Rehabilitation of Executive Functions in Users of Addictive Substances. Study Protocol

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BACKGROUND: Substance use increases the risk of damage to executive and cognitive functions. Manifested by a range of clinical symptoms, such impairments may affect people's coping with everyday activities and their abilities to establish and maintain good social links. Substance users are an at-risk population in this respect. **AIMS:** Two cognitive rehabilitation interventions will be experimentally implemented into clinical practice and their effectiveness compared. The levels of impairment of the patients' executive and cognitive functioning will be investigated. **METHODS:** The first rehabilitation modality under study is the Neurop3 computer program. The second, a pen-and-paper-based cognitive rehabilitation programme, will be devised by the authors. Initially, each patient will be screened using a test battery. If a deficit is identified, the patient will be offered the opportunity to participate in a rehabilitation programme. The components of the screening battery and the subsequent rehabilitation programmes will be chosen in such a way as to ensure that their administration falls within the competencies of an addiction specialist. The patients will be randomised into three groups according to the cognitive rehabilitation approach applied: 30 patients will be exposed to computer-assisted cognitive rehabilitation, 30 patients will undergo pen-and-paper rehabilitation, and 30 patients will constitute a control group. The study sample will comprise patients from the outpatient addiction treatment clinic at the Department of Addictology of the General University Hospital. The duration of all three programmes will be eight weeks. **DISCUSSION:** The research study explores the potential of rehabilitation programmes and explains the importance of cognitive rehabilitation for addiction patients. The results suggest that two cognitive rehabilitation programmes, in particular, may be promising in clinical practice. The research study is designed in such a way as to make it possible for an addiction specialist to administer it.

Keywords | Executive Functions – Cognitive Functions – Dysexecutive Deficit – Cognitive Rehabilitation – Addictology

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1 BACKGROUND

The literature defines executive functions in various terms. No single definition of this concept has been determined yet and different authors vary in their interpretations. Several definitions and approaches to the understanding of executive functions are provided below.

Kulišťák (2017) defined executive functions as a set of cognitive domains, including working memory, planning, cognitive inhibition, organisation, fluency, judgement, and estimation. The individual functions are interlinked and work as a whole rather than in isolation. Damage to one function may affect the correct operation of another. In addition, Kulišťák (2017) divides the domains into subdomains, which include abstract reasoning, creativity, hypothesising, self-control, fluency, behaviour regulation, and anticipation. Huizinga et al. (2018) refer to executive function as an umbrella term for a variety of cognitive processes, including thoughts, emotions, goal-directed behaviour, cognitive flexibility, and quick and flexible adaptation to new situations.

Executive functions constitute a compound of mental functions which are necessary for the correct operation of a range of cognitive processes. They are involved in correct reasoning, planning, problem solving, and managing day-to-day tasks, working memory, and attention. In addition, executive functions work to inhibit automatic and learnt responses to stimuli. In other words, these functions can inhibit an individual's deep-rooted behaviour and assist in the strategic focus of attention. The functions are directly influenced by the emotional state of an individual. Executive functions tend to deteriorate under stress. Instances of apathy and boredom have the same effect (Blair, 2017).

Executive functions are higher-order cognitive functions which have a direct effect on the manifestation of human behaviour. This group of functions includes planning ability, cognitive flexibility, self-regulation, inhibition, and behavioural control (Clark & Goodwin, 2008). With regard to the dysregulation of executive functions, the literature refers to the dysexecutive syndrome, which is defined as a group of clinical symptoms which typically occur as a result of evident damage to executive functions. A list of the 20 most common clinical symptoms of this syndrome was provided by Gurd et al. (2010). They include aggression, reduced efficiency, loss of interest in social rules, disruption of abstract thinking, agitation, and social disinhibition. According to Swann et al. (2009), executive impairments are manifested in reduced problem-solving abilities, increased impulsivity, sustained poor task performance, and the inability to plan.

