HEALTH PLANS
UNIVERSITY OF UTAH

Medical Policy

Flicker Fusion

Policy MP-047

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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:

Sensory function, particularly in the visual domain, has long been studied in the context of cognitive aging. Common explanations for this connection are that sensory failure in older individuals is both a gateway to cognitive decline (e.g., by reducing informational input) and/or a biomarker for deleterious change in the brain. Although changes in spatial vision, when well characterized, do appear to predict age-related changes in at least some aspects of cognitive performance, perhaps an even better measure is processing speed. Visual processing speed is one of the most common modalities tested and can be assessed relatively simply.

Critical flicker fusion frequency (CFF or CFFF) is defined as the frequency at which flickering light can be perceived as continuous and it is used to assess the processing of temporal vision. The upper level of one's abilities in visual processing is described as the critical flicker fusion threshold (or threshold for flicker fusion, TFF), which represents the maximum speed of flickering light that can be perceived by the visual system. Because of its efficiency in detecting rapid changes, it is used as an index of cerebral nervous system (CNS) function that is described as alertness and cortical arousal in humans. CFF has been used in various clinical circumstances such as encephalopathy, epilepsy, dementia, obstructive sleep apnea and other conditions. The clinical evidence, however, remains insufficient to permit conclusions on the health outcome effects of critical flicker fusion in the diagnosis of visual acuity.

Policy Statement and Criteria

1. Commercial Plans/CHIP

U of U Health Plans considers critical flicker fusion (CFF) experimental/investigational for ALL indications as the effectiveness of this approach to assessing individuals has not been established in the clinical literature.

Specific Indications for which is Excluded from Coverage include the following (not an all-inclusive list)

A. Diagnosis of low-grade (minimal) hepatic encephalopathy

B. Diagnosis of visual acuity

C. Differential diagnosis of demyelinating optic neuritis and ischemic optic neuropathy

D. Assessment or prediction of cognitive function

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

Visual Acuity

A 2004 study (Vianya-Estop et al) assessed whether critical flicker fusion CFF thresholds fulfill the criteria for a potential vision test (PVT) by being unaffected by media opacity yet affected by retinal disease. CFF thresholds for 3 different stimulus sizes (0.5, 1.0, and 1.5 degrees) were measured in 72 patients (mean age of 78.43 +/- 7.07 years) comprising 31 subjects with media opacity, 21 with macular disease (MD), and 20 with pseudophakia. There were no statistically significant differences between CFF values from the media opacity and the pseudophakia groups for any target size ($p > 0.10$). However, CFF values were significantly lower in patients with MD for all the target sizes $p < 0.05$). Analysis of a subset of 6 subjects with media opacity and 7 subjects with MD and visual acuity (VA) of 20/200 or worse showed the media opacity group still had similar CFF values as the pseudophakia group and had significantly higher CFF than the MD group. The authors concluded that CFF testing is shown to fulfill the requirements for a PVT and may prove to be particularly useful for patients with dense media opacity. However, further more robust studies are needed to validate these findings.

In 2006, Del Romo et al discussed the details of the clinical utility of CFF as a PVT (which attempts to predict the visual outcome that might be expected as a result of a cataract operation). CFF thresholds were determined in 31 subjects with age-related idiopathic cataract and no other eye disease, 19 subjects with macular disease (MD) and clear ocular media, and 24 age-matched control subjects. In addition, the CFF technique was administered before cataract surgery in 52 patients and compared with

the information provided by pre-surgical case history and ocular examination alone (ophthalmological judgment [OJ]) and results from 2 commonly used PVTs (the retroilluminated pinhole and the potential acuity meter). Critical flicker fusion thresholds obtained in the nonsurgical cataract group were unrelated to cataract severity and were similar to those in the control group. In contrast, CFF scores were significantly related to visual acuity (VA) in the MD group. In the pre- and post-surgical studies, OJ predicted postoperative VA very well in patients with moderate cataract and normal fundi and better than all the PVTs. Ophthalmological judgment performed less well in patients with comorbid eye disease and dense cataracts, when information from the PVTs would probably have been useful. Critical flicker fusion provided the most accurate predictions of postoperative VA in the small sample of patients with dense cataracts. The authors found that "CFF was unaffected by cataract, yet sensitive to MD, and provided useful information about the postoperative visual outcome beyond that obtained through history and ocular examination in patients with dense cataracts".

