HEALTH PLANS
UNIVERSITY OF UTAH

Medical Policy

Cognitive Rehabilitation Therapy

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Disclaimer:

1. Policies are subject to change in accordance with State and Federal notice requirements.
2. Policies outline coverage determinations for U of U Health Plans Commercial, CHIP and Healthy U (Medicaid) plans. Refer to the "Policy" section for more information.
3. Services requiring prior-authorization may not be covered, if prior-authorization is not obtained.
4. This Medical Policy does not guarantee coverage or payment of the service. The service must be a benefit in the member's plan and the member must be eligible for coverage at the time of service. Additional payment guidelines may be applied that are not included in this policy.

Description:

Cognitive rehabilitation therapy (CRT) is defined as a set of therapies designed to help improve damaged intellectual, perceptual, and behavioral skills, as opposed to sensorimotor skills or strictly emotional function. This therapy is directed toward "brain-behavior" deficits, such as attention, memory and learning, affect and expression, and executive functions. The goals of cognitive rehabilitation are to improve the patient's capacity to process and interpret information and to function in family and community life while maximizing their degree of return to their previous level of functioning. Ninety-five percent of rehabilitation facilities serving the needs of persons with brain injury provide some form of cognitive rehabilitation, including combinations of individual, group, and community-based therapies.

Policy Statement and Criteria

1. Commercial Plans/CHIP

U of U Health Plans covers cognitive rehabilitation therapy (CRT) as part of a comprehensive physical, occupational, and/or speech rehabilitation/therapy program for patients who have suffered either a cerebrovascular accident (CVA, stroke) or traumatic brain injury (TBI).

U of U Health Plans does NOT cover cognitive rehabilitation therapy (CRT) for any other indication as the lack of evidence to support clinical utility and statistical validity meets the plan's definition of experimental/investigational.

Conditions excluded from coverage include but are not limited to:

- Behavioral/psychiatric disorders such as addiction, attention-deficit/hyperactivity disorder (ADD/ADHD), bipolar disorder, depression, schizophrenia, social phobia, substance use disorders, and autism spectrum disorders (ASD)
- Brain tumors
- Cancer treatment that causes "chemobrain" or "chemofog"
- Cerebral palsy
- Cognitive decline in multiple sclerosis (MS)
- chronic obstructive pulmonary disease (COPD)
- Coma stimulation (aka the responsiveness program)
- Dementia (e.g., from Alzheimer's disease, HIV infection or Parkinson's)
- Intellectual or learning disabilities
- Long-haul Covid "brain fog"
- Treatment of epilepsy or seizure disorders

U of U Health Plans does NOT cover eye movement analysis (EyeBOX® device) for the evaluation and management of traumatic brain injury, concussions or any other indication, as it is considered investigational.

U of U Health Plans does NOT cover virtual reality (VR) therapy for rehabilitation of any acquired cognitive disorders (e.g., CVA/stroke, traumatic brain injury, and neurodegenerative diseases) or any other indications as VR therapy is considered experimental and investigational.

2. Medicaid Plans

Coverage is determined by the State of Utah Medicaid program; if Utah State Medicaid has no published coverage position and InterQual criteria are not available, the U of U Health Plans Commercial criteria will apply. For the most up-to-date Medicaid policies and coverage, please visit their website at: https://medicaid.utah.gov/utah-medicaid-official-publications/ or the Utah Medicaid code Look-Up tool

CPT/HCPCS codes covered by Utah State Medicaid may still require further evaluation to determine medical necessity for coverage.

Clinical Rationale

Behavioral/Psychiatric Disorders

In a 2021 meta-analysis, Therond et al., looked at the use of cognitive rehabilitation therapy (CRT) as an intervention in individuals with major depressive disorder (MDD), as they often experience cognitive deficits, to demonstrate improving cognition in psychiatric disorders. They analyzed results from 8 studies to estimate the effectiveness of CRT on global cognition and on 6 cognitive domains. These investigators also examined 3 potential moderators, namely session format (individual versus group), treatment duration, and participants' age. Cognitive rehabilitation therapy was found to improve global cognition ($g = 0.44$), verbal memory ($g = 0.60$), attention/ processing speed ($g = 0.41$), working memory ($g = 0.35$), and executive functioning ($g = 0.30$). The authors found no significant improvements for visuo-spatial memory and verbal fluency. In addition, no significant moderating effect of participant's age, session duration or session format were observed. The authors concluded that a moderate effect size and effectiveness varied between cognitive domains with the use of CRT in improving global cognition in adults with MDD. However, these conclusions were limited by a small number of studies, heterogeneity in cognitive measures, and the lack of indicators of everyday functioning.

In a 2022 systematic review, Shahmoradi et al., investigated 2 new emerging treatment approaches both in virtual reality (VR) and CRT that can be used to strengthen cognitive functions in patients, both children and adults, with autism spectrum disorder (ASD). The authors identified 688 studies related to this topic and then extracted the effects of interventions on cognitive outcomes. A total of 17 studies met the inclusion criteria, in which 226 persons with ASD had taken place. The sample size in the selected studies ranged from 1 to 56 participants (median of 8, Q1: 3.5, Q3: 15.5); 4 of the studies were case-control studies, 10 were pre-test/post-test studies, and 3 were randomized control trials (RCTs). Results of 16 studies showed significant progress in various cognitive indexes, such as task learning, attention, executive functioning, and daily skills in patients with ASD. In most studies, virtual technologies had beneficial effects on reducing cognitive problems, but existing limitations could reduce their effectiveness. Limitations of this review included the cost of VR devices, inappropriate size of software, the weight of devices, potential addiction, intolerance of wearing glasses or headsets by patients with autism (especially in children), and the possibility of eye injury. Drawbacks and challenges of the review included the difficulty of comparing studies due to the heterogeneity of the results and exclusion of published studies other than English language ones. In conclusion, the authors found that applying appropriate virtual-based approaches could improve cognitive indexes in patients with ASD. However, further, more robust studies are needed to examine the long-term effects of these technologies, along with improving the challenges and drawbacks found in this review.

Brain Tumors

A 2021 study (Weyer-Jamora et al.) assessed the effectiveness of post-acute cognitive rehabilitation across the continuum of care for adult patients with a brain tumor. Most treatment focus has been on acute rehabilitation, but emerging evidence supports outpatient and post-acute settings. The cognitive impairments including processing speed, attention, memory, and executive function resulted in positive outcomes with a multidisciplinary approach to treatment. Ongoing development of cognitive screenings and planning during the medical course of care are suggested to improve cognitive rehabilitation outcomes and supported in the clinical practice of treatment of this population. In conclusion, the authors found that the multidisciplinary approach and cognitive intervention was beneficial for cognitive outcomes in patients diagnosed with a brain tumor across programs. However, additional research is warranted to differentiate the specific outcomes resulting from cognitive rehabilitation for varying tumor grades and stages.

Dementia

A 2015 meta-analysis (Huntley et al) questioned if cognitive interventions in dementia improved general cognition. Thirty-three studies with interventions divided into categories such as cognitive training, cognitive stimulation, and cognitive rehabilitation were included. Studies classified as cognitive stimulation had a significant effect as measured on the Mini-Mental State Examination (MMSE) and the Alzheimer's Disease Assessment Scale-Cognitive Subscale (ADASCS). The authors concluded that cognitive stimulation improves scores on MMSE and ADAS-Cog in dementia, but benefits on the ADAS-Cog are generally not clinically significant and difficulties with blinding of patients and use of adequate placebo controls make comparison with the results of dementia drug treatments problematic. Therefore, further, more appropriate comparison studies are needed to demonstrate clinical significance.

