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Mental fatigue measurement using eye metrics: A systematic literature review

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Abstract

Mental fatigue measurement techniques utilize one or a combination of the cognitive, affective, and behavioral responses of the body. Eye-tracking and electrooculography, which are used to compute eye-based features, have gained momentum with increases in accuracy and robustness of the lightweight equipment emerging in the markets and can be used for objective and continuous assessment of mental fatigue. The main goal of this systematic review was to summarize the various eye-based features that have been used to measure mental fatigue and explore the relation of eye-based features to mental fatigue. The review process, following the preferred reporting items for systematic reviews and meta-analyses, used the electronic databases Web of Science, Scopus, ACM digital library, IEEE Xplore, and PubMed. Of the 1,385 retrieved documents, 34 studies met the inclusion criteria, resulting in 21 useful eye-based features. Categorizing these into eight groups revealed saccades as the most promising category, with saccade mean and peak velocity providing quick access to the cognitive states within 30 min of fatiguing activity. Complex brain networks involving sympathetic and parasympathetic nervous systems control the relation of mental fatigue to tonic pupil size and have the potential to indicate mental fatigue in controlled experimental conditions. Other categories, like blinks, are derived from the field of sleep research and should be used with caution. Several limitations emerged in the analysis, including varied experimental methods, use of dim lighting during the experiment (that could possibly also induce sleepiness), and use of unclear data analysis techniques, thereby complicating comparisons between studies.

KEYWORDS

electrooculography, eye metrics, eye movements, eye-tracking, mental fatigue, pupillometry

1 | INTRODUCTION

Mental fatigue affects people in professions like transportation (Itoh et al., 2000; LeDuc et al., 2005; Wise et al., 2019), construction (Li, Li et al., 2019), and health care (Nielsen et al., 2019; Schlosser et al., 2012), that often include long hours in demanding environments and where it is critical to be vigilant to avoid accidents and injury. Even in the absence

of injury prone situations, fatigue affects the productivity and mental health of the workers, resulting in a lower quality of life (Ricci et al., 2007). Furthermore, mental fatigue impacts people with hearing impairment (Wang et al., 2017) or diagnosed with multiple sclerosis (Bryant et al., 2004; Finke et al., 2012; Mills & Young, 2008; Niepel et al., 2013), amyotrophic lateral sclerosis (Gibbons et al., 2013), or traumatic brain injury (Johansson et al., 2010). It is one of the

most common complaints made by patients, and it has a severe impact on communication and everyday life (Bryant et al., 2004). Reliable measurement of fatigue under these circumstances is the first step to obtaining a deeper understanding of ways to reduce, manage, and counter this complaint.

Gaze-tracking equipment has become robust, inexpensive and accurate, and gaze sensors may soon be included in computers, phones, tablets, and head-mounted displays (Barz et al., 2018; Hu & Lodewijks, 2020). The use of eye-based physiological signals derived from blinks (Martins & Carvalho, 2015; Stern et al., 1984), eye movements (Cazzoli et al., 2014; Hirvonen et al., 2010), and pupils (Marandi et al., 2019; Morad et al., 2000), recorded using eye-tracking (Hopstaken et al., 2015b; Itoh et al., 2000; Li, Chen et al., 2019; Li, Li et al., 2019; Maffei & Angrilli, 2018; Marandi et al., 2018) and electro-oculography (EOG) (Hirvonen et al., 2010; Tag et al., 2019), have received increased scrutiny in the past years as a means of measuring fatigue (Dawson et al., 2014; Eckstein et al., 2017; Kramer, 1991; Martins & Carvalho, 2015). Several authors have reviewed fatigue measurement (Aaronson et al., 1999; Hu & Lodewijks, 2020; Martins & Carvalho, 2015; Monteiro et al., 2019; Tran et al., 2020); nevertheless, a review summarizing mental fatigue measurement techniques using eye-based technologies is still lacking. The goal of this systematic review is to present an overview of mental fatigue measurement using eye-based features derived from physiological signals.

1.1 | Defining mental fatigue

Fatigue is the effect of exertion caused by physical and/or cognitive activity, and the impact on an individual depends on factors like pain, sleep deprivation, circadian rhythm, diet, fitness level, and environment (Phillips, 2015). Numerous classifications have been developed to facilitate a better understanding of fatigue (Finsterer & Mahjoub, 2014). Fatigue is classified based on its association with an underlying condition into pathological and physiological fatigue. Pathological fatigue that occurs in some medical disorders, such as multiple sclerosis, depression, and rheumatism, is not easily predictable and may be chronic (Chaudhuri & Behan, 2004; Kluger et al., 2013). In contrast, physiological fatigue is independent of the diagnosis of a medical condition; it is a transient phenomenon caused by sustained exertion and is attenuated by rest (Kluger et al., 2013).

Mental fatigue, a type of physiological fatigue and the focus of this literature review, occurs as a consequence of cognitive processing on a task for a period of time that results in a reduction in cognitive capacity and motivation to continue with the task; it is sometimes accompanied by deteriorated task performance (Boksem & Tops, 2008; Hopstaken et al., 2015, 2015a; Pattyn et al., 2018; Tanaka et al., 2014).

Mental fatigue of a transient nature has been termed acute mental fatigue in the literature (van der Linden, 2011). Cognitive load caused by the task and the time spent on the task modulate the degree of the acute mental fatigue experienced during and after the task (Borragán et al., 2017). Motivation and the expected cost and benefits of performing a task determine the amount of effort individuals exert on the task to achieve success (Richter et al., 2016), and thereby modulate the degree of mental fatigue. In this review, fatigue and mental fatigue are used interchangeably and denote acute mental fatigue.

Another concept associated with fatigue and important to define is fatigability. Some authors have defined fatigability as the objective measurement of reduced performance caused by fatigue; and in this case, fatigue is characterized solely as a subjective feeling (Finsterer & Mahjoub, 2014; Linnhoff et al., 2019). We derive our definition from physiology and sports science research, where muscle fatigability is described as the failure to maintain force during a sustained contraction (Chaudhuri & Behan, 2004; Zijdwind et al., 2016). Fatigability indicates how fast a specific level of fatigue is achieved and is especially relevant for understanding fatigue in persons with neurological disorders and concussions, who often experience pathological fatigue independent of performing a task. We define mental fatigability as the inability to maintain processing during a sustained cognitive task. People with lower mental fatigability have the capacity to do more before reaching the same fatigue level compared with people with higher fatigability (Eldadah, 2010).

Despite a general agreement in these definitions, fatigue and mental fatigue are often confused with other similar concepts like sleepiness, drowsiness, daytime sleepiness, and weakness (Ream & Richardson, 1996). Patients and clinicians alike are unable to deconstruct fatigue from the closely associated experience of sleepiness and often combine both feelings under the umbrella term of “tiredness” (Shen et al., 2006). Researchers also tend to use fatigue and sleepiness interchangeably (May & Baldwin, 2009; Morad et al., 2000) or use sleep deprivation to induce and measure fatigue (Morad et al., 2000; Shen et al., 2008). This lack of differentiation in the papers has been recognized as an important issue in research (Neu et al., 2010), as have attempted to differentiate between the related concepts (Hu & Lodewijks, 2020). Sleepiness has been defined as the propensity to sleep, whereas the solution for fatigue is rest but not necessarily sleep (Mairesse et al., 2017). Both sleepiness and fatigue are associated with a reduction in arousal levels (Pattyn et al., 2018).

While the distinction between sleepiness and fatigue is an important one to identify, so is the difference between boredom and fatigue. Low demand in cognitive resources, as a result of monotonous vigilance tasks and boredom, result in an underload condition, whereas a higher than manageable

demand in cognitive resources leads to a condition of overload, or mental fatigue (Pattyn et al., 2008).

1.2 | Measurement of mental fatigue

Two characteristics of fatigue are important considerations for its measurement: (a) fatigue is a subjective phenomenon and (b) fatigue is associated with cognitive, behavioral, and affective responses of the body (Ream & Richardson, 1996). Measurement of mental fatigue can be summarized in four categories: (1) subjective questionnaires, which often include aspects of affective reaction to fatigue (Piper et al., 1998), (2) attention tests, denoting cognitive response to fatigue, (3) reduced task performance, depicting the behavioral response to fatigue and (4) physiological measurements, such as heart rate, brain activity, and pupil size.