The regular use of psychotropic substances causes damage to people's executive functioning. Such impairments are typically associated with decision-making abilities, cognitive fluency, memory, the ability to process new information and the speed at which this takes place, the ability to learn new things, and verbal skills (Zhao et al., 2021). In the Czech Republic an estimated 44,900 high-risk users of illegal substances were reported as of 2022. The estimates indicate that a total of 34,700 individuals engaged in high-risk use of methamphetamine and 10–11 thousand were high-risk opioid users. An estimated 1.5–1.7 million Czech residents engaged in risky alcohol use. No less than 250,000 adults were estimated to be at-risk cannabis users. An estimated 1.5 million individuals engaged in the problematic use of psychoactive medication. 29% of adolescents aged 15–16 had tried at least one illicit substance at some point in their lives (Chomynová et al., 2022). Spinola et al. (2017) reported pronounced deficits in executive functioning among chronic drinkers. Such impairments may lead to the development of risk-taking behaviour and self-regulation issues.

Describing a sample of stimulant-dependent patients, Schulte et al. (2014) found that the most common impairments among this group of patients were associated with working memory, attention, inhibition, verbal fluency, fine motor skills, abstract thinking, and emotional regulation. However, certain improvements in executive and cognitive functioning could be observed no later than after several weeks of full abstinence.

Charvát and Švachová (2017) published a research study exploring the impact of alcohol use on the condition of executive and cognitive functions in which they noted that it was useful to be aware of any deficits to that effect in the treatment process. Another study investigating the relationship between alcohol and the condition of executive functions was conducted by Fama et al. (2004). Specifically targeted at male participants in the study, their research was designed as a correlational analysis. It involved two groups of men (from the non-clinical population and alcoholics in treatment). The results showed that the males in treatment for alcohol dependency displayed marked deficits in executive functioning.

In the event that an executive deficit develops, interventions of choice vary across the professional community. The majority of authors, nevertheless, rely on cognitive rehabilitation, although approaches to cognitive rehabilitation and the methods used for it may vary. Kulišťák (2017) promotes the application of what is referred to as cognitive remediation, which involves a therapy aimed at enhancing cognitive processes and is based on individual behavioural training. Feuerstein (2014) proposes Feuerstein Instrumental Enrichment (FIE), a method designed to enhance the cognitive strategies of an individual. Others, including SAMCO (2015), argue that the most progressive approaches involve interventions based on digital technologies. The German company SAMCO offers Neurop-3, a computer program developed as a means of neuropsychological rehabilitation and diagnosis. The use of information technology for cognitive rehabilitation is also advocated by Preiss and Kučerová (2006) in their account of a model referred to as Cognitive Enhancement Therapy (CET). Widely used around the world, the programme employs computer-assisted rehabilitation to facilitate education, social cognition training, and training in selected cognitive domains. Dobson (2010), on the other hand, points out the potential of a method known as Problem Solving Therapy (PST). This approach is distinct from the alternative models in that its interventions may be administered live, both individually and in group settings.

2 AIMS

The main objective of the study is to compare two selected cognitive rehabilitation programmes in terms of their effectiveness and patient outcomes. The programmes will be incorporated into frontline work with selected addiction patients. The Neurop 3 computer-assisted intervention and a pen-and-paper-based rehabilitation programme developed by the authors will be used for the purposes of the study. A control group will also be compiled to meet the objectives of this research project. The study seeks to demonstrate the competences of an addiction specialist to intervene in this area from an addiction-specific perspective. Through this research investigation, we would like to bring a new area to the field of addictology that addiction specialists can address. The results of this study may serve as inspiration or guidance to other addiction specialists who may need to intervene in the same or similar way in their clinical work.

The following research questions were identified as part of the research study:

1) Can training using the selected methodology improve executive and cognitive performance in selected addiction patients with proven cognitive deficits?

2) How will the objective effectiveness of the selected rehabilitation programs differ?

3) Will completion of cognitive training lead to an increase in psychological well-being, quality of life of patients and improvement in subjective assessment of cognitive performance?

3 HYPOTHESES

H01: The executive and cognitive performance of patients enrolled in a computer-based rehabilitation program (Neurop 3 program) improves after completing the entire program.

H02: The executive and cognitive performance of patients enrolled in a pencil-paper rehabilitation programme will improve after completing the entire programme.

H03: Executive and cognitive performance after completing the rehabilitation programs will differ between patients assigned to the intervention groups and those in the control group.

