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Original research article

Psychosocial sequelae following cardiac arrest

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ABSTRACT

Background: Cardiac arrest (CA) leads to cerebral hypoxia resulting in multifactorial brain injury. Cognitive impairment and a higher degree of depressive symptoms are the most frequently described mental health problems after CA. The aim of the present study is to characterize psychosocial sequelae of CA.

Methods: The study population included 113 subjects. 63 patients after CA were matched to 51 healthy controls according to demographic characteristics and premorbid intelligence level. Cognitive test (MoCA), inventories of depressive (BDI-II) and anxiety symptoms (STAI) and midlife crisis scale (MCS) were administrated to study participants.

Results: The analysis showed that CA patients have a decreased level of cognitive performance ($p = 0.016$) and a higher degree of state anxiety symptoms ($p = 0.023$). There was no significant difference between CA patients and control subjects in the degree of depressive ($p = 0.435$) and trait anxiety symptoms ($p = 0.542$). Ex-post facto analysis based on logistic regression indicated that the strongest predictors of being classified as having had a cardiac arrest was male gender and state anxiety (OR = 4.45 and .50). Discriminant function analysis showed that group prediction was sensitive to age, cognitive performance, and state anxiety ($\lambda = 0.81$, $p = 0.028$).

Conclusions: Our results show that CA has significant cognitive and neuropsychiatric sequelae. The integration of psychosocial care and neuropsychiatric treatment into the complex medical care of CA patients seems to be justified.

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Introduction

Resuscitated cardiac arrest (CA) and sudden cardiac death are fatal complications of cardiovascular disease [1]. In health care systems with well-functioning prehospital emergency care and hospital complex intensive care, including the standard use of target temperature management, the percentage of surviving patients has been increasing [2,3]. Frequently, it has become possible to reach a satisfactory neurological outcome, which enables survivors to return to a normal life [3,4]. Nevertheless, even in these patients, the quality of life and their psychosocial functioning have been shown to be decreased [3–7].

During CA, many pathological processes take place, the most serious of which is cerebral hypoxia [8]. Long-term psychosocial effects of the hypoxic-ischemic injury may be manifested as a cognitive deficit or higher levels of anxiety and depressive symptoms [9,10,34].

Regarding the tolerance of brain tissue toward hypoxia, the most sensitive are the white matter and the temporal neocortex [11]. Following their injury, a cognitive deficit of the vascular type is often observed [6,12]. This is manifested as a decrease in memory function and attention accompanied by disorders of certain executive functions, such as mental flexibility, set shifting and decreased the motor speed of upper limbs [12].

The extent of cerebral hypoxia sequelae can be derived from the behavioral performance of patients which is measured by a five-point scale Cerebral Performance Category (CPC) [13]. Previously published data indicate that while CA survival rate is 21%, 17% of CA patients achieve a favorable neurological outcome as classified by CPC stage 1–2 [14,15]. Both the survival and the neurological outcomes depend on initial rhythms, i.e. shockable (ventricular fibrillation/tachycardia) and non-shockable (asystole, pulseless electrical activity) [16]. CA patients with shockable rhythms demonstrate the higher resilience of neurological decline after CA and have more favorable prognosis [16,17].

Decreased quality of life in CA survivors has also been linked to the increased occurrence of anxiety and depression symptoms [5,18,33]. Their morphological basis is the hypoxic injury of the brain centers for behavioral control, i.e. the white matter of the left prefrontal lobe connected to the amygdala and the limbic system [8,9]. Anxiety and depressive symptoms are often described as a comorbidity of CA in connection with a poorer ability of cognitive functioning, especially in learning new information [19,20]. CA can also cause changes in the social functioning, mainly regarding the interactions between the patients and their close relatives [21–23]. These psychosocial changes are the result of a combination of the post-hypoxic brain injury and the reflection on patient's confrontation with death, which can cause experiences resembling those in midlife crisis [21,23]. Attention focus on the patient's health, restriction of social life and increased responsibility are the psychosocial sequelae of cardiac arrest, influencing both the patient himself and his close relatives [21].

In the present study, the main goal was to describe whether the cognitive performance and mood significantly impact the psychosocial functioning of CA survivors.

Methods

Study design

Between November 2012 and December 2014, 62 survivors of CA were recruited from three cardiac arrest centers, i.e. the Department of Cardiology, Institute for Clinical and Experimental Medicine in Prague, Second Department of Internal Medicine, Cardiovascular Medicine, General University Hospital in Prague and Tomas Bata Regional Hospital in Zlin (the patient sample, Table 1). A control sample consisted of 51 healthy individuals examined at the Department of Neurology, 1st Faculty of Medicine and General University Hospital in Prague (Table 1). The project was performed in a manner consistent with the Ethical Principles of Charles

Table 1 – Demographic and clinical characteristics of cardiac arrest (CA) and control sample (CS).

	CA patients ($N = 62$)	CS ($N = 51$)	Statistical test	p value
Gender (% male)	79	49	11.2[a]	0.001*
Age (years)	59.5 ± 14.3	55.1 ± 14.8	1284[b]	0.087
Education (years)	12.7 ± 3.1	13.0 ± 2.5	1736[b]	0.374
NART/CRT	110.3 ± 11.6	113.9 ± 10.1	1887[b]	0.078
Time since CA (months)	47.4 ± 31.9	–	–	–
CA duration (minutes)	20.7 ± 19.5	–	–	–
CA classification (% shockable rhythm)	96			

CA = cardiac arrest; CS = control sample; M = mean; SD = standard deviation; data presented as M ± SD or frequency (percentage); NART/CRT = National Adult Reading Test/Czech Reading Test (measure of premorbid intelligence level expressed as number of errors in the test transformed into IQ score based on regression equation from Wechsler Adult Intelligence Scale—Revised/WAIS-R); Time since CA (months) = time elapsed since CA till test administration in number of months; CA duration (minutes) = time since receiving the call to restoration of heart function in minutes; CA classification = percentage of CA patients with shockable rhythm.

[a] χ^2 test.

[b] Mann–Whitney U-test.

* $p \leq 0.05$.

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University in Prague and was reviewed and accepted by the institutional IRB.

Patients

Patients meeting the following requirements were enrolled into the clinical sample: survivors of out-of-hospital CA comatose and mechanically ventilated on admission to hospital, minimum of 2 months following CA, application of guidelines recommended CA treatment including target temperature management, hospital discharge in a stabilized and good neurological condition assessed by Cerebral Performance Categories (CPC 1–2) and able to follow an out-patient rehabilitation care [24–26].

The present study has the following exclusion criteria: Patients and subjects from control sample who in the health questionnaire indicated following diagnoses with possible influence on testing: ongoing treatment for psychiatric illness, dementia, history of stroke and (or) other neurological impairment or injury were not included in the study. To eliminate potential testing bias, the control sample was matched with the patient sample by demographic parameters (age, education, and premorbid intelligence prior to the CA event, see below). Any healthy subject who reached the cutoff of −1.5 SD below the normative means adjusted for age and education as based on the Czech normative data of Montreal Cognitive Assessment (MoCA) [27] was excluded from the control sample.

Test battery

A test battery consisting of two performance tests, i.e. MoCA for the evaluation of cognitive function and the National Adult Reading Test/Czech Reading Test (NART/CRT) for the evaluation of premorbid intelligence were administered to all participants [27,28]. NART/CRT is a widely accepted and commonly used method in clinical settings for estimating premorbid intelligence levels of Czech-speaking patients with cognitive impairment in neuropsychological research. Such tests are called hold tests as these abilities are thought to be spared, or "held" following neurological injury, such as following CA. The test comprises 50 written words in Czech which all have irregular spellings (e.g. "faux pas"), so as to test the participant's vocabulary rather than their ability to apply regular pronunciation rules.

In addition, the test battery included tests of personal characteristics: Strait-Trait Anxiety Inventory (STAI X-1 evaluating the level of current "state" anxiety, STAI X-2 determining the long-term "trait" anxiety) and Beck Depression Inventory (BDI-II) to assess the level of depressive symptoms [29–31]. Patients after CA were also tested by the Midlife Crisis Scale (MCS) [23].

For statistical analysis, the premorbid level of intelligence using the NART/CRT test was transformed to total IQ metric according to WAIS-R (Wechsler Adult Intelligence Scale-Revised) Czech version. The cognitive performance in the MoCA test was transformed from the raw score to scaled score (percentile) based on the Czech normative data study of the MoCA and similarly the level of the state and trait anxiety was assessed by STAI X-1, X-2 based on the normative data from the Czech population [27,31]. As results of the BDI-II and MCS have no normative standards, only the raw scores were used.

Statistical analysis

Statistical data analysis was performed using the IBM SPSS 20 and JASP 0.6.6. Based on the visual appearance of the Q-Q graphs and the Shapiro–Wilk test, the samples do not show a normal distribution. For this reason, the nonparametric Mann–Whitney *U*-test (MWU) for two independent samples was used to compare differences between the clinical and control samples. Furthermore, in the ex-post facto analysis the logistic regression was applied to assess the impact of a number of factors on the likelihood that respondents are patients with CA. Afterwards, in the same direction of ex-post facto analysis, we performed discriminant function analysis to predict a categorical dependent variable (CA) by one or more independent variables (predictor variables). The significance level was set at $\alpha < 0.05$.

Results

Demographic data

A total of 113 subjects (62 CA survivors and 51 healthy controls) were enrolled. Regarding the demographic characteristics of the two samples, no statistically significant differences were found, corresponding to the predefined selection of control subjects (Table 1). The characteristics of the patient sample in terms of time since CA event and CA duration are depicted in Table 1, psychosocial characteristics in Table 2.

Analysis of the test battery results

The analysis of differences between the patient sample and healthy controls revealed a statistically significant difference in cognitive performance (MWU = 1996; $p = 0.016$) and in state

Table 2 – Between group differences in cognitive and neuropsychiatric measures.