Mental fatigue has been assessed in clinics using numerous questionnaires, like the Fatigue Impact Scale (Fisk et al., 1994), Chalder Fatigue Scale (Chalder et al., 1993), Multidimensional Fatigue Inventory (Smets et al., 1995), and Checklist Individual Strength (Beurskens et al., 2000). These questionnaires assess factors like physical fatigue, mental fatigue, motivation based on a range of 11 to 40 questions (Whitehead, 2009). Using these can result in bias due to subjective reporting (Chaudhuri & Behan, 2004; Monteiro et al., 2019), and the subjective reports do not always correlate with known objective measures of fatigue (Bailey et al., 2007).

The second method of fatigue measurement is analyses of performance on attention tasks, like the Psychomotor Vigilance Task (Dinges & Kribbs, 1991), Eriksen Flanker Task (Eriksen & Eriksen, 1974), and Attention Network Task (Fan et al., 2002). These tasks show effects of fatigue via reduction in performance accuracy and reaction to stimuli. Inevitably, these tasks require a break from the ongoing task and performing an additional, non-familiar task.

The third method associated with mental fatigue and its measurement is the measurement of the behavioral response to fatigue. Reduced performance on an ongoing task, such as reduced accuracy on a working memory task, can depict fatigue. While definitions often align fatigue with reductions in performance, what is often not mentioned in these definitions is that, prior to the performance level decrease, there may be an attempt to maintain the performance by expending more effort. At that stage, therefore, although the person experiences fatigue, there is no reduction in performance (Meijman, 1997).

The use of the fourth method of physiological signals and gaze behavior for mental fatigue measurement has increased in frequency, with the increasingly mobile and accurate technologies of electroencephalography (EEG; Gergelyfi et al., 2015; Guo et al., 2018; Hopstaken et al., 2015, 2015a, 2016; Sengupta et al., 2017; Wang et al., 2019), electrocardiography (ECG; Abbasi et al., 2018; Horiuchi et al., 2018), EOG

and eye-tracking. Continuous fatigue measurement using these technologies provides data that is unhampered by subjective bias and does not require taking a break from an ongoing task. Among these, eye-tracking and EOG are the technologies that do not rely on time-consuming setup and have minimal contact with the skin (Hu & Lodewijks, 2020). The recent improvements in terms of accuracy, size of equipment and ease of use for eye-tracking and EOG systems developed in the last years have transpired in the form of ordinary eyeglasses.^{1,2} Although the use of eye-tracking and EOG in the measurement of mental fatigue has increased, no summary of the various eye-based features has been presented that can be reliably used to navigate the measurement of mental fatigue.

1.3 | Objectives and research questions

The main goal of this systematic review is to determine eye-based features, as derived from psycho-physiological signals and gaze behavior, which are useful for mental fatigue measurement. The research questions are outlined as follows: (1) Which eye-based features have been used in the literature to measure mental fatigue? (2) How do the eye-based features relate to mental fatigue? To answer these questions, we have conducted a systematic review of studies that have measured mental fatigue using eye-based features.

The results of the eye-based metrics used to measure mental fatigue will be provided in a qualitative manner (increase or decrease with increasing mental fatigue), rather than in a quantitative manner (effect size or correlation), due to the variation in the eye-based metrics and units used, as well as the variation in the methods used to induce and record gaze data.

2 | METHOD

We conducted and reported this review as per the guidelines by the Preferred Reporting Items for Systematic reviews and Meta-Analyses statement (PRISMA; Moher et al., 2009). The review protocol was registered in the Open Science Foundation (Bafna & Hansen, 2020).

2.1 | Inclusion and exclusion criteria

We included papers that met the following criteria: (1) a study involving mental fatigue and using a task where the

¹<https://jins-meme.com/en/>

²<https://www.tobiipro.com/product-listing/tobii-pro-glasses-3/>

fatigue could be subjectively measured, and/or assumed to have incidence after a prolonged time-on-task; (2) eye-based features computed and analyzed for effects of mental fatigue.

We excluded original papers using the following conditions: (1) no English version of the full paper was available; (2) record was not peer-reviewed; (3) fatigue was not mentioned, induced or measured in the experiment described in the paper; (4) the study was performed with non-human participants; (5) the experimental protocol depicted measurements of stress, cognitive load, eye/visual fatigue, drowsiness, or sleepiness, although the title or keywords mentioned fatigue.

2.2 | Search strategy

We searched five databases—Scopus, Web of Knowledge, ACM Digital Library, PubMed, and IEEE Xplore—for articles published from 1900 to December 2019. Based on keywords found related to the original terms, we modified the search terms used to search in the title, abstract or keywords of the databases. The search string was constructed to include papers measuring mental fatigue using eye-based measures. The detailed search strategy is provided in online Appendix A1. Search terms used to denote fatigue were “fatigue,” “tiredness,” “fatigability,” or “tired,” which were used in conjunction with “mental or mentally” or “cognitive or cognitively.” Use of eye-based features was denoted by incorporating the terms “pupil,” “pupillometry,” “eye or eyes,” “gaze,” or “pupillography,” and measurement of fatigue was indicated by including the wildcard version of the terms detect, model, analyze and measure. Subsequently, the main author (TB) conducted the cited reference search.

2.3 | Study selection

After the removal of duplicates and papers in a language other than English, we examined the retrieved studies in two phases. In the screening phase, the main author (TB) excluded studies based on the title and the abstract, using the exclusion criteria of measuring stress, cognitive load, mental workload, eye fatigue, visual fatigue, drowsiness, and sleepiness. The next phase was the inclusion phase, where both authors read the full text of the articles to exclude papers that did not follow the inclusion–exclusion criteria. Each author selected the papers independently, and any discrepancies were sorted by mutual agreement. In a final stage, the main author (TB) performed backward reference search from the papers selected for the final

inclusion, based on title and abstract, and added them to the screening phase.

2.4 | Data extraction

The main author (TB) examined and extracted the following data into a pre-defined database: (a) reference of the paper indicating the first author and the year of publication, (b) the fatiguing task, (c) time spent on the task, (d) number of participants and distribution of sex and age characteristics, (e) eye-based criteria used, their definitions and outcome of the analyses, (f) lighting conditions of the experiment and (g) other methods used to assess fatigue. We added the lighting condition in the database following its mention in multiple papers.

2.5 | Quality assessment

The papers studied in this review do not fall under the category of randomized controlled trials, so they have no known quality assessment criteria. We created our own criteria, based on previous literature reviews on mental fatigue (Tran et al., 2020) and on factors that were deemed important by us in a paper measuring fatigue using eye-based features. The use of eye-based features is not yet standardized, as in the case of well-established methods like EEG (Tran et al., 2020). Hence, we monitored the definitions and signal processing techniques used in the computation of the eye-based features to evaluate the feasibility of re-using the features and reproducing the experiment. For each category of features, we have listed in online Appendix A2 the sub-criteria used to verify the signal processing techniques used, such as the specification of the stable luminance level for pupil size-based metrics. Partial points were given if some of the sub-criteria were fulfilled. To avoid confounding mental fatigue caused by the task with drowsiness arising from inadequate sleep or varied time used for the experiment, we evaluated the quality of the study based on the instructions given to the participants regarding sleep and the use of a standard time of day in the experimental design. The use of substances like alcohol or coffee has been known to affect fatigue, so we investigated the studies and their instructions to participants regarding this variable, based on the quality assessment criteria in previous literature reviews on mental fatigue (Tran et al., 2020). We gave partial points if one of the substances was included as a restriction in the instructions. Finally, we also evaluated if mental fatigue had been confirmed by another method, such as attention test, questionnaires or technologies such as EEG or ECG. The complete criteria, with their weights, are catalogued in Table 1.