A 2019 study (Bahar-Fuchs et al.,) assessed the use of CRT for people with mild to moderate dementia. Thirty three RCTs published between 1988 and 2018 were included in this study. Most RCTs were small and single-site, with sample sizes of 20 patients or below in each trial arm. Participants in most trials had a mean age between 70 and 80 years, and the presumed etiology of the cognitive dysfunction was Alzheimer dementia. Limitations of this study included lack of allocation concealment and lack of blinding of participants and personnel. In conclusion, based on low or very low quality evidence, the authors found no clear effect of CRT on any outcome, including global cognition and function, 3 to 12 months following treatment. Therefore, further studies with a longer duration of follow-up beyond 12 months post-treatment are needed.

In a 2019 multicenter RCT, Clare et al., outlined results on Individual Goal-oriented Cognitive Rehabilitation to Improve Everyday Functioning for People with Early-stage Dementia (GREAT). The study compared individual goal-oriented cognitive rehabilitation to treatment as usual in individuals with early-stage dementia. The majority of participants were diagnosed with Alzheimer dementia. Their mean age was 78.56 years, and their mean MMSE score was 23.82 points. The primary outcome was self-reported goal attainment at 3 months. Goals were identified using the semi-structured Bangor Goal Setting Interview (BGSI). Attainment was assessed based on a 0 to 10 scale. Reporting included self-reported self-efficacy (Generalized Self Efficacy Scale), mood (Hospital Anxiety and Depression Scale), dementia specific health related quality of life, memory (story recall from the Rivermead Behavioural Memory Test), attention (elevator counting and elevator counting with distraction subtests from the Test of Everyday Attention), or executive function (verbal letter fluency from the Delis-Kaplan Executive Function System). The authors noted that an improvement of 2 points in the goal attainment rating was considered to be clinically significant. In conclusion, the authors found that improvement in goal attainment was significantly greater in the therapy group than in the control group both at 3 months and at 9 months. However, no measure of functional ability was assessed and there were no significant between-group differences on any of the secondary outcomes at 3 or 9 months.

In a 2022 systematic review and meta-analysis, Kiper et al., stated that mild cognitive impairment (MCI), a neurodegenerative disease leading to Alzheimer's disease (AD) or dementia, is often associated with physical complaints. Combined physical and CRT has been employed to examine their effects on cognitive function; however, its impact on motor functions and activities of daily living (ADL) has not been explored yet. The combination of physical and cognitive training may be a valuable non-pharmacological intervention that could preserve motor function and quality of life (QOL). These authors examined if combined CRT is effective at improving motor performance in patients with an MCI. A systematic electronic literature search and a meta-analysis were performed. The following criteria were compulsory for inclusion in the study: RCT design; combined CRT compared to motor training alone or no intervention; motor outcomes as a study's endpoint. A total of 9 studies met the inclusion criteria. Results showed that CRT significantly enhanced balance compared to motor training alone (SMD 0.56; 95 % CI: 0.07 to 1.06; I2 = 59 %; 160 participants), whereas a significant improvement was found for mobility in the CRT group when compared to no intervention (MD -1.80; 95 % CI: -2.70 to -0.90; I2 = 0 %; 81 participants). However, there was no evidence that individuals with MCI experienced an increase in gait speed and QOL at the end of their practice sessions. Limitations of the report included a small number of studies (n = 5), low quality of reporting in some studies, and 3 studies were by the same authors, which made it impossible to detect whether the population analyzed in those studies were different or the same. In conclusion, the authors determined that further investigation with larger samples and a longer period of monitoring after intervention should be undertaken.

Cancer Treatment

A 2016 meta-analysis reported on neuropsychologic intervention for cognitive function in non-central nervous system (CNS) cancer survivors (Zeng et al). Three case-control studies and 7 RCTs with 433 patients (range, 22 to 98 patients), published between January 2010 and September 2015, were included. Most trials assessed the effects of the intervention immediately post-intervention or at short-term follow-up (≤ 6 months). More than half of the trials were conducted in breast cancer survivors. Three trials assessed the effects of cognitive rehabilitation programs and the weighted mean difference for the intervention effect at post-intervention follow-up was -0.19 (95% CI, -2.98 to 2.61). Limitations of the study included trials with small sample sizes. In conclusion, the authors found that neuropsychological interventions can improve cognitive function in non-CNS cancer survivors, however, further research is needed using larger sample sizes to confirm these findings.

In a 2019 systematic review, Fernandes et al., examined cognitive rehabilitation programs in adults with non-central nervous system (CNS) cancers. It included 1,124 participants (n range, 11 to 242) from 19 studies published between 2007 and 2018, of which the majority were RCTs (N=12). Waitlist was the most common comparator in the RCTs. As with the previous reviews, the authors found that most studies assessed the effects of the intervention immediately post-intervention or at short-term follow-up (≤ 6 months), and most trials were conducted in breast cancer survivors. The authors did not find any meta-analyses and limitations included that participants were not blinded to group assignment. Findings across the studies were mixed. In conclusion, the authors found that among the RCTs and nonrandomized controlled studies "87% found short-term improvements on at least one objective cognitive measure," which pertained to measurements taken immediately post-intervention. Therefore, among the longest-term (26-month follow-up) and largest trials (n=242) included, there were no significant effects on various objective cognitive measures. Only 63% of studies found improvements in short-term quality of life measures and none found any improvements in functional outcomes.

In a 2019 single-center small randomized control trial (N=46), Akel et al., evaluated CRT in children with cancer from an inpatient treatment clinic of the Department of Pediatric Oncology at University Hospital in Ankara, Turkey. Cognitive skills targeted by the CRT included place and time orientation, internal and external spatial perception, praxis, attention, visio-motor construction, and thinking operations. Children were characterized by a mean age of 10 years and 55% were male. Cancer diagnoses included non-Hodgkin lymphoma (40%), Hodgkin lymphoma (30%) and bone tumors (30%). Outcomes were evaluated only immediately post-intervention. Although compared to the routine therapy groups, numerically larger effect sizes for change in fatigue and functional independence were reported for the cognitive rehabilitation group. However, it is unknown whether the differences were clinically or statistically significant as the comparative treatment effects were not calculated and clinically significant difference were not pre-specified. In conclusion, the authors did find significant improvements in cognitive measures that were reported pre/post in the intervention group, however, no data was reported for the routine therapy group on this outcome. In addition to these inadequate outcome assessment methods, interpretation of these findings are limited by other methodological shortcomings including lack of blinding of participants and long-term follow-up. Since this evidence is not sufficient to draw conclusions on the effect of health outcomes, further, more robust studies are needed.

Coma Stimulation

In a 2002 systematic review Lombardi, et al., evaluated the effectiveness of sensory stimulation programs in patients in a coma or vegetative state. The Cochrane review evaluated randomized controlled trials and nonrandomized controlled clinical trials comparing any type of stimulation programs to standard rehabilitation in patients in a coma or vegetative state. Three studies, including (one randomized controlled trial and two nonrandomized controlled trials) with 68 traumatic brain injured patients in total, met the inclusion criteria. The overall methodological quality was poor, and the studies differed widely in terms of study design and conduct. Also, due to the diversity in reporting of outcome measures, a quantitative meta-analysis was not possible. None of the three studies in the Cochrane review provided useful and valid results on outcomes of clinical relevance for coma patients. The Cochrane researchers concluded that there is no reliable evidence to support or rule out the effectiveness of multisensory programs in patients in a coma or vegetative state. The researchers further stated that the need to improve knowledge in this field and the lack of effective treatments indicates that treatment interventions based on sensory stimulation should be provided only in the context of well-designed, adequately sized, randomized controlled trials.