In another 2006 study (Vianya-Estopa et al) assessed the usefulness of a battery of PVTs including potential acuity meter (PAM), laser interferometer (LI), CFF, super illuminated pinhole at distance (SPH(d)) and near (SPH(n)), and optimal reading speed (ORS) by their independence of the effects of cataracts and sensitivity to MD in 76 patients with age-related cataract and no other eye disease, 52 patients with MD and clear ocular media, and 28 patients with normal, healthy eyes. Potential vision tests were independent of the degrading effects of cataract up to a visual acuity (VA) level of 20/200 or worse (CFF), 20/125 (ORS and SPH), and 20/40 (PAM and LI). A high degree of association was found between PVT scores and distance VA in the MD group for SPH(d) (r2 = 0.93), SPH(n) (r2 = 0.89), and PAM (r2 = 0.71). A moderate correlation was found for LI (r2 = 0.55), CFF (r2 = 0.50), and ORS (r2 = 0.45). The authors concluded, "in regard to critical flicker/fusion frequency that while the test showed the greatest ability to bypass cataracts, its ability to predict VA in patients with early MD was limited".

In continuing to develop a potential vision test based on the CFF phenomenon by using a brighter stimulus and optimizing its size, Shankar and Pesudovs (2007) reported the results of a prospective non-randomized study in which 225 participants were assigned to 1 of 4 groups: normal, media opacity only, retinal/neural disease only, and cataract plus retinal/neural disease. The CFF thresholds were measured for 3 stimulus sizes: 0.5 degree, 1.0 degree, and 1.5 degrees. Discrimination between groups was tested by analysis of variance and receiver operating characteristic analysis. The relationship between visual acuity and CFF in eyes without media opacity was determined by linear regression and used to predict visual outcomes in 23 eyes having cataract surgery. The mean age of the 225 participants was 71.4 years +/- 13.2 (SD); 134 (59.8%) were women. The normal group had 41 participants, and the other 3 groups had 61 participants each. Critical flicker fusion thresholds were reduced in retinal/neural disease but resistant to image degradation from media opacity. The 1.5-degree stimulus had 88% sensitivity and 90% specificity for discriminating groups. Visual acuity after cataract surgery was accurately predicted within +/-1 line in 43% of eyes, +/-2 lines in 83%, and +/-3 lines in 100% All eyes with poor visual acuity (greater than 0.50 logMAR) or dense cataract (greater than 4.0 Lens Opacities Classification System III) were predicted within +/-2 lines. The authors concluded that CFF effectively discriminated between subjects with and without retinal/neural disease and accurately predicted visual outcome after cataract surgery. The use of a brighter stimulus enhanced performance in cases of dense media opacity. However, these findings need to be validated by further, larger and more robust studies.

Hepatic Encephalopathy

In a 2013 comparison study, Goldbecker et al noted that hepatic encephalopathy (HE) is a common complication of liver insufficiency. While there is widespread acceptance of its importance, there is no consensus on how best to diagnose and monitor HE. These investigators compared the 4 most favored methods for the diagnosis of HE. A total of 170 patients who were on the waiting list for liver

transplantation as well as 86 healthy controls were included in the study. All patients and controls underwent the porto-systemic encephalopathy syndrome test yielding the psychometric hepatic encephalopathy score (PHES), the repeatable battery for the assessment of neuropsychological status (RBANS), the inhibitory control test (ICT) and CFF measurement. Psychometric hepatic encephalopathy score and ICT targets had the best sensitivity (85.7% versus 85.7%) and specificity (96.5% versus 97.6%) for the diagnosis of overt HE. Critical flicker fusion showed inferior sensitivity (40.9%) for the diagnosis of HE and dependency from previous alcohol abuse ($p = 0.015$). Multiple regression analysis showed that all test results apart from PHES were influenced by secondary diagnoses such as diabetes mellitus and renal insufficiency. The authors found that in the German population of patients awaiting liver transplantation, PHES is the most robust method for the diagnosis and follow-up of HE. However, the study along with others underlines the difficulty to define MHE by only one test.