TABLE 1 Quality assessment criteria

Number	Quality assessment question	Weight assigned
QA1	Are the eye-based features and the signal processing techniques to compute the eye-based features clearly defined?	Yes: 2 No: 0
QA2	Is the confounding effect of circadian rhythm addressed in the experiment design?	Yes: 1 Not mentioned: 0
QA3	Is the confounding factor of substance use addressed during the experiment or data analysis?	Yes: 1 No: 0
QA4	Is the confounding effect of sleep addressed in the experiment design?	Yes: 1 No: 0
QA5	What is the number of participants in the study?	≥ 20 participants or power analysis performed: 2 10–19 participants: 1.5 6–9 participants: 1 1–5 participants: 0.5 Not specified: 0
QA6	Has mental fatigue been confirmed using attention tests, questionnaires or technology such as EEG, ECG?	Yes: 1 No: 0

3 | RESULTS

The results obtained from the studies included in the review are structured as follows; Section 3.1 summarizes the study selection process. Sections 3.2 and 3.3 provide the experimental context to the results on the eye-based features and provide an overview of the methods used to induce fatigue and to record fatigue, respectively. They also present a perspective on the variety of methods used, in both inducing fatigue and measuring it. Section 3.4 describes the main results on the various eye-based features, including machine learning results. Lastly, section 3.5 provides the quality assessment results from the studies.

3.1 | Study selection

A total of 1,384 papers were identified from all the sources—Web Of Science (359), Scopus (796), ACM

Digital Library (20), IEEE Xplore (54), and PubMed (155). An additional paper was found in the personal records of the main author (TB). From these, 895 records were included, after the duplicates and papers not written in English were removed. These 895 records were screened by reading their title and abstract, if they measured mental fatigue and were peer-reviewed, which resulted in 125 papers to be read completely. Based on the inclusion criteria, 32 papers were identified and included in this review. These 32 papers cited 60 relevant papers, as per their title and abstract, which were added to the screening step. Papers that were read completely from these were 18 in number, and two were selected for the final inclusion list, resulting in 34 papers. The process of selection is depicted in Figure 1. These 34 papers had alert participants at the beginning of the study, who reached a state of fatigue at the end of a fatiguing task. Studies that induced fatigue using circadian rhythm were excluded from the review. However, one of the included studies employed both time-on-task and circadian rhythm to induce fatigue and attempted to dissociate both conditions (Cazzoli et al., 2014). Table 2 provides details on the study characteristics and the fatigue-inducing methods (columns 2, 3, and 6) and measurement techniques (column 7).

3.2 | Mental fatigue inducing methods

Various tasks were used to induce fatigue during the experiment. The tasks associated with each study are provided in column 2 of Table 2, and are depicted in Figure 2.

The experiment duration used in the studies followed a range from 20 min (Maffei & Angrilli, 2018; Tian et al., 2012) to 18 hr (Di Stasi et al., 2013), and the details are provided in column 3 of Table 2. The distribution of the studies and the total experimental duration is shown in Figure 3. The experiments were generally divided into trials, where tasks were continuously performed without a break. The trial time of the experiment is given in brackets in column 3 of Table 2, if it differed from the experiment time. Each type of fatiguing task was performed for a broad range of experiment duration, except in the case of driving tasks, which were all performed for 2–3 hr.

Twenty-three of the 34 papers reported on the lighting conditions, as controlled in the experimental protocols, and are depicted in column 6 of Table 2. However, 17 of these studies used words like "dim" and "dark" to describe the lighting conditions. We found this detail interesting in the context of fatigue measurement, since fatigue is closely associated with sleepiness, and dim lighting is generally used in sleep measurement protocols (Wei et al., 2019).

FIGURE 1 Review procedure following the PRISMA strategy

3.3 | Mental fatigue recording methods

In 29 of the 34 papers, a fatigue questionnaire was used to confirm that the task applied in the experiment resulted in a change in the subjective feeling of fatigue. The fatigue questionnaires used are provided in column 7 in Table 2. Two studies used known sleepiness questionnaires (Li, Li et al., 2019; Marandi et al., 2018) instead of a fatigue questionnaire, and one of these studies used a workload questionnaire (NASA-TLX) additionally (Li, Li et al., 2019). The rest of the studies (7) assumed that time-on-task would generate fatigue and did not confirm the presence of fatigue at the end of the experiment (Cazzoli et al., 2014; Di Stasi et al., 2015, 2016; Gao et al., 2015; Maffei & Angrilli, 2018; Tian et al., 2012).

The objective method of fatigue confirmation via attention tasks was performed in only three studies (Gao et al., 2015; Li, Chen et al., 2019; Renata et al., 2018) of the 34 included in the review, and two of these also performed the gaze recording during the attention task (Li, Li et al., 2019; Renata et al., 2018).

In most studies, the physiological measurement of fatigue using eye-based features took place simultaneously as the fatiguing task. In 10 studies, however, an additional gaze-recording task was administered before and after the fatiguing task, with the sole purpose of measuring fatigue by recording the physiological signals. The gaze-recording task

is given in column 2 of Table 2, in brackets, with the fatiguing task. The fatiguing tasks that were accompanied by these fatigue measurement tasks were largely real-life fatiguing tasks involving professionals in surgery (Di Stasi, McCamy, Macknik, et al., 2013), aircraft flying (Di Stasi et al., 2016; Diaz-Piedra et al., 2016; LeDuc et al., 2005), and traffic control operation (Li, Li et al., 2019). Di Stasi et al. (2012) conducted gaze-recordings during the fatiguing task of driving as well as during a guided saccade task before and after the driving task.

Nine of the studies conducted multi-modal measurement of fatigue using EEG (Gergelyfi et al., 2015; Guo et al., 2018; Hopstaken et al., 2015, 2015a, 2016; Sengupta et al., 2017; Wang et al., 2019), ECG (Abbasi et al., 2018; Horiuchi et al., 2018), and functional near-infrared spectroscopy (fNIRS; Borragán et al., 2018) and were able to confirm the corresponding measurements of mental fatigue using eye-based metrics.

3.4 | Eye-based features

The eye-based features are categorized into the following eye-metric categories: pupil, percentage of eye closure, blinks, saccades, fixations, microsaccades, ocular drift, and eye activity. Table 3 portrays 21 of the features deemed useful as per the quality assessment criteria and so does not

TABLE 2 Summary of the papers that met the inclusion criteria

Fatigue inducing methods					Fatigue recording methods			
Reference	Fatiguing task (Gaze-recording task, if not same as fatiguing task)	Time-on-task (Without breaks, if not the same as time-on-task)	Participants		Lighting condition of experiment room	Subjective Questionnaire/Attention task	Eye-based features	Quality assessment
			N (Female)	Age (yr): mean $\pm$ SD or range				
Abbasi et al. (2018)	Cognitive task	0.5 hr	35 (0 F)	23 $\pm$ 3	$\geq$ 300 lx	VAS-f	Eye activity	5
Borrágán et al. (2018)	Custom cognitive task	1 hr (16 min)	22 (16 F)	23 $\pm$ 2.28		VAS-f	Blink count	4
Burke et al. (2018)	Cognitive task	2 hr 40 min	35 (21 F)	63–84		Current fatigue question	Normalized baseline pupil diameter	7
Cazzoli et al. (2014)	Circadian rhythm and free visual exploration task	25 min (6 min)	18 (7 F)	24.89	Dimly lit		Saccade mean velocity Saccade magnitude Mean fixation duration	4.5
Di Stasi, McCamy, Catena, et al. (2013)	Cognitive task (Guided saccade tasks)	2 hr	12 (2 F)	30 $\pm$ 3.8	Darkened and quiet	Borg Scale of Perceived Exertion	Microsaccade peak velocity-magnitude slope Saccade peak velocity-magnitude slope Mean drift velocity	7.5
Di Stasi et al. (2012)	Driving task (Guided saccade tasks)	2 hr	10 (5 F)	23.9 $\pm$ 4.9	Dimly lit	Chalder Fatigue Scale	Saccade duration Saccade peak velocity	7.5
Di Stasi et al. (2015)	Driving task	2 hr	10 (5 F)	23.9 $\pm$ 4.9	Dimly lit		Microsaccade peak velocity-magnitude slope Microsaccade mean velocity-magnitude slope Microsaccade duration-magnitude slope Microsaccade peak velocity Microsaccade mean velocity Microsaccade duration Microsaccade magnitude Saccade frequency Blink frequency	3.5
Di Stasi, McCamy, Macknik, et al. (2013)	Surgery duty (Guided saccade task)	13–18 hr	12 (6 F)	30 $\pm$ 2.2	Darkened and quiet	Borg Scale of Perceived Exertion ^a	Saccade peak velocity-magnitude slope	7