A 2006 RCT of 60 patients was performed to determine the efficacy and benefits of early stimulation therapy in pediatric patients who were in a coma due to non-traumatic neurological insult (Karma and Rawat). Patients were randomized to the study group, who received stimulation to each of the six senses five times a day for two weeks (n=30) or to the control group, who received no stimulation (n=30). The level of consciousness was measured using the Glasgow Coma Scale (GCS) and AVPU (A = the child is awake and alert, or V = responds to voice, or P = responds to pain e.g., pinching or pulling frontal hair, or U = unconscious) scale prior to and after stimulation therapy. The authors reported statistically significant improvement in coma in the treatment group compared to the control group, as measured by GCS and AVPU when the stimulation started less than 15 days from onset of coma. In conclusion, the authors found that stimulation therapy can reduce the duration for children in non-traumatic coma. However, due to the small sample size and short duration of follow-up, larger studies are needed to affirm these results.

Li et al. (2021) performed a literature review on the progress of sensory stimulation (SS) to enhance coma arousal after traumatic brain injury. They included all original studies published in English with patients presenting severe disorders of consciousness due to traumatic brain injury who had received SS and whose behavioral/neural responses had been measured. Authors compared data on ten selected studies and analyzed the SS effects in comatose patient outcomes after TBI. They concluded that the literature suggests the SS program improves coma arousal after TBI. However, high-quality clinical trials are needed to establish standard SS protocols.

In a 2022 systematic review Weaver et al., assessed the effectiveness of interventions to improve arousal and awareness of people with disorders of consciousness (DoC) following a TBI. Twenty-seven studies were included and grouped thematically. The authors concluded that unimodal auditory stimulation, familiar voices telling structured stories, and transcranial direct current stimulation had a moderate level of evidence. Multimodal sensory stimulation had the strongest evidence in support of its use in clinical practice. However, further studies are needed to confirm these findings.

Eye Movement Assessment for TBI/Concussion

According to the FDA (2017), the EyeBOX® is an eye movement assessment aid which tracks patient's eye movements to provide an interpretation of the functional condition of the patient's brain. The EyeBOX is a 4-min test that was created to assist physicians in the evaluation of patients with suspected concussions and is appropriate for individuals aged 5 to 67 years. This device is an assessment aid that is not intended for standalone detection or diagnostic purposes.

In a 2018 systematic review and meta-analysis, Mani et al investigated the effect that TBI has on oculomotor functions (OM) from papers that objectively measured saccades and smooth-pursuit eye movements in mild and severe TBI. The overall impact of TBI on OM functions was moderate and significant with an effect size of 0.42 from 181 OM case-control comparisons. The heterogeneity, determined using the random effect model, was found to be significant ($Q (180) = 367$, $p < 0.0001$, $I2 = 51$) owing to the variety of OM functions (reflexive saccades, anti-saccades, memory-guided saccades, self-paced saccades and pursuits) measured and varying post-injury periods. The overall effect on OM functions were similar in mild and severe TBI despite differences in combined effect size of various OM functions. OM functions involving complex cognitive skills such as anti-saccades (in mild and severe TBI) and memory-guided saccades (in mild TBI) were the most adversely affected, suggesting that OM deficits may be associated with cognitive deficits in TBI. In conclusion, the authors found that TBI often results in long-standing OM deficits and the experimental measures of OM assessment reflect neural integrity and may provide a sensitive and objective biomarker to detect OM deficits following TBI. However, further, more robust studies are needed to demonstrate these findings.

In another 2018 systematic review and meta-analysis, Snegireva et al evaluated evidence for the use of eye-tracking technology in sports-related concussion assessment and monitoring. A search was run for literature published between January 1980 and May 2018. Included were empirical research studies in English where at least 50% of the research subjects were athletes, the subject were individuals with a diagnosis of concussion, and eye movements were measured using an eye-tracking device. Twenty one publications were integrated on sports-related concussion and eye-tracking technology, 9 of which qualified for the meta-analysis. Overall, the literature reported significant findings for variables in each of the 4 classes of eye-tracking measurements (movement, position, count, and latency). Meta-comparison was made for 7 variables for the acute concussions (the difference between the concussed and the control groups was significant for all of them) and 1 variable for the latent concussions (the difference was not significant). The authors concluded that most saccadic and pursuit deficits may be missed during clinical examination, and thus eye-tracking technology may be a useful and sensitive screening and monitoring tool for sports-related concussions. The inconsistencies between the eye movement metrics and methodology still make inferences challenging; however, using tasks that are closely related to brain areas involved in executive functions (such as memory-based saccade or anti-saccade tasks) in the acute injury phase holds promise in differentiating between athletes who have a concussion compared to those who do not.

Yaramothu et al (2019) noted that the Vergence Endurance Test (VET), a quantitative and objective eye movement assessment, was used to differentiate control from concussed subjects. A total of 9 symptomatic concussed (2 men; 30.8 ± 11 years) and 9 asymptomatic control (6 men; 25.1 ± 1.4 years) subjects participated in the VET. Symmetrical disparity vergence step targets were presented with and without visual distractors. A masked data analyst measured vergence latency, peak velocity, response amplitude, settling time, and the percentage of trials that contained blinks. A Binocular Precision Index (BPI) and a Binocular Accuracy Index (BAI) were calculated to quantify the changes that occur in the vergence parameters over the duration of the VET. Convergence and divergence peak velocity, divergence response amplitude, the percentage of trials that contained blinks during the transient portion of the response, and the BAI were significantly ($p < 0.05$) different between the concussed and the control subjects. For these parameters, the BAI and divergence response amplitude yielded the greatest accuracy, 78%, in their ability to discriminate between the groups. The authors found that the techniques developed within this study have the potential to evaluate the effectiveness of different vision therapy/vergence rehabilitation protocols leading to additional improvements in oculomotor function and treatments required for recovery post-concussion. However, further, more robust studies are needed to determine whether the trends observed here generalize to a larger population. By assessing the differences between control and concussed subjects and how vergence eye movements recorded during the VET may improve after therapeutic interventions or natural recovery.

In 2019, Vakil et al evaluated the "Context-Effect" (CE) which is the facilitation of memory for target stimuli due to the similarity of context in the learning and testing phases. Previous studies reported that traumatic brain injury (TBI) affects memory for contextual information when tested directly. However, the indirect effect of contextual information on memory of target (i.e., CE) is preserved. Several studies have demonstrated that CE is composed of multiple, distinct cognitive processes. The present study included 4 context conditions to enable identification of the exact process affected by TBI. In addition, eye movements were monitored to test 3 hypotheses: first, that the TBI group's dwell time on target (DTOT) at encoding would be less than that of controls. Second, that DTOT at encoding would be more highly associated with recognition at test for the control group than for the TBI group. Third, that overall DTOT at encoding on new, as compared to old items ("repetition effect"), would be less pronounced for the TBI group as compared to controls. A total of 24 patients with mild-to-severe TBI and 23 matched controls participated in this study. These researchers presented subjects with photographs of male faces shown wearing distinctive, trial-unique hats (yielding specific Target-Context pairing). Eye movements were recorded throughout the test task. Memory for faces following TBI is impaired compared to that of controls. The magnitude and pattern of CE were the same for both groups. The TBI group had a lower DTOT compared to that of controls. However, the relative length of DTOT in the various conditions was similar in both groups. The authors found that behavioral results indicated that although the TBI group had impaired memory for faces, the CE pattern was similar to that of controls. Similarly, in terms of eye movements, although the TBI group focused less on target, relations between the various conditions were similar in both groups. However, further, more robust studies are needed to confirm these findings in a larger population.

