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SYSTEMATIC REVIEW

How to Tackle Mental Fatigue: A Systematic Review of Potential Countermeasures and Their Underlying Mechanisms

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Abstract

Introduction Mental fatigue (MF) is a psychobiological state that impairs cognitive as well as physical performance in different settings. Recently, numerous studies have sought ways to counteract these negative effects of MF. An overview of the explored countermeasures for MF is, however, lacking.

Objectives The objective of this review is to provide an overview of the different MF countermeasures currently explored in literature. Countermeasures were classified by the timing of application (before, during or after the moment of MF) and type of intervention (behavioural, physiological and psychological).

Methods The databases of PubMed (MEDLINE), Web of Science and PsycINFO were searched until March 7, 2022. Studies were eligible when MF was induced using a task with a duration of at least 30 min, when they assessed MF markers in at least two out of the three areas wherein MF markers have been defined (i.e., behavioural, subjective and/or [neuro]physiological) and used a placebo or control group for the countermeasure.

Results A total of 33 studies investigated one or more countermeasures against MF. Of these, eight studies assessed a behavioural countermeasure, 22 a physiological one, one a psychological countermeasure and two a combination of a behavioural and psychological countermeasure. The general finding was that a vast majority of the countermeasures induced a positive effect on behavioural (e.g., task or sport performance) and/or subjective MF markers (e.g., visual analogue scale for MF or alertness). No definitive conclusion could be drawn regarding the effect of the employed countermeasures on (neuro)physiological markers of MF as only 19 of the included studies investigated these measures, and within these a large heterogeneity in the evaluated (neuro)physiological markers was present.

Discussion Within the physiological countermeasures it seems that the use of odours during a MF task or caffeine before the MF task are the most promising interventions in combating MF. Promising behavioural (e.g., listening to music) and psychological (e.g., extrinsic motivation) countermeasures of MF have also been reported. The most assumed mechanism through which these countermeasures operate is the dopaminergic system. However, this mechanism remains speculative as (neuro)physiological markers of MF have been scarcely evaluated to date.

Conclusion The present systematic review reveals that a wide range of countermeasures have been found to successfully counteract MF on a subjective, (neuro)physiological and/or behavioural level. Of these, caffeine, odours, music and extrinsic motivation are the most evidenced for countering MF. To provide in-detail practical guidelines for the real-life application of MF countermeasures, more research must be performed into the underlying mechanisms and into the optimal dosage and time of application/intake.

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Key Points

The cognitive and/or physical impairments caused by mental fatigue can be partially countered by using a physiological, behavioural or psychological countermeasure.

Caffeine, odours, music and extrinsic motivation seem promising countermeasures against mental fatigue. However, the heterogeneity in the protocols to induce and determine mental fatigue makes it difficult to draw firm conclusions.

Future studies should evaluate the impact of the most promising countermeasures on (neuro)physiological markers of mental fatigue and on optimizing mental fatigue-combating interventions by combining multiple strategies.

1 Introduction

Mental fatigue (MF), which can be defined as a psychobiological state caused by prolonged episodes of cognitive exertion, has already been demonstrated to decrease accuracy and increase reaction time during cognitive tasks [1] and to deteriorate endurance performance [2–4], as well as technical and tactical aspects in team sports [5, 6]. Subsequently, in real-world settings such as car driving, within the workplace or in a sport setting, this leads to an elevated risk for accidents, injuries and/or incidents [7–9]. As such, research to counteract, avoid or habituate against MF has soared in recent years.

Countermeasures against MF have been evaluated within multiple settings, such as non-physical cognitive performance [10], as well as sport-specific settings [11, 12]. One example of this is the use of creatine to combat the MF-associated decrements in both cognitive and psychomotor performance [13, 14]. Van Cutsem et al. [13] argued that the occurrence of MF is associated with a drop in the phosphocreatine concentration in the brain; as such, creatine supplementation might be able to increase brain energy resources, postpone the drop in phosphocreatine and subsequently also the occurrence of MF. They discovered that creatine supplementation successfully counteracted the MF-associated decrease in cognitive performance, but not psychomotor performance [13]. Another example of a potential MF countermeasure is the adenosine receptor antagonist caffeine [15, 16]. Caffeine is a natural xanthine alkaloid that is able to cross the blood–brain barrier and block the adenosine receptors to alter central nervous system (CNS) function [15, 16]. Adenosine inhibits the release of brain excitatory neurotransmitters (e.g., dopamine) and reduces arousal and spontaneous behavioural activity. Indeed, the interplay between adenosine and dopamine may play an important mechanistic role in the MF-associated decrease in performance [17, 18]. Martin et al. [17] argued that mental exertion could result in an accumulation of cerebral adenosine, an inhibitory neuromodulator, increasing the excitatory stimulus required (leading to a higher perception of effort), as well as directly impacting both dopamine release and binding to its receptor. If true, this would provide a clear neurophysiological pathway through which caffeine can reduce MF and provide an easy-to-implement MF countermeasure within multiple contexts (e.g., work and sport) [11, 12, 19]. Moreover, non-nutritional interventions, for example the use of music, have also been found to counteract the negative impact of MF [20]. It has been proposed that music may act through increasing important neurotransmitter levels and, as such, attenuating feelings of pain and physical exertion experienced during physical performance [21, 22]. Therefore, the use of music is another promising countermeasure against MF which could be easily implemented in multiple settings.

Despite recent scientific interest in MF countermeasures, investigations into the methods, routines or substances are still in their infancy. Some studies [2, 11, 13, 14] have provided preliminary insight in the search for optimal MF countermeasures, but further understanding of the MF mechanisms is necessary to develop new and/or optimize already existing interventions. As no systematic review on possible MF countermeasures has been published, a possible consequence is that counter-, or preventative measures for MF are either being neglected or sub-optimally employed [23, 24]. Therefore, to optimise their use, the purpose of this review is to create an overview of the available MF countermeasures and their effectiveness.

To create a clear overview of the currently available MF countermeasures, we restricted this review to acute countermeasures. For the sake of clarity, we use the word 'countermeasure' to refer to an intervention or action taken to counteract or compensate for the effect(s) of something else. In this regard, the word countermeasure also includes measures that can work preventively or curatively against the negative consequences of MF on human functioning (i.e., subjectively, behaviourally and/or [neuro]physiologically). MF countermeasures can be considered to be acute, working within a few days after implementation (e.g., caffeine, creatine etc.) or chronic, with longer implementation periods (e.g., Brain Endurance Training, mindfulness etc.) [11, 13, 25, 26]. In the current review, we focused on interventions applied up to 7 days before a mentally fatiguing activity, i.e., acute countermeasures. The arbitrary choice for a maximum time interval of 7 days between the application/intake of a countermeasure and the actual activity that might trigger MF was based on the assumption that MF countermeasures that require more than 7 days to positively impact MF will be more challenging to implement in most settings (e.g., time consuming, not worth the investment) and therefore are less applicable. Within the acute countermeasures we further classified the interventions based on (1) the timing of application of the countermeasure (before/during/after engaging in a task that possibly triggers MF); and on (2) the nature of the countermeasure (behavioural, e.g., taking a break [27], psychological, e.g., increase of motivation [28] or physiological, e.g., nutritional, pharmacological interventions [11]). These distinctions are likely to further support understanding and the real-world implications of such interventions. This classification should, in the end, serve to apply the available MF countermeasures more easily and optimally in the relevant context.

2 Methods

This systematic review was completed using the PRISMA (Preferred Reporting Items for Systematic review and Meta-analyses) guidelines [29].

2.1 Eligibility Criteria

To establish the keywords for this systematic review, PICOS categories (Population, Intervention, Comparison, Outcome and Study design) were used (see Table 1). For the population, studies using healthy adults (aged 18–50 years) were included in this review. In terms of the intervention, the focus was on acute (up to 7 days prior) MF countermeasures with a physiological, behavioural or psychological basis. Additionally, a placebo or control group had to be included in the design in order to obtain studies of high quality. Concerning the main outcomes, studies were only found eligible if they assessed at least two out of the three areas in which markers of MF have been defined: behavioural (e.g., performance on a cognitive/physical task), subjective (e.g., perception of MF using a visual analogue scale [VAS]) or (neuro)physiological MF markers (e.g., brain activity through electroencephalography), after performing a MF-inducing task with a duration of at least 30 min. In one of our previous systematic reviews on the effects of mental fatigue on physical performance [2], studies from ego depletion literature (i.e., where prior cognitive exertion most often lasts < 30 min) were excluded. Although two recent meta-analyses have demonstrated decrements in physical performance subsequent to shorter (< 30 min) and longer (> 30 min) cognitive tasks [3, 30], this time cut-off was maintained. When task difficulty is similar, task duration negatively affects subsequent task performance [31, 32] with 30 min appearing to be a consistent threshold for MF-related performance impairments [2, 33, 34]. In addition, the vigilance decrement that typically occurs after 20–30 min of continuous work in the literature on sustained attention [2, 33], and the typical 30-min time range in which an increase in perceived mental fatigue is often observed in the literature on mental fatigue [2, 34], further supports the 30-min time cut-off. Lastly, in terms of study design, only randomized controlled trials (RCTs) or non-randomized controlled trials (nRCTs) were included for further review.

2.2 Information Sources and Search Strategy

Three electronic databases, PubMed, Web of Science (WoS) (all databases) and PsycINFO were searched until March 7, 2022. Medical subject heading (MeSH) terms, if available in PubMed, were used for a qualitative literature search. See Table 2 for an overview of the keywords that were used in the different databases. In addition, the reference lists of included studies, and studies that cited the included studies, were screened.