	CA patients (N = 63)	CS (N = 51)	Statistical test	*p* value
MoCA (percentile)	40	55	1996[a]	0.016*
BDI-II (median)	8	7	1422[a]	0.435
STAI X1 (median)	5	4	501[a]	0.023*
STAI X2 (median)	4	3	668[a]	0.542

CA = cardiac arrest; CS = control sample; MoCA = Montreal Cognitive Assessment (raw scores were transformed into percentiles according to Czech normative data study of the MoCA); BDI-II = Beck Depression Inventory, Second Edition (raw score); STAI = Spielberger Stait (X1) and Trait (X2) Anxiety Inventory (raw scores were transformed into sten (a sten score is defined by reference to a standard normal distribution and has a midpoint of 5.5 and SD of 1.0) according to Czech normative data study).

[a] Mann–Whitney *U*-test.

* $p \leq 0.05$.

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Table 3 – Logistic regression in ex post facto model of cardiac arrest.

	B	SE	Wald	df	p	Odds Ratio	95.0% CI for Odds Ratio	
							Lower	Upper
Gender	1.492	0.689	4.695	1	0.030*	4.446	1.153	17.147
Age (years)	−0.045	0.021	4.848	1	0.028*	0.956	0.918	0995
Education (years)	−0.119	0.127	0.871	1	0.351	0.888	0.692	1.140
NART/CRT(perc)	0.049	0.049	1.603	1	0.205	1.050	0.974	1.132
MoCA (perc)	0.013	0.011	1.443	1	0.230	1.013	0.992	1.035
BDI-II (raw score)	0.062	0.061	1.053	1	0.305	1.064	0.945	1.198
STAI-X1 (sten score)	−0.684	0.239	8.221	1	0.004*	0.504	0.316	0.805
STAI-X2 (sten score)	0.010	0.177	0.003	1	0.956	1.010	0.714	1.427

NART/CRT (perc) = National Reading Test/Czech Reading Test (measure of premorbid intelligence level expressed as number of errors in the test transformed into IQ score based on the percentile score from regression equation from Wechsler Adult Intelligence Scale—Revised/WAIS-R); MoCA (perc) = Montreal Cognitive Assessment (raw scores were transformed into percentiles according to Czech normative data study of the MoCA); BDI-II = Beck Depression Inventory, Second Edition (raw score); STAI = Spielberger Stait (X1) and Trait (X2) Anxiety Inventory (raw scores were transformed into sten according to Czech normative data study); B = value obtained in multiple regression analysis (positive values for positive relationship); Wald = Wald test; p value = significant less than 0.05; Odds Ratio = the change in odds of being in group of CA patients when the value of predictors increase by one unit.

* $p \leq 0.05$.

anxiety (MWU = 501; $p = 0.023$). On the contrary, no significant difference was shown when comparing the level of depressive symptoms (MWU = 1422; $p = 0.435$) and trait anxiety (MWU = 668; $p = 0.542$; Table 2).

Correlation analysis of variables in the patient sample

Correlation analysis of relations between the tests in the patient sample showed an inverse relationship between the level of depressive symptoms and cognitive performance ($r = -0.45$; $p < 0.001$). Depressive level further correlated with state anxiety ($r = 0.32$; $p = 0.018$) and trait anxiety ($r = 0.34$; $p = 0.012$). Neither of the tests correlated significantly with the results in MCS. Regarding the demographic characteristics, a significant correlation was demonstrated between patients' age and both state ($r = -0.36$; $p = 0.008$) and trait anxiety ($r = -0.33$; $p = 0.015$). The clinical parameters (length of CA, time from CA) were not significantly linked to any of the applied tests.

Table 4 – Standardized canonical discriminant function coefficients (canonical variable – relevance to group of cardiac arrest patients).

Predictor	Function 1
Age (years)	0.570
NART/CRT (perc)	−0.238
MoCA (perc)	0.460
BDI-II (raw score)	−0.418
STAI X1 (sten score)	1.007
STAI X2 (sten score)	−0.121

NART/CRT (perc) = National Reading Test/Czech Reading Test (measure of premorbid intelligence level expressed as number of errors in the test transformed into IQ score based on regression equation from Wechsler Adult Intelligence Scale—Revised/WAIS-R); MoCA (perc) = Montreal Cognitive Assessment (raw scores were transformed into percentiles according to Czech normative data study of the MoCA); BDI-II = Beck Depression Inventory, Second Edition (raw score); STAI = Spielberger Stait (X1) and Trait (X2) Anxiety Inventory (raw scores were transformed into sten according to Czech normative data study).

Logistic regression

The model contained eight independent variables: Gender, Age (years), Education (years), NART/CRT (perc), MoCA (perc), BDI-II (raw score), STAI-X1 (sten score), STAI-X2 (sten score; Table 3). The full model containing full predictors was statistically significant, χ^2 (8, $N = 118$) = 22.02, $p = 0.005$, indicating that the model was able to distinguish between respondents who were patients with CA and control group. The model as a whole explained between 24.3% (Cox and Snell R square) and 33.9% (Nagelkerke R square) of the variance in CA and correctly classified 77.2% of cases. As shown in Table 3, only two of the independent variables made a unique statistically significant contribution to the model (age and STAI X-1). The strongest predictor of having a cardiac arrest in ex-post facto design was gender, recording an odds ratio of 4.45. This predictor indicated that male respondents were over four times more likely to be classified as having had a cardiac arrest when compared to the control sample, controlling for all other factors in the model. The second predictor, STAI-X1, found those with higher scores almost twice as likely to be classified as having had a cardiac arrest. Note that the "twice as likely" speaks to the 0.5 odds ratio for a negative score which is the same as 1/0.5 = 2 for a positive score.

Discriminant function analysis of CA patients group

The first function significantly differentiated control and CA groups, Wilks Lambda = .807, Chi-square (7) = 15.74, $p = 0.028$. The highest loadings have STAI X-1, age, and MoCA in predicting group membership (Table 4). Especially STAI X-1 has the capability to predict cardiac arrest in ex-post facto design. The overall structure matrix indicates that group prediction was sensitive to age, cognition, and anxiety. Importantly, all three of these features appear to work together in effectively classifying CA and control participants.

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Discussion

The main findings of the present study can be summarized as follows. First, CA survivors had decreased cognitive performance when compared with healthy controls. Second, the patients did not have an increased occurrence of depressive symptoms but had a higher level of state anxiety compared with healthy controls. Third, in an ex-post facto model of CA, male gender and high level of state anxiety have a significant, non-specific relation to CA. These factors are to be considered from the ex-post facto perspective as sequelae of CA, but it can also be hypothesized that they are important factors in the evolution of CA. However, we cannot surmise these play a causal role in triggering CA. Finally, CA contrasted by healthy controls can be correctly classified using a high level of state anxiety, cognitive performance, and age. Specifically, more anxious and older individuals who are less cognitively intact are more likely to be classified as having CA from ex-post facto perspective.

The decline in cognitive function performance of CA survivors in the present study corresponds to the previously published data [3,7,8]. Even adherence to available guidelines and implementation of target temperature management resulting in the decrease in overall mortality and the improvement of neurological outcomes following CA, the development and the persistence of a significant cognitive deficit may still result from the hypoxic-ischemic cerebral injury following CA [26,32,34]. In contrast to the previously published studies, where the influence of age, education, and premorbid intelligence on cognitive performance was not taken into account, in the present study, we aimed to homogenize the patient sample with the control sample with respect to demographic characteristics and consider this a major advantage of this study.

Apart from the decreased cognitive performance in patients after CA, previous studies have indicated a higher occurrence of depression and anxiety symptoms [5,10,21]. A higher level of depression was not found in this study in patients following CA. This finding may be influenced by a relatively long average time from the CA episode in the clinical sample. The evaluated levels of depression reflected the 14 days prior to the assessment and in the case of a long period following the CA, the depressive symptoms might have diminished due to sufficient adaptation and medical care. In contrast to other studies published so far [5,6,18], in the current study, the reason for not having found a significant difference in depression between the control and the patient samples could also be caused by the rigorous matching of patients (i.e. not only demographic data was taken into account).

The role of anxiety after having CA corresponds to the previously published data [6,18,34]. State anxiety is significantly connected with CA and is considered from ex-post facto perspective as a statistical predictor of CA as well as higher age [35–37]. CA may affect patients at any age, and it is likely that age plays an important role in the ability to adapt to life after CA. In our sample, age had a significant influence on state anxiety symptoms in patients after CA, where in older patients the anxiety symptoms were less pronounced [14]. We speculate that this can be explained by the fact that younger patients often present the CA event as a sudden, unexpected, and serious diagnosis, which interferes more with the patient's previous life concept and requires broader adaptation effort. In contrast, older people may accept the CA event as less surprising and unexpected in their age group and be able to adapt more easily. The experience of this life-threatening cardiac event endangering its functional structure may lead to increased level of currently experienced anxiety in younger subjects.

An impaired cognitive performance and increased the occurrence of depressive and anxiety symptoms in patients after CA influence the patients' quality of life [12]. Specific experiences accompanying the psychosocial changes in patients' lives can in many ways resemble the experiences of people in midlife crisis [14–16]. For this reason, a Midlife Crisis Scale (MCS) was administered in this study. In our analysis, however, a significant association in the context of prediction or the degree of explanation between the tested midlife crisis symptoms and CA was not found.

Our data show conclusively that some neuropsychiatric features such as state anxiety in connection with certain demographic characteristics (age and male gender) are associated with CA. To our best knowledge, there is a lack of studies researching this relationship, and these findings can be useful for cardiologists working with cardiac patients at risk of CA. In the case, the patient fulfills the psychosocial profile outlined by our analyses (high level of state anxiety or depression, male in older age) the cardiologist should be aware of the higher risk of CA in these patients.