(Continues)

TABLE 2 (Continued)

Reference	Fatigue inducing methods			Fatigue recording methods			
	Fatiguing task (Gaze-recording task, if not same as fatiguing task)	Time-on-task (Without breaks, if not the same as time-on-task)	Participants		Lighting condition of experiment room	Subjective Questionnaire/Attention task	Eye-based features
			<i>N</i> (<i>n</i> Female)	Age (yr): mean $\pm$ SD or range			
Di Stasi et al. (2016)	Aircraft flying task (Guided saccade task)	1–2 hr	26 (0 F)	29 $\pm$ 4.6	Dark		Saccade peak velocity-magnitude slope Saccade mean velocity-magnitude slope Saccade duration-magnitude slope Saccade peak velocity Saccade mean velocity Saccade magnitude Saccade duration
Diaz-Piedra et al. (2016)	Aircraft flying task (Guided saccade task)	2.5 hr	5 (0 F)	27.6 $\pm$ 1.7	Darkened and quiet	Borg Scale of perceived exertion	Area under the curve of saccade peak velocity-magnitude slope
Gao et al. (2015)	Attention task	1 hr	6 (0 F)	~20	Gentle light	Psychomotor vigilance test	Machine learning features
Gergelyfi et al. (2015)	Custom cognitive task	4–5 hr (190 min)	18 (8 F)	25.72 $\pm$ 3.54	Dimly illuminated	MFI ^a	Blink frequency Median blink duration Long blink ratio
Guo et al. (2018)	Driving task	2.5 hr (1.5 hr)	60 (30 F)	23.25 $\pm$ 2.5	Dimly lit	POMS-SF	PERCLOS
Herlambang et al. (2019)	Cognitive task	2.5 hr	20 (12 F)	24.95 $\pm$ 3.01		VAS-f	Blink count Mean blink duration
Hopstaken et al. (2015a), Hopstaken et al. (2015)	Cognitive task	2 hr (18 min)	20 (17 F)	19.9 $\pm$ 2.0	Dimly lit	Current fatigue question	Baseline pupil diameter
Hopstaken et al. (2015)	Cognitive task	1 hr (10 min)	82 (63 F)	20.95 $\pm$ 3.9	Dimly lit	Current fatigue question	Baseline pupil diameter Peak pupil dilation
Hopstaken et al. (2016)	Cognitive task	1.5 hr (15 min)	47 (32 F)	20.5 $\pm$ 1.8	Dimly lit	Current fatigue question	Baseline pupil diameter
Hopstaken et al. (2015b)	Cognitive task	1 hr 48 min (18 min)	33 (18 F)	21.2 $\pm$ 3.7	Dimly lit	Current fatigue question	Baseline pupil diameter Peak pupil dilation

(Continues)

TABLE 2 (Continued)

Reference	Fatigue inducing methods			Fatigue recording methods			Quality assessment
	Fatiguing task (Gaze-recording task, if not same as fatiguing task)	Time-on-task (Without breaks, if not the same as time-on-task)	Participants Age (yr): mean $\pm$ SD or range	Lighting condition of experiment room	Subjective Questionnaire/ Attention task	Eye-based features	
Horiuchi et al. (2018)	Cognitive task	1 hr (8 min)	16 (3 F) 21–24		Jikaku-sho Shirabe test	Standardized blink count Standardized blink burst count Standardized blink burst frequency Standardized blink duration Standardized blink velocity	4.5
Lavine et al. (2002)	Attention and cognitive task	0.5 hr	20 (10 F) 20–54		SAM fatigue scale	Mean fixation duration per event Number of fixations per event Fixation distance	6
LeDuc et al. (2005)	Aircraft flying task (Fitness Impairment Tester)	1.2 $\pm$ 0.62 hr	53 32 $\pm$ 7.03	Illuminated with standard fluorescent light	Current fatigue question	Baseline pupil diameter Pupil constriction amplitude Pupil constriction latency Saccade mean velocity	5
Li, Li et al. (2019)	Traffic control operator job (Attention task)	8.5 hr (2 hr)	8 30–50		Samm-Perelli scale + Mackworth clock test	Features for machine learning	5
Li, Li et al. (2019)	Construction equipment operator task	1 hr 40 min (12 min)	12 (0 F) 27.92 $\pm$ 3.2	Bright and stable daylight conditions	Stanford sleepiness questionnaire + NASA-TLX	Blink count Mean blink duration Mean pupil diameter Percent change in pupil diameter	4.5
Maffei and Angrilli (2018)	Attention task	20 min (7 min)	33 (33 F) 21–26			Normalized blink ratio Blink probability	5
Marandi et al. (2018)	Cognitive task	40 min (3 min)	38 (20 F) 39.58 $\pm$ 5.29	Indoor controlled environment	Karolinska sleepiness questionnaire	Mean blink duration Blink frequency Pupil dilation range Fixation Duration Saccade peak velocity Saccade duration	7

(Continues)

TABLE 2 (Continued)

Reference	Fatigue inducing methods		Fatigue recording methods			Quality assessment
	Fatiguing task (Gaze-recording task, if not same as fatiguing task)	Time-on-task (Without breaks, if not the same as time-on-task)	Participants		Subjective Questionnaire/ Attention task	Eye-based features
			<i>N</i> (<i>n</i> Female)	Age (yr): mean $\pm$ SD or range		
McGarrigle et al. (2017a)	Listening task	50 min (20 min)	24	18–30	VAS-f	Pupil dilation as a function of time
McGarrigle et al. (2017b)	Listening task	40 min (15 min)	41 (23 F)	9.25 $\pm$ 0.98	Custom scale on “fatigue right now”	Pupil dilation as a function of time
Paladini et al. (2016)	Saccade task	1 hr 8 min (16 min)	30 (19 F)	28.7 $\pm$ 5.7	VAS-f	Saccade peak velocity Saccade accuracy Saccade latency
Renata et al. (2018)	Verbal reasoning task (Attention task)	2.5 hr	14		Samm-Perelli scale + Choice reaction time test	Saccade peak velocity Saccade magnitude
Sengupta et al. (2017)	Cognitive task	40–50 min (4.66 min)	30 (6 F)	25.16 $\pm$ 5.78	Current fatigue question	Saccade peak velocity
Song et al. (2015)	Control of spacecraft support system	1 hr 45 min (15 min)	3		Current fatigue question	Mean blink duration Variance of blink duration Standard deviation of blink duration Variation coefficient of blink duration
Tian et al. (2012)	Control of space vehicle	20 min (10 min)	10 (0 F)	26–31		Mean blink duration PERCLOS
Wang et al. (2019)	Driving task	3 hr (30 min)	12 (2 F)	32 $\pm$ 1.6	Samm-Perelli scale	Eye activity per minute
Yamada and Kobayashi (2018)	Cognitive task (Natural viewing task)	34 min (3 min)	20 (8 F)	47.5 $\pm$ 20.5	Current fatigue question	Mean pupil dilation Blink duration per minute Features for machine learning

Abbreviations: SD, standard deviation; min, minutes; hr(s), hour(s); yr, years; VAS-f, visual analog scale for fatigue; MFI, multidimensional fatigue inventory; POMS-SF, profile of mood states—short form; SAM, school of aerospace medicine.

^aAdapted/modified.

FIGURE 2 Fatigue-inducing tasks used by the included studies

FIGURE 3 Experiment duration of the included studies

include features introduced and used only by papers that have a quality assessment score less than 5. The table also does not cover the papers that used machine learning algorithms (Gao et al., 2015; Li, Chen et al., 2019; Yamada & Kobayashi, 2018), as the relation between individual features and mental fatigue was not shown. Additionally, the operational definitions of the features and their relation to mental fatigue, as observed in the included studies, are provided. For a full list of the 52 features covered in all the studies, refer to online Appendix A4.