2.3 Study Selection

After executing the search strategy, all studies from the different databases were gathered and imported into Rayyan [35]. After removing duplicates, two authors (MP and JH) screened the studies, independently and blinded from each other, on title and abstract. Studies were included and excluded following the inclusion and exclusion criteria (see Table 3). Conflicts concerning the included or excluded studies at this stage of screening were resolved, then full texts of the remaining studies were screened by the same

Table 1 PICOS (population, intervention, comparison, outcome and study design)

PICOS	Keywords
Population	Humans, healthy, adults (18–50 years)
Intervention	Mental fatigue countermeasures (physiological, behavioural, psychological)
Comparison	Placebo or control group
Outcome	Mental fatigue (subjective, behavioural, [neuro]physiological markers) induced by a task lasting ≥ 30 min
Study design	RCT, nRCT

nRCT non-randomized controlled trial, *RCT* randomized controlled trial

Table 2 Number of hits for the complete search strategy for the different databases

Database	Complete search string	Hits (07/03/2022)
PubMed	(("Humans"[Mesh]) OR ("Participants") OR ("Athletes") OR ("Athletes"[Mesh]) OR ("Men"[Mesh]) OR ("Women"[Mesh]) OR ("Adult"[Mesh]) OR ("Students"[Mesh]) OR ("Healthy Volunteers"[Mesh])) AND (("Countermeasures") OR (Nutritional Sciences[Mesh]) OR (Nutrition) OR (Pharmacology[Mesh]) OR (Pharmacology) OR (Chemicals and Drugs Category[Mesh]) OR ("Caffeine"[Mesh]) OR ("caffeine") OR ("Vitamins"[Mesh]) OR ("Vitamins") OR ("Rhodiola"[Mesh]) OR ("Rhodiola") OR (Panax[Mesh]) OR (Ginseng) OR (ginkgo biloba) OR (flavanol) OR ("Creatine") OR ("Iron") OR ("Magnesium") OR ("Carbohydrates") OR ("Nitrates") OR (" Mouth Rinse") OR ("Chewing Gum") OR ("Polyphenols") OR ("Tea") OR ("Coffee") OR (Behavior and Behavior Mechanisms[Mesh]) OR ("Behavioural") OR ("napping") OR ("task switching") OR ("Exercise"[Mesh]) OR ("Exercise") OR ("Music"[Mesh]) OR ("Music") OR ("Binaural beats") OR (Mental Processes[Mesh]) OR ("Self Efficacy") OR ("Mindfulness") OR ("Motivation") OR ("Energy drinks")) AND (("Mental Fatigue"[Mesh]) OR ("Mental Fatigue") OR ("Central Fatigue") OR ("Cognitive Fatigue") OR ("Cognitive Exertion") OR ("Mental Exertion") OR ("Ego Depletion") OR ("Mental Strain") OR ("Cognitive Strain") OR ("Mental exhaustion") OR ("Driving Fatigue")) NOT (("Multiple Sclerosis"[Mesh]) OR ("Neoplasms"[Mesh]) OR ("Stroke"[Mesh]) OR ("Disease"[Mesh]) OR ("Infections"[Mesh]) OR ("Immune System Diseases"[Mesh]) OR ("Endocrine System Diseases"[Mesh]) OR ("Digestive System Diseases"[Mesh]) OR ("Animal Diseases"[Mesh]) OR ("Respiratory Tract Diseases"[Mesh]) OR ("Patients") OR ("Burnout") OR ("Parkinson"))	2580
Web of Science	TS = ((("Humans") OR ("Participants") OR ("Athletes") OR ("Men") OR ("Women") OR ("Adult") OR ("Students") OR ("Healthy Volunteers")) AND (("Countermeasures") OR ("Nutritional Sciences") OR (Nutrition) OR (Pharmacology) OR (Chemicals and Drugs Category) OR ("Caffeine") OR ("Vitamins") OR ("Rhodiola") OR (Panax) OR (Ginseng) OR (ginkgo biloba) OR (flavanol) OR ("Creatine") OR ("Iron") OR ("Magnesium") OR ("Carbohydrates") OR ("Nitrates") OR (" Mouth Rinse") OR ("Chewing Gum") OR ("Polyphenols") OR ("Tea") OR ("Coffee") OR (Behavior and Behavior Mechanisms) OR ("Behavioural") OR ("napping") OR ("task switching") OR ("Exercise") OR ("Music") OR ("Binaural beats") OR (Mental Processes) OR ("Self Efficacy") OR ("Mindfulness") OR ("Motivation") OR ("Energy drinks")) AND (("Mental Fatigue") OR ("Central Fatigue") OR ("Cognitive Fatigue") OR ("Cognitive Exertion") OR ("Mental Exertion") OR ("Ego Depletion") OR ("Mental Strain") OR ("Cognitive Strain") OR ("Mental exhaustion") OR ("Driving Fatigue")) NOT (("Multiple Sclerosis") OR ("Neoplasms") OR ("Stroke") OR ("Disease") OR ("Infections") OR ("Immune System Diseases") OR ("Endocrine System Diseases") OR ("Digestive System Diseases") OR ("Animal Diseases") OR ("Respiratory Tract Diseases") OR ("Patients") OR ("Burnout") OR ("Parkinson")))	1049
PsycINFO	(("Humans") OR ("Participants") OR ("Athletes") OR ("Men") OR ("Women") OR ("Adult") OR ("Students") OR ("Healthy Volunteers")) AND (("Countermeasures") OR (Nutritional Sciences) OR (Nutrition) OR (Pharmacology) OR (Chemicals) OR (Drugs) OR ("Caffeine") OR ("caffeine") OR ("Vitamins") OR ("Rhodiola") OR (Panax) OR (Ginseng) OR (ginkgo biloba) OR (flavanol) OR ("Creatine") OR ("Iron") OR ("Magnesium") OR ("Carbohydrates") OR ("Nitrates") OR ("Mouth Rinse") OR ("Chewing Gum") OR ("Polyphenols") OR ("Tea") OR ("Coffee") OR (Behavior) OR (Behavior Mechanisms) OR ("Behavioural") OR ("napping") OR ("task switching") OR ("Exercise") OR ("Music") OR ("Binaural beats") OR (Mental Processes) OR ("Self Efficacy") OR ("Mindfulness") OR ("Motivation") OR ("Energy drinks")) AND (("Mental Fatigue") OR ("Central Fatigue") OR ("Cognitive Fatigue") OR ("Cognitive Exertion") OR ("Mental Exertion") OR ("Ego Depletion") OR ("Mental Strain") OR ("Cognitive Strain") OR ("Mental exhaustion") OR ("Driving Fatigue"))	1061

Table 3 Inclusion and exclusion criteria

Inclusion	Exclusion
Healthy population (aged 18–50 years)	Elderly patients
Mental fatigue-inducing task ≥ 30 min	Animal studies
Mental fatigue measured at a minimum of 2 of the 3 different markers (subjective, behavioural or physiological)	Disorders (multiple sclerosis, Alzheimer's disease etc.)
Placebo/control group/task	Intervention > 1 week
Intervention ≤ 1 week	

two authors (MP and JH). In addition, the reference lists of included studies (i.e., backward screening), and studies that cited the included studies (i.e., forward screening) were screened to make the search as complete as possible.

2.4 Data Extraction

To answer the research question, all details concerning the effect on MF (subjectively, behaviourally or [neuro] physiologically), type, timing of application and possible effects of the countermeasures were extracted from the included studies and are summarized in Table 4. Other extracted information included study design, participant demographics, sample size, control/placebo groups and MF intervention. As already mentioned in Sect. 1, included studies were further classified based on (1) the timing of application of the countermeasure (before/during/after engaging in a task that possibly triggers MF); and on (2) the nature of the countermeasure (behavioural, psychological or [neuro] physiological). We are well aware that this classification is arbitrary and that, certainly in terms of the classification based on the nature of the countermeasures, multiple evaluated countermeasures could fit in multiple subdivisions. For example, the countermeasure ‘taking a break’ was classified as a behavioural countermeasure because it requires a behavioural change by the individual to take a break. However, classifying ‘taking a break’ as a psychological countermeasure because a motivational effect is expected might also be considered. In general, countermeasures that primarily required an individual to undertake or undergo a specific activity that is different from the MF-inducing task were classified as ‘behavioural countermeasures’. Countermeasures that were primarily developed to impact an individual’s perception were classified as ‘psychological countermeasures’. Countermeasures that primarily aimed to impact the body’s physiology, via the intake of some kind of nutritional/pharmacological agent or the application of stimulation techniques, were classified as ‘physiological countermeasures’.

2.5 Risk of Bias Assessment

All included studies were individually assessed for risk of bias (RoB). Since both within- (i.e., crossover) and between-subject study designs were included, separate RoB tools were utilized dependent on the study design. For studies using a within-subject design, the revised Cochrane risk-of-bias tool for randomized crossover trials (RoB 2 for crossover trials) was utilised. The revised Cochrane risk-of-bias tool for randomized trials (RoB 2) [36] was used for between-subject studies. Two authors (MP and JH) performed this RoB assessment. Finally, conflicts between the authors were resolved through discussion until consensus was reached and an overall risk of bias, following the recommended protocol, was made for each study.

3 Results

3.1 Study Selection

The systematic literature search yielded 4690 studies from all selected databases. Due to duplicate records, 735 studies were removed resulting in a total of 3955 studies for further evaluation. Figure 1 displays a flow diagram of the selection process. After the first round, 86 studies were selected for further screening. The full-text evaluation resulted in 30 included studies. Forward and backward screening provided three additional papers, resulting in a total of 33 studies that were included in the present systematic review. The level of blinded agreement for title plus abstract and for the full-text screening were 97.1% and 98.1%, respectively.

3.2 Risk of Bias

All 33 included studies, of which ten are between-subject and 23 within-subject design studies, were screened for risk of bias (see Figs. 2, 3). This assessment determined that 25 studies [12, 14, 20, 26, 27, 37–56] had a high risk of bias, three studies [57–59] had some concerns of bias and five studies [11, 13, 60–62] had a low risk of bias.

