the degree of impairment of high-order EF often observed in people who have developed substance-related or behavioural addiction disorders. The set of tests and tasks that constitutes the BFE-A was selected based on their relevance, as highlighted by empirical literature, and their diagnostic potential, as highlighted by available psychometric and clinical evidence. In the scenario of cognitive assessment practices, the use of a screening battery created ad hoc for the target clinical population—possibly followed, if needed, by second-level diagnostic investigations—constitute, indeed, a good compromise between the accuracy of a complete evaluation and the specificity of an assessment that is completely tailored on the individual patient and that, therefore, may require remarkable clinical experience to be properly set up.

Given the interest in creating a tool that could be efficiently administered in different clinical contexts and in services dedicated to the treatment and diagnosis of addiction pictures, the BFE-A was developed in compliance with the following principles:

- *Informativity*: ability to provide an overall profile of integrity of the examinee's EF and higher cognitive skills that could then possibly be complemented by second-level neuropsychological assessment, thus optimizing the resources dedicated to assessment procedures.
- *Psychodiagnostic value and clinical relevance*: optimal coverage of executive deficits associated with substance-related and behavioural addiction, as well as ability to provide information related to peculiar executive and higher cognitive functions known for their impairment in different addiction pictures.
- *Modularity*: possibility of using the tests of the BFE-A also as independent tests or of creating subsets of tests for specific diagnostic investigations, in addition to

the use of the BFE-A as a unitary tool for screening the executive functioning of the examinee.

– *Clinical usability*: rapid administration and correction times, as well as selection of materials and methods of administration that could be easily implemented and are simple to use in real-life clinical settings.

In particular, the intrinsic modularity and flexibility of the BFE-A allows outlining a first general profile of executive functioning in the examinee and, at the same time, to get specific pieces of information concerning strengths and weaknesses across explored cognitive domains. Furthermore, each subtest has been associated to performance and error indices that are both functionally and metrically comparable. That allows the examiner to outline intra-individual comparisons between the investigated functions, to draw parallels between the examinee's performances at the various subtests, and to identify specific effects of an implemented treatment protocol by weighing them transversely to the investigated cognitive domains, thus providing valuable hints for the optimization or efficiency testing of different care and assistance plans.

3.5 Presentation of an Empirical Validation Study

To sum up, the above-presented BFE-A was developed to try and answer clinical and methodological needs for a usable, valid, and brief screening tool, able to properly sketch a profile of residual skills and weaknesses concerning higher cognition and EF in substance-related and/or behavioural addiction. We will now briefly present the outcomes of the empirical validation study aimed at testing the feasibility, informativity, and robustness of the novel neurocognitive screening battery.

A total of 207 volunteers were enrolled by the Research Unit in Affective and Social Neuroscience of the Catholic University of the Sacred Heart of Milan and by the Canzio Drug Addiction Service of the ASST Fatebenefratelli-Sacco in Milan, with the additional support of the Alcoholic and Double Diagnosis Community of Castelfranco Veneto (TV). The total sample was divided into a clinical normative cohort constituted by 151 patients diagnosed with substance-use disorder and a control normative cohort constituted by 56 healthy volunteers. All of enrolled participants provided their informed consent for participation in the validation study, as well as for storage and treatment of related data. The project and related experimental procedures have been reviewed and approved by the relevant Ethics Committee, and comply with the rules and standards of the Declaration of Helsinki and its subsequent revisions.

All of participants included in the clinical cohort were diagnosed with substance-use disorder (diagnostic criteria by DSM-5; APA, 2013) and were involved in diagnostic and/or supportive programs by the above-mentioned drug assistance/treatment centres. Patients with secondary/concurrent diagnosis of neurological conditions or previous neurological clinical history were excluded from enrolment, as well as participants who reported clinical instability in the 48 h prior to assessment session. In addition, volunteers with neurological or psychiatric clinical history, experience of recreational use of psychoactive substances (except alcohol), or first-degree relationship, professional, or volunteering experience with individuals who have been diagnosed with substance-use disorders were excluded from the control normative cohort so to prevent potential confounds.