In 2020, Murray et al (2020) determined that smooth pursuit eye movements (SPEMs) and saccadic eye movements are both commonly impaired following sport-related concussion (SRC). Typical oculomotor assessments measure individual eye movements in a series of restrictive tests designed to isolate features such as response times. These measures lack ecological validity for athletes because athletes are adept at simple tasks designed for the general population. Yet, because eye movement metrics are sensitive and well-characterized neuroanatomically, it would be valuable to examine if athletes exhibit abnormal eye movements with more challenging tasks. To address this gap in knowledge, these researchers collected eye-tracking data during a sport-like task to gain insight on gaze behavior during active self-motion. SPEMs and saccadic eye movements were recorded during a sport-like visual task within 24 to 48 hours following SRC. A total of 36 Division I student-athletes were divided into SRC and control (CON) groups. All subjects completed 2 blocks of the Wii Fit© soccer heading game (WF) while wearing a monocular infra-red eye tracker. Eye movement classification systems quantified saccadic amplitude (SA), velocity (SV), and count (SC); as well as SPEM velocity (SPV) and amplitude (SPA). Separate Mann-Whitney U tests evaluated SPA and SC and found no significant effects (SPA, $p = 0.11$; SC, $p = 0.10$). A multi-variate analysis of variance for remaining variables revealed SPV was significantly greater in CON ($p < 0.05$), however, the SRC group had greater SA and SV ($p < 0.05$). The authors concluded that to maintain foveation during a sport-like task, SRC subjects used larger amplitude, faster saccades, but exhibited slower SPEMs. Furthermore, measuring oculomotor function during ecologically valid, sport-like tasks may serve as a concussion biomarker and provide insights into eye movement control following SRC. However, this is one of the first studies to provide evidence of abnormal SPEMs and saccades during a sport-line task. Thus, additional research is needed with larger studies to demonstrate these findings.

In another 2020 study, Horan et al) reviewed technological advances to provide an opportunity to refine tools that examine CNS performance. These researchers examined the test-retest reliability and convergent and ecological validity of a newly developed, virtual-reality, concussion assessment tool, "CONVIRT", which uses eye-tracking technology to examine visual processing speed, and manual reaction time (pushing a button on a riding crop) to evaluate attention and decision-making. Subjects (n = 165), were evaluated with CONVIRT, which uses virtual reality to give the user the experience of riding a horse during a horse-race. Subjects were also assessed with standard Cogstate computer-based concussion measures in-between 2 completions of the CONVIRT battery. The physiological arousal induced by the test batteries were assessed via measures of heart rate (HR) and HR variability (low-frequency (LF) to high-frequency (HF) ratio). Satisfactory test-retest reliability and convergent validity with Cogstate attention and decision-making subtests and divergent validity in visual processing speed measures were observed. CONVIRT also increased HR and LF/HF ratio, which may better approximate subject arousal levels in their work-place. The authors concluded that CONVIRT may be a reliable and valid tool to examine elements of cognition and CNS disruption. The increased ecological validity may also mean better informed "return-to-play" decisions and stronger industry acceptance due to the real-world meaningfulness of the assessment. However, further, more robust studies are needed to demonstrate the sensitivity of the CONVIRT tool and its battery before efficacy can be determined.

Finally, a 2020 UpToDate review on "Sideline evaluation of concussion" states that a number of tools are being developed to assist with the evaluation of athletes with a possible concussion. The King-Devick test consists of printed cards with numbers that the athlete reads to assesses saccadic eye movements. According to a 2017 systematic review of critical elements of sideline screening, this test shows promise in small studies as a possible sideline assessment tool. Head impact sensors (helmet sensors, or sensors in mouth guards, headbands, or directly applied to skin) have not been shown to provide helpful information to sideline evaluators about concussion. Some institutions are developing applications for smart phones and hand-held devices for on-field concussion assessment. Further study is needed before recommendations can be made about adopting such tools for sideline evaluation".

<u>Long-haul Covid "Brain Fog"</u>

In a retrospective, single-center, chart review, Olezena et al (2021) examined the functional impairments of a cohort of patients undergoing inpatient rehabilitation after surviving severe COVID-19 illness to better understand the ongoing needs of this patient population. This study consisted of consecutive patients hospitalized for COVID-19 and admitted to a regional inpatient rehabilitation hospital from April 29 to May 22, 2020. Patient demographics, clinical characteristics and complications from acute hospitalization were examined. Measures of fall risk (Berg Balance Scale), endurance (6 Minute Walk Test [6MWT]), gait speed (10 Meter Walk Test [10MWT]), mobility (transfer and ambulation independence), cognition, speech and swallowing (American Speech and Hearing Association National Outcomes Measurement System Functional Communication Measures) were evaluated at rehabilitation admission and discharge. The study population included 29 patients (70 % men, 58.6 % white, mean age of 59.5). The mean length of acute hospitalization was 32.2 days with a mean of 18.7 days intubated. Patients spent a mean of 16.7 days in inpatient rehabilitation and 90 % were discharged home. Patients demonstrated significant improvement from admission to discharge in measures of fall risk, endurance, gait speed, mobility, cognition, speech and swallowing, ($p < 0.05$). At discharge, a significant portion of the population continued to exhibit deficits in cognition (attention 37 %; memory 28 %; problem solving 28 %), balance (55 %) and gait speed (97 %). The authors concluded that patients admitted to inpatient rehabilitation following hospitalization with COVID-19 demonstrated deficits in mobility, cognition, speech and swallowing at admission and improved significantly in all of these domains by discharge. However, a significant number of patients exhibited residual deficits at discharge highlighting the post-acute care needs of this patient population. These researchers stated that study limitations included small sample size (n = 29), single-center, retrospective design and lack of standardized rehabilitation protocol for COVID-19 patients. Moreover, baseline functional status and psychiatric complications were not examined in this study.

Houben and Bonnechere (2022) stated that there is accumulating evidence that patients with severe COVID-19 disease may have symptoms that continue beyond the acute phase, extending into the early chronic phase. This prolonged COVID-19 pathology is often referred to as "Long COVID". Simultaneously, case investigations have shown that COVID-19 individuals might have a variety of neurological problems. The accurate and accessible assessment of cognitive function in patients post-COVID-19 infection is thus of increasingly high importance for both public and individual health. Little is known regarding the influence of COVID-19 on the general cognitive levels but more importantly, at sub-functions level. These researchers examined the current level of evidence supporting the negative impact of COVID-19 infection on cognitive functions. A total of 27 studies were included in the systematic review representing a total of 94,103 participants (90,317 COVID-19 patients and 3,786 healthy controls). These investigators then carried out a meta-analysis summarizing the results of 5 studies (959 participants, 513 patients) to quantify the impact of COVID-19 on cognitive functions. The overall effect, expressed in SMDs, was -0.41 (95 % CI: -0.55 to -0.27). The authors concluded that the COVID-19 crisis has profoundly changed society's organization and challenged the different healthcare systems. While re-validation services have been greatly impacted during the different waves (acute management of patients), rehabilitation specialists are now faced with the challenge of managing long-term complications. Among these complications, these investigators have shown in this review important complaints in cognitive functions. Even if most of these disorders diminish with time, on average 6 months after the 1st infection, it is important to develop strategies to improve the situation. There is currently little work that has been carried out focusing on the rehabilitation of cognitive functions; however, the current evidence suggests that the best option would be a combination of physical rehabilitation exercises combined with cognitive training. The latter can be performed using computerized solutions. In the future, it is important to think about the best way to integrate cognitive stimulations within physical rehabilitation since cognitive disorders are frequently associated with many pathologies requiring rehabilitation, not only COVID-19 as have been discussed in this paper, but also for example stroke, multiple sclerosis, and Parkinson's disease.