3.4.1 | Pupil

Phasic changes in pupil diameter have been used in various ways to depict mental fatigue. The following pupil-based features reduced as a function of mental fatigue: mean pupil dilation, peak pupil dilation, pupil dilation range (Hopstaken et al., 2015b; Hopstaken et al., 2015; Marandi et al., 2018;

Yamada & Kobayashi, 2018). The tasks used to induce as well as measure fatigue were cognitive tasks performed for 30 min to 1.5 hr, except for Yamada and Kobayashi (2018), who used a natural viewing task to measure fatigue. Mean pupil diameter, also depicting phasic variations, decreased with time-on-task on a construction equipment operator task of ~2 hr (Li, Li et al., 2019).

Tonic changes in pupil diameter were obtained using baseline pupil diameter, computed for a short duration before a trial, and were shown to reduce with time-on-task for four of the six studies that used this metric. The four studies showing a decrease in pupil diameter used cognitive tasks for a duration of 1–2.5 hr to induce fatigue (Burke et al., 2018; Hopstaken et al., 2016; Hopstaken et al., 2015a; Hopstaken, et al., 2015). The fifth study that used the baseline pupil diameter also employed a cognitive task of ~2 hr, but failed to show a pattern in the data (Hopstaken et al., 2015b). The remaining study compared pupil size before and after an aircraft flying task, and showed an increase in the baseline pupil diameter after the ~1-hr task (LeDuc et al., 2005).

A pupil-based metric defined by the light conditions—the pupil response to light, was shown to decrease in size and become increasingly delayed under the effect of fatigue caused by ~1 hr of aircraft flying task (LeDuc et al., 2005).

3.4.2 | Blink

Three metrics from the blink category were positively correlated with mental fatigue: the blink count, the blink frequency, and the normalized blink ratio, in all the eight studies that measured these. The fatigue inducing as well as measuring task in these studies was mainly a cognitive task (Borrágán et al., 2018; Gergelyfi et al., 2015; Herlambang et al., 2019; Horiuchi et al., 2018; Maffei & Angrilli, 2018; Marandi et al., 2018). One study used a driving task

TABLE 3 Eye metrics used to measure mental fatigue, their definitions, and their relation with mental fatigue. ↑ indicates an increase in the metric with increasing mental fatigue, ↓ indicates a decrease in the metric with increasing mental fatigue

Category	Metric	Operational definition	Mental fatigue relation	References
Pupil	Baseline pupil diameter	Mean of pupil diameter for time 't' before the trial, where t = 200 ms or 500 ms	↓	Hopstaken et al. (2015b), Hopstaken et al. (2015a), Hopstaken et al. (2015), Hopstaken et al. (2015) ^c , Hopstaken et al. (2016), LeDuc et al. (2005) ^b
	Normalised baseline pupil diameter	Ratio of the baseline pupil diameter for time 't' before the trial to the baseline pupil diameter during the first task, where t = 200 ms	↓	Burke et al. (2018)
	Pupil dilation as a function of time	Mean of pupil dilation in steps of time 't', where pupil dilation is the difference between the trial pupil diameter and baseline pupil diameter, and t = 500 ms, 100 ms	↓	McGarrigle et al. (2017a), McGarrigle et al. (2017b)
	Peak pupil dilation	First positive peak of the difference between the trial pupil diameter and baseline pupil diameter within the time 't', where t = 1,500 ms	↓	Hopstaken et al. (2015, 2015b)
	Pupil dilation range	Range of change in pupil dilation, after subtractive normalisation	↑	Marandi et al. (2018)
	Pupil constriction amplitude	Difference in initial and minimum pupil diameter, in response to a flash of light	↓	LeDuc et al. (2005)
	Pupil constriction latency	Delay between the flash of light and pupil constriction	↑	LeDuc et al. (2005)
Percentage of eye closure	Percentage of eye closure (PERCLOS)	Ratio of time the pupil diameter is at 20% of its normal pupil diameter to the total measurement time	↑	Guo et al. (2018), Tian et al. (2012) ^a
Blinks	Blink count	Number of blinks in a trial	↑	Borragán et al. (2018), Herlambang et al. (2019), Li, Li et al. (2019)
	Blink frequency	Number of blinks in a trial divided by the trial time	↑	Di Stasi et al. (2015), Gergelyfi et al. (2015), Marandi et al. (2018)
	Mean blink duration	Mean of the blink durations during the trial	↑	Herlambang et al. (2019), Li, Li et al. (2019), Marandi et al. (2018) ^b , Song et al., 2015, Tian et al. (2012) ^a
Saccades	Saccade duration	Duration of the saccade	↑	Di Stasi et al. (2012 ^a , 2016) ^c , Marandi et al. (2018) ^b
	Saccade peak velocity	Maximum of the instantaneous velocity during a saccade	↓	Marandi et al. (2018), Paladini et al. (2016), Renata et al. (2018), Sengupta et al. (2017), Di Stasi et al. (2012, 2016)
	Saccade peak velocity-magnitude slope	Slope (m) of the saccade peak velocity-magnitude relationship, where saccade peak velocity = $m * \ln(\text{magnitude}) + b$	↓	Di Stasi, McCamy, Catena, et al. (2013), Di Stasi, McCamy, Macknik, et al. (2013), Di Stasi et al. (2016)
	Area under the curve (AUC) of the saccade peak velocity-magnitude	Area under the curve by integration of the saccade peak velocity-magnitude relationship	↓	Diaz-Piedra et al. (2016)
Microsaccades	Microsaccade peak velocity-magnitude slope	Slope (m) of the microsaccade peak velocity-magnitude relationship, where microsaccade peak velocity = $m * \ln(\text{magnitude}) + b$	↓	Di Stasi, McCamy, Catena, et al. (2013); Di Stasi et al. (2015)

(Continues)

TABLE 3 (Continued)

Category	Metric	Operational definition	Mental fatigue relation	References
Eye activity	Eye activity	Electrical activity of the eye	↑	Abbasi et al. (2018)
	EEG-derived eye activity per minute	Number of eye movements per minute	↓	Wang et al. (2019)
Fixation	Number of fixations per event	Total number of fixations for each event	↓	Lavine et al. (2002)
	Mean fixation duration	Mean of the fixation durations	↓	Cazzoli et al. (2014) ^c ; Lavine et al. (2002); Marandi et al. (2018) ^c
	Fixation distance	Mean of the distance from fixations to the geometric center of the target	↑	Lavine et al. (2002)
Ocular drift	Mean ocular drift velocity	Slow random movement occurring during a fixation	↑	Di Stasi, McCamy, Catena, et al. (2013)

^aThe metric was not significant for the reference.; ^bThe reference showed the opposite relation between the metric and mental fatigue.; ^cThe reference could not show a notable pattern between the metric and mental fatigue.

(Di Stasi et al., 2015) and another one used a simulated construction work (Li, Li et al., 2019). The task durations varied from 25 min to 4–5 hr.

Mean blink duration was tested by five studies (Herlambang et al., 2019; Li, Li et al., 2019; Marandi et al., 2018; Song et al., 2015; Tian et al., 2012), with mixed results. One study showed a decrease in mean blink duration with increasing mental fatigue on a task of duration ~2 hr (Song et al., 2015), while another reported no significant results on a 20-min fatiguing task (Tian et al., 2012). Both of these studies induced and measured fatigue using a task of controlling space vehicles, as compared to the tasks used by studies that resulted in a positive correlation—cognitive tasks and a simulated construction task, all of which had a duration of 40 min to 2.5 hr.

PERCLOS, another derivative of blink duration, also had inconsistent results across the two studies that computed it (Guo et al., 2018; Tian et al., 2012).

3.4.3 | Saccade and microsaccade

Two metrics from the category of saccade—peak velocity and mean velocity—were inversely proportional to mental fatigue according to each of the eight studies that used them. Seven of the eight studies generated voluntary saccades using fatiguing tasks such as free visual exploration task (Cazzoli et al., 2014), driving (Di Stasi et al., 2012), aircraft flying (Di Stasi et al., 2016; LeDuc et al., 2005), cognitive tasks (Marandi et al., 2018; Renata et al., 2018; Sengupta et al., 2017). The remaining study involved pro-saccades, a type of saccade generated by following a visual cue, in a gap-overlap saccade task (Paladini et al., 2016). In four of

the eight studies, additional fatigue measurement tasks such as a guided saccade task, generating pro-saccades (Di Stasi et al., 2012, 2016; LeDuc et al., 2005) and an attention task, generating voluntary saccades (Renata et al., 2018) were performed before and after the fatiguing task. The duration of these tasks ranged from 25 min to 2.5 hr.