The age range of enrolled participants was 18–60 years (M = 40.10 years; SD = 11.39), while their level of education varied between 4 and 22 years (M = 13.37 years; SD = 3.59). The sample was primarily constituted by males (males = 134; females = 73) mainly due to gender differences in the clinical cohort, which mirror commonly reported empirical and clinical observations concerning the prevalence distribution of addiction pictures.

The BFE-A has been administered by licensed psychologists trained in psychodiagnostic and neuropsychological testing in a single session. The complete assessment procedure lasted, on average, about 45 min. Scoring of participants' performance at the battery subtests was performed by the expert examiners and then checked by a second expert in neuropsychological testing, acting as additional blinded judge.

Performance data for each subtest of the BFE-A were, then, analysed to investigate the validity, reliability, and clinical potential of the tool. A first set of statistical analyses, which will be here briefly reported, focused on between-group comparisons in order to test for the capacity of the BFE-A to highlight significant differences between the performance of the control and clinical cohorts. Specifically, behavioural measures of performance were analysed via independent-samples t-tests ($\alpha = 0.05$) including Group (Control vs. Clinical) as the main factor. Finally, the size of significant effects was estimated via Cohen's d values to better appraise the relevance of observed between-group differences. Effect sizes have been deemed as small, medium, or large in agreement with Cohen's norms (1988).

Statistical analyses consistently showed worse cognitive performance in patients diagnosed with substance use disorder compared to healthy controls, both at neuropsychological tests of cognitive flexibility, focused attention, verbal memory, and working memory, and at neurocognitive tasks tapping on the efficiency of attention regulation, control of interference, and behavioural inhibition skills. Such scenario hints, in line with available clinical studies and observations concerning neurocognitive sequelae of addiction pictures, at the presence of a generalized impairment of regulatory mechanisms involved in orientation of attention/cognitive resources, inhibition of behaviour, and task-irrelevant information, as well as information processing and consolidation. Notably, the outcome of inferential statistics becomes richer if effect size estimates are taken into account. The analysis of Cohen's d values, indeed, has pointed out that the clearest and most sizeable between group differences concern short- and long-term memory (VMT subtest) and focused attention (FAT subtest), with large effect size estimates, followed by verbal (VFT subtest) and non-verbal fluency (NFT subtest) and inhibitory control (MGTA subtest), with medium-to-large effect size estimates. Subtests tapping on working memory (WMT) and efficiency of mechanisms for suppression of interference (MSTA), instead, highlighted significant though less considerable effects, these being associated to small-to-medium effect size estimates.

To sum up, above-presented preliminary findings further stress the link between peculiar executive deficits and the substance-use disorder and provide first evidence in favour of the potential of the above-presented BFE-A as a quick yet valid neurocognitive screening tool, able to consistently highlight differences in higher-cognition and executive control efficiency between a cohort of patients diagnosed with substance-use disorder and a cohort of matched healthy subjects, as well as to outline a peculiar profile of stronger and weaker points in such high-level cognitive functions.

3.6 Structure of the BFE-A

3.6.1 Verbal Memory Test

Altered learning and memory processes are thought to lie at the core of dysfunctional motivational and reward mechanisms that, in addiction disorders, amplify the reinforcing value associated with specific behaviours or substances of abuse. Notably, the very same neural structures involved in those implicit dysfunctional learning mechanisms also underlie higher explicit mnestic functions. Such association is corroborated by a quite ample set of clinical studies, which consistently showed that processes mediating short-term maintenance and subsequent long-term storage of information are often impaired in people presenting addiction (Fernández-Serrano et al., 2011; Gould, 2010). Explicit, or declarative, memory involves conscious encoding and retrieval of information, facts and events from long-term memory after they went through short-term memory processing and maintenance, and is typically measured through recall or recognition tasks. Focusing on neurocognitive sequelae of addiction, in the majority of available studies, memory impairments were tested and quantified via learning and memory tests based on verbal material, such as word lists or short stories.