3.3 Study Characteristics

A summary of included study characteristics can be found in Table 4. All studies included healthy individuals, covering a total population of 1012 participants (53% male when sex reported). Nine studies used a male-only population [11, 12, 43, 47–49, 52, 58, 62], one study a female population [55] and three studies did not report the sex of their participants (93 participants of the total) [44, 45, 61]. The average age of all participants was 26 years old, ranging between 18 and 45 years old. A total of six studies included a physical task whereby information on the physical fitness of the participants was mentioned [11, 13, 43, 49, 61, 62]. Table 5 provides an overview of the different types and timing of application of the evaluated countermeasures.

3.4 Type of Countermeasure

3.4.1 Behavioural

Ten studies used a behavioural countermeasure (see Sect. 2 for a definition) [20, 26, 27, 40, 45–47, 54, 55, 59]. Of these, five studies used a physical sensation-based intervention (e.g., physical activity and massage) [40, 45, 47, 54, 59], four other studies utilized an auditory intervention (e.g., listening to music) [20, 26, 40, 45], and two studies [27, 46] assessed the effect of a nap on MF. As well as utilising a nap, Hayashi et al. [27] incorporated a moment of rest in the middle of the task as an extra countermeasure in their study. Tanaka and colleagues [55] provided the only investigation into the effect of sitting in an open space connected to nature on the restoration of performance after MF. In a combined approach, Lim et al. [45] sought to understand if the use of a mechanical massage chair in conjunction with binaural beats

Table 4 Overview of the characteristics across all included studies

Study	Sample	Design	Interventions	Outcome measures	Results
Behavioural countermeasures					
Guo et al. [20]	*N:* 36 (18 ♀, 18 ♂) Age: 20.33 ± 1.26 years	Between subjects	*MF-CM*: ● CM1: Instrumental folk music ● C: No music *MOA:* During MF task *MF task*: 60-min AX-CPT	*Before and after MF-inducing task:* ● 15-min Go/NoGo task (with a rest every 5 min) *After each cognitive task:* ● VAS for: alert/concentrated, anxious, energetic, confident, irritable, jittery/nervous, sleepy, talkative *During Go/NoGo task*: ● EEG (ERP) ● EOG	CM1 vs C: ↑ VAS for alert/concentrated, energetic, confident + ↑ Go-P3 and NoGo-P3 amplitudes in EEG C vs CM1: ↑ RT in Go/NoGo task
Hayashi et al. [27]	*N:* 10 (6 ♀, 4 ♂) Age: 21.7 ± 2.5 years	Within subjects	*MF-CM*: ● CM1: Nap ● C: Rest *MOA:* In the middle of MF task, for 20 min *MF task*: VDT, a memory search task, for 120 min	*Every 10 min during MF task*: ● VAS for sleepiness, fatigue, work motivation *Beginning and end of MF task and before and after the 20-min intervention*: ● Fatigue questionnaire *Throughout the study*: ● EEG (BO) ● EOG ● EMG submentalis ● VDT Task performance	CM1 vs C: ↑ VDT task performance + ↑ VAS for work motivation + ↓ VAS for sleepiness + ↓ VAS for fatigue
Jacquet et al. [40]	*N*: 37 (30 ♀, 7 ♂) Age: 20.7 ± 0.7 years	Between subjects	*MF-CM*: ● CM1: Physical activity (15 min on an ergo-cycle, moderate intensity) ● CM2: Music (15 min) ● C: Rest/talking (10 min) *MOA:* After MF task *MF task*: 32-min TLDB	*Before experimental session:* ● Saint Mary's Hospital Sleep Questionnaire *During MF task:* ● EEG (BO) ● EOG ● MF task performance *At the start, after MF task, after MF-CM:* ● EEG (BO) ● M-VAS *After MF-CM:* ● VAS for pleasantness *Before MF task and after MF-CM:* ● Arm-pointing task	C vs CM1 & CM2: ↑ Movement duration of arm-pointing task CM1 vs CM2: ↑ Alpha power of EEG (BO) + ↓ errors in arm-pointing task

Table 4 (continued)

Study	Sample	Design	Interventions	Outcome measures	Results
Lim et al. [45]	*N:* 25 (? ♀, ? ♂) Age: 20–50 years	Within subjects	*MF-CM*: ● CM1: Mechanical massage (20 min) ● CM2: Mechanical massage + binaural beats (20 min) ● C: Relax (20 min) *MOA:* Before and after MF task *MF task*: 40 min of cognitive tests (d2test, Digit span test, Corsi block-tapping test, Picture recognition test, Face recognition test)	*Throughout the study:* ● EEG (BO) ● Task performance of cognitive tests	CM2 vs CM1 & C: ↓ MF in both EEG indices + ↑ test scores on Digit span test and Picture recognition test CM2 & CM1 vs C: ↑ Test score of Face recognition test
Mizuno et al. [47]	*N:* 14 (14 ♂) Age: 22 ± 1.1 years	Between subjects	*MF-CM*: ● CM1: Mild-stream bathing (10 min) ● C: Normal bathing (10 min) *MOA:* After MF task *MF task*: Four sections of 30-min ATMT + 30-min 2-back test. Break of 40 min in the middle for lunch	*Before MF task:* ● M-VAS ● Task performance ATMT *Before and after MF-CM:* ● APG ● Muscle stiffness Blood pressure ● M-VAS ● HR ● Axillary temperature ● Blood samples ● Task performance ATMT	CM1 vs C: ↑ Δ HR + ↓ muscle stiffness + ↓ reaction times ATMT No differences for M-VAS
Oberste et al. [59]	*N:* 99 (47 ♀, 52 ♂) Age*:* 21.6 ± 3.6 years	Between subjects	*MF-CM*: ● CM: Aerobic exercise on cycle ergometer (30 min, 65–75% of VO_2 peak) ● Passive C: Watching sitcom (1 episode) ● Active C: Lower body stretching routine (30 min) *MOA:* After MF task *MF task*: 36-min continuous attention test (DAUF) + 9-min N-Back test + 15-min Stroop task = 60 min	*Before, after MF task and after MF-CM:* ● Cognitive flexibility using the task performance of part B of the Trail Making Test ● Multidimensional Mood State Questionnaire ● VAS for self-perceived cognitive performance ● VAS for motivation	After CM, Passive C and Active C: ↑ Cognitive flexibility + ↑ subjective wellbeing CM vs Passive C + Active C: ↑ Cognitive flexibility + ↑ mood + ↑ motivation + ↑ self-perceived cognitive performance
Tanaka et al. [54]	*N:* 16 (7 ♀, 9 ♂) Age: 28.9 ± 7.2 years	Between subjects	*MF-CM*: ● CM1: Sitting in a room with a pellet stove ● C: Looking at a monitor on which a pellet stove was displayed *MOA:* After the MF task they sat for 30 min in a room equipped with either CM1 or C *MF task*: 30-min 2-back test	*Before MF task, after MF task and after MF-CM:* ● ATMT performance ● VAS for fatigue; healing; comfort; warmth ● APG	CM1 vs C: ↓ Subjective scores for fatigue + ↑ comfort and warmth + ↓ change in total error counts + ↓ sympathetic nerve activity + ↑ parasympathetic nerve

Table 4 (continued)

Study	Sample	Design	Interventions	Outcome measures	Results
Tanaka et al. [55]	*N*: 16 (16 ♀) Age: 43.5 years	Between subjects	*MF-CM*: ● CM1: Sitting in a room with an open space connected to nature ● C: Sitting in a room without an open space connected to nature *MOA:* After the MF task they sat for 30 min in CM1 or C *MF task*: 30-min 2-back test	*Before MF task, after MF task and after MF-CM:* ● ATMT performance ● VAS for fatigue; relaxation; comfort; healing ● APG	CM1 vs C: ↑ Relaxation, comfort and healing + ↓ total error counts on ATMT performance No difference for APG
Physiological countermeasures					
Ataka et al. [56]	*N*: 17 (9 ♀, 8 ♂) Age: 36.5 ± 5.2 years	Within subjects	*MF-CM*: ● CM1: 4 × capsules (25 mg CAF and other neutral compounds) ● CM2: 4 × capsules (250 mg D-ribose and other compounds) ● P: 4 × capsules (no active compounds) *MOA:* 2/day for 1 wk before the experimental day + during the trials *MF task:* 4 × UKT (30 min) + ATMT (30 min)	*Before MF, right after MF and 3 h after MF:* ● VAS for fatigue VAS for motivation ● VAS for sleepiness ● ATMT task performance ● Blood sample (BCAAs)	CM1 (vs P): ↑ ATMT performance during fatigue-inducing mental tasks. No effect on subjective scales CM2 (vs P): No effect
Azevedo et al. [11]	*N:* 8 (8 ♂) Age: 24 ± 2 years	Within subjects	*MF-CM*: ● CM1: capsule with 5 mg/kg CAF ● P: capsule with no active compounds *MOA:* Before MF task, 90 min before cycling test *MF task:* 90-min AX-CPT	*During cycling tests:* ● EMG ● HR ● VO_2 ● VO_2 peak ● Peak HR ● RPE *Before and after MF task:* ● Glucose ● POMS (vigor + fatigue) *Before, immediately after, 3rd and 5th min of recovery:* ● Lactate	CM1 vs P: ↑ Δ Endurance capacity + ↑ W_{total} P vs CM1: ↑ RPE (2nd min) + ↑ Δ fatigue + ↓ Δ vigor (vs I1)
Bailey et al. [42]	*N:* 15 (9 ♀, 6 ♂) Age: 23 ± 1 years	Within subjects	*MF-CM*: ● CM1: Mouth rinse with a CHO solution (6.4% maltodextrin carbohydrate) ● P: Mouth rinse with a solution with no active compounds *MOA:* During MF task, between each bout *MF task:* 60-min Stroop Color Word Test	*During MF task:* ● Stroop Color Word Test task performance (reaction time & accuracy) *Before and after MF task:* ● Motor-evoked potential *After MF task:* ● M-VAS	CM1 vs P: No sig. effect of CM1 on Stroop Color Word test task performance (reaction time & accuracy) P vs CM1: ↑ Increase in M-VAS + ↑ relative reduction in motor-evoked potential

Table 4 (continued)