Bertuccelli et al (2022) stated that severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is a worldwide public health issue. Almost 2 years into the pandemic, the persistence of symptoms following the acute phase is a well-recognized phenomenon. These investigators carried out a scoping review to map cognitive domain impairments, their frequency, and associated psycho-affective disorders in individuals with a previous COVID-19 infection. They searched PubMed/Medline, Scopus, and PsycInfo to identify relevant reports published between December 1, 2019 and February 21, 2022. These researchers followed the PRISMA extension for scoping review guidelines. A total of 3 independent reviewers selected and charted 25 records out of 922. Memory, attention, and executive functions appeared to be the most affected domains. Delayed recall and learning were the most impaired domains of memory. Among the executive functions, abstraction, inhibition, set shifting, as well as sustained and selective attention were most commonly impaired. Language and visuo-spatial abilities were rarely affected, although this finding might be biased by the scarcity of reports. Neurological and respiratory conditions were often reported in association with cognitive deficits. Results on psycho-affective conditions were inconclusive due to the low frequency of reported data. Admission to an intensive care unit (ICU) is not related to cognitive deficits. This review highlighted a potential effect of a previous post-COVID-19 infection on a pattern of memory, attention, and executive functions impairments. These investigators stated that these findings need to be confirmed on larger cohorts with comprehensive neuropsychological batteries and correlated to neurophysiological and neurobiological substrates. The authors stated that despite rising evidence, a clear picture of the cognitive alterations following COVID-19 infection is missing. Characterizing the post-COVID-19 pattern of cognitive impairments and their frequency will contribute to a better understanding of its pathophysiology. The final aim is to set up appropriate care and rehabilitation pathways.

National Institute for Health and Clinical Excellence (NICE)'s guideline on long COVID (Venkatesan, 2022) does not mention the use of cognitive rehabilitation. In 2021, NICE issued a rapid guideline on managing the long-term effects of COVID-19. The guideline recommends using a "multidisciplinary approach to guide rehabilitation, including physical, psychological and psychiatric aspects of management." Cognitive rehabilitation was not specifically addressed. Assessing the clinical effectiveness of "different service models of multimodality/multidisciplinary post-COVID-19 syndrome rehabilitation in improving patient-reported outcomes (such as quality of life)" was listed as a key recommendation for research.

Furthermore, an UpToDate's "Patient education: Recovery after COVID-19 (The Basics) "written by the doctors and editors at UpToDate" (January 4, 2023) as well as UpToDate reviews on "COVID-19: Evaluation and management of adults following acute viral illness (long COVID)" (Mikkelsen and Abramoff, 2022) and "Geriatric rehabilitation interventions" (Hoenig and Cary, 2022) do not mention cognitive rehabilitation as a management / therapeutic option.

Other Neurological Disorders

A 2018 systematic review of literature from 2007 through 2016 (Goverover et al) determined clinical recommendations for cognitive rehabilitation of people with multiple sclerosis (MS), based on Searches of Medline, PsycINFO, and CINAHL with a combination of the following terms: attention, awareness, cognition, cognitive, communication, executive, executive function, language, learning, memory, perception, problem solving, reasoning, rehabilitation, remediation, training, processing speed, and working memory. A total of 129 articles were identified and underwent initial screening; 59 articles were selected for inclusion after initial screening; and 19 studies were excluded after further detailed review; 40 studies were fully reviewed and evaluated. Articles were assigned to 1 of 6 categories, including:

- Attention,
- Learning and memory,
- Processing speed and working memory,
- Executive functioning,
- Metacognition, or
- Non-specified/combined cognitive domains

This authors yielded 6 class I studies, 10 class II studies, and 24 class III studies. One intervention in the area of verbal learning and memory received support for a practice standard, 2 computer programs received support as practice guidelines (in the area of attention and multi-cognitive domains), and several studies provided support for 5 practice options in the domains of attention and learning and memory. In conclusion, the authors found that substantial progress has been made since the previous review regarding the identification of effective treatments for cognitive impairments in persons with MS. However, they stated that much work remains to be done to optimize rehabilitation potential by applying the most methodologically rigorous research designs to provide more class I evidence in support of a given treatment strategy.

In 2020 Svaerke et al., assessed the deterioration of working memory (WM) as a common cognitive deficit in Parkinson's disease (PD), which severely influences the ability to lead an independent life. Interventions that could delay the impact of WM deficits could positively impact the independence and QOL of patients. Authors of included studies were contacted to detect unpublished data or articles not found by database-search. Broad selection criteria were applied because literature was expected to be limited. Studies were eligible for inclusion if they examined the effects of CBCRT on WM in a sample consisting of at least 50% PD patients, or in which the results of PD patients could be isolated. Studies were further eligible for inclusion in a planned meta-analysis if the effects of the CBCRT intervention could be isolated, the CBCRT intervention was compared to active or passive control groups consisting solely of PD patients, and the WM outcome measure could be isolated. Only 6 studies were included despite broad inclusion criteria. Study results were heterogeneous, and the risk of bias in study methodology was either unclear or high; 2 studies were eligible for meta-analysis. A meta-analysis was not performed because these studies used different measures of WM that were not rated as equally valid and reliable. In conclusion, the authors found that existing literature is sparse and provides insufficient evidence to conclude if CBCRT benefits WM in PD patients. The authors found several drawbacks this study. First, the small number of studies that met the inclusion criteria for this meta-analysis limited the precision of the publication bias. Furthermore, the lack of data or the use of different methods in the analyses limited the possibility of making a comparison between all the studies included in the systematic review. On the one hand, the variability of trained cognitive functions allowed studies divided by different cognitive domains to be compared, although not all the cognitive domains were trained in all the studies and so, in some cases, the comparison would be limited. On the other hand, some of the studies measured the cognitive domains differently. Thus, when the specific cognitive domains were grouped according to the tests used, only studies that reported those tests independently could be included.

In a 2021 systematic review and meta-analysis, Sanchez-Luengos et al., evaluated the effectiveness of CRT in non-demented PD patients cognitive deficits. In order to reduce the impact of cognitive impairment in PD, CRT programs have been developed. A total of 12 articles were selected according to PRISMA guidelines that demonstrated attention, working memory, verbal memory, executive functions and processing speed were the most frequently improved domains. Results showed moderate effects on global cognitive status (g = 0.55) and working memory (g = 0.50); small significant effects on verbal memory (g = 0.41), overall cognitive functions (g = 0.39) and executive functions (g = 0.30); small non-significant effects on attention (g = 0.36), visual memory (g = 0.29), verbal fluency (g = 0.27) and processing speed (g = 0.24); and no effect on visuo-spatial and visuo-constructive abilities (g = 0.17). Depressive symptoms showed small effect (g = 0.24) and QOL showed no effect (g = -0.07). A meta-regression was carried out to examine moderating variables of overall cognitive function effects, although moderators did not explain the heterogeneity of the improvement following CRT. The authors concluded that these findings suggested that CRT may be beneficial in improving cognition in non-demented PD patients, although further studies are needed to analyze the effectiveness of CRT in patients with PD at the cognitive level and on the instrumental ADL, functionality and QOL. Furthermore, it would be interesting to analyze individual factors such as age, lifestyle, personality and genetic factors, which may be applicable to personalized medicine, in order to design more specific and individualized interventions.