The Verbal Memory Test (VMT) of the BFE-A, then, aims at assessing short- and long-term memory through immediate and delayed recall trials. Specifically, it taps on encoding, consolidation, and retrieval processes for verbal material presented in auditory mode. The administration procedure is based on a list of 15 words, which is presented 5 times. After each presentation, the examinee is asked to verbally recall of the stimulus list. Then, after 10 min, the examiner asks the examinee to recall the list of stimuli again, with no additional cues.

The VMT was created starting from a conceptual and methodological revision of the most diffused neuropsychological tests for immediate and delayed recall of verbal items and, in particular, of the Rey Auditory Verbal Learning Test (Rey, 1958). Such classical neuropsychological test proved to be able to highlight memory deficit in a variety of neuropsychological clinical conditions (Andersson et al., 2006;

Bravin et al., 2000; Carlesimo et al., 1996; Schoenberg et al., 2006; Vakil et al., 2012). It was also used to assess memory deficits related to alcohol and substance abuse (Carbia et al., 2017; Fox et al., 2009; Hoffman et al., 2006; Jang et al., 2007; Solowij et al., 2011); though the analysis of literature highlighted a few critical issues concerning the item list included in the Italian version of the test and the general structure of the test. Specifically, the presence of latent semantic associations between the items of the word list may cause facilitation and favour intrinsic encoding strategies. Furthermore, the items in the list is constituted by both concrete and abstract words, which, however, have peculiar semantic features and a different representation in the conceptual linguistic system. Also, the length of the items presents significant variability. And again, preliminary clinical observations collected in a pilot study suggested that the test might be simple for some types of patients with addiction, especially in the younger ones.

Building on such preliminary observation and critical notes, during the development of the VMT we have created a new set of items, selected from the list of lemmas of the COLFIS corpus (Bertinetto et al., 2005) on the basis of stringent psycholinguistic properties: lexical class (nouns), category (concrete), number of letters (4–6), total relative frequency (≥100). In addition, we opted for words that did not have direct latent associations (for example, sun-garden-window) or that did not belong to the same proximal semantic-conceptual network (for example, home-school). Moreover, in order to make the test more discriminative and sensitive even in the case of slight deficits in memory functions, in the VMT the examinee is asked to perform a serial recall task. Serial recall, indeed, compared to free and guided recall, requires a greater allocation of cognitive resources.

3.6.2 Working Memory Test

Deficits of working memory—being such function crucial for complex information-processing and, therefore, for any higher cognitive function—have been the object of extensive investigation in relation with both substance-related and behavioural addiction (Fernández-Serrano et al., 2011; Ioannidis et al., 2019; Yücel et al., 2007). Working memory is commonly defined as a limited capacity portion of the human memory system, where information is temporarily stored and kept accessible to consciousness so that is can be manipulated and processed in the service of higher cognition. As part of EF, working memory is often altered in people who developed addiction pictures and, in typical neuropsychological assessment procedures, is assessed via digit span or repetition tests.

The Working Memory Test (WMT) of the BFE-A aims, in particular, at assessing the working memory span for numerical material presented in auditory mode. Specifically, it taps on the mechanisms for storage and active processing of information in the short term. The administration procedure includes the presentation of numerical sequences of increasing length. After the presentation of each sequence, the examinee is asked to repeat the series of numbers rearranged from the highest to the lowest.