Study	Sample	Design	Interventions	Outcome measures	Results
Brietzke et al. [43]	*N:* 20 (20 ♂) Age: 35 ± 7 years	Within subjects	*MF-CM*: ● CM1: Mouth rinse with a CHO solution (64 g of maltodextrin diluted in 1L of P solution) ● P: Mouth rinse with a solution with no active compounds ● C: Nothing *MOA:* After the MF task, at the end of the warm-up + at 25%, 50% and 75% of the MIT *MF task*: 40-min RVIP test	*Throughout the MIT:* ● W_{peak} ● Time to exhaustion ● Gas exchange (VE, VO_2, VCO_2) ● EEG (BO) ● RPE *Before and after MF task:* ● M-VAS	CM1 vs P & C: ↑ W_{peak} + ↑ time to exhaustion CM1 & P vs C: ↑ PFC activation during MIT
Franco-Alvarenga et al. [61]	*N:* 12 (? ♀, ? ♂) Age: 34.3 ± 6.2 years	Between subjects	*MF-CM*: ● CM1: Capsule with 5 mg/kg CAF ● P: capsule with no active compounds *MOA:* Before MF task, ± 50 min before TT20km *MF task*: 40-min RVIP test	*Throughout the TT20km:* ● RPE ● Motivation ● FAS ● Feeling scale ● RPEw *Before and after MF task:* ● M-VAS ● FAS ● Motivation *During 3-min rest, before and after the MF task:* ● EEG (BO) *Throughout the study:* ● RVIP task performance ● TT20km (Time to complete and W_{mean})	CM1 vs P: ↓ FAS + ↑ TT20km performance No sig. effect on motivation, RVIP task performance, EEG, RPE and RPEw
Ishihara et al. [38]	*N:* 37 (36 ♀, 1 ♂) Age: 20.5 years	Within subjects	*MF-CM*: ● CM1: CRT unit on (creating a magnetic field) ● CM2: CRT unit off (no magnetic field) *MOA:* During MF task *MF task*: 90 min of VDT work	*Before and after MF task:* ● Saliva samples ● Urine samples ● ISP questionnaire	CM1 vs CM2: No statistical sig. differences between both groups after MF task
Kato et al. [39]	*N:* 24 (8 ♀, 16 ♂) Age: 23.6 years	Within subjects	*MF-CM*: ● CM1: Odours (Citral, green (cis-3-hexanal) and menthol) ● C: No odour *MOA:* During MF task, from block 5 to 12 for 35 s every 145 s *MF task*: 60 min of Go/NoGo task (12 blocks, 30 s in between blocks)	*Before and after experimental session:* ● Fatigue scale ● Perceived intensity and pleasantness of each odour *During MF task:* ● EEG (ERP) ● EOG ● MF task performance	CM1 vs C: ↓ Time-on-task RT increase, no changes for accuracy of Fatigue scale ↑ In Go- and NoGo-P3 amplitudes

Table 4 (continued)

Study	Sample	Design	Interventions	Outcome measures	Results
Kennedy & Scholey [44]	Study 1: *N*: 30 (? ♀, ? ♂) Age: 21.5 ± 3.5 years Study 2: *N*: 26 (? ♀, ? ♂) Age: 21 ± 3 years	Between subjects	*MF-CM*: ● Study 1: ● CM1.1: 38 mg of CAF and 68 g of glucose in 380-mL drink ● CM1.2: 46 mg of CAF and 68 g of glucose in 380-mL drink ● P1: 380-mL drink with no active compounds Study 2: ● CM2.1: 33 mg of CAF and 60 g of glucose in 330-mL drink ● P2: 380-mL drink with no active compounds *MOA:* Study 1 + Study 2: 10 min before MF task *MF task*: Study 1 + Study 2: 6 × 10-min CDB (2-min Serial Threes, 2-min Serial Sevens, 5-min RVIP, 1-min M-VAS)	*During MF task:* ● M-VAS ● MF task performance	CM1.1, CM1.2, CM2.1 vs P1 & P2: ↑ Accuracy on RVIP CM1.2, CM2.1 vs P1 & P2: ↓ M-VAS CM1.2 vs P1: ↑ Accuracy on the Serial Sevens task
Kennedy et al. [60]	*N:* 130 (70 ♀, 60 ♂) Age: 21 ± 1.6 years	Within subjects	*MF-CM*: ● CM1: Vitamin/mineral/guarana tablet (Berocca Boost®) dissolved in 200 mL water ● P: Placebo drink with no active compounds *MOA:* 30 min before MF task *MF task*: Six × 10-min CDB (2-min Serial Threes, 2-min Serial Sevens, 5-min RVIP, 1-min M-VAS)	*During MF task:* ● M-VAS ● MF task performance *Pre-intervention and 30-min post-intervention:* ● Saliva samples	CM1 vs P: ↑ Speed and accuracy of performing RVIP + ↓ M-VAS
Kennedy et al. [57]	*N:* 24 (15 ♀, 9 ♂) Age: 25.2 ± 6.8 years	Within subjects	*MF-CM*: ● CM1: 100 µL Mentha piperita essential oil consumed with 200 mL full-fat milk ● CM2: 50 µL Mentha piperita essential oil consumed with 200 mL full-fat milk ● P: Placebo capsules with no active compounds *MOA:* 60 min before first cognitive assessment *MF task*: 4 × 10-min CDB (2-min Serial Threes, 2-min Serial Sevens, 5-min RVIP, 1-min M-VAS)	*Before the Cognitive Demand Battery*: ● STAI ● Bond-Lader Mood Scales ● Word, Picture, Face/Name Presentation ● Immediate Word Recall ● CRT ● RVIP ● Corsi Blocks *During the Cognitive Demand Battery:* ● M-VAS *After the Cognitive Demand Battery:* ● Peg and Ball Task ● Delayed Word recall (2 times), Name/Face recall, Picture recognition	CM1 vs P: ↓ M-VAS at 3 h post-dose ↑ Accuracy of performing RVIP at 1 h and 3 h post-dose ↑ Correct Serial Threes at 3 h post-dose

Table 4 (continued)

Study	Sample	Design	Interventions	Outcome measures	Results
Li et al. [41]	*N:* 40 (20 ♀, 20 ♂) Age: 27.4 ± 2.6 years	Within subjects	*MF-CM*: ● CM1: Magnitopunctures applied to the Dazhui (DU14) point and Neiguan (PC6) points ● C: Magnitopunctures were applied to non-acupuncture points *MOA:* In the last 60 min of the 180-min MF task *MF task*: High-speed driving continuously for 180 min	*During MF task:* ● Heart rate *Before and after MF task:* ● Vigilance task performance ● CFF *After MF task* ● Borg's category ratio	C vs CM1: ↓ Vigilance task performance (reaction time + correc-tive rate) + ↑ CFF + ↑ some fatigue symptoms of Borg scale
Nagai et al. [48]	*N:* 20 (20 ♂) Age: 21.1 years	Within subjects	*MF-CM*: ● CM1: 140 mL of Brand's Essence of Chicken ● C: 140 mL of placebo with no active compounds *MOA:* For 7 days in the morning, before the experimental day *MF task*: MAT for 40 min + SMT (20 tri-als of memorizing 9 digit numbers)	*Before and after MF task* ● Blood samples ● POMS *During MF task* ● MAT + SMT task performance	CM1 vs C: ↑ Recovery of mean cortisol level + ↑ 'Anger' + ↑ 'Ten-sion' + no change in fatigue pre-post + ↑ performance on MAT + SMT C vs CM1: ↑ Fatigue pre-post
Penna et al. [49]	*N:* 10 (10 ♂) Age: 30 ± 6 years	Within subjects	*MF-CM*: ● CM1: tDCS (Left temporal cortex) (30 min) ● C: Sham (30 min) *MOA:* Last 30 min of MF task *MF task*: 45 min of the paper version of the Stroop Colour test	*Before and after MF task + MF-CM:* ● M-VAS *After MF task + MF-CM:* ● M-VAS for MF ● VAS for motivation Swimming performance (time taken) *During Swimming Performance:* ● RPE	CM1 vs C: No sig. differences for M-VAS, VAS for motivation and swimming performance
Rattray et al. [62]	*N:* 13 (13 ♂) Age: 23 ± 4 years	Between subjects	*MF-CM*: ● CM1: 400 mg modafinil ● P: Placebo *MOA:* 90 min before MF task *MF task*: 90 min of modified incongruent Stroop task	*Before MF-CM, 75 min after MF-CM, after MF task:* ● M-VAS ● VAS for motivation ● AX-CPT task performance *After MF task:* ● BRUMS ● NASA-TLX ● SIMs ● Performance TTE ● Stroop Task performance *During MF task and TTE* ● HR *During TTE:* ● RPE	CM1 vs P: ↑ TTE performance + ↓ reaction time of Stroop + ↓ mental demand, physical demand, frustration No sig. differences for M-VAS and motivation-VAS

Table 4 (continued)