The limitation of our research is a relatively small sample given by the limited availability of the eligible patients, which could be the source of type II statistic error, i.e. the failure to reject the null hypothesis as a result of low statistical power. On the other hand, we have aimed to carefully select the subjects included in the control sample with an attempt to eliminate the possible confounding factors (e.g. premorbid intelligence level). This selection has not been performed in previously published studies. Second, the long average time from the CA event might have led to the vanishing of some of the studied symptoms, and it would be beneficial to concentrate on different stages of adaptation to the hypoxic trauma in further research. Third, on average, only 10% of CA patients are survivors, and it can be only hypothesized if 90% of CA patients who did not survive CA have the same neuropsychiatric characteristics as the CA survivors in our sample. Fourth, a vice versa interpretation of our results would be possible: is not state anxiety and male gender predictive of CA survival? Because these patients are CA survivors, and it could be hypothesized that these factors play a protective role in their survival. Fifth, the results of logistic regression should be interpreted with caution, e.g. when we write "predictor" we have a statistical predictor in ex-post facto model of CA in mind, not a causal predictor of CA.

Conclusion

Survivors of CA with favorable neurological outcome suffer from decreased cognitive performance and symptoms of state anxiety even after a relatively long time following the CA treatment ($M = 47.4 \pm SD = 31.9$ in months). Male gender and

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state anxiety are associated with higher risk of having CA in ex-post facto model. More importantly, age, cognitive performance and state anxiety appear to work together in effectively classifying CA and control participants. In conclusion, psychosocial symptoms and demographic variables outlined above play a significant role in the clinical picture of CA and should be taken into account by cardiologist beside other somatic factors when treating patients at risk of CA.

Conflict of interest

None declared.

Ethical statement

Authors state that the research was conducted according to ethical standards of University.

Funding body

None.

Informed consent

I declare, on behalf of all authors, that informed consent was obtained from the patient participating in this study.

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Effects of continuous positive airway pressure on neurocognitive and neuropsychiatric function in obstructive sleep apnea

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Abstract

The aim of this study was to determine the neurocognitive and neuropsychiatric effects of continuous positive airway pressure treatment on patients with obstructive sleep apnea. This cross-sectional, prospective, observational study included 126 patients with sleep apnea. The following tests were performed: the Montreal Cognitive Assessment for the evaluation of cognitive impairment, the Beck Depression Inventory, and the State-Trait Anxiety Inventory, together with the Epworth Sleepiness Scale for the evaluation of neuropsychiatric symptoms and a person's general level of daytime sleepiness. The first measurement did not show neurocognitive impairment or a higher level of depressive and anxiety symptoms in 126 patients with obstructive sleep apnea in comparison to normative standards. After the 3-month treatment indicated for 43 patients with obstructive sleep apnea, we did not find any significant improvement in cognitive performance ($p = .213$). However, patients with sleep apnea with continuous positive airway pressure treatment did show significantly less daytime sleepiness, anxiety and depressive symptoms (all $p < .001$). In conclusion, short-term (3 months) treatment of patients with obstructive sleep apnea can substantially alleviate their daytime sleepiness, as well as depressive and anxiety symptoms.

KEYWORDS
affective disorders, anxiety, cognition, depression, sleep disorders

1 | INTRODUCTION

Obstructive sleep apnea (OSA) is a sleep-related breathing disorder associated with respiratory cessation as a result of obstruction of the upper airway during sleep (Lal, Strange, & Bachman, 2012; Tulek, Atalay, Kanat, & Suerdem, 2013; Zhou, Camacho, Tang, & Kushida, 2016). Complete (apneas) or partial (hypopneas) obstructive events in OSA, resulting in intermittent hypoxaemia, disturb sleep, causing its fragmentation, which is then a condition leading to excessive daytime sleepiness (EDS) (Barbe et al., 2001; Bucks, Olaithe, & Eastwood, 2013; Slater & Steier, 2012; Zhou et al., 2016). The resulting reduced blood oxygen saturation and disturbed sleep architecture may determine neurocognitive dysfunction and mood disorders in patients with OSA (Bucks et al., 2013; Jackson, Howard, & Barnes, 2011; Lal et al., 2012; Naqvi, Wang, Glozier, & Grunstein, 2014; Zhou et al., 2016). Cognitive impairment with OSA is mainly characterized by a lower level of attention and vigilance, reduced learning and memory, and decreased executive performance (Jackson et al., 2011; Lal et al., 2012; Rouleau, Decary, Chicoine, &

Montplaisir, 2002; Tulek et al., 2013; Zhou et al., 2016). From the pathophysiological point of view, some studies explain cognitive impairment by damage to some cerebral areas following hypoxaemia (Quan et al., 2011). On the other hand, cognitive impairment may be a consequence of EDS due to sleep fragmentation (Zhou et al., 2016). In the context of mood disorders with OSA, a higher degree of depressive and anxiety symptoms is frequently described (Acker et al., 2017; Cai, Xu, Wei, Sun, & Chen, 2017; Ejaz, Khawaja, Bhatia, & Hurwitz, 2011; Schroder & O Hara, 2005). Depression in particular is closely linked with OSA due to common clinical symptoms (Acker et al., 2017; BaHammam et al., 2016; Ejaz et al., 2011; Fidan, Unlu, Sezer, Gecici, & Kara, 2007; Naqvi et al., 2014). Both neuropsychiatric consequences of OSA, cognitive dysfunction and mood changes, may also be affected by frequently described co-morbidities, such as hypertension or diabetes (Fidan et al., 2007).

Continuous positive airway pressure (CPAP) therapy is a standardly used and effective OSA treatment that improves subjectively but also objectively measured EDS and sleep quality (Kushida et al., 2012; Lau, Eskes, Morrison, Rajda, & Spurr, 2013; Pan, Deng, Xu, Liu, & Liu, 2015; Zhou et al., 2016). However, the positive impact of CPAP on the cognitive performance of patients with OSA is inconsistent. Previous studies have partly discovered an improvement in cognitive performance due to CPAP use, especially on vigilance and attention, but not in executive functioning or constructional ability (Aloia, Arnedt, Davis, Riggs, & Byrd, 2004; Bucks et al., 2013; Ferini-Strambi et al., 2003; Zhou et al., 2016). Persistent cerebral damage following hypoxaemia may explain the irreversibility of cognitive impairment caused by OSA (Bardwell et al., 2007; Sforza & Roche, 2012). When the effect of CPAP is detected, improvement depends on the duration of CPAP use, both in the context of an average number of hours per night and the number of months since the start of CPAP treatment (Antic et al., 2011; Ferini-Strambi et al., 2003; Sforza & Roche, 2012). Most studies on the subject have reported a significant association between CPAP treatment and decreased depressive and anxiety symptoms (Cai et al., 2017; Celik et al., 2016). Longitudinally, CPAP treatment improves mood disorders and vigilance, which is associated with a lower frequency of traffic accidents (Jackson et al., 2011; Yamamoto, Akashiba, Kosaka, Ito, & Horie, 2000). There is a lack of OSA studies describing the impact of CPAP treatment on the cognitive and affective functioning of patients with OSA.

The objective of this study is to compare the level of neurocognitive performance and the number of neuropsychiatric symptoms (depression and anxiety) pre- and post-CPAP usage in a group of patients with OSA. We hypothesized that cognitive decline and a higher degree of depressive and anxiety symptoms in patients with OSA would significantly associate with the severity of OSA.

2 | PATIENTS AND METHODS

The sample consisted of 126 consecutive patients (101 men and 25 women, all Caucasian aged 56.9 ± 12.8 years) recruited in INSPAMED in Prague during May and April 2015. All patients had been diagnosed with OSA (according to American Academy of Sleep Medicine [AASM] version 2.2 criteria – apnea–hypopnea index [AHI] ≤ 5 events per hour) using a home sleep apnea test (HSAT) offered in the form of a type III device (Berry et al., 2015; Punjabi, Aurora, & Patil, 2013). The only exclusion criterium was ongoing treatment of a degenerative or oncological illness; two patients were thus excluded. Mild, moderate and severe OSA were differentially diagnosed in accordance with ICSD-3 for polysomnographic data (American Academy of Sleep Medicine, 2014). Whereas there are no official rules specific for HSAT diagnosis of OSA, we used the ICSD-3 manual, which is a standardly followed procedure in outpatient practice (American Academy of Sleep Medicine, 2014; Berry et al., 2015; Punjabi et al., 2013). Subsequently, patients with moderate-to-severe OSA ($n = 115$) were indicated for CPAP treatment (CPAP model Air Sense 10 Elite from ResMed) by a somnologist (according to AASM version 2.2 criteria, i.e. AHI > 15 events per hour), while eight patients with a complicated diagnosis and seven patients with borderline mild-to-moderate OSA (AHI = 15 or 16) were indicated to repeat the HSAT after some time, as determined by the somnologist. Table 1 shows the demographic and clinical characteristics of the participants.

Of the 98 patients with moderate-to-severe OSA indicated for CPAP, 43 were eligible for a prospective psychological retest after 3 months of continuous treatment with auto-CPAP. The inclusion criteria for the retest research sample were: auto-CPAP therapy prescribed by the treating somnologist; patient's acceptance of CPAP (nine patients refused CPAP treatment); successful completion of the CPAP titration (18 patients did not complete it within the set deadline due to, i.e. stress, need of bilevel positive airway pressure, illness, etc.); patient's acceptance of the psychological retest (11 patients refused retesting); and a minimum CPAP usage of more than 4 hr per night/at least one record on the CPAP SD card (17 patients used CPAP less).

The Montreal Cognitive Assessment (MoCA) for the evaluation of cognitive impairment, the Beck Depression Inventory (BDI-II) and the State-Trait Anxiety Inventory (STAI), together with the Epworth Sleepiness Scale (ESS) for the evaluation of neuropsychiatric symptoms and a person's general level of daytime sleepiness, were recorded at the time of diagnostic HSAT for each patient and also after 3 months of CPAP treatment in patients prospectively followed-up (Beck, Steer, & Brown, 1996; Johns, 1991; Kopecek et al., 2017; Kvaal, Ulstein, Nordhus, & Engedal, 2005). Patients with OSA utilized the CPAP machines for 99.2 ± 23.82 days on average and 4.4 ± 1.97 hr per night. We considered CPAP usage of more than 4 hr per night to be good adherence (Rotenberg, Murariu, & Pang, 2016).