The WMT was created starting from a conceptual and methodological revision of the most-diffused neuropsychological tests used to assess working memory defects and, in particular, the Digit Backward Test (Hebb, 1961; Wechsler, 1939). While the classic version of the backward digit paradigm appeared for the first time in the Wechsler Bellevue Intelligence Scale (Wechsler, 1939), several versions differing in materials, presentation methods, and scoring algorithms were developed in the following years. In its original version, the examiner verbally presents sequences of digits and then asks the examinee to repeat them in reverse order. Such test is commonly used during neuropsychological assessment of various clinical conditions in neurology, from head trauma, to stroke, neurodegenerative disorders, and others (Black, 1986; Laures-Gore et al., 2011; Luerding et al., 2008; Sartori & Edan, 2006). As a part of more extensive assessment batteries, it was also used for the evaluation of cognitive deficits in people presenting substance-related addiction (Cannizzaro et al., 2014; Copersino et al., 2009; Grohman & Fals-Stewart, 2004), especially from cannabis (e.g. Meier et al., 2012).

In order to overcome some critical issues concerning the structure of sequences that were pointed out during the critical analysis of the relevant literature, the WMT was equipped with new items, which was created using one-digit natural numbers, by controlling for the internal structure of the sequences and so to prevent the presence of ordered digit chunks and to avoid chunks constituted by contiguous even (or odd) numbers. Moreover, in order to increase the complexity and, therefore, the discriminating potential of the test, the WMT requires the examinee to mentally manipulate the information stored in the temporary buffers (i.e. before being produced, the sequence of numbers must be rearranged in descending order), thus increasing the cognitive workload and allowing to evaluate the efficiency of working memory during a challenging task.

3.6.3 Focused Attention Test

Among other executive deficits, the reduction of the ability to orient attention toward specific stimuli, to keep attention resources consistently on a continuous task, and maintain the focus while inhibiting distracters is commonly reported as a side-effect of substance use and addiction disorders (Fernández-Serrano et al., 2011; Gould, 2010). The ability to focus attention on a target task or stimulus for any period of time, thus making it possible to quickly and efficiently detect relevant information and plan appropriate responses is commonly referred to as focused attention. Such complex process, which is often inefficient in both acute substance administration and chronic drug abuse (Gould, 2010), plays a critical role in supporting higher cognition, together with working memory. Its impairment might thus worsen the efficiency of executive control and, therefore, of self-regulation skills of people who developed addiction.

The Focused Attention Test (FAT) of the BFE-A aims at investigating the ability to identify and parse out relevant stimuli while ignoring distracters during a challenging task. Specifically, it taps on the integrity of focused attention processes with visual-spatial material. The FAT is based on a decoding task involving graphics and numerical materials. The examinee is presented with a grid of graphic symbols and an encryption key displaying the association between numbers and symbols, and has to convert each symbol in the grid based on the encryption key within a limited time.

The FAT was created starting from a conceptual and methodological review of the most-diffused neuropsychological tests used to evaluate the efficiency of focused attention and, in particular, the Symbol Digit Modalities Test (Smith, 1973). Such test, inspired by Wechsler Digit Symbol test (Wechsler, 1939) was thought to tap on several components of attention, as well as information processing and working memory skills (Shum et al., 1990).

Performance at the Symbol Digit Modalities Test was found to be deficient in various categories of neurology patients (Owens et al., 2018; Reekes et al., 2020; van Walsem et al., 2018; Wu et al., 2020) and to be worsened in presence of concurrent anxiety or depression (Goretti et al., 2014; Joosub et al., 2017). Impaired performance at the test was also found in individuals who developed addiction to alcohol or substances, such as heroin, cocaine, amphetamines, MDMA, and cannabis (Cuyàs et al., 2011; Harvey et al., 2007; Jovanovski et al., 2005; O'Malley et al., 1992). Yet, the score of the original version of the test is known to be influenced by age, education, gender, and cultural factors (Kennepohl et al., 2004), as well as practice (Roar et al., 2016; Strauss et al., 2006).

During the design of the FAT, we performed an accurate revision of the graphic symbols used in the new version of the test and of its internal structure. Specifically, we have selected and validated new symbols and excluded graphical signs that could have recalled mathematical operators that, when coupled with numerical digits, could have evoked implicit facilitating associations. Furthermore, the encryption key has been rearranged in order to avoid that graphically similar signs were contiguous to each other, again to avoid any facilitation effect due to implicit learning of the sequence.