Study	Sample	Design	Interventions	Outcome measures	Results
Reay et al. [50]	*N:* 30 (16 ♀, 14 ♂) Age: 22.6 ± 5.5 years	Between subjects	*MF-CM*: ● CM1: 200 mg Panax Ginseng extract (2 capsules of 100 mg) + 2 capsules of placebo ● CM2: 400 mg Panax Ginseng (4 capsules of 100 mg) ● P: Four capsules of placebo *MOA:* 60 min before MF task *MF task*: 6 × 10-min CDB (2-min Serial Threes, 2-min Serial Sevens, 5-min RVIP, 1-min M-VAS)	*During MF task:* ● M-VAS ● MF task performance *Baseline, 1 h after MF-CM and after the third and sixth completion of CDB* ● Blood glucose	CM1 & CM2 vs P: ↓ Blood glucose levels CM1 vs CM2 & P: ↑ Correct responses Serial Sevens + ↓ subjective ratings of MF on completion 2–6 of CDB CM2 vs CM1 & P: ↓ Subjective ratings of MF on completion 3 of CDB
Reay et al. [51]	*N:* 27 (10 ♀, 17 ♂) Age: 21.9 ± 4.6 years	Between subjects	*MF-CM*: ● CM1: 200 mg Panax Ginseng (capsules)/0 mg glucose (drink) ● CM2: 0 mg Panax Ginseng/25 g glucose ● CM3: 200 mg Panax Ginseng/25 g glucose ● P: 0 mg Panax Ginseng/0 mg glucose *MOA:* Capsules: 60 min before MF task; Drinks: 30 min before and 30 min after MF task *MF task*: 6 × 10-min CDB (2-min Serial Threes, 2-min Serial Sevens, 5-min RVIP, 1-min M-VAS)	*During MF task:* ● M-VAS ● MF task performance *Baseline, 1 h after MF-CM and after the sixth completion of CDB* ● Blood glucose	CM2 & CM3 vs CM1 & P: ↑ Blood glucose 1 h post-dose CM1 vs CM2, CM3 & P: ↓ Blood glucose levels 1 h post-dose + ↑ number of performed Serial Threes subtractions at completion 3, 4 and 6 of CDB + ↓ subjective ratings of MF on completion 5 and 6 of CDB CM2 vs CM1, CM3 & P: ↑ Number of performed Serial Threes subtractions at completion 3, 4 and 6 of CDB + ↓ subjective ratings of MF on completion 5 and 6 of CDB
Saito et al. [52]	*N:* 17 (17 ♂) Age: 33.8 ± 11.7 years	Between subjects	*MF-CM*: ● CM1: MCMP (honey-like floral odour) ● C: No odour *MOA:* During MF task, mist was sprayed twice every 5 min *MF task*: 40-min 2-back test	*During MF task:* ● M-VAS ● MF task performance *Before and after MF task:* ● Task performance on Simple Color reaction test (3 min) ● Task performance on modified Stroop colour-word test (6 min) ● APG ● M-VAS	CM1 vs C: ↓ Difference value of the correct response rate in the modified Stroop colour-word test No sig. differences for APG and M-VAS

Table 4 (continued)

Study	Sample	Design	Interventions	Outcome measures	Results
Scholey et al. [53]	*N:* 30 (17 ♀, 13 ♂) Age: 21.9 ± 0.61 years	Between subjects	*MF-CM*: ● CM1: 520 mg of cocoa flavanols ● CM2: 994 mg of cocoa flavanols ● P: 46 mg of cocoa flavanols *MOA:* 90 min before MF task *MF task*: 6 × 10-min CDB (2-min Serial Threes, 2-min Serial Sevens, 5-min RVIP, 1-min M-VAS)	*After baseline and post-treatment:* ● Saliva samples *Pre and post intervention* ● State-Trait Anxiety Inventory state scale *During MF task:* ● M-VAS ● MF task performance	CM1 & CM2 vs P: ↑ Number of correct Serial Threes subtractions CM1 vs P: ↑ Number of correct Serial Threes subtractions at all time points CM2 vs P: ↑ Number of correct Serial Threes subtractions at first four timepoints CM1 vs CM2 & P: ↓ Subjective ratings of MF at all time points except third one
Van Cutsem et al. [12]	*N:* 10 (10 ♂) Age: 23 ± 2 years	Between subjects	*MF-CM*: ● CM1: 10 s mouth rinse of same solution as placebo with 1.2% CAF and 6.4% maltodextrin powder ● P: 10 s mouth rinse of placebo *MOA:* Before the start and every 12.5% completion of the MF task *MF task*: 90-min incongruent Stroop task	*During all trial:* ● HR ● EEG (BO + ERP) *Before and after MF task:* ● POMS ● SIMS ● Flanker task performance ● Glucose *Before and after the intervention, before and after MF task, every 12.5% completion of MF task:* ● M-VAS ● VAS for motivation ● Stroop task performance	CM1 vs P: ↓ M-VAS + ↑ accuracy Stroop in the eighth and last blocks + ↑ Flanker task performance + ↑ blood glucose + ↑ P2 amplitude (EEG) in third and last time interval

Table 4 (continued)

Study	Sample	Design	Interventions	Outcome measures	Results
Van Cutsem et al. [13]	*N:* 14 (4 ♀, 10 ♂) Age: 24 ± 3 years	Between subjects	*MF-CM*: ● CM1: 20 tablets/day of creatine (1 g of creatine monohydrate/tablet) ● P: Tablets of calcium lactate *MOA:* For 7 days before day of trial, 20 tablets/day at 4 equally spaced intervals *MF task*: 90-min incongruent Stroop task	*During all trial:* ● HR *Before and after MF task:* ● Handgrip strength endurance task ● Sport-Specific Visuomotor Task performance ● Flanker task performance ● Glucose ● POMS ● Session RPE ● Motivation and intrinsic motivation scales *Before and after the intervention, before and after MF task, during MF task:* ● M-VAS ● VAS for motivation ● Stroop task performance	CM1 vs P: ↑ Accuracy Stroop + ↑ strength endurance in non-dominant hand No sig. difference for RT of sport-specific visuomotor task + M-VAS
Watanabe et al. [14]	*N:* 24 (5 ♀, 19 ♂) Age: 24.4 ± 9.1 years	Between subjects	*MF-CM*: ● CM1: 8 tablets/day of creatine (1 g of creatine monohydrate/tablet) ● P: Tablets of calcium lactate *MOA:* For 5 days before day of trial, total of 8 tablets/day, spread over 4 times *MF task*: 35-min UKT	*During MF task:* ● NIRS (cerebral haemoglobin oxygenation) ● UKT performance	CM1 vs C: ↑ UKT performance in second part of the task + ↑ average deoxyHb during former half of the second half of MF task
Yamano et al. [58]	*N:* 20 (20 ♂) Age: 37.7 ± 0.8 years	Between subjects	*MF-CM*: ● CM1: 70 mL of Brand's Essence of Chicken twice daily ● P: 70 mL of placebo twice daily *MOA:* During 7 days prior to day of trial *MF task*: 40-min 2-back test	*Before and after MF task and after rest session:* ● Simple Color reaction test performance ● Modified Stroop Color-word test performance ● M-VAS	CM1 vs C: ↓ Reaction times in the modified Stroop colour-word test + ↓ subjective level of fatigue
Psychological countermeasures					
Hopstaken et al. [37]	*N:* 47 (32 ♀, 15 ♂) Age: 20.5 ± 1.8 years	Between subjects	*MF-CM*: ● CM1: Time reward manipulation to induce motivation ● C: No reward manipulation *MOA:* In the last block of the MF task *MF task*: Seven time-on-task blocks for a total duration of 105 min	*Before and after the MF task:* ● RSME ● VAS for fatigue, engagement *During MF task*: ● Task performance ● Pupil diameter ● Gaze position ● EEG (ERP)	CM1 vs C: ↓ VAS for fatigue + ↑ VAS for engagement + ↑ Task performance + ↑ pupil diameter

Table 4 (continued)

Study	Sample	Design	Interventions	Outcome measures	Results
Combination of behavioural and psychological countermeasures					
Axelsen et al. [26]	*N:* 90 (47 ♀, 43 ♂) Age: 34.5 ± 10.6 years	Between subjects	*MF-CM*: ● CM1: Binaural beats ● CM2: Novice mindfulness ● CM3: Experienced mindfulness ● C: Sit and relax *MOA:* After MF task for 12 min *MF task:* 90-min AX-CPT	*Before and right after MF:* ● BRUMS *Before MF and after intervention:* ● SART task performance *All trial:* ● HR	CM1 (vs PRE): ↑ HR + ↑ Subjective feelings of fatigue + ↑ SART performance CM2 (vs PRE): ↑ HR + ↑ Subjective feelings of fatigue + ↓ SART performance CM3 (vs PRE): ↑ HR + ↑ Subjective feelings of fatigue + ↓ SART performance C (vs PRE): ↑ HR + ↑ Subjective feelings of fatigue + ↓ SART performance
Loch et al. [46]	*N:* 24 (14 ♀, 10 ♂) Age: 22.8 ± 3.6 years	Between subjects	*MF-CM*: ● CM1: Power nap (20 min) ● CM2: Systematic breathing (20 min) ● CM3: Systematic breathing + mental imagery (20 min) ● C: Reading collection of comics (20 min) *MOA:* After MF task and cognitive task *MF task*: 60-min AX-CPT	*Before MF task, after cognitive task, after MF-CM:* ● SRSS ● VAS for MF, PF and concentration *Before MF task* ● SOMNOwatch + EEG (BO) *Before and after MF task:* ● Task performance of Reaction Time Test and Vienna Test System	No significant differences between CM1, CM2, CM3 and C

APG Accelerated plethysmography, *ATMT* Advanced trail making tests, *AX-CPT* AX-continuous performance test, *BCAAs* Branched-chain amino acids, *BO* Brain oscillations, *BRUMS* Brunel Mood Scale, *C* Control, *CAF* Caffeine, *CDB* Cognitive demanding battery, *CFF* Critical flicker fusion frequency, *CHO* carbohydrate, *CM1* Countermeasure 1, *CM2* Countermeasure 2, *CM3* Countermeasure 3, *CRT* Cathode Ray Tube, *EEG* Electroencephalography, *EMG* Electromyography, *EOG* Electrooculography, *ERP* Event-related potentials, *FAS* Felt Arousal Scale, *HR* Heart rate, *ISP* Incredibly short profiles of mood states, *MAT* Mental arithmetic test, *MF* Mental fatigue, *MF-CM* Countermeasure against mental fatigue, *MF task* to induce mental fatigue, *MIT* Maximal incremental test, *MOA* Moment of application, *M-VAS* Visual analogue scale for mental fatigue, *NASA-TLX* NASA Task Load Index, *NIRS* near infra-red spectroscopy, *P* Placebo, *PFC* Prefrontal cortex, *POMS* Profile of Mood State, *RPE* Rating of perceived exertion, *RSME* Rating scale mental effort, *RT* Reaction Time, *RVIP* Rapid Visual Information Processing, *SART* Sustained Attention to Response Task, *SIMS* Situational Motivation Scale, *SMT* Short-term memory test, *SRSS* Short Recovery and Stress Scale, *STAI* State-Trait Anxiety Inventory, *tDCS* Transcranial Direct Current Stimulation, *TLDB* Time Load Dual Back, *TT* time trial, *TTE* Time to exhaustion, *UKT* Uchida–Kraepelin test, *VAS* Visual Analogue Scale, *VDT* Visual display terminals, *VE* Minute ventilation, W_{peak} Peak power output, W_{total} Total power output