2.1 | Home sleep apnea testing

Overnight HSAT with portable sleepmonitor type III (RemLogic version 2.0, Embla Systems), which is standardly used in clinical outpatient practice in INSPAMED, was used for OSA screening (Collop et al., 2007). HSAT contains: nasal airflow due to the cannula

TABLE 1 Demographic, sleep, cognitive and neuropsychiatric characteristics of the complete OSA sample (n = 126)

OSA	M ± SD
Demographic and clinical characteristics	n = 126
Gender (male, %)	101.0 (80.2)
Age (years)	56.9 ± 12.8
Education (years)	14.0 ± 3.2
NART/CRT (premorbid IQ)	114.6 ± 18.2
Hypertension (% positive)	75.0 (59.5)
Diabetes mellitus-II (% positive)	35.0 (27.8)
Psychiatric diagnosis (% positive)	4.0 (5.0)
Generalized anxiety disorder (% positive)	1.0 (0.8)
Mixed anxiety and depressive disorder (% positive)	1.0 (0.8)
Bipolar disorder, currently in remission (% positive)	1.0 (0.8)
Major depressive disorder, single episode, mild (% positive)	2.0 (1.6)
Psychopharmaceuticals (% treated)	20.0 (15.9)
Benzodiazepines (% treated)	6.0 (4.8)
Antidepressants (% treated)	12.0 (9.5)
Hypnotics (% treated)	6.0 (4.8)
Antiepileptics (% treated)	1.0 (0.8)
Antipsychotics (% treated)	3.0 (2.4)
BMI (kg/m^2)	32.8 ± 5.7
Sleep characteristics	
OSA severity	
Mild (%)	11.0 (8.7)
CPAP (%)	0 (0.0)
Moderate (%)	41.0 (32.5)
CPAP (%)	16.0 (39.0)
Severe (%)	74.0 (58.7)
CPAP (%)	27.0 (36.5)
AHI (apnoe-hypopnea event per 1 hour/ night)	41.2 ± 24.0
ODI (oxygen-desaturation event per 1 hour/ night)	40.8 ± 24.3
SAT (oxygen saturation %)	91.0 ± 7.2
SAT90 (oxygen saturation index lower than 90% in %)	21.7 ± 25.1
ESS (raw score in ESS, 24 points at maximum)	9.8 ± 7.0
Symptomatic, ESS≥10 (%)	58.0 (46.0)
Cognitive and neuropsychiatric data	
MoCA (percentile)	52.8 ± 29.4
MoCA time (minutes)	6.4 ± 1.7
BDI-II (percentile)	59.9 ± 29.0
STAI X-1 (percentile)	47.5 ± 19.3
STAI X-2 (percentile)	42.8 ± 23.3

Data presented mean (M) ± standard deviation (SD) or frequency (percentage). OSA, obstructive sleep apnea; NART/CRT, National Adult Reading Test/Czech Reading Test (measure of premorbid intelligence level expressed as number of errors in the test transformed into IQ score based on regression equation from Wechsler Adult Intelligence Scale-Revised/WAISR); BMI = body mass index; OSA severity: Mild = AHI 5-15, Moderate = AHI 16-30, Severe = AHI ≥ 30; AHI, apnoe/hypopnoe index; ODI, oxygen desaturation index; SAT, average oxygen saturation level; SAT90, oxygen saturation level of 90%; ESS, Epworth sleepiness scale; MoCA, Montreal Cognitive Assessment total score transformed into percentile; MoCA time, mean length of MoCA administration in minutes; BDI-II, Beck Depression Inventory, Second Edition transformed into percentile; STAI, Spielberger's Stait (X-1) and Trait (X-2) Anxiety Inventory transformed into percentile.

pressure transducer; thoracabdominal movements due to elastic bands; oxygen saturation and heart rate due to the pulse oxymetry (sensor) attached to the little finger; leg movements due to lower limb electrodes/and body position (Collop et al., 2007; Punjabi et al., 2013).

Data obtained from HSAT included in the analysis are as follows: AHI; oxygen desaturation index (ODI; number of times per hour when the level of blood oxygen dropped by 3% from baseline); SAT (average percentage of oxygen saturation in the blood); and SAT90 (percentage of sleep during which oxygen saturation was under 90%; Aloia et al., 2004; Boland et al., Collop et al., 2007; Roure et al., 2008). HSAT data were scored according to the HSAT Rules for Adults, which is a part of the AASM Manual for the Scoring of Sleep and Associated Events, version 2.2, and were visually screened by a somnologist (Berry et al., 2015; Boland et al., 2002).

2.2 | Statistical analysis

Variables are expressed as the arithmetic mean ± SD or the median in the case of non-normal data distribution. In correlational analysis, the data were evaluated by Spearman's coefficient of rank correlation (due to the non-normal distribution of the data) to evaluate the relationship between different variables or test measures, in case of nominal variables by point-biserial correlation coefficient. Between-groups differences in OSA severity were analysed using the Mann–Whitney U-test. The analysis between repeated measurements was performed by the Wilcoxon signed-rank test. For post hoc comparisons, we used Bonferroni correction. All analyses were performed using IBM SPSS 20.0 for Windows. Statistical significance was considered to be present when $p < .05$.

3 | RESULTS

We analysed data from 126 patients (101 men and 25 women, all Caucasian aged 56.9 ± 12.8 years) with OSA. Patient characteristics are shown in Table 1. The mean MoCA score in patients with OSA was 52.8 ± 29.4, and we did not find any patient who showed signs of cognitive impairment, defined as being below 1.5 SD according to the Czech normative data study (Kopecek et al., 2017). Similarly, no patients with OSA showed signs of higher depression or anxiety (Table 1).

There were 15 patients with OSA who suffered from different neurological conditions (e.g. cerebral haemorrhage), which may have significantly interfered with further examinations. However, analysis of OSA without (n = 111) and OSA with neurological conditions (n = 15) showed no difference between these groups (Table 2).

TABLE 4 Between-groups differences in MoCA mean administration time based on OSA severity

		Mild OSA (n = 11)	Moderate OSA (n = 41)	Severe OSA (n = 71)
Mild OSA (n = 11)	U	–	106.0	196.5
	p value		.004*	.003*
Moderate OSA (n = 41)	U	106.0	–	1764.0
	p value	.004*		.074
Severe OSA (n = 74)	U	196.5	1764.0	–
	p value	.003*	.074	

Post-hoc comparisons are based on Mann-Whitney U test (U). OSA Mild = AHI 5–15, Moderate = AHI 16–30, Severe = AHI ≥ 30. * $p \leq .01$

TABLE 5 Differences between pre-test (pretreatment) and post-test (posttreatment) in clinical, cognitive and neuropsychiatric performance of OSA patients using CPAP (n = 43)

	Pre-test	Post-test	W	p value
ESS (raw score)	10.8 ± 10.2	6.0 ± 3.5	685.0	<.001*†
AHI (apnea-hypopnea event per hour of night)	45.7 ± 22.5	1.8 ± 1.9	861.0	<.001*†
MoCA total score (raw score)	25.9 ± 3.0	26.3 ± 2.5	198.0	.213
MoCA Visuospatial-Executive (raw score)	4.6 ± 0.5	4.6 ± 0.7	95.0	.000
MoCA Naming (raw score)	3.0 ± 0.4	3.0 ± 0.0	9.0	.824
MoCA Memory (raw score)	3.0 ± 1.3	3.2 ± 1.4	119.5	.381
MoCA Attention (raw score)	5.4 ± 1.1	5.6 ± 0.7	40.5	.149
MoCA Language (raw score)	2.4 ± .8	2.1 ± 0.8	178.5	.015‡
MoCA Abstraction (raw score)	1.7 ± .6	1.9 ± 0.3	15.0	.053†
MoCA Orientation (raw score)	5.9 ± .4	5.9 ± 0.3	5.0	.572
MoCA time (seconds)	6.5 ± 1.8	5.8 ± 1.2	625.5	.012‡
BDI-II (raw score)	9.4 ± 7.1	4.5 ± 4.6	663.0	<.001*†
STAI X-1 (raw score)	39.4 ± 10.6	37.5 ± 9.7	454.0	.123
STAI X-2 (raw score)	41.1 ± 9.5	37.6 ± 8.7	540.0	.001††

Data presented mean (M) ± standard deviation (SD) and pre-test vs post-test comparisons are based on Wilcoxon Signed-Rank Test (W). ESS, Epworth Sleepiness Scale; AHI, apnoe/hypopnoe index; MoCA, Montreal Cognitive Assessment (raw scores; min. 0–max. 30), MoCA subtest Visuospatial and Executive function (0–5 points raw score), MoCA Naming (0–3), MoCA Memory/Delayed recall (0–5), MoCA Attention (0–6), MoCA Language (0–3); MoCA Abstraction (0–2), MoCA Orientation (0–6); MoCA time, mean administration time in minutes; BDI-II, Beck Depression Inventory, Second Edition (raw score); STAI, Spielberger's State (X-1) and Trait (X-2) Anxiety Inventory (raw scores). *$p < .001$; †$p < .01$; ‡$p < .05$; ††still significant after Bonferroni correction for 12 comparisons ($p < .004$).

the data we can see several notable medium correlations of polysomnographic findings (AHI, ODI, SAT) and higher daytime sleepiness, as measured by the ESS (Table 6). Furthermore, higher daytime sleepiness is related to a higher level of depressive symptoms in pre-tests as well (rho = .280, p = .035) as in post-tests (rho = .321, p = .038), and AHI is inversely related to better attention (rho = –.324, p = .039; Table 6). More importantly, MoCA Memory and the Delayed Recall subtest had a medium association with the number of hours using the CPAP machine (rho = .315, p = .048; Table 7).