3.6.4 Verbal Fluency Test

Fluency is one of the main facets of the complex construct of cognitive flexibility, which can be described as the ability to direct and re-orient cognitive resources between different operations, stimuli, or responses, and to flexibly adapt mental processes, mindset, and behaviour in relation to different tasks, schemas, or changes in the environment. Fluency itself is commonly mirrored by the extent and variety of information retrieved from memory within restricted search parameters (e.g. the amount of unique words pertaining to specific semantic categories). To be efficient, it requires executive control over cognitive processes, such as selective attention and inhibition, set shifting, and self-monitoring (Patterson, 2011). Cognitive flexibility proved to be affected by structural and functional alterations associated with addiction disorders (Antons et al., 2020; Brand et al., 2019; Fernández-Serrano et al., 2011; Koob & Volkow, 2016) and verbal fluency tasks are likely the most diffused methods for assessing such higher executive function in both neurology and psychiatric departments.

The Verbal Fluency Test (VFT) of the BFE-A aims at assessing the integrity of lexical access and selection mechanisms and the efficiency of self-monitoring and cognitive flexibility when dealing with verbal material. The administration procedure includes three 60-s trials. In each trial, the examinee is asked to produce as many words as possible that begin with a given letter (phonemic rule), excluding proper nouns and derived names with the same root.

The VFT was created starting from a conceptual and methodological revision of the most-diffused neuropsychological tests tapping on verbal fluency skills and, in particular, of the Controlled Verbal Fluency Task (Borkowski et al., 1967). Starting from the original version, numerous variants of the verbal fluency test have been developed based on different languages and letter sets (Kavé, 2005; Kosmidis et al., 2004; e.g. Novelli et al., 1986; Pena-Casanova et al., 2009; Raoux et al., 2010). Such tests proved to be valid and sensitive in identifying deficits of cognitive flexibility and impairment of verbal EF in the presence of frontal lesions or dysfunctions (Alvarez & Emory, 2006; Davidson et al., 2008; Henry & Crawford, 2004; Metternich et al., 2014), as well as neurodegenerative disorders, mild cognitive impairment, neurodevelopmental disorders, and depressive syndromes (Andreou & Trott, 2013; Libon et al., 2009; Obeso et al., 2012; Vaughan et al., 2018). Deficits of verbal fluency and cognitive flexibility have also been reported using phonemic fluency tests in individuals with alcohol and substance-related addiction (Kelley et al., 2005; McHale & Hunt, 2008; van Holst & Schilt, 2011). Yet, validation studies present a remarkable variability of core factors modulating examinees' performance (Ardila et al., 2000; Auriacombe et al., 2001; Loonstra et al., 2001).

Since the critical analysis of those evidence has mainly highlighted methodological shortcomings related to the stimulus letters, which were often chosen randomly, in designing the novel VFT, we have especially focused on the selection of such stimuli. In particular, in order to minimize potential biases caused by the originally random choice of the stimulus letters and to the consequent differences in the extension of the related vocabulary in different languages, in the present version of the phonemic verbal fluency test the stimulus letters have been selected following the following principles: presence of two consonants and one vowel; minimum number of lemmas starting with the stimulus letter in the reference vocabulary equal to 10.000 for the consonants or 25.000 for the vowel (based on the De Mauro's New Dictionary of the Italian Language); number of lemmas in the Italian vocabulary starting with the three newly selected stimulus letters equal to or greater than the number of lemmas associated with the original letters.

3.6.5 Non-verbal Fluency Test

While tests based on verbal fluency represent a sort of standard for the assessment of verbal EF in both neurology and psychiatry departments, non-verbal fluency tasks are remarkably less used in clinical practice, notwithstanding their clinical and diagnostic potential. Such tasks, indeed, allow to evaluate the integrity and efficiency of executive control on selective attention and inhibition, set shifting, and creativity not relying on verbal materials, thus overcoming potential biases or barriers due to cultural or linguistic differences.