H04: Life satisfaction (measured by the Life Satisfaction Questionnaire) of patients assigned to the intervention groups will differ after completing rehabilitation.

H05: Subjective self-assessment of cognitive performance of patients assigned to intervention groups will differ before and after completing rehabilitation programs.

4 STUDY SAMPLE

All data will be collected at the outpatient addiction clinic operated by the Department of Addictology of the General University Hospital in Prague. In order to be included in the study, each patient will have to meet the eligibility criteria as described below. The minimum age limit has been set to 18 years. There is no maximum age limit. No account will be taken of the patients' educational attainment in recruiting them for the study sample. Gender representation of men and women will be the same in each group.

Inclusion criteria:

1) minimum 18 years of age (completed)

2) total willingness to participate

3) demonstrated deficits in executive functions

4) formally diagnosed with at least one of the predefined ICD-11 diagnoses (F10.1, F10.2, F11.1, F11.2, F12.1, F12.2, F14.1., F14.2., F15.1, F15.2, F16.1, F16.2, F19.1, F19.2)

5) at least a month of abstinence prior to rehabilitation

6) at least a month of abstinence prior to screening

Exclusion criteria for admission to the study are the presence of one or more of the following diagnoses: epilepsy, brain surgery or trauma, seizures, neurological disorders, or psychotic disorders.

The study sample will comprise a total of 90 patients of the outpatient addiction clinic operated by the Department of Addictology of the General University Hospital. In this respect, we build on a meta-analysis by Jean et al. (2010), according to whom the majority of research studies of cognitive rehabilitation work with experimental groups of up to 30 individuals. Our study sample will consist of patients who are active users of the (both individual and group) therapeutic services provided by the outpatient facility.

The study participants will be divided into three basic groups. Quota sampling will be used to assign the patients to different study groups on the basis of the following predetermined quota variables: gender, age category, education, and type of addiction-specific diagnosis. The researchers aspire for both rehabilitation groups under consideration to be mutually proportionate in size. Patients will be divided into two intervention groups by randomization. In practice. We will roll the dice for the patients. If an odd number is rolled, they will be assigned to the computer rehabilitation group. If an even number is rolled, they will be assigned to the pencil-paper rehabilitation program.

The first patient group will be exposed to the Neurop 3 rehabilitation program. This group of 30 patients will undergo computer-assisted rehabilitation only. The second group, also comprising 30 patients, will experience rehabilitation without the use of electronic devices. The latter model, to be developed

by the authors, will be based on paper worksheets and consist of exercise blocks targeted at various cognitive skills. The third group will be a control group compiled from 30 patients of the outpatient addiction clinic. The control group will be subjected to the initial screening and subsequently tested at a three-month follow-up, as will the two intervention groups. The control group will have a passive status; it will not participate in the rehabilitation programmes. The patients in this group will function in their lives with no intervention. The significance of the engagement of the control group lies primarily in controlling for the test-retest effect. If there is anybody from the control group interested in being included in the rehabilitation process, they will be offered such an option after the completion of the observation and the follow-up assessment. However, such a person's outcomes will not be included in the research findings because of possible bias.

We will measure patients' abstinence through toxicological testing. The toxicological testing will be conducted using the patients' urine. Through this examination, we will be able to confirm or rule out the use of various addictive substances. Patients who violate abstinence during the rehabilitation program will be excluded from the research study.

5 METHODS

The design of the research study as a whole is adapted to reflect the requirements for a rehabilitation programme addressing the needs of people experiencing substance use-related deficits in their executive functions. A test battery and interviews with the study participants will be used to assess the efficacy, effectiveness, and general benefits of the rehabilitation programme.

All the study data will be generated by means of a test battery described in greater detail below.

In their choice of the test battery, the authors build on their previous research activities. The test battery described below is a modified version of the test battery used in an original research study, Screening for Damage to Executive Functions in Alcohol Users: an Addiction Professional Perspective (Votavová, 2020). Two additional screening instruments – Controlled Oral Word Association Test (COWAT) and Five Point Test – were added and the Barthel Index and the Instrumental Activity of Daily Living were excluded from the battery.