TABLE 6 Correlations between polysomnographic findings, daytime sleepiness cognitive and neuropsychiatric variables

Condition	Variable	rho	p value
pre-test (n = 126)	ESS–AHI	.261	.004
	ESS–ODI	.337	<.001
	ESS–SAT	.228	.012
	ESS–SAT90	.242	.008
	ESS–BDI-II	.280	.035
post-test (n = 43)	AHI–MoCA Attention	–.324	.039
	ESS–BDI-II	.321	.038

rho, Spearman's rank order correlation coefficient; ESS , Epworth Sleepiness Scale; AHI, apnoe/hypopnoe index; ODI, oxygen desaturation index; SAT, average oxygen saturation level; SAT90, oxygen saturation level of 90%; BDI-II, Beck Depression Inventory, Second Edition (raw score), MoCA Attention subtest.

3.4 | The effect of continuous positive airway pressure on patients with and without excessive daytime sleepiness

Before treatment, 58 patients (46%) reported the occurrence of EDS, which is one of the clinical parameters of OSA (Johns, 1991;

TABLE 7 Correlations between post-test characteristics and CPAP use parameters after 3 months (n = 43)

		CPAP days	CPAP hours
AHI (apnea-hypopnea event per hour of night)	*rho*	−.075	−.352
	p value	.647	.026*
MoCA Memory/Delayed recall (raw score)	*rho*	.110	.315
	p value	.500	.048*

rho, Spearman_s rank order correlation coefficient; CPAP days, average length of CPAP use in days; CPAP hours, average length of CPAP use in hours per night; AHI, apnea/hypopnea index; MoCA Memory/Delayed recall.

Slater & Steier, 2012). The ESS is a frequently used tool for identyfying EDS in clinical practice. According to the ESS, the criteria for significant symptomatology of EDS is an ESS ≥ 10 points (out of 24 total points; Johns, 1991). In our research sample, 43 retested patients scored on average 14 points ± 3.6 SD in ESS before the treatment start. After 3 months of CPAP usage, the average score in ESS decreased to 7 points ± 4.2 SD.

Analysis showed a significant difference between symptomatic and non-symptomatic retested patients with OSA regarding the CPAP effect on the MoCA test, which was measured by the substraction of the pre-test from the post-test MoCA score (rMoCA; U = 522.0, z = −2.246, p = .025; the complete results can be found in Table 8). No other significant effect of CPAP on patients with and without sleepiness was found.

TABLE 8 Between-group differences in MoCA, BDI-II, STAI X-1/X-2 in patients with (n = 21) and without (n = 22) EDS (OSA patients with excessive daytime sleepiness according to ESS) prior to CPAP treatment

	Md				
	EDS	No-EDS	*U*	*z*	*p* value
rMoCA (RS)	0	−1	522.0	−2.246	.025*
MoCA post-test (RS)	26	26	645.0	−.978	.328
rMoCAtime (S)	−33	−18	651.0	−.733	.464
MoCA time post-test (S)	335	361	599.0	1.273	.203
rBDI-II (RS)	4	3	212.0	−.215	.830
BDI-II post-test (RS)	4	3	227.0	−.098	.922
rSTAI X-1 (RS)	5	3	176.5	−.380	.708
STAI X-1 post-test (RS)	37	35	225.5	−.134	.894
rSTAI X-2 (RS)	4	5	171.5	−.521	.607
STAI X-2 post-test (RS)	35	37	227.5	−.085	.932

Post-hoc comparisons are based on Mann-Whitney U Test (U), z-score (z) and p value. EDS, group of OSA patients with excessive daytime sleepiness according to ESS (≥10 point from 24 points at maximum); no EDS, group of OSA patients without excessive daytime sleepiness according to ESS (<10 point from 24 points at maximum); rMoCA, pre-test – post-test in raw score; rMoCA time, pre-test – post-test in seconds; rBDI-II, pre-test – post-test in raw score; rSTAI X-1, pre-test – post-test in raw score; rSTAI X-2, pre-test – post-test in raw score; RS, raw-score; S, seconds. *p < .05.

3.5 | The effect of continuous positive airway pressure on patients with good adherence to treatment

Acceptance and adherence are important conditions for good CPAP compliance (Rotenberg et al., 2016). Adherent patients are usually defined as those who use CPAP for an average of 4 hr per night on 70% of nights (Rotenberg et al., 2016).

We found a significant difference between adherent and non-adherent retested patients with OSA in CPAP effect regarding the time of MoCA administration, which was measured by the mathematical difference between pre-test and post-test MoCA administration (rMoCAtime; U = 58.5, z = −2.472, p = .012; Table 9). Patients who used CPAP more than 4 hr per night had faster psychomotor speed in MoCA test than less adherent patients. No other significant effect of CPAP on adherent or non-adherent patients was found.

4 | DISCUSSION

We aimed at describing the clinical picture of patients with OSA regarding their neurocognitive and neuropsychiatric characteristics (pre-test) in relation to 3 months of CPAP treatment (post-test). We thus aimed at proving the beneficial effects of CPAP treatment on the neurocognitive and neuropsychiatric symptoms that are often observed in patients with OSA (Acker et al., 2017; BaHammam et al., 2016; Ejaz et al., 2011; Fidan et al., 2007; Naqvi et al., 2014).

In the pre-test, we did not find any significant cognitive impairment in patients with OSA in comparison to normative data, which is consistent with previous research on cognitive functioning by OSA. We also did not find any above-average level of depressive state and trait anxiety symptoms in comparison to normative data. As a result, we were able to compare in both pre-test and post-test a group of patients with OSA treated with CPAP that was relatively asymptotic of cognitive or neuropsychiatric co-morbidities, and to observe the effect of CPAP on OSA functioning without the mediating influence of other co-morbidities.

We found that 3 months of CPAP treatment has no significant effect on cognitive performance in patients with OSA, as measured by the MoCA. These findings are concordant with the results of previous studies (Barbe et al., 2001; Ferini-Strambi et al., 2003; Quan et al., 2011). On the other hand, we monitored in the study a declining tendency of cognitive functioning 3 months after starting CPAP treatment in patients with OSA, who upon diagnosis did not feel an EDS versus those who did feel daytime sleepiness. Patients without significant symptomatology before starting treatment moderately worsened in cognitive functioning after 3 months of using CPAP. Although the difference found is with the greatest probability caused by too small a sample size, we assume that the indication of non-symptomatic patients with OSA regarding CPAP treatment may be for patients smaller relief than for patients who prior to treatment complained of EDS, which may be a manifestation of an undesired effect of the treatment.

However, after 3 months of CPAP usage, patients with OSA performed the test significantly faster, which may be related to their

TABLE 9 Between-group differences in MoCA, BDI-II, STAI X-1/X-2 between group of patients with good (n = 31) and poor (n = 9) adherence to CPAP treatment

	Md				
	Adherent	Non-adherent	*U*	z	*p* value
rMoCA (RS)	0	−1	111.5	−1.037	.659
MoCA post-test (RS)	25	27	94.5	−1.037	.300
rMoCAtime (S)	−38	1	58.5	−2.472	.012*
MoCA time post-test (S)	338	351	106.0	−0.841	.400
rBDI-II (RS)	−4	−5	131.0	−0.134	.894
BDI-II post-test (RS)	3	7	104.5	−1.146	.252
rSTAI X-1 (RS)	−5	1	96.0	−.610	.542
STAI X-1 post-test (RS)	35	49	89.5	−1.621	.105
rSTAI X-2 (RS)	−4	−1	100.5	−0.439	.660
STAI X-2 post-test (RS)	35	46	97.0	−0.168	.177

Post-hoc comparisons are based on Mann-Whitney U Test (*U*), z-score (z) and *p* value. EDS, group of OSA patients with excessive daytime sleepiness according to ESS (≥10 point from 24 points at maximum); no EDS, group of OSA patients without excessive daytime sleepiness according to ESS (<10 point from 24 points at maximum); rMoCA, pre-test – post-test in raw score; rMoCA time, pre-test – post-test in seconds; rBDI-II, pre-test – post-test in raw score; rSTAI X-1 = pre-test – post-test in raw score; rSTAI X-2, pre-test – post-test in raw score; RS, raw-score; S, seconds. *$p < .05$.

faster information processing as a result of CPAP treatment. The study further demonstrates that the faster processed information 3 months after starting CPAP treatment corresponds to the measure of instrument use by the patients. Patients with good treatement adherents who used the device at least 4 hr per night on 70% of the monitored nights had a more rapid cognitive performance versus those who used it less. Furthermore, the information processing speed in the MoCA was OSA-severity dependent, as was also confirmed by previous research (Antic et al., 2011; Ferini-Strambi et al., 2003; Sforza & Roche, 2012). The result, therefore, cannot be solely explained by test–retest practice effect, but rather by a specific effect of CPAP treatment on the information processing speed in patients with OSA.

A higher level of depressive symptoms in OSA has been well documented by previous research on the neuropsychiatry of OSA (Naqvi et al, 2014; Zhou et al., 2016). Higher depression is caused by daytime sleepiness, and the resulting fatigue and, vice-versa, higher level of depressive symptoms can be understood as a risk factor in the development of EDS (Aloia et al., 2004; Antic et al., 2011). We found that 3 months of CPAP treatment of patients with OSA had a beneficial effect on the level of depressive and trait anxiety symptoms (Acker et al., 2017; BaHammam et al., 2016; Ejaz et al., 2011; Fidan et al., 2007; Naqvi et al., 2014; Ryan, Bayley, Green, Murray, & Bradley, 2011; Sanchez, Buela-Casal, Bermudez, & Casas-Maldonado, 2001). These effects were highly significant, because they survived Bonferroni correction. We surmise that the effect of CPAP is mediated by a reduction in the number of AHI during sleep, which results in less daytime sleepiness and a concomitant lower level of depression.