The Non-verbal Fluency Test (NFT) of the BFE-A aims at testing the efficiency of cognitive flexibility mechanisms and the integrity of generative and creative processes based on visual-spatial patterns and graphical design. The test material consists of a series of 80 matrices constituted by 5 squared dots arranged according to a fixed schema (4 corners and a dot in the middle). According to the administration procedure, the examinee is asked to produce the greatest number of different graphic configurations by connecting, with straight lines, at least two of the five squared dots of the matrices, within a limited time.

The NFT was created starting from a conceptual and methodological revision of the few neuropsychological tests developed to evaluate cognitive flexibility and fluency via non-verbal material and, in particular, of the Five Point Test (Regard et al., 1982). Such neuropsychological test, which was initially created to offer a more structured and methodologically sound alternative to available visual-spatial fluency tests, had the merit to introduce different scores indicative of executive functioning, such as productivity, flexibility, use of strategic planning, as well as errors due to violations of the rules (Cattelani et al., 2011; Goebel et al., 2009). Several studies show that such test is sensitive to brain damage and, in particular, to structural and functional alterations of the frontal lobes (Goebel et al., 2013; Hansen et al., 2017; Lee et al., 1997; Tucha et al., 1999). Despite the clinical potential of the test and the relevance of cognitive flexibility deficits associated with addiction patterns, the use of non-verbal fluency tests for neurocognitive assessment of individuals with substance use disorder or behavioural addictions is poorly documented (Al-Zahrani & Elsayed, 2009).

The critical analysis of relevant literature, together with pilot testing of the BFE-A, resulted in a review of the test materials and in the updating of some scoring criteria. Namely, in the novel NFT, the matrices consist of a configuration of five squared dots, instead of round points, in order to optimize the figure-background contrast. In addition, the initial set of examples has been revised by adding a third configuration to clarify to the examinee that even the drawings formed by separate lines (for example, two parallel lines) are valid for the purposes of the test. Finally, in the NFT, the use of strategies in producing graphic configurations is of remarkable interest and is considered a peculiarly critical factor in evaluating the efficiency of high-order EF. For this reason, the defining criteria for identifying strategies in answers to the test have been expanded, including the use of rotation rules (serial reproduction of the same graphic configuration but rotated around its central point), the use of enumeration rules (serial reproduction of similar graphic configurations, but created by addition or subtraction of traits), and the use of semantic-conceptual rules (for example, the sequential reproduction of the letters of the alphabet or of graphic patterns representing numerical digits).

3.6.6 Modified Stroop Task for Addiction

Further components of EF that proved to be critically impaired in people presenting substance-related or behavioural addiction are attention regulation and interference inhibition (Antons et al., 2020; Brand et al., 2019; Fernández-Serrano et al., 2011; Koob & Volkow, 2016). In particular, reduced executive control over endogenous vs. exogenous orienting of attention and inhibitory mechanisms aimed at lowering the subjective relevance of interfering stimuli might contribute to the severity of self-regulation deficits in addiction. And again, ineffective control over the distribution of the attention focus and available cognitive resources, especially when cognitive reserve is fading, may make it more difficult to refrain from automatic dysfunctional behaviours.

The Modified Stroop Task for Addiction (MSTA) of the BFE-A is a computerized neurocognitive task devised to investigate the integrity of those attention regulation processes and of mechanisms allowing for the control of interference due to semantic incongruence or salience of addiction-related stimuli. The task uses verbal material and quantifies the outcome in terms of accuracy, omitted responses, and response times. In the MSTA, the examinee has to respond to quickly-presented verbal stimuli by indicating the colour in which the stimulus words are written (four possible responses: red, green, blue, and yellow). The task includes both the classic contrast between congruent colour-word stimuli (e.g. the word "yellow" presented in yellow) and incongruent colour-word stimuli (e.g. the word "red" presented in blue), and a further contrast between neutral words (e.g. "canoe") and words associated with contexts and situations of substance abuse and dependence (e.g. "drunk"). Four alternative though comparable versions of the MSTA were created, focused on specific addiction pictures and different primary substances of abuse: stimulants, opioids/sedatives/hypnotics, alcohol, and cannabis/THC.