Stroke-CVA/Traumatic Brain Injury (TBI)

A Hayes health technology assessment (2017-reviewed 2021) observed that cognitive rehabilitation therapy (CRT) for traumatic brain injury (TBI) can improve cognitive functioning. Overall, the report concluded, however, that "the efficacy of cognitive rehabilitation, and which forms are most effective, are not possible at this time due to heterogeneity in the patient populations (comorbid conditions, variable time since TBI, nature and severity of injury), variability in the targeted domains and outcome measures, and heterogeneity in treatment characteristics (components of therapy as well as the setting, intensity, duration of treatment)”.

A Cochrane analysis in 2017 (Kumar et al.) reported that there is insufficient good-quality evidence to support the role of cognitive rehabilitation when compared to no intervention or conventional rehabilitation in improving return to work, independence in ADL, community integration or quality of life in adults with TBI. There is moderate-quality evidence that cognitive rehabilitation, as an in-home program, is like hospital-based cognitive rehabilitation in improving return to work status among active duty military personnel with moderate-to-severe TBI. Moderate-quality evidence suggests that two strategies do not differ in achieving return to work in veterans or military personnel with TBI.

In a 2019 systematic review Cicerone et al., evaluated cognitive rehabilitation in a total of 491 articles (109 class I or IA, 68 class II, and 314 class III). These articles made 29 recommendations for evidence-based practice of cognitive rehabilitation (9 Practice Standards, 9 Practice Guidelines, and 11 Practice Options). Evidence from this review supports Practice Standards for attention deficits after TBI or stroke; visual scanning for neglect after right-hemisphere stroke; compensatory strategies for mild memory deficits; language deficits after left-hemisphere stroke; social-communication deficits after TBI; metacognitive strategy training for deficits in executive functioning; and comprehensive-holistic neuropsychological rehabilitation to reduce cognitive and functional disability after TBI or stroke.

A 2019 multicenter, assessor-blinded, RCT (das Nair et al) was conducted to evaluate a group memory rehabilitation program for people with TBI in 9 sites in England. The program included 328 patients and involved 10 weekly sessions, each lasting about 1.5 hours, which were delivered by a trained Assistant Psychologist to groups of between 4 to 6 participants. The intervention focused on retraining memory functions and strategies to improve encoding and retrieval. The control group received usual care, which typically included employment rehabilitation services, self-help groups, or specialist charity support. Between 2013 and 2015, 328 individuals were randomized to therapy (N=171) or usual care (N=157). The participants were characterized by a mean age of 45.1 years, median GCS closest to admission of 11.5 (25th, 75th centile=6, 14), a length of initial hospital stay for TBI of 84.2 days, and time since TBI of 100.9 months. Limitations of the study included lack of an active control arm, incomplete assessment of intervention fidelity, and exclusion of over 20% of the sample from the primary analysis. On the primary outcome of frequency of memory failures in daily life assessed using the Everyday Memory Questionnaire-patient version at 6 months’ follow-up, the between-group difference was not clinically important (adjusted difference in mean scores –2.1 ; 95% confidence interval [CI] –6.7 to 2.5; p=.37). For secondary outcomes, there was a significant improvement in goal attainment both at 6 and 12 months, but no differences on others such as mood or quality of life. In conclusion, the authors found that the group memory rehabilitation delivered in this trial is very unlikely to lead to clinical benefits or to be a cost-effective treatment for people with TBI in the community. Therefore, future studies should examine the selection of participants who may benefit most from memory rehabilitation.

In a 2019 systematic review, Svaerke et al., assessed studies concerning the effects of computer-based cognitive rehab therapy (CBCRT) on visuospatial neglect (VN) after stroke, to summarize the current state of knowledge in this research field and make recommendations for future research. A total of 4 electronic databases were systematically searched. Authors of relevant studies were contacted to detect unpublished data or articles not found by searching databases. Data were extracted from included studies using predefined coding schemes and characteristics and results of individual studies were summarized qualitatively. Studies were included if at least 50% of the included patients had a stroke, if the studies explored the effects of CBCRT as a primary intervention for rehabilitation of VN and if they included neuropsychological outcome measures for the presence of VN. A total of 7 studies were included; 6 of the 7 studies suggested positive effects of CBCRT on VN after stroke. Limitations include that the studies consisted of small samples, varied greatly in design and had various methodological quality. In conclusion, the authors found that it is not currently possible to either support or reject the effects of CBCRT on VN after stroke, as the existing literature is very sparse and studies have various methodological limitations. Therefore, further, more robust studies are needed to compare CBCRT with active and passive control conditions in randomized and blinded designs to determine health outcomes.

Alashram et al (2023) stated that TBI can cause numerous cognitive deficits. These deficits are associated with disability and reduction in QOL. Non-invasive brain stimulation (NIBS) provides excitatory or inhibitory stimuli to the cerebral cortex. In a systematic review, these investigators examined the effectiveness of NIBS (i.e., transcranial magnetic stimulation [rTMS] and transcranial direct current stimulation [tDCS]) on cognitive functions in patients with TBI. PubMed, SCOPUS, PEDro, CINAHL, Medline, REHABDATA, and Web of Science were searched from inception to May 2021. The risk of bias in the RCTs was assessed using the Cochrane Collaboration's instrument. The Physiotherapy Evidence Database (PEDro) scale was employed to examine the risk of bias in the non-RCTs. A total of 10 studies met the inclusion criteria – 6 studies used rTMS, and 4 used tDCS as cognitive rehabilitation interventions. The results showed heterogenous evidence for the effects of rTMS and tDCS on cognitive function outcomes in individuals with TBI. The authors concluded that the evidence for the effects of NIBS on cognition following TBI was limited; tDCS and rTMS were safe and well-tolerated interventions post-TBI. However, the optimal stimulation sites and stimulation parameters remain unknown. These researchers stated that combining NIBS with traditional rehabilitation interventions may contribute to greater enhancements in cognitive functions post-TBI.

UpToDate has a multitude of studies that discuss cognitive rehabilitation. Some examples are dementia, epilepsy, post-concussion syndrome, multiple sclerosis and in cancer survivors after treatment. The following are conclusions made from these studies: “Cognitive rehabilitation techniques (for multiple sclerosis) are another approach, but data related to clinical application of these methods are limited. Further research into the application of cognitive rehabilitation techniques is clearly needed.” “Studies regarding the efficacy of this approach (cognitive therapy) are limited by the lack of standardized techniques (for dementia).” “Cognitive rehabilitation for cancer patients is not yet based on solid evidence-based research and oftentimes uses the guidelines approached for traumatic brain injury and stroke patients.” “Formal neuropsychologic assessment and cognitive rehabilitation, although understudied, may be helpful for some patients with cognitive complaints. Only small studies have shown the role of cognitive rehabilitation to improve memory after temporal lobe epilepsy surgery.” Therefore, further, more robust studies are needed to prove the effectiveness of cognitive rehab with epileptic patients. “The use of cognitive rehabilitation for cognitive difficulties after mild TBI is controversial. Although a systemic review found good support for its use in military/veteran populations, studies in other populations are lacking.” “Interventions aimed at developing compensatory strategies for cognitive issues prior to or during treatment for cancer have been studied in breast cancer populations and in children treated for leukemia. However, there are few randomized clinical trials assessing many of these interventions in cancer patients or survivors.”