We also observed a post-test beneficial trend in cognitive performance, especially in MoCA language and to a lesser extent in abstraction. These improvements, albeit statistically non-significant, may be related to better night-time cerebral perfusion as a result of CPAP treatment (Bucks et al., 2013; Lal et al., 2012; Zhou et al., 2016). Nocturnal apneas are associated with profound changes in cerebral blood flow, and apnea-induced hypoxaemia, combined with reduced cerebral blood, may predispose patients with OSA to nocturnal cerebral ischaemia. MoCA language and abstraction subtests include verbal fluency, two complex sentences repeat and a conceptualization task that may be very sensitive to impaired cortical integrity caused by chronic nocturnal cerebral sub-ischaemic insults and resulting sleep architecture disruption due to OSA (Ferini-Strambi et al., 2003; Roure et al., 2008).

There are limitations related to the study sample. Our sample size was relatively small, especially after splitting the sample into OSA severity subgroups. On the other hand, it is unrealistic to expect large numbers of patients with mild OSA, because due to the low level of OSA symptomatology these patients are rarely indicated to specialized medical help in a sleep laboratory by a practitioner or have no reason to seek such help. Also, there was significant drop-out of patients with OSA before retesting. Furthermore, our sample has no comparison control group, and the comparisons were done by normative data comparisons from the Czech population. Regarding methods, HSAT was used to diagnose OSA instead of standard polysomnography. Limitations of HSAT are recorded mainly in scoring respiratory events due to the fact that monitoring in HSAT is greater than total sleep time (Pan et al., 2015). In type III, HSAT total recording time is based on the time in bed and it is not possible to determine total sleep time in as rigorous a way as it is possible in polysomnography (Zhao et al., 2017). This affects AHI, which tends to be underestimated (Zhao et al., 2017). Another method limitation was by using the ESS we obtained subjective estimates of daytime sleepiness that were not validated by another objective measure of daytime sleepiness. Also, the trends in information processing speed and cognitive performance, such as mental flexibility (fluency) and conceptualization, and depressive and anxiety symptoms level should

be observed longitudinally to confirm the significant influence of CPAP treatment on these neurocognitive and neuropsychiatric characteristics in patients with OSA.

In conclusion, this study showed a significant beneficial effect of 3 months of CPAP treatment on the neurocognitive and neuropsychiatric characteristics of patients with OSA. In particular, CPAP treatment leads to improvement of information speed processing, which is OSA-severity dependent, and further to a highly significant alleviation of depressive and anxiety symptoms, besides lesser daytime sleepiness. We also showed possible new directions regarding the efficiency of CPAP treatment for ameliorating the cognitive performance of patients with OSA. Finally, CPAP treatment seems to be a promising tool for the treatment of not only sleep disruptions as expressed by AHI but also for alleviation of suffering from higher levels of depression, anxiety and slowed psychomotor speed due to OSA.

CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

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The Clinical Impact of Systematic Screening for Obstructive Sleep Apnea in a Type 2 Diabetes Population—Adherence to the Screening-Diagnostic Process and the Acceptance and Adherence to the CPAP Therapy Compared to Regular Sleep Clinic Patients

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Obstructive sleep apnea (OSA) is a common disorder in Type 2 diabetes (T2D) patients further increasing their already high cardiovascular risk. As T2D patients typically not report OSA symptoms, systematic screening for OSA in this population is warranted. We aimed to determine the readiness of T2D patients to undergo screening and to compare their adherence to continuous positive airway pressure (CPAP) therapy with "regular" sleep clinic patients who typically seek medical advice on their own initiative. We therefore recruited 494 consecutive T2D patients and offered them OSA screening using home sleep monitoring (type IV device). All participants in high risk of moderate-to-severe OSA were recommended home sleep apnea testing (HSAT) followed by CPAP therapy. Patients were followed-up for 12 months and outcomes compared to 228 consecutive sleep clinic patients undergoing HSAT. Among 307 screened T2D patients, 94 (31%) were identified at high risk of moderate-to-severe OSA. Subsequently, 54 patients underwent HSAT, 51 were recommended, and 38 patients initiated CPAP (acceptance 75%). Among 228 sleep clinic patients, 92 (40%) were recommended and 74 patients initiated CPAP (acceptance 80%). After 1 year, 15 (39%) T2D and 29 (39%) sleep clinic patients showed good CPAP adherence (use $\geq$ 4 h/night $\geq$ 70% nights). In conclusion, 20 T2D patients needed to be screened in order to obtain one successfully treated patient. OSA screening in T2D patients identified 31% with moderate-to-severe OSA. Once diagnosed, their CPAP acceptance and adherence did not differ from sleep clinic patients. However, the reasons for the high dropout during the screening-diagnostic process impacting the overall success of the screening program need to be identified and addressed.

Keywords: sleep apnea, diabetes, screening, CPAP acceptance, CPAP adherence

guidelines. This study was carried out in accordance with the recommendations of the Ethical Committee of the Third Faculty of Medicine, Charles University, Prague with written informed consent from all subjects. All subjects gave written informed consent in accordance with the Declaration of Helsinki. The protocol was approved by the Ethical Committee of the Third Faculty of Medicine, Charles University, Prague.

Determination of Acceptance and Adherence

CPAP usage data of both, Type 2 diabetes and sleep clinic patients were analyzed at 3 and 12 months after establishing optimal mask fit, treatment pressure and regime (titration). Acceptance was defined as the patient's agreement to CPAP therapy after titration. Adherence was assessed using reports downloaded from CPAP machines. Patients using CPAP ≥4 h per ≥70% of nights were considered having "Good" adherence, while lower CPAP usage was considered as "Poor" adherence.

Sleep Study Protocol

OSA Screening Study

Screening for the presence of OSA was performed using a type IV device (ApneaLink, ResMed, San Diego, CA, United States) that recorded hemoglobin saturation, heart rate and nasal airflow during sleep in a home setting. Subjects were instructed to set-up the device and keep regular sleep habits. Support in the form of a non-stop phone help-line was established and the devices were returned to investigators the next morning. Automatic scoring of respiratory events with a 4% desaturation threshold was performed, apneas defined as a ≥90% reduction in airflow for at least 10 s and hypopneas defined as a ≥30% reduction in airflow for at least 10 s together with hemoglobin desaturation of ≥4%. Patients with REI ≥15 were considered as being at high risk of moderate-to-severe OSA. For 13 patients the oxygen desaturation index (ODI) was used due to a poor airflow signal.

Diagnostic Sleep Study

Sleep recordings were performed using a type III device that recorded hemoglobin saturation, heart rate, nasal airflow, ECG, chest and abdominal respiratory efforts (Nox T3, Nox Medical, Reykjavik, Iceland) in a home setting. The recordings were evaluated by a board-certified sleep medicine physician according to AASM criteria (apnea defined by a ≥ 90% reduction in airflow for at least 10 s and hypopnea defined as a ≥ 30% reduction in airflow for at least 10 s together with ≥ 4% desaturation). Patients with moderate-to-severe OSA (REI ≥ 15) were recommended to initiate CPAP treatment.

Statistical Analysis

Statistical analysis was performed using Prizm 5 for Windows Software (GraphPad Software Inc., La Jolla, CA, United States). Differences in anthropometrical parameters between the patient groups were analyzed using a *T*-test and differences in frequencies were analyzed using a Chi-Square test. Data are presented as mean ± SEM, counts or proportions (%). Statistical significance was set to $p < 0.05$.

RESULTS

OSA Screening Outcomes in Type 2 Diabetes Patients

Out of 483 consecutive Type 2 diabetes patients who fulfilled the inclusion criteria, 321 patients consented to undergo OSA screening, resulting in 307 analyzed sleep recordings of an acceptable quality. Among successfully screened patients, 31% (63 men and 31 women) were identified as being in a high risk of moderate-to-severe OSA and thus invited for a diagnostic sleep study. However, such a sleep study was performed for only 60% of them due to the unwillingness of patients to further continue with the diagnostic process (**Figure 1**).

The Type 2 diabetes patients who accepted the diagnostic home sleep apnea testing (HSAT) were characterized by 42% higher REI (32.6 ± 2.4 vs. 22.9 ± 1.5, $p < 0.05$) and a 49% higher score in Epworth sleepiness scale (7.6 ± 0.6 vs. 5.1 ± 0.5, $p < 0.05$) than the Type 2 diabetes patients who declined HSAT. No differences in anthropometric and demographic parameters or associated comorbidities were observed (**Table 1**).

CPAP Acceptance and Adherence in Type 2 Diabetes and Sleep Clinic Patients

Based on the results of home sleep apnea testing, 51 Type 2 diabetes patients were recommended to initiate CPAP treatment. However, 13 patients dropped out before or during the CPAP titration, resulting in a CPAP acceptance rate of 75% (38 treated patients). A similar acceptance rate of 80% ($p > 0.05$) was observed in sleep clinic patients—74 patients were treated out of 92 patients recommended for CPAP (**Figure 2**).

Type 2 diabetes patients who were recommended to initiate the CPAP treatment were, in comparison to sleep clinic patients who received same recommendation, older (64.4 ± 1.3 vs. 52.3 ± 1.4, $p < 0.05$), had a lower score in the Epworth sleepiness scale (7.7 ± 0.7 vs. 10.3 ± 0.7), and they were more frequently treated for hypertension and dyslipidemia. There were no significant differences in REI and time spent in saturation < 90% between the Type 2 diabetes and the sleep clinic patients who were recommended CPAP (**Table 2**).

Sleep clinic patients who accepted CPAP exhibited more severe OSA than patients not accepting CPAP (REI 46.0 ± 2.4 vs. 24.8 ± 2.5, $p < 0.05$). This difference was not observed in Type 2 diabetes patients accepting and not accepting CPAP (REI 40.8 ± 3.0 vs. 36.3 ± 3.7, $p > 0.05$), where some patients with lower REI determined by screening had already declined diagnostic home sleep apnea testing. Hypoxic exposure evaluated by time spent at saturation < 90% correlated with CPAP acceptance in both Type 2 diabetes and sleep clinic patients (**Table 2**).