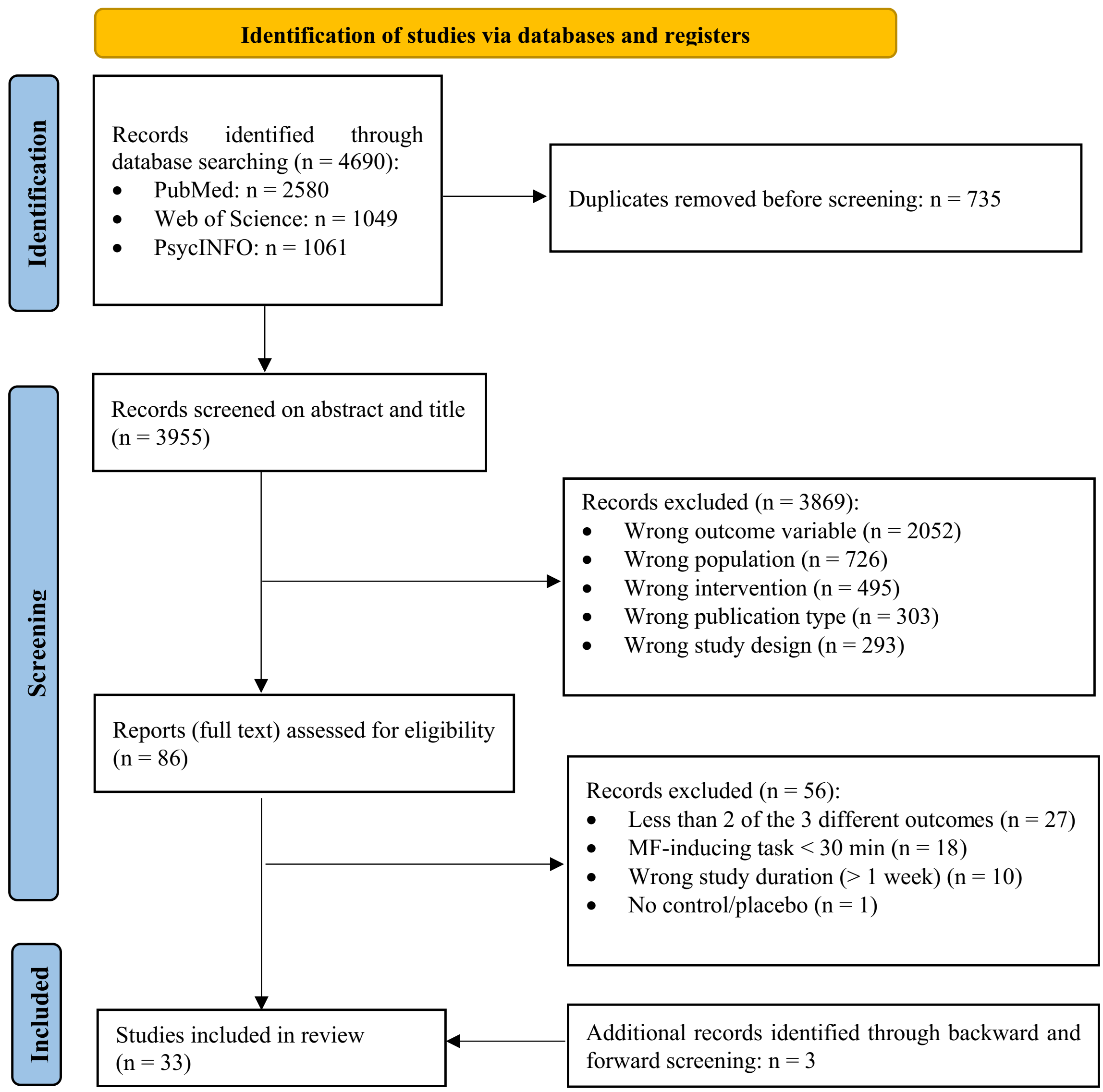


Fig. 1 Flow diagram of the selection process

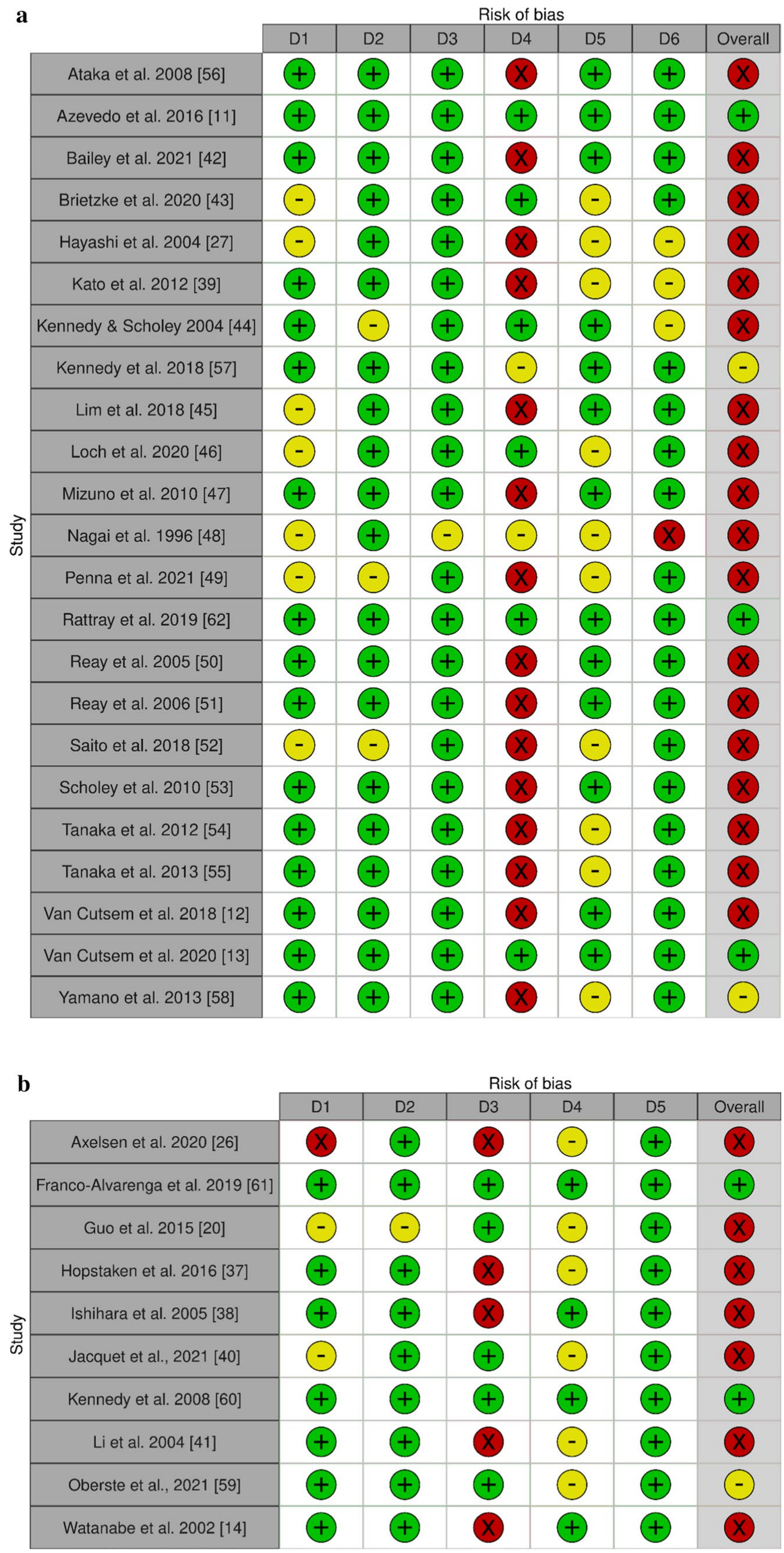
could act as a countermeasure against MF (see Table 4 for an overview of the evaluated countermeasures).

Nine of the ten studies reported significant differences on a behavioural marker (e.g., flanker task performance or a physical task performance; see Table 4 for further details on this matter and Table 6 for an overview of the effects) with a MF countermeasure [20, 26, 27, 40, 45, 47, 54, 55, 59]. Eight studies used subjective reports of MF, with a visual analogue scale for MF (M-VAS) most commonly employed, but only four found that the intervention had an effect [20, 27, 54, 55] (see Table 4). Nine studies employing behavioural countermeasures assessed (neuro)physiological indices (e.g., heart rate, electroencephalography or accelerated plethysmography). However, only four of them observed benefits due to the countermeasure on their outcomes [20, 45, 47, 54] (see Table 4). Only Loch et al. [46] failed to observe an impact of their countermeasure(s) (a powernap, systematic breathing and combined systematic breathing plus mental imagery intervention) on any marker of MF in the studies collated. Further details of the intervention and study details are presented in Table 4.