Test battery:

1. Anamnestic record
2. Beck Anxiety Inventory
3. Beck Depression Inventory
4. Addenbrooke Cognitive Test
5. Frontal Assessment Battery
6. Trail Making Test (Part A, Part B)
7. Dysexecutive Questionnaire
8. Life Satisfaction Questionnaire
9. Five Point Test
10. Controlled Oral Word Association Test

The above test battery will be administered to each patient prior to their rehabilitation and then again after the due completion of the rehabilitation programme, not later than within three months following the intervention. All patients will be post-tested at the same time. Comparisons will be made of the test scores achieved. The post-testing will be used as an evaluation tool.

The test battery is intentionally designed in such a way as to make it possible for an addiction specialist to use it in clinical practice. The individual components of the battery can be administered by addiction specialist, psychologists, psychiatrists, occupational therapists, and other professionals. The test battery refers to another area of care which addiction specialist may encounter in their clinical practice. They may use the test battery to screen the patients for relevant deficits and intervene accordingly where applicable.

The patients who test positive for deficits in their executive functions will be offered the opportunity to participate in a rehabilitation programme. Two types of rehabilitation programmes were selected for the purposes of the present study. They are described in the following section.

5.1 Interventions

The first programme that was chosen is NEUROP 3. It involves a computer-assisted intervention developed by the SAMCO company. The first version of the software was created in 1993. Since then, it has undergone three modifications. The latest version is NEUROP 3. The program was created by a neuropsychologist, Dr. Laco Gaál, for the purposes of the cognitive rehabilitation of patients with demonstrated deficits in this area. While originally in the German language, at present it can also be purchased in Czech, English, and Slovak. NEUROP 3 comprises a total of 57 modules, or subprograms, addressing specific executive and cognitive functions. The program is flexible enough to make it possible for a practitioner to devise their own modules or exercises to reflect patients' individual needs. TOUCH-NEUROP, a version of the software intended specifically for tablets and other touch-screen devices, is also available. Another version of the program, HNP/THNP NEUROP, enables patients to rehabilitate in their home settings using their personal devices (Pulkrabková, 2017).

The second programme under study will be developed by the authors for the purposes of the research project and will consist purely of a pen-and-paper-based intervention. It will consist of 16 blocks. Twice a week, the patients will attend 60-minute sessions during which predetermined rehabilitation blocks will be administered to them, each of them consisting of various cognitive exercises. The content of the blocks will be the same for all the patients. The entire programme will be scheduled to span a period of eight weeks. Between the sessions, the patients will be assigned homework tasks which will help them practise their executive and cognitive functioning in their home settings too. The exercises will include anagrams, riddles, word formation, solving logical tasks, distinguishing shapes, creating a story, drafting an advertisement, solving sudoku, searching for information in a text, completion tasks, memory games, and word searches.

5.2 Ethical aspects

Ethical standards will be adhered to throughout the research study. Participation in the study must be fully voluntary and the participants must be assured of absolute anonymity at the very beginning of the recruitment process. Each patient will be able to choose whether they are interested in participating in the study. In addition, each patient will be thoroughly briefed about all the particulars of the research. All patients must be informed that the study data will be handled securely in compliance with the Czech legislation governing the protection of personal data and the Code of Ethics applicable to the field of addictology.

Before being engaged in the study, each patient will be given an informed consent form. It will provide general information about the purpose of our meeting and the contact details of the investigator and the senior expert supervisor of the research project. The study as a whole was approved by the General University Hospital Ethics Committee in January 2022. In 2023 we will submit an updated version of the study to the Ethics Committee and apply for reapproval. Each patient will be advised of their right to withdraw from the study at any time.

5.3 Data analysis and statistical processing

Data analysis will be carried out using two computer programs, specifically Microsoft Excel from the Microsoft Office package and the IBM SPSS statistical software.