The CPAP recordings obtained after a 1-year follow-up showed "good" adherence to CPAP treatment defined as CPAP usage ≥ 4 h in ≥ than 70% of nights in 15 out of 38 Type 2 diabetes patients and 29 out of 74 sleep clinic patients who initiated CPAP treatment resulting in a 39% adherence rate in both groups (**Table 3**). A comparison of patients with "good" adherence and "poor" adherence to CPAP revealed that sleep clinic patients with "good" adherence were characterized by a higher REI and a longer time spent in saturation < 90%, while

TABLE 1 | Characteristics of type 2 diabetes patients screened for OSA by home sleep monitoring.

	All	REI < 15	REI ≥ 15	REI ≥ 15	
				declined HSAT	examined by HSAT
Patients, *n* (%)	307 (100%)	213 (69%)	94 (31%)	37 (39%)	56 (60%)
Men, *n* (%)	177 (58%)	114 (54%)	63 (67%)	24 (65%)	38 (68%)
Age (years)	64.0 ± 0.5	63.7 ± 0.6	64.8 ± 1.0	65.1 ± 1.6	64.3 ± 1.3
BMI (kg/m^2)	31.2 ± 0.3	30.4 ± 0.3	33.0 ± 0.6*	32.4 ± 0.8	33.4 ± 0.9
Hypertension, *n* (%)	255 (83%)	172 (81%)	83 (88%)	32 (86%)	46 (82%)
Dyslipidemia, *n* (%)	262 (85%)	182 (85%)	80 (85%)	32 (86%)	41 (73%)
CV disease, *n* (%)	46 (15%)	28 (13%)	18 (19%)	6 (16%)	10 (18%)
ESS, *n*	3.2 ± 0.2	5.8 ± 0.3	6.6 ± 0.4	5.1 ± 0.5	7.6 ± 0.6**
REI_screening study, *n*	12.5 ± 0.8	5.3 ± 0.3	28.7 ± 1.6	22.9 ± 1.5	32.6 ± 2.4**
REI_diagnostic study, *n*					37.7 ± 2.4
T90, %					23.6 ± 3.4

BMI, body mass index; CV disease, cardiovascular disease defined as myocardial infarction, percutaneous coronary intervention or stroke, REI, respiratory event index; T90, percentage of total sleep time with oxygen saturation < 90%; HSAT, home sleep apnea testing; ESS, Epworth Sleepiness Scale.
*Data represent mean ± SEM or proportions (%), *p < 0.5 for differences between REI < 15 group and REI ≥ 15.group (T-test, Chi-squared test), **p < 0.05 for differences between declined HSAT group and examined by HSAT group (T-test, Chi-squared test).*

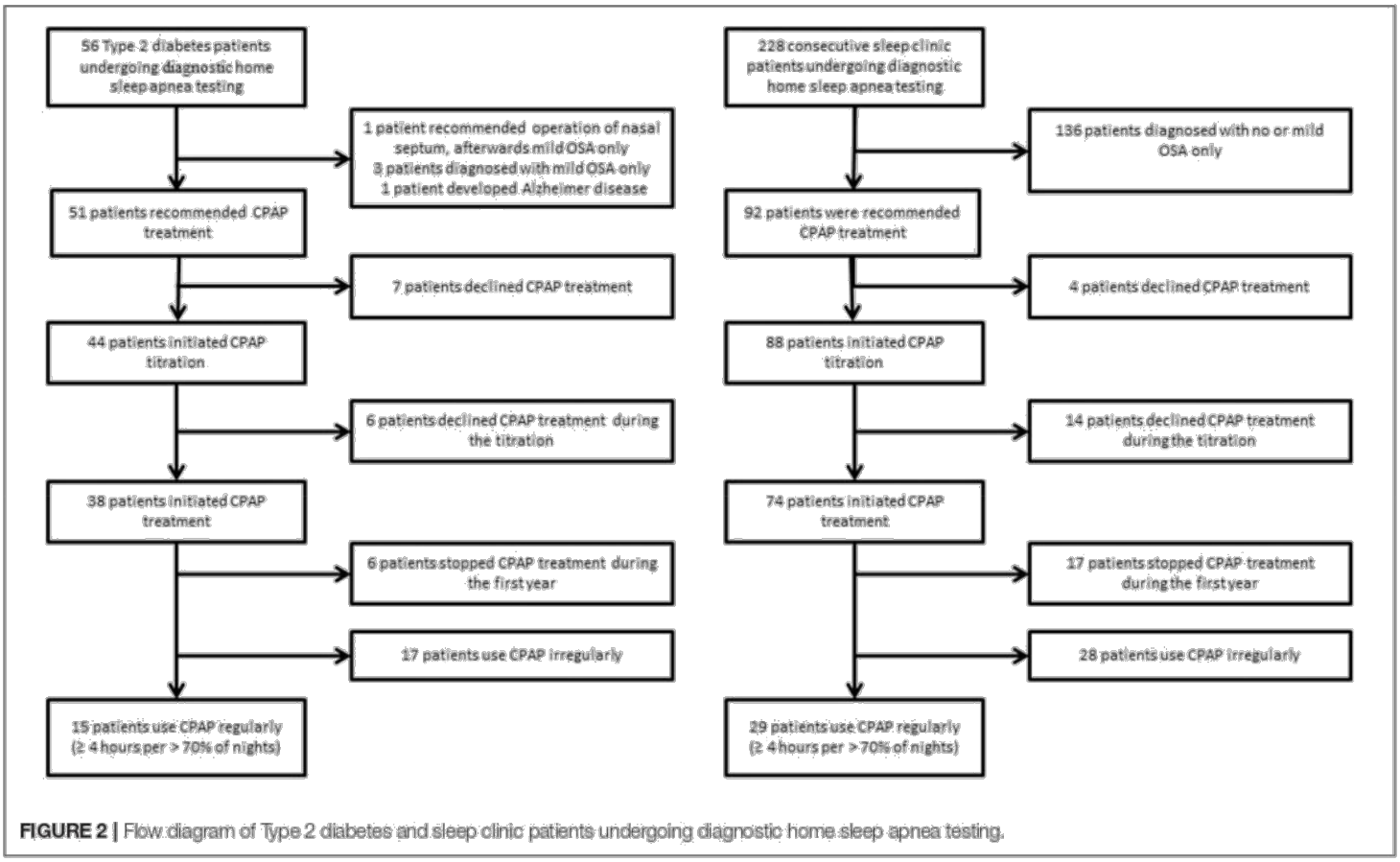

FIGURE 2 | Flow diagram of Type 2 diabetes and sleep clinic patients undergoing diagnostic home sleep apnea testing.

treatment (25). Similarly, a study in heart failure patients showed that ∼ 12% of patients in high risk of moderate-to-severe OSA participated in a full diagnostic process, accepted the CPAP treatment and subsequently exhibited good adherence to CPAP (24). The present study identified two key dropout points in the screening diagnostic process. First, when the patient is recommended to enter the screening program (dropout rate 34%). Second, after obtaining the screening results, when the patient is advised to continue with the diagnostic sleep study (dropout rate 39%). However, once diagnosed with moderate-to-severe OSA, CPAP acceptance and adherence rates in patients with Type 2 diabetes were not different compared to a sleep clinic population. Sleep clinic patients who accepted and better adhered adequately to CPAP exhibited more severe OSA then those who

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Příloha III. Informace pro pacienty, kteří prodělali srdeční zástavu s resuscitací

Informace

pro pacienty, kteří prodělali

srdeční zástavu s resuscitací

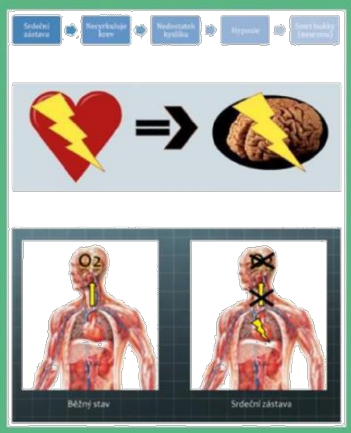
Úvod

Pokud jste prodělal/a srdeční zástavu s úspěšnou resuscitací a daří se Vám zotavovat se po fyzické stránce, přesto se můžete Vy sám/sama i Vaši blízcí setkat s nepříjemnými změnami v prožívání, komunikaci či chování. Takové problémy mohou být důsledkem psychické adaptace na prodělaný kritický životní moment nebo jsou následkem poškození mozku během srdeční zástavy. U mnoha takto postižených pacientů je možné během období rehabilitace dosáhnout jejich zlepšení.

Cílem tohoto materiálu je usnadnit Vám a Vašim nejbližším rozpoznání příznaků posthypoxického postižení mozku a vyrovnat se s nimi. Dále Vám chceme dát informace o tom, jakou pomoc můžete vyhledat, a jak podpořit a urychlit návrat do běžného života.

Co je srdeční zástava?

Při srdeční zástavě dochází k okamžitému přerušení funkce srdce jako pumpy. Krevní oběh se zastaví a k orgánům těla se nedostává kyslík potřebný k jejich správné činnosti. Během 15–20 sekund nastává kolaps a bezvědomí s nehmatným pulsem a následně zástavou dechu.



Příčiny srdeční zástavy

Příčinou srdeční zástavy je nejčastěji maligní (zhoubná) komorová arytmie (fibrilace komor) nebo méně často zástava srdce (asystolie). Při asystolii zcela vymizí elektrická i mechanická činnost srdečních komor a srdce netepe. Fibrilace komor znamená pouze chaotické a mechanicky neúčinné chvění srdce s frekvencí. Je možné ji ukončit defibrilačním výbojem, který opět nastolí normální srdeční rytmus.

Co je resuscitace?

Správně vedená kardiopulmonální resuscitace může nemocného se srdeční zástavou v mnoha případech zachránit. Pokud se pacientovi s náhlou srdeční zástavou dostane účinné první pomoci do jedné minuty od začátku potíží, má vysokou naději na přežití. S každou minutou trvání zástavy klesá šance na přežití. Uplyne-li od nehody do poskytnutí první pomoci a obnovení krevního oběhu 10–12 minut, snižuje se již pacientova šance na přežití na 5 %.