Di Stasi, McCamy, Catena, et al. (2013) tested features of saccades and microsaccades that are a combination of the known existing features. They hypothesized that the main sequence slope (the slope relationship between the saccade/microsaccade magnitude, duration, and velocity) would be affected by cognitive processes such as mental fatigue. They computed the slopes of the main sequences and found that the saccade velocity-magnitude slopes reduced with increasing mental fatigue. The fatiguing tasks in the four studies that used these metrics were all different—aircraft flying (Di Stasi et al., 2016), health-care shift (Di Stasi, McCamy, Macknik, et al., 2013), driving (Di Stasi et al., 2015), and cognitive tasks (Di Stasi, McCamy, Catena, et al., 2013). Three of the four studies used an additional guided saccade task before and after the fatiguing tasks, in order to measure the mental fatigue using pro-saccades (Di Stasi, McCamy, Catena, et al., 2013; Di Stasi, McCamy, Macknik, et al., 2013; Di Stasi et al., 2016). All except one study controlled the experiment duration to 2 hr; the exception used an experiment duration of 13–18 hr, to generate a health-care shift. In one study, saccade latency, or the reaction time of saccade generation in response to a visual cue, was used to measure the effect of fatigue on attentional disengagement on a gap-overlap task, and found that the saccade latency to shift attention from one visual cue to another (or the cost to disengage) increased with increasing fatigue (Paladini et al., 2016).

3.4.4 | Machine learning features and methods

The features described in Table 3 were analyzed using methods from descriptive statistics. Three papers, however, presented results from inferential statistical methods, so the interpretation of the contribution of individual features to the results is not easy. Gao et al. (2015) used the features blink duration, closing time of the eye, reopening time, blink duration, blink intervals, the velocity of eye closure, the velocity of eye reopening, the energy of blinks, slow eye movement duration and proportions, number of rapid eye movements (REM), and the duration and energy of REMs and used support vector machines (SVM) for fatigue classification. Li, Chen et al. (2019) combined the features gaze velocity probability and entropy to classify fatigue. The data were divided into two states—"fatigue," and "alert," and the researchers used bagged trees to classify fatigue. Yamada and Kobayashi (2018) computed 181 features from four categories—oculomotor (saccades, fixations, blinks, and pupil size), saliency-based features, eye movement directions, and gaze allocation (based on probability and entropy of gaze bins)—to achieve binary classification using a radial basis function kernel SVM.

3.5 | Quality assessment

Total scores for the quality assessment criteria are given in column 9 of Table 2, and the individual criterion scores are detailed in online Appendix A3. From a total score of 8, the studies that obtained a score of 5 or above ($>60\%$) were considered acceptable in terms of scientific quality. Only 19 of the 34 studies obtained a score of 5 or above, and three studies obtained the highest score of 7.5 (Di Stasi, McCamy, Catena, et al., 2013; Di Stasi et al., 2012; Wang et al., 2019). Twenty studies obtained a full score on the quality assessment criterion 1 and provided an explicit definition of the metrics and the signal processing techniques used on the metric.

We used quality assessment criteria to identify studies that removed the possible causes of sleepiness—a good night's sleep (QA4) and circadian rhythm (QA2), and another criterion to confirm mental fatigue (QA6), to identify the features that were more sensitive to mental fatigue than sleepiness. Five studies fulfilled all three criteria (Burke et al., 2018; Di Stasi, McCamy, Catena, et al., 2013; Di Stasi, McCamy, Macknik, et al., 2013; Di Stasi et al., 2012; Wang et al., 2019). These five studies had used seven different features—normalized baseline pupil diameter, saccade peak velocity-magnitude slope, microsaccade peak velocity-magnitude slope, saccade duration, saccade peak velocity, mean ocular drift velocity, and EEG-derived eye activity per minute—to measure mental fatigue.

4 | DISCUSSION

This systematic review reports on the eye metrics associated with mental fatigue and describes the relation of the metrics to mental fatigue. Among the 34 studies included in the review, 21 useful eye-based metrics were used to measure mental fatigue, which was induced using a variety of tasks, including cognitive, driving, and attention tasks, for a duration of 20 min to 18 hr. It is crucial, at this stage of research, to provide an overview of the literature and to understand the direction in which the mental fatigue measurement research is headed.

4.1 | Relation between mental fatigue and eye metrics

The most promising metrics for fatigue detection were based on saccadic movements. Bahill and Stark (1975) and Schmidt et al. (1979) were the first researchers to study the effects of fatigue on saccade characteristics. Saccade duration was found to increase, while saccade magnitude and velocity reduced for fatigued participant (each study had one fatigued participant). Moreover, Bahill and Stark (1975) claimed that the saccadic points during a fatigued state do not belong to the main sequence (using data from one fatigued participant). Conversely, Di Stasi et al. (2012) plotted the saccade peak velocity versus saccade magnitude data from fatigued participants and the plot follows the expected main sequence curve, but with a different slope. They hypothesized that the slope of the saccadic, as well as microsaccadic main sequence, reduced as a result of fatigue. The slope was found to be significantly reduced due to the effect of mental fatigue, and at the same time, the individual saccade characteristics—saccade magnitude and peak velocity—reduced as an effect of mental fatigue. Although this has not been discussed in the papers, a possible explanation could be that the decrease in saccade peak velocity was higher than the decrease in saccade magnitude, resulting in an overall decrease in their slope. Another observation that supports this theory is that the slope of saccade duration and magnitude is not found to show a notable effect of mental fatigue. Saccade duration and magnitude are known to increase and decrease with time, respectively, and a simultaneous constant change in the slope would mathematically not be possible. Deeper inspection of the reason behind the simultaneous reduction of the saccade velocity-magnitude slope and the individual features with time is required.

Saccade generation is controlled by a structure in the mid-brain called superior colliculus (SC). SC is involved in the computation of eye displacement to reach the target and the saccadic velocity (Purves et al., 2001). Another region associated with saccade generation is the brainstem, specifically

the omnipause neurons. The inhibitory activity of omnipause neurons coincides with the occurrence of saccades, and they have been recently theorized to increase the sensitivity of the saccade-generating neurons—excitatory burst neurons—to the stimuli from SC (Optican, 2008). This increased sensitivity is also responsible for the switch from fixation to saccadic movement. Lesions in omnipause neurons have been linked to a subsequent increase in saccade duration and reduction in saccade velocity (Miura & Optican, 2006), similar to the effects of fatigue. However, the neural mechanisms preceding these effects of fatigue on saccades are not yet completely understood and need further research.

Pupil size and electrophysiology have previously been exploited using adaptive gain theory, which has been developed in neuroscience to explain the activity of locus coeruleus (LC) neurons and their relation to task engagement and arousal (Aston-Jones & Cohen, 2005). LC neurons have two modes of activity: phasic and tonic. During the phasic mode, norepinephrine is released in bursts which can be observed as an increase in pupil dilation locked to the task (or stimulus-evoked pupil dilation), while the ongoing task is exploited and task performance is improved. During the tonic mode, only baseline norepinephrine is released, and the phasic LC responses are reduced, leading to an exploration of tasks that best utilize the resources and subsequently task performance declines. Based on this theory, Hopstaken et al. (2015b) have proposed a third mode of working of the LC neurons—the disengagement mode. In this mode, both the stimulus-evoked pupil dilation and the baseline pupil diameter decrease in amplitude, and this is accompanied by disengagement from the current task and low attention levels. Using well-designed experiments and cognitive tasks, the baseline pupil diameter (pupil diameter before the task stimulus appeared) was shown to decrease with time-on-task in three out of the five papers that studied it (). Following the same theory, peak pupil dilation was confirmed to reduce with time-on-task. However, this theory on the third output mode of the LC needs further investigation with respect to the LC activity, cognitive load, and the behavioral outcomes of the task.