3.4.2 Physiological

Twenty-two studies that met the inclusion criteria investigated a physiological countermeasure against MF (see Sect. 2 for a definition) [11–14, 38, 39, 41–44, 48–53, 56–58, 60–62], of which five were not substances administered orally. Of the 17 oral-consumption-based interventions, five studies focused on caffeine as a countermeasure

Fig. 2 Risk of bias in **a** individual crossover studies; **b** individual randomized controlled studies. **a** *D1* bias arising from the randomization process, *D2* bias arising from period and carryover effects, *D3* bias due to deviations from intended intervention, *D4* bias due to missing outcome data, *D5* bias in measurement of the outcome, *D6* bias in selection of the reported result, *X* high risk of bias, − some concerns regarding bias, + low risk of bias. **b** *D1* bias arising from the randomization process, *D2* bias due to deviations from intended intervention, *D3* bias due to missing outcome data, *D4* bias in measurement of the outcome, *D5* bias in selection of the reported result, *X* high risk of bias, − some concerns regarding bias, + low risk of bias



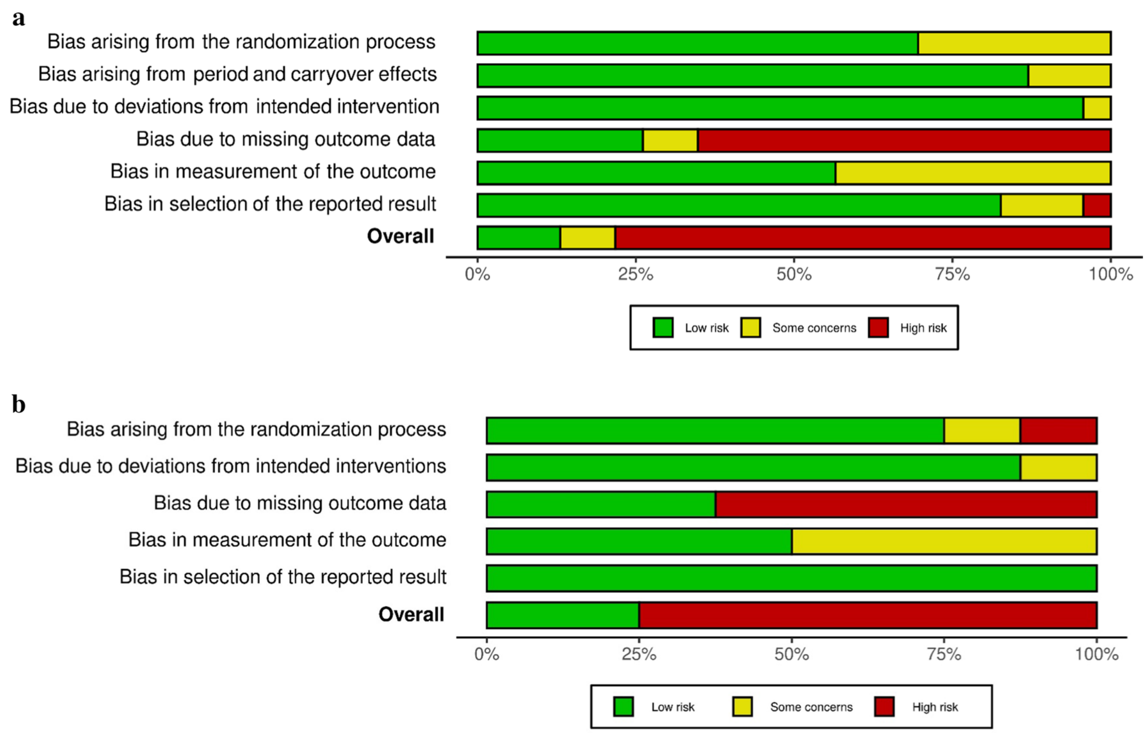


Fig. 3 Risk of bias for **a** all crossover studies; **b** all randomized controlled studies

Table 5 Overview of the different countermeasures used in the included studies, classified by timing of application and type of intervention

Type of intervention	Time of application			
	Up to 1 week before MF-inducing activity	On same day as MF-inducing activity	During MF-inducing activity	After MF-inducing activity
Behavioural			Music [20] Nap [27]	Aerobic exercise [59] Binaural beats [26] Mechanical massage with and without binaural beats [45] Mild-stream bathing [47] Music [40] Power nap [46] Open space connected to nature [55] Pellet stove [54] Physical activity [40]
Physiological	Caffeine or D-ribose [56] Chicken essence [48, 58] Creatine [13, 14]	Caffeine [11, 61] Caffeine/glucose mix [44] Cocoa flavanols [53] Mentha piperita essential oil [57] Modafinil [62] Panax Ginseng [50] Panax Ginseng with and without glucose [52] Vitamin/mineral/guarana tablet [60]	Caffeine-maltodextrin mouth rinse [12] Carbohydrate mouth rinse [42] Magnetic field [38] Magnitopuncture [41] Odour [39, 52] tDCS [49]	Carbohydrate mouth rinse [43]
Psychological			Extrinsic motivation [37]	Mindfulness [26] Systematic breathing with and without mental imagery [46]

MF mental fatigue, *tDCS* transcranial direct current stimulation

Table 6 Overview of the observed impact of the different countermeasures, that were evaluated in the included studies, on the different markers being behavioural (e.g., performance on a cognitive/physical task), subjective (e.g., perception of MF using a visual analogue scale (VAS)) or (neuro)physiological MF-markers (e.g., brain activity through electroencephalography)

Countermeasure	Marker for mental fatigue		
	Behavioural	**Subjective**	**(Neuro)physiological**
Behavioural			
Aerobic Exercise [59]	+	+	/
Binaural Beats[a] [26]	+	=	=
Binaural Beats with mechanical massage[b] [45]	+	/	+
Mechanical massage[b] [45]	+	/	=
Mild-stream bathing [47]	+	=	+
Music[c] [40]	+	=	=
Music [20]	+	+	+
Nap [27]	+	+	/
Open space connected to nature [55]	+	+	=
Pellet stove [54]	+	+	+
Physical activity[c] [40]	+	=	=
Powernap[d] [46]	=	=	=
Physiological			
Caffeine [11]	+	+	/
Caffeine [61]	+	+	=
Caffeine[e] [56]	+	=	/
Caffeine/glucose mix [44]	+	+	/
Caffeine-maltodextrin mouth rinse [12]	+	+	+
Carbohydrates mouth rinse [42]	=	+	+
Carbohydrates mouth rinse [43]	+	/	=
Chicken essence [48]	+	+	+
Chicken essence [58]	+	+	/
Creatine [13]	+	=	=
Creatine [14]	+	=	+
Cocoa Flavanols [53]	+	+	/
D-Ribose[e] [56]	=	=	/
Glucose[f] [51]	+	+	/
Magnetic field [38]	/	=	=
Magnitopuncture [41]	+	+	/
Mentha piperita essential oil [57]	+	+	/
Modafinil [62]	+	+	/
Odour [39]	+	=	+
Odour [52]	+	=	=
Panax Ginseng [50]	+	+	/
Panax Ginseng[f] [51]	+	+	/
Panax Ginseng with glucose[f] [51]	=	=	/
tDCS [49]	=	=	/
Vitamin/mineral/guarana tablet [60]	+	+	/
Psychological			
Extrinsic motivation [37]	+	+	+
Mindfulness[a] [26]	-	=	=
Systematic breathing with mental imagery[d] [46]	=	=	/
Systematic breathing without mental imagery[d] [46]	=	=	/

+ indicates significant positive effect of the countermeasure on this marker; = indicates no significant effect of the countermeasure on this marker; – indicates negative effect of the countermeasure on this marker; / indicates marker not used in study; *MF* mental fatigue, *tDCS* transcranial direct current stimulation

[a]Same study

[b]Same study

[c]Same study

[d]Same study

[e]Same study

[f]Same study

[11, 12, 44, 56, 61]. Kennedy and Scholey [44] trialled caffeine in combination with glucose, Van Cutsem et al. [12] used it as a mouth rinse combined with maltodextrin, and Ataka et al. [56] compared caffeine with a D-ribose supplement and placebo in a 1-week intervention. Four other 1-week interventions included either creatine [13, 14] or chicken essence [48, 58]. Similar to Van Cutsem et al. [12], Brietzke et al. [43] and Bailey et al. [42] used a mouth rinse countermeasure, with carbohydrates as the only active ingredient. Brietzke et al. [43] used it after the MF-inducing task, while Bailey et al. [42] applied it during the task. Five other included studies assessed the effect of less common oral-consumption-based interventions. Of these, Reay et al. [50, 51] conducted two studies with Panax Ginseng, Kennedy et al. [60] and Kennedy et al. [57] investigated a commercial vitamin complex and a specific type of essential oil, respectively, and Scholey et al. [53] researched the effects of cocoa flavanols on MF. Lastly, Rattray et al. [62] were the only investigators using a pharmacological intervention (i.e., modafinil). The five studies that used non-orally administered countermeasures employed a non-invasive brain stimulation or odour-based intervention. Ishihara et al. [38] evaluated the effect of a magnetic field caused by liquid crystal display, while Li et al. [41] used magnitopuncture, a more localised magnetic-based intervention. Penna et al. [49] employed a transcranial direct current stimulation (tDCS) protocol during the MF task in an attempt to counter its negative effects. Two studies made use of odour as an intervention against MF [39, 52].

Regarding the effects on the different indicators of MF, of which an overview can be found in Table 6, 20 of the physiological countermeasures were evaluated against a behavioural marker (performance on a specific battery of cognitively demanding tasks). Of these, 16 studies reported improvements in performance following use of the countermeasure [11–13, 41, 43, 44, 50–53, 56–58, 60–62] (see Table 4 for further details on this matter). Only Bailey et al. [42], Nagai et al. [48], Penna et al. [49] and Watanabe et al. [14] found no effect on the behavioural marker. All studies except Watanabe et al. [14] used subjective markers of MF. Of these 21 studies, 14 [11, 12, 41, 42, 44, 48, 50, 51, 53, 57, 58, 60–62] showed a significant difference following the physiological countermeasure (see Table 4 for further details on this matter). Also (neuro)physiological markers were monitored in ten studies investigating physiological MF countermeasures, half of which provided positive results [12, 14, 39, 42, 48] (see Table 4). Details regarding the specific MF markers that were employed can be found in Table 4.