A large body of literature suggests that cognitive rehabilitation therapies may improve cognitive functioning as measured by neuropsychological tests; mostly in patients with TBI. There is evidence that it may be valuable in post stroke patients. However, there is not enough evidence to recommend this therapy for the remainder of the neurologic disorders (e.g., multiple sclerosis, Parkinson’s disease, dementia, epilepsy, etc.) or in the treatment of cognitive problems resulting from cancer treatments ("chemobrain" or "chemofog"). As there is great heterogeneity in therapy methods, which limits conclusions about which techniques are most effective, and a lack of literature examining whether these cognitive changes result in any functional or health improvements over time.

Cognitive rehabilitation therapy (CRT) has been proposed for numerous other conditions that cause, or may cause, impaired cognitive function, including:

- ADD, ADHD
- Cerebral palsy
- COPD
- Developmental delay
- Learning disabilities
- Pervasive developmental disorders
- Seizure disorders

There is insufficient evidence in the published medical literature to support the use of CRT for these conditions. The role of CRT for the treatment of conditions other than moderate to severe traumatic brain injury or stroke/cerebral infarction has not been established.

Applicable Coding

<u>CPT Codes</u>

<u>Possibly Covered:</u>

96125	Standardized cognitive performance testing (eg, Ross Information Processing Assessment) per hour of a qualified health care professional's time, both face-to-face time administering tests to the patient and time interpreting these test results and preparing the report
97129	Therapeutic interventions that focus on cognitive function (eg, attention, memory, reasoning, executive function, problem solving, and/or pragmatic functioning) and compensatory strategies to manage the performance of an activity (eg, managing time or schedules, initiating, organizing, and sequencing tasks), direct (one-on-one) patient contact; initial 15 minutes
97130	; each additional 15 minutes (List separately in addition to code for primary procedure)
92507	Treatment of speech, language, voice, communication, and/or auditory processing disorder; individual

<u>Not Covered:</u>

0770T	Virtual reality technology to assist therapy (List separately in addition to code for primary procedure)

<u>HCPCS Codes</u>

<u>Not covered:</u>

S9056	Coma stimulation per diem

References:

1. Akel BS, Åahin S, Huri M, et al. Cognitive rehabilitation is advantageous in terms of fatigue and independence in pediatric cancer treatment: a randomized-controlled study. Int J Rehabil Res. Jun 2019; 42(2): 145-151. PMID 30741725
2. Alashram AR, Padua E, Annino G. Noninvasive brain stimulation for cognitive rehabilitation following traumatic brain injury: A systematic review. Appl Neuropsychol Adult. 2023;30(6):814-829.

3. Bahar-Fuchs, A., A. Martyr, A. M. Goh, J. Sabates and L. Clare (2019). "Cognitive training for people with mild to moderate dementia." Cochrane Database Syst Rev 3(3): CD013069.
4. Bertuccelli M, Ciringione L, Rubega M, et al. Cognitive impairment in people with previous COVID-19 infection: A scoping review. Cortex. 2022;154:212-230.
5. Cicerone KD, Goldin Y, Ganci K, et al. Evidence-Based Cognitive Rehabilitation: Systematic Review of the Literature From 2009 Through 2014. Arch Phys Med Rehabil. 2019;100(8):1515-1533. doi: 10.1016/j.apmr.2019.02.011
6. Clare L, Kudlicka A, Oyebode JR, et al. Individual goal-oriented cognitive rehabilitation to improve everyday functioning for people with early-stage dementia: A multicentre randomised controlled trial (the GREAT trial). Int J Geriatr Psychiatry. May 2019; 34(5): 709-721. PMID 30724405
7. das Nair R, Bradshaw LE, Carpenter H, et al. A group memory rehabilitation programme for people with traumatic brain injuries: the ReMemBrIn RCT. Health Technol Assess. Apr 2019; 23(16): 1-194. PMID 31032782
8. Fernandes HA, Richard NM, Edelstein K. Cognitive rehabilitation for cancer-related cognitive dysfunction: a systematic review. Support Care Cancer. Sep 2019; 27(9): 3253-3279. PMID 31147780
9. Food and Drug Administration (FDA). (2017). De Novo Classification Request for EyeBOX®. Submission #DEN170091. Device Type: Traumatic Brain Injury Eye Movement Assessment Aid. Regulation #21 CFR 882.1455. Accessed: August 8, 2024. Available at: https://www.accessdata.fda.gov/cdrh_docs/reviews/DEN170091.pdf
10. Goverover Y, Chiaravalloti ND, O'Brien AR, DeLuca J. Evidenced-based cognitive rehabilitation for persons with multiple sclerosis: An updated review of the literature from 2007 to 2016. Arch Phys Med Rehabil. 2018;99(2):390-407.
11. Hayes®, Inc. (2017). "Cognitive Rehabilitation Therapy For Traumatic Brain Injury (TBI)". Annual Review: Nov 4, 2021. Accessed: April 16, 2024. Available at: https://evidence.hayesinc.com/report/dir.cognitivetbi605
12. Hoenig H, Cary M. Geriatric rehabilitation interventions. UpToDate [online serial]. Waltham, MA: UpToDate; reviewed December 2022.
13. Horan B, Heckenberg R, Maruff P, Wright B. Development of a new virtual reality test of cognition: Assessing the test-retest reliability, convergent and ecological validity of CONVIRT. BMC Psychol. 2020;8(1):61.
14. Houben S, Bonnechere B. The impact of COVID-19 infection on cognitive function and the implication for rehabilitation: A systematic review and meta-analysis. Int J Environ Res Public Health. 2022;19(13):7748.
15. Huntley JD, Gould RL, Liu K, et al. Do cognitive interventions improve general cognition in dementia? A meta-analysis and meta-regression. BMJ Open. Apr 02 2015; 5(4): e005247. PMID 25838501
16. Karma D, Rawal AK. Effect of stimulation in coma. Indian Pediatr. 2006. Oct; 43(10):856-60.
17. Kiper P, Richard M, Stefanutti F, et al. Combined motor and cognitive rehabilitation: The impact on motor performance in patients with mild cognitive impairment. Systematic review and meta-analysis. J Pers Med. 2022;12(2):276.
18. Kumar, K. S., S. Samuelkamaleshkumar, A. Viswanathan and A. S. Macaden (2017). "Cognitive rehabilitation for adults with traumatic brain injury to improve occupational outcomes." Cochrane Database Syst Rev 6(6): CD007935.
19. Li J, Cheng Q, Liu FK, Huang Z, Feng SS. Sensory stimulation to improve arousal in comatose patients after traumatic brain injury: a systematic review of the literature. Neurol Sci. 2020;41(9):2367-2376. doi:10.1007/s10072-020-04410-9
20. Lombardi F, Taricco M, De Tanti A, Telaro E, Liberati A. Sensory stimulation of brain-injured individuals in coma or vegetative state. Cochrane Database of Systematic Reviews 2002, Issue 2, Art No. CD001427.
21. Mani R, Asper L, Khuu SK. Deficits in saccades and smooth-pursuit eye movements in adults with traumatic brain injury: A systematic review and meta-analysis. Brain Inj. 2018;32(11):1315-1336.
22. Mikkelsen ME, Abramoff B. COVID-19: Evaluation and management of adults following acute viral illness (Long COVID). UpToDate [online serial]. Waltham, MA: UpToDate; reviewed December 2022.
23. Mitchell S, Bradley VA, Welch JL, Britton PG. Coma arousal procedure: a therapeutic intervention in the treatment of head injury. Brain Injury 1990;4(3):273–279.
24. Murray NG, Szekely B, Islas A, et al. Smooth pursuit and saccades after sport-related concussion. J Neurotrauma. 2020;37(2):340-346.
25. National Institute for Health and Care Excellence (NICE). COVID-19 rapid guideline: managing the long-term effects of COVID-19 [NG188]. November 11, 2021; https://www.nice.org.uk/guidance/ng188
26. National Institute of Neurological Disorders and Stroke (NINDS). Disorders. Coma Information Page. Date last modified: May 24, 2017. Accessed May 22, 2023. Available at URL address: https://www.ninds.nih.gov/Disorders/All-Disorders/Coma-Information-Page
27. Olezene CS, Hansen E, Steere HK, et al. Functional outcomes in the inpatient rehabilitation setting following severe COVID-19 infection. PLoS One. 2021;16(3):e0248824.
28. Richard NM, Bernstein LJ, Mason WP, et al. Cognitive rehabilitation for executive dysfunction in brain tumor patients: a pilot randomized controlled trial. J Neurooncol. May 2019; 142(3): 565-575. PMID 30847839
29. Sanchez-Luengos I, Balboa-Bandeira Y, Lucas-Jimenez O. Effectiveness of cognitive rehabilitation in Parkinson's disease: A systematic review and meta-analysis. J Pers Med. 2021;11(5):429.
30. Shahmoradi L, Rezayi S. Cognitive rehabilitation in people with autism spectrum disorder: A systematic review of emerging virtual reality-based approaches. J Neuroeng Rehabil. 2022;19(1):91.