Cílem resuscitace je záchrana života prostřednictvím obnovení krevního oběhu, spontánního dýchání a zabránění nevratnému poškození mozku. Proto se dnes resuscitace nazývá kardio-pulmo-cerebrální (srdeční, plicní a mozková). Provádí se standardním doporučeným způsobem a je rozdělena na základní laickou a odbornou profesionální resuscitaci.

Přestože k obnově spontánní cirkulace dochází u 60 % obětí srdeční zástavy se zahájenou resuscitací, propuštění z nemocniční péče se dožije jen 30 % z nich. Bohužel mnoho z těchto pacientů trpí v dalším období nějakou formou neurologického poškození.

Co znamená posthypoxické postižení mozku a jak se projevuje?

Činnost mozku je závislá na nepřetržité dodávce kyslíku. Mozek a nervová tkáň spotřebovává až 20 % veškerého vdechnutého kyslíku. Při srdeční zástavě proto dochází v mozkové tkáni velmi časně k poškození z nedostatku kyslíku, které rozhoduje o přežití pacienta se srdeční zástavou a jejích následcích. Prognóza mozkové hypoxie a její projevy závisí na tom, jak dlouho byl mozek vystaven nedostatku kyslíku a které jeho části byly poškozeny.

Problémy, se kterými se můžete po prodělané srdeční zástavě setkat

Poškození mozku po prodělané srdeční zástavě a psychické reakce na něj se mohou projevovat různým způsobem. Z psychologického hlediska lze tyto změny rozdělit do třech úrovní.

a) **ZMĚNY POCITŮ A NÁLAD**
Projevují se jako ztráta schopnosti prožívat radost, častá smutná až depresivní nálada, neschopnost zapojit se do komunikace s okolím, vnitřní napětí, neklid, vznětlivost až výbušnost.

b) **ZMĚNY V MYŠLENÍ**
Mezi tyto příznaky patří zhoršená paměť nebo pozornost, zpomalení tempa přemýšlení či řeči, obtíže v orientaci v čase nebo v prostoru, těžkosti v řešení každodenních problémů, neschopnost příjmu a vstřebávání nových informací.

c) **ZMĚNY V CHOVÁNÍ**
Změny v chování se mohou projevit narušením vztahů s blízkými osobami, neschopností komunikace s okolním světem, vyřazením z pracovního procesu, závislostí na druhých, tendencí unikat k nežádoucímu chování nebo závislostem

Pokud prožíváte některé z těchto problémů, můžete vyhledat pomoc odborníků a organizací, specializovaných na tyto problémy. **Psycholog** Vám může pomoci zjistit a pojmenovat Váš konkrétní problém a poradit Vám, jak a s kým ho můžete řešit. **Psychiatrická pomoc** je na místě v případě závažných obtíží, kdy může být nutná a prospěšná i farmakologická léčba. **Psychoterapeutická péče** obvykle spočívá v intenzivním diagnostickém a léčebném vztahu s vyškolenými psychology nebo psychiatry. Některé obtíže související s rehabilitací tělesnou, mentální i psychickou jsou předmětem zájmu a aktivity různých **organizací**, které sdružují osoby s podobnými problémy, snaží se jim poskytnout podmínky pro zlepšení stav, znovuzískání ztracených schopností nebo dovedností a návratu do běžného života. Mezi tyto organizace patří i **pacientské skupiny**, sdružující lidi s podobnými zdravotními obtížemi, jejichž cílem je sdílení zkušeností a zlepšování podmínek pro úspěšnou diagnostiku, léčbu a dlouhodobou mimonemocniční a rehabilitační péči podobně postižených pacientů.

Nezapomeňte také na **své blízké**, neboť i oni prožívají Vaše onemocnění s Vámi a v určitých fázích mohou čelit vysokému a bez pomoci těžko zvládnutelnému stupni zátěže. Začleňte je do procesu Vaší léčby, rehabilitace a do návratu zpět do normálního života! Můžete využít i služeb organizací, které pracují nejen s pacienty, ale i jejich s rodinnými příslušníky! Právě ty mohou dopřát prostor také Vašim nejbližším a usnadnit tak Vaši léčbu.

Možnosti, jak se s problémy po srdeční zástavě vyrovnat a kde hledat pomoc

Možnosti během Vašeho pobytu v IKEM:

Během Vašeho pobytu Vám budeme nápomocni poskytnutím potřebných informací, rehabilitační péčí a možností konzultace psychologa a neurologa.

Možnosti po propuštění z IKEM:

Pokud po propuštění z nemocnice zjistíte, že Váš celkový fyzický a psychický stav neodpovídá Vašim zkušenostem a očekáváním nebo pokud si Vaše okolí nevíš určitými věcmi ve vašem psychickém a fyzickém stavu rady, je vhodné vyhledat odbornou pomoc. V dalším textu jsme pro Vás připravili seznam odborných organizací, jejichž pomoci a asistence můžete využít. Do budoucna bychom rádi podpořili vznik svépomocné skupiny pacientů a lidí s podobným postižením a umožnili jim organizovat společná setkání a sdílet cenné zkušenosti.

PRAHA:

1. Cerebrum: tréninky kognitivních funkcí, fyzioterapii, ergoterapie, rekondiční pobyty, hipoterapie, poradenství
Křižíkova 56/75A, 186 00 Praha 8
+420 226 807 048
info@cerebrum2007.cz
www.cerebrum2007.cz

2. AV institut s.r.o.: zaměstnávání osob se zdravotními komplikacemi
Poděbradská 924/46B, 190 00 Praha 9
+420 230 233 603, +420 734 793 008;
info@sante-institut.cz
www.av-institut.cz

3. Klinika rehabilitačního lékařství: rehabilitační služby (ambulantní i lůžkové) pro pacienty s poškozením mozku - kognitivní, fatické, pohybové problémy
Albertov 7, 128 00 Praha 2
+420 224 968 491
???@???.cz
rehabilitace.lf1.cuni.cz

4. Oddělení kognitivních poruch, Národní ústav duševního zdraví: organizace léčby pacientů s kognitivními poruchami
Topolová 748, 250 67 Klecany
+420 283 088 160
ales.bartos@nudz.cz
www.nudz.cz

5. Pečující: organizace pomáhající laickým pečovatelům o chronicky nemocné
www.pecujici.cz
Šrobárova 50, Praha 10
+420 267 163 154
tamara.tosnerova@ecn.cz

6. Manuál ucelené péče na území Prahy pro lidi s poškozením mozku: na webu je přehledný rozcestník pro nabídku různých druhů služeb (neurolog, rehabilitace, psycholog, psychiatr...)
+420 774 372 796
info@navraty.info
www.navraty.info

7. Psychosomatická klinika: skupinová i individuální psychoterapie, fyzioterapie, psychiatrie, neurologie, komplexní péče o zdraví
Patočkova 712/3, 169 00 Praha 6
+420 233 351 741, +420 731 620 200
klinika@psychosomatika.cz
poradna@psychosomatika.cz
www.psychosomatika.cz

8. Psychoterapeutická a psychosomatická klinika ESET: péče o psychosomatická onemocnění, zaměření na stres, psychoterapie individuální i skupinová, vhodné i pro opatrovníky pacientů
Vejvanovského 1610, 149 00 Praha 4 - Jižní Město
+420 272 940 880
klinikaeset@volny.cz, info@klinikaeset.cz
www.klinikaeset.cz

BRNO:

1. Práh: kognitivní trénink (skupinové i individuální setkávání pacientů s poškozením mozku)
Tuřanská 12, 620 00 Brno
+420 545 229 339, +420 539 051 122
info@prah-brno.cz
www.prah-brno.cz

2. Klinika LOGO: soukromá klinika pomáhající lidem s poruchou komunikace na úrovni logopedie, kognitivního tréninku, ale i relaxace
www.moje-klinika.cz
Vsetínská 20, 639 00 Brno
+420 543 420 666, +420 543 232 323, +420 777 675 233
www.moje-klinika.cz/napiste-nam

HAVLÍČKŮV BROD:

1. Mnémé: kognitivní trénink
Jana Vejsadová, Jihlavská 3206, Havlíčkův Brod
+420 737 171 318
jana.vejsadova@gmail.com
info@mneme.cz
www.mneme.cz

JIHLAVA:

1. Psychoambulance: KBT psychoterapie s nácvikem, relaxace
Heleníská ulice 97, 586 01 Jihlava
+420 721 358 365
kbtjihlava@seznam.cz
www.psychoambulance.wz.cz

ROUDNICE NAD LABEM:

1. Psychoterapie roudnice nad Labem: kognitivní trénink
Lidická 1637, 413 01 Roudnice n. L.
+420 777 783 159, +420 603 210 933
info@psychoterapie-roudnice.cz
www.psychoterapie-roudnice.cz

CELÁ ČR:

1. Svaz postižených civilizačními chorobami v České republice, z. s.: 330 okresních organizací pomáhajících lidem s civilizačními chorobami, rehabilitační a rekondiční programy pro opětovné začlenění do společnosti
www.civilky.cz

Dostupná literatura pro laickou veřejnost:

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Křivohlavý, J. (2009). **Trénování paměti a poznávacích schopností.** Grada Publishing, a.s. Praha
Suchá, J. (2009). **Cvičte si svůj mozek-pracovní sešit pro pacienty s lehkou kognitivní poruchou (střední úroveň obtížnosti).** Gerontologické centrum Praha, Pfizer, spol. s.r.o.
Brockert, S. (1993). **Ovládání stresu.** Melantrich, Praha.

PC programy na trénink kognitivních funkcí:

- **NEUROP**, **HappyNeuron**, **CogRehab**, **CogMed** (přítomné v rehabilitačních střediscích)
- možnost PC programů pro nácvik kognitivních funkcí (tzv. brainjogging) na stránkách: **www.brainjogging.cz**

Informace o péči v různých městech by měl poskytnout každý Rehabilitační ústav nebo centra pro neurorehabilitaci.

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