Pupil response to light, moreover, exhibits delayed effects and a reduced pupil size due to fatigue. This response is a part of the Fitness Impairment Test (FIT), commercially developed to test the fitness of shift workers (Portman-Tiller, 1998). Although the results of the original FIT testing did not show correlations between the pupil constriction amplitude and mental fatigue (Portman-Tiller, 1998), LeDuc et al. (2005) successfully showed the effects of mental fatigue using pupil constriction amplitude and latency.

The studies using blinks to indicate fatigue depicted an increase in blink frequency and mean blink duration with time-on-task. John A. Stern et al. (1984) attributed a reduction of blink frequency during a task (visual as well as non-visual) to increased attention to the task, followed by a compensation

by an increase in the number of blinks on the completion of the task. Eckstein et al. (2017) have theorized that this reduction in blink frequency during the task leads to the lack of moisture in the eyes and the subsequent increase in blinks toward the end of long experiments.

Neurologically, blink frequency has been used as a non-invasive measure of the neurotransmitter—dopamine due to the robust correlation between the two (Eckstein et al., 2017; Jongkees & Colzato, 2016; Nieoullon, 2002). This relationship also explains the lower blink frequency in Parkinson's patients, in whom the dopaminergic neurons are degenerating (Lou, 2009). Dopamine is involved in a network of the self-regulation of cognition (Lou, 2009), in the decision-making process of the exploitation of the ongoing task versus the exploration of different tasks (Boksem & Tops, 2008). When the network in the brain determines that the rewards from the ongoing task do not fulfill the expectations from the task, dopamine level reduces, resulting in the perception of fatigue. This reduction in dopamine is associated with a reduction in blink frequency. This suggests that the explanation of mental fatigue via neuroscience would indicate a decrease in blink frequency. The combined effects of the reduced dopamine, eye moisture, and the compensation for blink suppression, could affect blink measures due to mental fatigue. The increased blink frequency observed in the studies in this review could be due to an overall increase in blink frequency to compensate for blink suppression during the task and to regulate eye moisture. The relative changes in blinks due to each of the above factors need to be further researched.

Similar to blink duration, PERCLOS was hypothesized to increase with fatigue, but it is linked to the propensity to close the eyes during a state of drowsiness, as per the development of the metric for the detection of drowsiness during driving (Wierwille et al., 1994).

Some of the metrics used have no basis in prior hypotheses—pupil dilation range, mean ocular drift velocity, and fixation distance. They showed the effects of mental fatigue in one study each. These metrics are indicators of instability in the gaze and pupil, and they depict an increase in the instability due to mental fatigue (Di Stasi, McCamy, Macknik, et al., 2013).

By employing quality assessment scores, we identified features that could be more sensitive to mental fatigue than sleepiness, using criteria to eliminate the causes of sleepiness, such as inadequate sleep the night before the experiment or circadian effects. This set of features was derived from saccades, microsaccades, pupil, and eye movement. Saccade peak velocity seems the most promising among these, as it was consistent and verified by multiple studies. Another promising feature is normalized baseline pupil diameter, depicting the tonic changes in pupil size as a measure of mental fatigue. The only problem with this feature is the requirement of a controlled environment, to prevent changes in the pupil

due to varying illumination. This problem has been depicted in the studies included, which employed saccade features in varied indoor and outdoor settings, compared to the controlled laboratory settings where pupil size features were used to analyze effects of mental fatigue. Saccade and microsaccade peak velocity-magnitude slopes were introduced as features by Di Stasi, McCamy, Catena, et al. (2013) and shown to measure fatigue using various fatigue-inducing tasks such as cognitive tasks, surgery duty, aircraft flying, and driving. The tasks used to record eye movements, in the three of the four studies above were guided saccade task, generating prosaccades, and a driving task, causing voluntary saccades, in the last one. These features have shown to be responsive to mental fatigue in varied experimental conditions. Saccade duration, moreover, showed inconsistent results across the three studies it was used in, and requires further research. The last one of the features—eye movement—was computed using EEG frontal cortex electrodes (Wang et al., 2019). The study confirmed mental fatigue using questionnaires as well as using the power spectrum from the EEG signals. Further research is needed to resolve this feature in terms of the eye-based signal from the current EEG signal. An important note here is that none of the above features included blinks, which indicates that blinks are less sensitive to mental fatigue than sleepiness.

4.2 | Definition of mental fatigue

Although a definition of mental fatigue is not the basis for this review, it is a foundation for the understanding and measurement of mental fatigue. From the 17 papers that provided their understanding of mental fatigue, the following definition emerged as the accumulated one: mental fatigue is a subjective feeling associated with a reduction in mental resources, including attention and information processing abilities, and a reduced motivation that develops with sustained cognitive effort over time and that can impact task performance.

However, some papers either included drowsiness as a symptom of mental fatigue (Paladini et al., 2016), equated mental fatigue with fatigability (Burke et al., 2018), or provided no explicit understanding of mental fatigue (Di Stasi et al., 2015, 2016; Diaz-Piedra et al., 2016; Horiuchi et al., 2018; Lavine et al., 2002; LeDuc et al., 2005; Li, Chen et al., 2019; McGarrigle et al., 2017a, 2017b; Wang et al., 2019).

There are several existing theories on the generation of mental fatigue, as reviewed by (Pattyn et al., 2018). A traditional theory on fatigue describes a fixed pool of resources, depletion of which results in fatigue. However, this resource theory does not include the influence of motivation on fatigue. We shortly describe two theories which we expect to

have merit—the motivational control theory of fatigue and the cost-benefit theory. Both explain a series of computations on the cost of pursuing the current action and the benefits of the goals achieved, but while the latter suggests that the realization that the costs (efforts) required by the task are high and the rewards are low results in a reduced motivation on the task and subsequent increase in fatigue, the former theory suggests that repeated computations of costs and benefits and performing a task with low motivation is the cause for fatigue (Boksem & Tops, 2008; Hockey, 2010). Boksem & Tops have backed the cost-benefit theory with neuro-biological evidence on the cost-benefit computations.

4.3 | Behavior and mental fatigue

Mental fatigue definitions are generally associated with reductions in performance (Herlambang et al., 2019; Hopstaken et al., 2015a, 2016, 2015; Li, Li et al., 2019; Sengupta et al., 2017), as also proven in 10 of the 34 studies. However, in practice, the feeling of fatigue is often caused by an attempt to maintain performance on the task (Burke et al., 2018; Di Stasi et al., 2015; Marandi et al., 2018), which would result in no or minimal variation in the overall performance. Burke et al. (2018) verified this, as the reaction time on the cognitive task increased, but accuracy did not change, which could indicate that the participants, in an attempt to maintain the accuracy, took even more time to complete the task. Another reason for the low variation in performance could be a temporary increase in arousal levels in order to complete a short and simple task (Di Stasi, McCamy, Macknik, et al., 2013; Hopstaken et al., 2015a, 2015). In other studies, performance measures like accuracy were affected more by motivation (Herlambang et al., 2019) or task difficulty (Di Stasi, McCamy, Catena, et al., 2013; McGarrigle et al., 2017a) than by time.

4.4 | Limitations

4.4.1 | Experimental methods

When combining the studies and investigating the relation between mental fatigue and the eye-based metrics, it quickly became clear that a meta-analysis would not be possible due to the diversity in the experimental methods used. Comparison of the same metric between the studies was difficult for a number of reasons, including the duration of the experiment that varied from 20 min to 18 hr and the use of various combinations of fatigue, stress, or sleepiness questionnaires to detect the subjective feeling of fatigue. While Tian et al. (2012) obtained a positive correlation between the time-on-task and the mean blink duration for a space-vehicle

control task of 20 min, they concluded that the task did not cause mental fatigue. However, the results could not be verified due to a lack of analysis of a fatigue questionnaire or behavioral measures. In contrast, Song et al. (2015) found a negative correlation between the mean blink duration and the fatigue score, although the fatigue score increased with time on a spacecraft-support control task that lasted for 1 hr 45 min. Another inexplicable result is the lack of a pattern for the baseline pupil diameter in one study (Hopstaken et al., 2015b), although the same cognitive task performed for a similar amount of time (~2 hr) in similar experimental conditions resulted in a decrease in the baseline pupil diameter (Hopstaken et al., 2015a, 2015).