31. Snegireva N, Derman W, Patricios J, Welman KE. Eye tracking technology in sports-related concussion: A systematic review and meta-analysis. Physiol Meas. 2018;39(12):12TR01.
32. Svaerke K, Niemeijer M, Loekkegaard A. The effects of computer-based cognitive rehabilitation on working memory in patients with Parkinson's disease: A systematic review. J Parkinsons Dis. 2020;10(1):47-57.
33. Svaerke K, Niemeijer M, Mogensen J, Christensen H. The effects of computer-based cognitive rehabilitation in patients with visuospatial neglect following stroke: A systematic review. Top Stroke Rehabil. 2019;26(3):214-225.
34. Therond A, Pezzoli P, Abbas M, et al. The efficacy of cognitive remediation in depression: A systematic literature review and meta-analysis. J Affect Disord. 2021;284:238-246.
35. UpToDate. Patient education: Recovery after COVID-19 (The Basics). UpToDate [online serial]. Waltham, MA: UpToDate; January 4, 2023.
36. UpToDate®. "Cognitive function after cancer and cancer treatment" Topic last updated: Jan 18, 2023. Literature current through: March 2024. Topic: 16347. Version: 27.0 Accessed: April 16, 2024. Available at: https://www.uptodate.com/contents/cognitive-function-after-cancer-and-cancer-treatment?search=cognitive%20rehabilitation&source=search_result&selectedTitle=2%7E46&usage_type=default&display_rank=2#H811910843
37. UpToDate®. "Comorbidities and complications of epilepsy in adults". Topic last updated: Aug 03, 2023. Literature current through: Mar 2024. Topic: 114559. Version: 29.0. Accessed: April 16, 2024. Available at: https://www.uptodate.com/contents/comorbidities-and-complications-of-epilepsy-in-adults?search=cognitive%20rehabilitation&source=search_result&selectedTitle=6%7E46&usage_type=default&display_rank=6#H739439901
38. UpToDate®. "Management of the patient with dementia". Topic last updated: Feb 22, 2023. Literature current through: Mar 2024. Topic: 5080. Version: 29.0. Accessed: April 16, 2024. Available at: https://www.uptodate.com/contents/management-of-the-patient-with-dementia?search=cognitive+rehabilitation&source=search_result&selectedTitle=8%7E46&usage_type=default&display_rank=8
39. UpToDate®. "Physical rehabilitation for cancer survivors". Topic last updated: Jan 24, 2023. Literature current through: Mar 2024. Topic: 2827. Version: 35.0. Accessed: April 16, 2024. Available at: https://www.uptodate.com/contents/physical-rehabilitation-for-cancer-survivors?search=cognitive%20rehabilitation&source=search_result&selectedTitle=9%7E46&usage_type=default&display_rank=9#H1241210
40. UpToDate®. "Postconcussion Syndrome" Topic last updated: Jul 30, 2021. Literature current through: March 2024. Topic: 5091. Version: 33.0 Accessed: April 16, 2024. Available at: https://www.uptodate.com/contents/postconcussion-syndrome?search=cognitive%20rehabilitation&source=search_result&selectedTitle=3%7E46&usage_type=default&display_rank=3#H3933537658
41. UpToDate®. "Sideline Evaluation of Concussion". Topic last updated: September 29, 2023. Litrature current through: July 2024. Accessed: August 8, 2024. Available at: https://www.uptodate.com/contents/sideline-evaluation-of-concussion?search=Sideline%20evaluation%20of%20concussion&source=search_result&selectedTitle=1%7E111&usage_type=default&display_rank=1#H8087873
42. UpToDate®. "Symptom management of multiple sclerosis in adults" Topic last updated: Oct 05, 2023. Literature current through: Mar 2024. Topic: 1690. Version: 40.0. Accessed: April 16, 2024. Available at: https://www.uptodate.com/contents/symptom-management-of-multiple-sclerosis-in-adults?search=cognitive%20rehabilitation&source=search_result&selectedTitle=7%7E46&usage_type=default&display_rank=7#H1126331
43. Vakil E, Aviv O, Mishael M, et al. Direct and indirect measures of context in patients with mild-to-severe traumatic brain injury (TBI): The additive contribution of eye tracking. J Clin Exp Neuropsychol. 2019;41(6):644-652.
44. Venkatesan P. NICE guideline on long COVID. Lancet Respir Med. 2021;9(2):129.
45. Weaver, J. A., K. Watters and A. M. Cogan (2023). "Interventions Facilitating Recovery of Consciousness Following Traumatic Brain Injury: A Systematic Review." OTJR (Thorofare N J) 43(2): 322-336.
46. Weyer-Jamora C, Brie MS, Luks TL, Smith EM, Hervey-Jumper SL, Taylor JW. Postacute Cognitive Rehabilitation for Adult Brain Tumor Patients. Neurosurgery. 2021 Nov 18;89(6):945-953. doi: 10.1093/neuros/nyaa552. PMID: 33586764; PMCID: PMC8600173.
47. Yaramothu C, Greenspan LD, Scheiman M, Alvarez TL. Vergence endurance test: A pilot study for a concussion biomarker. J Neurotrauma. 2019;36(14):2200-2212.
48. Zeng Y, Cheng AS, Chan CC. Meta-Analysis of the Effects of Neuropsychological Interventions on Cognitive Function in Non-Central Nervous System Cancer Survivors. Integr Cancer Ther. Dec 2016; 15(4): 424-434. PMID 27151596