The MSTA was created starting from a conceptual and methodological revision of experimental procedures based on the Stroop effect and used as neuropsychological assessment tools for attention and emotional regulation deficits and executive control. The Stroop task was originally developed as a tool to quantify the processing speed of complex information and the cognitive cost of interference. Subsequently, a growing interest in the impact of emotion on cognition and inhibitory control mechanisms provided the background for the development of the Emotional Stroop Test (Williams et al., 1996), an adaptation of the traditional Stroop task for the measurement of interference caused by the emotional salience of a stimulus.

Specific versions of the emotional Stroop test have been used for the assessment of interference control deficits in psychiatric patients (Rao et al., 2010; Wingenfeld et al., 2011), and of attentional-emotional bias in people with alcohol addiction (Adams et al., 2012) or substance-related addiction, such as cocaine (Kennedy et al., 2014), heroin (Yang et al., 2015), and nicotine (Mogg & Bradley, 2002). Yet, studies aimed at validating specific Stroop tests for addiction are still scant (Cane et al., 2009; Cox et al., 2006; Gardini et al., 2009). Furthermore, the reliability of those versions of the Stroop task, while being higher than that of other tasks used to investigate addiction-related attentional bias (Ataya et al., 2012), has been questioned. The design and development of the four versions of the novel MSTA task were, then, guided by the critical analysis of relevant literature concerning the paper-pencil and computerized versions of the Stroop test and, in particular, of its versions dedicated to the investigation of the interference effect due to emotional salience of the stimuli.

3.6.7 Modified Go/No-Go Task for Addiction

A complementary aspect of previously-noted higher executive impairments in addiction is represented by the alteration of prefrontal inhibitory control mechanisms, which plays a crucial role in modulating motivational incentives to maintain goal-directed behaviour and flexibility of stimulus–response associations (Antons et al., 2020; Brand et al., 2019; Fernández-Serrano et al., 2011; Koob & Volkow, 2016). Such mechanisms allow to suppress prepotent responses and to minimize the influence of irrelevant actions, feelings, and thoughts, thus enabling behavioural accommodation to changing goals, contexts, and contingencies. Relevant for addiction disorders, it has been recently proposed that the efficacy of general inhibitory control moderate affective, cognitive, and behavioural responses to exogenous or endogenous triggers, as well as the drive toward engaging in specific addictive behaviours (Hahn et al., 2017). Inhibitory control manifests through response selection or response stopping, and such processes lie at the core of the most diffused tasks devised to investigate and quantify the ability to suppress prepotent—though useless, irrelevant, or dysfunctional—thoughts or behaviours, such as the stop-signal task and the go/no-go task.

The Modified Go/No-go Task for Addiction (MGTA) of the BFE-A is a computerized neurocognitive task specifically devised to assess executive control and response inhibition in addiction. The task investigates the attentional bias for salient stimuli associated with addiction-related contexts or experiences, quantifying its impact (as mirrored, for example, by an increase in false alarms or by a modulation of response times) on behavioural inhibition mechanisms. To quantify such impact, the task allows for collecting different behavioural performance measures, including accuracy, number of omissions, false alarms, and response times.

In the MGTA, the examinee is asked to respond as quickly as possible to a given stimulus (Go stimulus, for example the letter “M”) by pressing a button while withholding his/her response when another stimulus (No-go stimulus, for example the letter "W") is presented on the screen. The associations between stimulus and response (or non-response) are defined at the beginning of the task. The task was devised to counterbalance such associations within the subjects to account for any perceptual bias. Specific to the MGTA, the task also involves the systematic manipulation of the background on which the Go and No-go stimuli are presented. The background can recall neutral semantic contexts (e.g. physical activity or environments/scenes of daily life) or be semantically associated with addiction-related contexts, tools, substances, or experiences. As for the MSTA, the MGTA includes four different though comparable sets of addiction-related backgrounds, associated with different primary substances of abuse: stimulants, opioids/sedatives/hypnotics, alcohol, and cannabis/THC.