The diversity in the understanding of mental fatigue in the studies is realized by the variety of fatigue questionnaires used to verify the subjective feeling of mental fatigue. Even when multiple studies used the same questionnaire, a visual analog scale, the original scale had 18 items, whereas McGarrigle et al. (2017a) used a subscale with 13 items, and still others used only one item (Abbasi et al., 2018; Borragán et al., 2018; Herlambang et al., 2019; Paladini et al., 2016).

A number of studies used a driving task to induce mental fatigue, and the conditions of the experiment were monotonous and uncomplicated in three of the four studies. In driving research, this fatigue is termed *passive task-related fatigue*, and it requires minimal cognitive as well as physical activity. This type of fatigue is related to underload conditions, where participants experience fatigue due to boredom and low cognitive activity, as opposed to overload conditions that require high cognitive demand (May & Baldwin, 2009). It is debatable to compare the mental fatigue caused by driving in monotonous conditions to cognitive tasks that are customised to generate maximal cognitive load that would still allow high performance (Borragán et al., 2018). The fourth study added a secondary attention task to the existing driving task, which increased the complexity of the mental fatigue experiment and would make the task comparable to other cognitive tasks inducing cognitive load. A possible solution to clarify the cause of mental fatigue would be to verify whether the fatiguing task increases the cognitive load for the participants.

The use of nervous system stimulants such as caffeine can have invigorating effects on humans and counter fatigue (Connell et al., 2017), which is why multiple included studies asked participants to refrain from caffeine before performing the fatigue measurement experiments. However, missing even a morning coffee by habitual caffeine drinkers can initiate withdrawal effects (Phillips-Bute & Lane, 1997). A step toward control for the effect of caffeine could be to analyse data while controlling for the effect of caffeine intake. Controlling for effects of confounding variables is a common practice in medical articles (Nyklíček & Vingerhoets, 2000), and can be adopted using analysis methods such as regression.

A final matter for the experimental design is the use of dark or dimly lit rooms during the experiment. Most of the studies were not specific about the luminance level of the environment or the screen the participants were facing, but dimly lit rooms indicate low illuminance, which has been linked to low attention (Zhu et al., 2019). A recent study has attempted to disassociate mental fatigue and sleepiness (Hu & Lodewijks, 2020), and while the papers in this review have attempted to control for every known factor that could induce sleep-related fatigue, performing the experiment in dimly lit rooms is a questionable practice that could be argued to cause drowsiness, either in addition to or instead of mental fatigue.

4.4.2 | Data analysis

Transparency in the signal processing techniques is one of the most important requirements of a paper, as it allows the experiment to be repeatable. About 40% (14 papers) of the papers included in this review did not expand on the signal processing techniques or provide a description of the metrics used. Clear signal processing techniques are especially important when the same signals are obtained using various technologies, like EEG, EOG, eye-tracking, or video cameras.

A number of the metrics used for the measurement of mental fatigue, such as PERCLOS, have been derived from sleep studies (Hu & Lodewijks, 2020; Wierwille et al., 1994), because the concept of mental fatigue being different from sleepiness has been developed only recently in the field of psychology (Borghini et al., 2014; Hu & Lodewijks, 2020; Lal & Craig, 2001). There might be some basis for deriving the objective metrics from sleep studies, since both mental fatigue and drowsiness are associated with low arousal; however, it is important to determine whether the metrics respond differently to a state of mental fatigue than they do to drowsiness.

4.5 | Future directions

The analysis of the papers included in this review has shown that the following areas need consideration when measuring mental fatigue using eye-based features:

4.5.1 | Studies with patients

Multiple studies have measured mental fatigability and have found it higher in people with depression (Hopstaken et al., 2015), multiple sclerosis (Niepel et al., 2013; de Rodez Benavent et al., 2017), traumatic brain injury (Maruta et al., 2014; Möller et al., 2019), and hearing impairment (McGarrigle et al., 2017a; Wang et al., 2017) compared to

healthy controls. Mental fatigability is a problem for these patients as a result of changing neurobiology (Chaudhuri & Behan, 2004), and results in an expeditious feeling of mental fatigue. However, acute mental fatigue has not been studied in the patients. Understanding the progress of mental fatigue and its indicators in the target population is crucial to reducing the mental fatigability and thereby, the quality of life of the patients. Although inducing mental fatigue in patients with an underlying condition, with possible adverse effects on their health, may be ethically questionable, this can be important for the understanding and management of fatigue for the patients as well as for their caregivers.

4.5.2 | Taking advantage of non-invasive equipment

The non-invasive eye-tracking and EOG equipment provide a unique opportunity to assess mental fatigue in naturalistic settings, without disturbing the subject by asking questions, requesting additional tasks, or requiring the use of uncomfortable equipment. However, the use of the equipment for fatigue detection has not been brought into real-time scenarios. This is also discernible when reading the papers that used real-life scenarios of fatigue development and detection, in fields like health care (Di Stasi, McCamy, Macknik, et al., 2013), the military (Diaz-Piedra et al., 2016; LeDuc et al., 2005), or transportation (Di Stasi et al., 2016, 2012; Li, Chen et al., 2019; Wang et al., 2019). These would be the ideal situations where non-invasive, wearable equipment could continuously track the physiological signals. The current studies do not exploit the full potential of eye-tracking and EOG or their ability to detect mental fatigue using eye behavior during natural tasks.

4.5.3 | Better understanding of mental fatigue

The concept of mental fatigue is not standalone. It depends on sleepiness; it is affected by motivation and cognitive load, and it has an effect on attention. For a comprehensive understanding of mental fatigue, the following concepts need to be studied in relation to mental fatigue:

Sleepiness

The concepts of sleepiness and mental fatigue have only recently been differentiated in their definitions and understanding (Hu & Lodewijks, 2020). A few metrics used for mental fatigue detection find their origin in sleep research, but it is crucial to establish whether these metrics are actually detecting mental fatigue. We have outlined a checklist on the quality of the experiment design in Table 1, which would ensure

that mental fatigue is measured. We also propose controlling for confounding variables, such as caffeine intake, during data analysis.

Cognitive load and motivation

Mental fatigue is expected to be accompanied by degradation in task performance; however, that is not always the case. The reasons for this discrepancy could stem from a high motivation to maintain task performance by applying more effort despite experiencing mental fatigue. Higher cognitive load and low motivation are known to generate increased mental fatigue (Boksem et al., 2006; Borragán et al., 2017). It would be helpful to use various eye-based features in further studies on cognitive load and motivation and how they relate to mental fatigue. Another reason why performance decreases are not observed could be that mental fatigue does not exist in binary levels (i.e., fatigue/no fatigue), but ascending degrees of mental fatigue could exist, with each degree of mental fatigue affecting performance and behavior in non-linear ways.

Detection of mental fatigue in real-time can have major implications in various fields, such as critical professions like transportation, to prevent individuals from committing gross errors; like health care, to improve the quality of life of people disrupted by extreme fatigue, especially when it involves a technology used for communication, such as augmented and assisted communication system or brain-computer interfaces; and like education, to vary the length of classes depending on the topic and cognitive load it can generate. The metric that can detect mental fatigue in real-time could become a standard tool for mental health, similar to the use of heart rate to determine physical fitness.

In conclusion, the existing evidence from 34 papers shows the promise of 21 eye-based features for assessing mental fatigue. Pupil size features of baseline pupil diameter and peak pupil dilation have been shown to decrease with time-on-task; however, pupil size is currently usable in controlled laboratory settings only. The mean and peak velocity of saccades seem to have the most reliable results, even for mental activity of less than 30 min, and are versatile in terms of environmental conditions and fatiguing tasks. The eye-based metrics found to be more sensitive to mental fatigue, than to sleepiness, were saccade peak velocity, normalized baseline pupil diameter, and EEG-derived eye movements. Blinks increase with time-on-task, indicating a decrease in arousal, but this might be an indicator of sleepiness rather than mental fatigue. This line of research requires further investigation with respect to the relationship between mental fatigue and sleepiness and the differentiation in the detection of both.

CONFLICT OF INTEREST

We have no known conflict of interest to disclose.

AUTHOR CONTRIBUTIONS

Tanya Bafna: Conceptualization; Investigation; Methodology; Writing-original draft; Writing-review & editing. **John Paulin Hansen:** Funding acquisition; Supervision; Writing-review & editing.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

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