In 2014, Kircheis et al noted that CFF and PHES analyses are widely used to diagnose HE, but little is known about their value in the diagnosis of low-grade HE. The diagnostic values of CFF and PHES were compared using a computerized test battery and West Haven criteria as reference. These investigators performed CFF analysis on 559 patients with cirrhosis and 261 without (controls). Of these 820 patients, 448 were evaluated using a modified PHES system and 148 were also evaluated using the conventional PHES system. Critical flicker fusion distinguished between patients with overt HE and without minimal or overt HE in the entire study population with 98% sensitivity and 94% specificity and in the subgroup of patients who were evaluated by conventional PHES with 97% sensitivity and 100% specificity. Conventional PHES identified patients with overt HE with 73% sensitivity and 89% specificity. Critical flicker fusion distinguished between patients with and without minimal HE with only 37% sensitivity but 94% specificity (entire study population). In the subgroup of patients evaluated by conventional PHES, CFF distinguished between patients with and without minimal HE with 22% sensitivity and 100% specificity; these values were similar to those for conventional PHES (30% sensitivity and 89% specificity). The modified PHES distinguished between patients with and without minimal HE with 49% sensitivity and 74% specificity. The diagnostic agreement values between CFF and conventional or modified PHES in patients with minimal HE were only 54% or 47%, respectively. The study concluded that in an analysis of patients with cirrhosis and controls, CFF distinguished between patients with overt HE and without minimal or overt HE. Also, that PHES testing produced a statistically significant difference among groups, but there was considerable overlap between controls and patients with overt HE. Moreover, these researchers stated that PHES, CFF, and a combination of PHES and CFF could not reliably distinguish patients with minimal HE from controls or those with overt HE. Therefore, further more robust studies are needed to validate the findings.

In a 2018 cohort study, Barone et al stated that a CFF of less than or equal to 39 Hz identifies cirrhotic patients with minimal HE (mHE) and predicts the risk of both overt HE (oHE) and mortality in patients with previous episodes of decompensation and/or oHE. The cohort study examined the effectiveness of CFF in predicting the 1st episode of oHE and survival in cirrhotics who had never experienced an episode of oHE. This trial included 134 patients and 150 healthy subjects. A CFF of greater than 39 Hz was considered normal and pathological when less than or equal to 39 Hz; the median follow-up was 36 months. At baseline, all controls had CFF of greater than 39 Hz; 93 patients had a CFF of greater than 39 Hz and 41 had a CFF of less than or equal to 39 Hz. The prevalence of CFF of less than or equal to 39 Hz significantly increased with the progression of the Child-Pugh class ($p = 0.003$). Moreover, the risk of oHE was increased by CFF of less than or equal to 39 ($p < 0.001$, by log-rank test) [hazard ratio [HR] = 7.57; CI: 3.27 to 17.50); $p < 0.0001$, by Cox model] and ammonia [HR = 1.02; CI: 1.01 to 1.03), $p = 0.0009$]. Both a CFF value of less than or equal to 39 Hz and Child-Pugh class were independent predictors of mortality by Cox model [HR = 1.97; CI: 1.01 to 3.95), $p = 0.049$; HR = 3.85; CI: 1.68 to 8.83),

p = 0.003]. In conclusion, the authors found that CFF predicted the 1st episode of oHE in cirrhotics that had never experienced oHE, and predicted mortality risk. Although these findings suggested that cirrhotic patients should be routinely screened by CFF, larger, well-designed studies are needed.