The MGTA was created starting from a conceptual and methodological revision of the available literature on the use of the Go/No-go paradigm for the evaluation of cognitive control skills and of the efficiency of inhibitory mechanisms, which was primarily based on experimental evidence. Since its first definition, the Go/No-go task took the form of an experimental paradigm used to study attention and inhibitory control mechanisms and their neurophysiological correlates (Donders, 1969; Huster et al., 2013). Factors such as the relative frequency of Go and No-go stimuli, the duration of the trial, or the inter-stimulus interval affect the level of inhibitory control required by the task and, then, the interpretation of performance measures (Leblanc-Sirois et al., 2018; Wessel, 2018; Young et al., 2018). The Go/No-go paradigm was also used to investigate whether the pathological condition of addiction induces attentional bias in favour of the substance of abuse and inhibitory control deficits (Wiers et al., 2013). In particular, the majority of studies focused on higher cognitive processes and cognitive control skills in cohorts of individuals who developed addiction to alcohol (Campanella et al., 2017; Noël et al., 2007; Pennington et al., 2019; Petit et al., 2014), using words or images associated with alcohol consumption as stimuli or as contextual frames (Campanella et al., 2017; Pennington et al., 2019). More scant are the studies using the paradigm with reference to other drugs of abuse, such as nicotine and heroin (Liang et al., 2014; Scholten et al., 2019). In designing and implementing the MGTA, we capitalized on the critical analysis of relevant literature concerning the computerized versions of the Go/No-go task and, specifically, of its modified version for the evaluation of inhibitory control and attention bias induced by salient stimuli associated with the use of substances or addiction-related experiences.

3.7 Conclusions

The above-presented empirical evidence—together with previously reported models, data, and remarks concerning the extent and core features of executive deficits that systematically pair with substance-related and behavioural addiction disorders—suggest that the BFE-A might represent a valuable alternative to aspecific cognitive screening tools that are actually used in clinical settings. Furthermore, taking into account the standards for cognitive assessment that are implemented by average drug assistance/treatment services, the novel battery provides an answer to the clinical need for informative and reliable neuropsychological assessment tools, as well as to the practical need for quick and usable measures.

Validation studies and data from normative samples support the diagnostic value of the battery, yet a few open questions and potential future developments have to be acknowledged. Firstly, conclusive remarks on the value of the BFE-A for clinical practice would benefit from further testing with different clinical cohorts, including representative samples of patients who developed behavioural addictions (e.g. pathological gambling, gaming disorder, problematic Internet or social-network use, compulsive buying, and others). In addition, the tool should be subjected to test-retest studies, so to better investigate the reliability of test outcomes over time. And again, future studies should focus on concurrent and divergent validity by testing the correlation between the battery outcomes and independent psychometric, behavioural, and cognitive measures, or by complementing current findings with paired neurofunctional data (e.g. EEG markers of information-processing, executive control, attention regulation, and cognitive effort; hemodynamic markers of functional neural activations or inefficient neural processing).

Furthermore, future investigations could also better explore the capability of the screening battery to discriminate between major executive deficits and subclinical dysfunctions, and test its sensitivity in detecting different degrees of cognitive impairment associated with different addiction pictures. Such goals might be pursued by devising and implementing additional subtests or complementary assessment tools to specifically explore, as an example, the integrity and efficiency of decision-making processes, which lie outside of the functions currently targeted by the BFE-A.

Again, by pushing forward the boundaries of assessment settings and by embracing a more ecological perspective on cognitive assessment, future versions of the screening battery might be completely converted into an easy-to-use (for example, totally digital) format that could be used even outside of care and assistance facilities (e.g. home-based testing) or might be improved to assess the efficiency of investigated functions in realistic and interactive contexts.

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