Each patient in the study sample will be subjected to two rounds of testing using the test battery specified above. Each test or questionnaire will be administered and evaluated according to the instructions provided by the authors. A variable to look for during the testing will be raw scores for the individual items, such as time and number of points. The data will be paired for all three groups (two experimental and one control group): it will include both pre- and post-test values. Each questionnaire or test will come with a record sheet into which all information and data will be entered throughout the testing. An individual folder will be created for each patient, in which record sheets will be kept. The raw scores generated by the tests will have to be converted using a preset formula. This is a statistical method used to process data called the percentile method and the SD-score method. This method is used to work with quantitative biomedical data and shows us the degree of deviation from the norm. The percentile method consists of comparing the results of the individual under investigation with data obtained from a control and representative group. This method produces a percentile chart on which the results of the subject under investigation are recorded. The formula below is used in this statistical method. The result is expressed in terms of standard deviations, which show how much the value of the individual deviates from the mean value in the population. For the correct application of this method, it is necessary that the parameter under study has a normal, or Gaussian, distribution (Šmahel, 2002). The converted result will be compared with the normal distribution curve. The preset evaluation scales are explained below:

- a value of standard deviation ranging from -1 to +1 = norm
- a value of standard deviation ranging from -1 to -2 = below average
- a value of standard deviation greater than -2 = extremely below average
- a value of standard deviation ranging from +1 to +2 = above average
- a value of standard deviation greater than +2 = extremely above average

The formula used for the conversion:

$$\frac{\text{test score - average value for the given age (and educational attainment)}}{\text{Standard Deviation (SD)}}$$

The effectiveness of the programmes in the two experimental groups will be measured using a non-parametric method, the Mann-Whitney test. The training outcomes will be measured using the Wilcoxon pair test. Measurements will be carried out in all three groups, i.e. the two experimental groups and the control one.

It was mentioned earlier in this paper how important it is that our executive and cognitive functions work properly without any impairments. Addictology clinical practice and a literature search indicate that impairments of executive functions and their subsequent rehabilitation are not common components of addiction care. The present research study therefore draws attention to a new area of care which, if employed in clinical work with patients to a greater degree, may provide another intriguing perspective on the profession of an addiction specialist. As part of the study, a detailed description will be provided of how to screen a patient for any suspected impairments of their executive and cognitive functions. This description may inspire other practitioners working in the field who may want to incorporate this screening method into their day-to-day clinical practice. Additionally, the two cognitive rehabilitation programmes will be compared and their effectiveness assessed. Again, addiction specialist or other practitioners may use this as inspiration and adopt the design for the benefit of their patients. In the Czech setting, research into this topic has been limited thus far. The authors of this paper therefore believe that they are highlighting a phenomenon which is given far less attention that it deserves.

6 DISCUSSION

In nearly all patients dealing with substance addiction, we can observe impairment in the areas of executive and cognitive functions (Mende, 2019; Motazedian et al., 2021; Meier et al., 2012). This impairment tends to be heterogeneous with a wide range of clinical manifestations. The quality of life also deteriorates for these patients as a result of these impairments. They face challenges in their jobs, schools, social circles, activities, and daily responsibilities. Interpersonal relationships are also often affected (Zhao et al., 2021). Basterfield et al. (2019) additionally mention a loss or decrease in motivation. Patients frequently lose their ability to work with motivation effectively and efficiently.

If we find that patients in our care have a cognitive deficit. We can begin cognitive rehabilitation. Until recently, cognitive rehabilitation in clinical practice was primarily used by occupational therapists and psychologists. The present study brings a new perspective on the subject matter by promoting an inspiring additional interventional approach involving screening for deficits in executive functions and their rehabilitation from an addiction specialist's perspective. According to Malia & Brannagan, (2010) the rehabilitation process takes a different amount of time for each patient. The length can range from a few months to several years. Cognitive rehabilitation is a long-term process that has several phases. Each phase requires different care and approach from the professional. Nowadays, there are a large number of rehabilitation programs that professionals can use in their clinical practices. In our research investigation we have chosen the computer program Neurop 3 and a pencil paper-based rehabilitation program.