Prediction of Executive Dysfunction

In a 2015 study, Mewborn et al noted that CFF, a measure of visual processing speed, has often been regarded as a basic metric underlying a number of higher cognitive functions. To test this, these researchers measured CFF, global cognition, and several cognitive subdomains. Because age is a strong co-variate for most of these variables, both younger (n = 72) and older (n = 57) subjects were measured. Consistent with expectations, age was inversely related to CFF and performance on all of the cognitive measures except for visual memory. In contrast, age-adjusted CFF thresholds were only positively related to executive function. Results showed that CFF predicted executive function across both age groups and accounted for unique variance in performance above and beyond age and global cognitive status. The authors concluded that the current findings suggested that CFF may be a unique predictor of executive dysfunction; further study in a more heterogeneous sample is needed to define any specific relation between CFF and brain function. The authors also noted that because CFF thresholds are quick and inexpensive to obtain, they may serve as a good biomarker of higher cognitive function, especially in clinical situations. However, these preliminary findings need to be validated further by well-designed studies.

Another 2015 study (Brooks) noted that Dr. Hendrik Scholl, head of visual neurophysiology at the Wilmer Eye Institute in Baltimore, stated the following "The findings are "potentially interesting", but he urged caution in their interpretation. The [probability] that this is a chance finding is not low, and the meaning of the finding is questionable because there is most likely no causality between critical fusion frequency and brain functions. You don't know, if your critical flicker frequency is high, if this is the reason that you do better on executive function. It's also not very plausible that the visual system and a specific dimension of the visual system should have any impact on executive function"

Another UpToDate review on "The mental status examination in adults" (last updated in 2019) does not mention critical flicker fusion as a diagnostic/management tool for executive functioning.

Differential Diagnosis of Demyelinating Optic Neuritis and Ischemic Optic Neuropathy

A 2018 review (Young et al) analyzed CFF in optic neuritis (ON) and non-arteritic anterior ischemic optic neuropathy (NAION). Multiple variables for eyes with ON or NAION using 2-sided t-test and Chi-square tests were measured. A multi-variate linear regression was performed for the dependent variable CFF. A receiver operating characteristic (ROC) curve was used to define a CFF threshold for distinguishing these entities. Unaffected eyes had an average CFF value of 31.5 Hz. CFF values for ON (20.7 Hz ± 7.36) and NAION (24.3 Hz ± 9.03) were not significantly different from each other (p = 0.06). However, the CFF for ON, 18.27 Hz ± 9.29, was significantly lower than for NAION, 23.92 Hz ± 7.02, p = 0.02 when limiting the comparison to moderate and severe disease. The ROC curve demonstrated that a CFF value of less than or equal to 24 Hz was 71% sensitive for ON and that a value greater than 24 Hz was 74% specific for excluding ON. A multi-variate linear regression model demonstrated that ON contributed to approximately an 8 Hz decrease in CFF compared to NAION. Patients with a CFF of less than or equal to 24 Hz had a 2.89 odds ratio (95% confidence interval [CI]: 1.76 to 4.01) of having ON. The authors concluded that CFF values in eyes with ON were significantly lower compared to eyes with NAION when evaluating moderate and severe disease; 24-Hz may be a useful CFF threshold value when trying to distinguish between these 2 entities. Nonetheless, these findings need to be confirmed in more robust, well-designed studies.

Applicable Coding

CPT Codes

Not covered

99172 Visual function screening, automated or semi-automated bilateral quantitative determination of visual acuity, ocular alignment, color vision by pseudoisochromatic plates, and field of vision (may include all or some screening of the determination(s) for contrast sensitivity, vision under glare) *[not covered for critical flicker fusion]*

99173 Screening test of visual acuity, quantitative, bilateral *[not covered for critical flicker fusion]*

HCPCS Codes

No applicable codes

ICD-10 Codes *(Not an all-inclusive list)*

H46.0-H46.9	Optic Neuritis
H47.011-H47.019	Ischemic optic neuropathy
H53.141-H53.149	Visual discomfort (fatigue)
H53.8	Other visual disturbances [loss of visual acuity]
K72.00-K72.91	Hepatic failure, not elsewhere classified
R41.844	Frontal lobe and executive function deficit

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