Neurop 3 was chosen for its comprehensiveness. The exercises included in the program can cover dozens of cognitive domains that may be impaired in patients. We view Neurop 3 as a very comprehensive program focusing on cognitive rehabilitation. The program is tailored to the individual needs of each patient. It adapts the difficulty of the exercises according to the cognitive performance of the individual. Gil-Pagés et al. (2022) state that computerized cognitive rehabilitation programs are particularly valuable because they give patients immediate feedback. This leads to an increase in patients' self-esteem, self-confidence and self-efficacy. The variety of tasks administered may also be attractive. The pencil-paper programme is not exactly selected at the moment. For this reason, we do not give a specific form in this article. Paper-and-pencil-based programs have a significant tradition. Georgopoulou et al. (2023) compared the effectiveness of computer-based and paper-based cognitive rehabilitation programs. The paper-and-pencil program was found to be more effective, especially in improving executive functions, overall cognitive functions, memory, attention, language abilities, and more. This viewpoint is supported by other research studies as well (Nousia et al., 2022; Groot et al., 2016; Man et al., 2011).

Some research studies have shown that it is very effective to include education in the rehabilitation process. This can relate to a variety of areas such as relaxation, movement, diet, sleep hygiene, prevention of damage to cognitive functions, etc. (Arnemann et al., 2015; Asher et al. 2019; Franck, 2021).

One of the main reasons why we perceive cognitive rehabilitation as important is that without intervention, existing deficits will continue to persist or worsen. Cognitive deficits in an individual can lead to problems within the family and in interpersonal relationships. Impairments in executive function and cognition can hinder a person's return to school or employment, and may impede the quality of that return (Malia & Brannagan, 2010).

We recognize several limitations in our study. The first weakness of our research sample could be the wide age range. Under ideal conditions, we would have preferred a more homogeneous age group in our research sample. Older patients were not disadvantaged by this aspect. Cognitive performance naturally declines with advancing age, but this decline does not occur uniformly across the population. It depends on various factors influenced by lifestyle or genetics. Different cognitive and executive domains exhibit varying sensitivity to this decline. Functions that tend to remain unimpaired even in older age typically include the processing speed of new information, episodic memory, and abstract thinking (Atalay et al., 2019). The research population will be very diverse. Patients will differ from each other in a number of factors (age, gender, educational attainment, occupational background). All of these factors may in turn influence cognition and certain patients may be at a significant advantage. For example, a disadvantage of the screening tests we use, such as the ACE-R test, is that the patient's scoring may in practice be influenced by the patient's education and language ability. Patients with higher educational attainment may be at a distinct advantage and may score higher (Shi et al., 2018). Another limitation of our work could be the concerns regarding potential relapses among the participating patients. In order for patients to be involved in the rehabilitation process, they must maintain strict abstinence throughout. If they violate abstinence, they will be excluded from the study. Here, there are concerns about the extent to which patients will be able to adhere to abstinence.

With this research study, we aim to highlight the importance of executive functions and their role in our daily lives. Our study provides inspiration for further research projects that could focus on this issue. There are many different approaches and possibilities to investigate and develop this phenomenon, and our work can serve as a starting point for further studies.

7 CONCLUSIONS

The core subject matter of the present study is executive functions. Despite some evidence demonstrating a relationship between substance use and the condition of executive functions, this topic is not frequently associated with the population of addiction patients.

This research study is based on the assumption that the prolonged and regular use of addictive substances increases the risk of damage to executive and cognitive functions. And if such damage occurs, proper interventions and cognitive rehabilitation, where applicable, are needed. Addictology is a field of study with multidisciplinarity as its typical feature. Therefore, addiction specialists' involvement in the cognitive rehabilitation of their patients appears self-evident. The present paper should serve as guidance for other addiction specialists who may be interested in cognitive rehabilitation and want to incorporate it into their everyday clinical practice. The information provided by this study should help other addiction specialists respond promptly and flexibly to any deficits that may be identified in their patients.

The findings will be used to describe effective and ineffective practices and factors of the programmes under study. The rehabilitation programmes should help patients in identifying their problems and gaining insight into their situation, as well as facilitating the improvement of their day-to-day functioning.

Finally, the entire process should highlight the specific nature of rehabilitation work with addiction patients.

Authors' contributions: The author AV designed the study and proposed the study design. The author AV designed the initial form of the article. The author AV conducted the literature review and prepared the summary of related work. The author LŠ participated in the preparation of the article. All authors contributed to the creation of the article and approved the final version of the manuscript.

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