3.4.3 Psychological

Three included studies used a psychological countermeasure against MF (see the Sect. 2 for a definition) [26, 37, 46]. Axelsen et al. [26] and Loch et al. [46] analysed the differences between a psychological and behavioural countermeasure (see Sect. 3.4.1). In the study of Axelsen et al. [26], the difference between binaural beats and mindfulness (where the authors made the additional distinction between novice and experienced practitioners) and their effects on MF was explored. Furthermore, Loch and colleagues [46] investigated the effect of systematic breathing with and without mental imagery in comparison with a powernap as recovery from MF. Lastly, one study conducted an experiment in which the researchers attempted to enhance motivation through a time-based reward manipulation during the MF-inducing task [37].

Table 4 presents the outcome measures of these studies. All three studies that evaluated a psychological countermeasure used performance on cognitive tasks as behavioural markers to determine whether the employed countermeasures were successful in counteracting MF. As such, Axelsen et al. [26] and Hopstaken et al. [37] observed significant results (see Table 6). The study of Hopstaken and colleagues [37] was the only one of the included studies that searched for and also found a significant difference in pupil diameter, which they used as a physiological marker of MF. In their study, Hopstaken et al. [37] evaluated the MF-counteracting properties of a reward manipulation (i.e., the length of the cognitive task depended on how well they performed). They observed a significant decrease in pupil diameter due to MF and an increase in it after introducing the reward manipulation. Three other studies [20, 27, 39] assessed electrooculography but failed to observe significant changes due to the countermeasure used (see Table 4). Subjective outcomes were utilised by two [37, 46] of these three studies, but the psychological manipulations only improved subjective markers of MF in one of these [37] (see Table 4 for more information on this matter).

3.5 Timing of the Countermeasure

3.5.1 Up to a Week Before the Mental Fatigue-Inducing Activity

A total of five studies investigated the implementation of a physiological countermeasure over a period of 5–7 days before the moment of MF [13, 14, 48, 56, 58]. Two of these protracted strategies [13, 14] were required due to the typical loading phase of creatine utilised [63]. While, on the other hand, the commercially available chicken essence used by Nagai et al. [48] and Yamano et al. [58] is traditionally used over a period of 7 days or longer due to its potential as remedy for physical and mental fatigue. A 7-day loading strategy was also utilised in a study of Ataka et al. [56], wherein the MF-counteracting properties of caffeine and D-ribose were compared. Ataka et al. [56] suggested that both interventions could possibly counteract MF via their potential to increase the adenine nucleotide availability (see Table 4 for details and Table 5 for an overview).

3.5.2 On the Same Day as the Mental Fatigue-Inducing Activity

Nine studies explored the effect of physiological countermeasures minutes to hours before the MF task [11, 44, 50, 51, 53, 57, 60–62]; full details on the moment of application can be found in Tables 4 and 5. Six of the studies used countermeasures, such as caffeine and cocoa flavanols, that have short-term impacts and were administered within an hour of the MF protocol [11, 44, 50, 51, 60, 61]. In the three other studies, countermeasures were given 90 min before the MF task [53, 62] or, in the case of Kennedy et al. [57], the MF task was employed 1, 3 and 6 h after the intake of the countermeasure.

3.5.3 During the Mental Fatigue-Inducing Activity

Ten studies investigated the effect of countermeasures during the MF task [12, 20, 27, 37–39, 41, 42, 49, 52] (see Table 5 for an overview). Six studies included countermeasures which did not directly interfere with the MF-inducing task [20, 38, 39, 41, 49, 52]. Two studies implemented an odour during the MF task [39, 52], three used a non-invasive brain stimulation intervention [38, 41, 49] and Guo et al. [20] implemented music during the MF task. The four other investigations [12, 27, 37, 42] were incorporated in the MF task, with two studies using mouth rinses at predetermined moments during the MF task [12, 42]. Hopstaken et al. [37] implemented a time-based reward in the last block of the MF task, and Hayashi and colleagues [27] investigated the difference between a 20-min nap or rest break in the middle of the task. The duration of each countermeasure can be found in Table 4.

3.5.4 After the Mental Fatigue-Inducing Activity

Nine studies assessed the restorative effect of countermeasures after the MF task [26, 40, 43, 45–47, 54, 55, 59], of which three studies inspected a countermeasure with a stress-relieving background [47, 54, 55] and one study used a carbohydrate mouth rinse after the MF task. Axelsen et al. [26] investigated the differences between binaural beats (i.e., an auditory intervention suspected to have an impact on cognitive functioning [64]) and mindfulness, and applied both interventions immediately after the MF task for a duration of 12 min. Loch et al. [46] used 20-min sessions of a powernap and systematic breathing with and without mental imagery as recovery strategies and applied these countermeasures 5 min after the mentally fatiguing task. Lim and colleagues [45] studied the combination of binaural beats and mechanical massage for 20 min as strategies to counteract MF 5 min after the MF task. Full details on the moment and duration of application can be found in Table 4.

4 Discussion

The purpose of this review was to provide an overview of countermeasures against the negative consequences of MF. A total of 33 studies were included in the present systematic review. Of these, eight studies investigated a behavioural countermeasure, 22 a physiological one, one study a psychological countermeasure and two studies investigated both a behavioural and psychological countermeasure. The vast majority of the included studies reported that, based on an observed positive impact on behavioural (e.g., task or sport performance) and/or subjective markers of MF (e.g., visual analogue scale for MF or alertness), the investigated countermeasure successfully counteracted MF. However, regarding the (neuro)physiological markers of MF, it is difficult to draw a strong conclusion as only half of the included studies evaluated the effect on these markers in addition to evaluating the effect on behavioural and/or subjective markers. Nonetheless, first indications show that the used countermeasures had a positive impact on MF-related brain activity changes (e.g., elevated P3-amplitudes and alpha activity in favour of the used countermeasure [20, 39, 40]). See Table 6 for a general overview.

4.1 Countermeasures and Their Mechanism(s)

4.1.1 Physiological Countermeasures

To counter and/or mitigate the effects of MF, 22 studies have evaluated interventions that are proposed to act directly through physiological pathways. Fourteen of them used a form of neuroenhancer, that is, a substance with the purpose to augment learning and memory, attention and vigilance, mood and behaviour [65]. Among the substances used to combat MF, the most tested is caffeine. Azevedo et al. [11] found that 5 mg.kg^{-1} caffeine resulted in a 14% increase in endurance performance. This was confirmed by Franco-Alvarenga et al. [61], who reported a reduced (1.7%) time to complete a 20-km cycling session and an increase (3%) in mean power. Based on these two studies, it appears that caffeine is able to reduce MF-related decrements in endurance performance and that a 5-mg.kg^{-1} dosage is sufficient to do so. Furthermore, caffeine also successfully countered the negative effect of MF on cognitive performance [44, 56]. Ataka et al. [56] found that after a 7-day intake period of 200 mg of caffeine per day, task performance on an advanced trail-making test in a mentally fatigued state was improved in comparison with the placebo. Further, Kennedy and Scholey [44] reported an improved cognitive performance following the combined intake of caffeine and carbohydrates, but only with the combination of 46 mg of caffeine with 68 g of glucose. Other combinations (38 mg of caffeine with 68 g of glucose and 33 mg caffeine with 60 g of glucose) were less successful in mediating the effects of MF. This would suggest that there is a certain minimal dose of caffeine required to counteract MF, which emphasizes the importance of using a relative dosage of caffeine that is based on body weight. Furthermore, Van Cutsem et al. [12] used a combination of caffeine and maltodextrin during the MF task, but as a mouth rinse. A beneficial effect of this solution was observed on the subjective feeling of MF and also improved task performance on the Stroop and flanker task (more specifically the accuracy) in a mentally fatigued state. This may be due to the activation of both the orbitofrontal and dorsolateral prefrontal cortex, which improved cognitive performance [66]. The use of solely a carbohydrate mouth rinse during the MF task also appears to be useful. The latter finding was demonstrated by Bailey et al. [42], who found improvements of both subjective and neurophysiological markers of MF. Additionally, Brietzke et al. [43] found a positive effect of mouth rinsing with carbohydrates on a maximal incremental test, but they applied it after the MF task. The above shows that nutritional MF countermeasures, such as caffeine, are currently known to work in two ways. The first follows ingestion and thus involves the mechanism of absorption via the gastrointestinal system. Caffeine ultimately crosses the blood–brain barrier and exerts its effect on brain neurotransmission. In other words, by blocking the adenosine receptors it counteracts most of the inhibitory effects of adenosine on neuroactivity, dopamine release and arousal (certainly in the prefrontal cortex and hippocampus, brain areas that could be linked to MF [16, 17]). Secondly, caffeine may act through the activation of specific taste receptors (specifically in the study by Van Cutsem et al. [12, 67], bitter taste receptors were suggested to play a role) that trigger a transduction cascade to the brain and thus may result in the activation of brain regions that play an important role in MF, such as the anterior cingulate cortex. Also, for carbohydrate mouth rinses a transduction cascade can occur. This was supported by research in which the limbic system as well as the primary sensorimotor cortex and neural networks involved in sensory perception were activated after the intervention [68].

The possible importance of receptors that are present in the mouth and nose to counteract MF, and as such the subsequent brain activation [69], is further substantiated by two studies that investigated the effect of odour on MF [39, 52]. Both studies found significant improvements in the odour conditions. Kato et al. [39] found a significantly reduced increase in reaction time in the MF group compared with the control group, while Saito et al. [52] found a better response rate when using a newly developed odour. This newly developed odour (called MCMP, a honey-like floral odour) was created to work on the Hex-Hex Mix receptors. Activating these receptors has been shown to attenuate fatigue and, as such, to effectively counteract MF [52]. However, more general and well-known odours, as used by Kato et al. [39], are also apparently able to counter MF. The suggested explanation for these findings currently is the connection of the olfactory bulb with higher brain centres like the amygdala-hippocampal complex [70]. The amygdala plays an important role in the process of the value of rewards associated with cognitive effort [71, 72], which is then projected to the anterior cingulate cortex for decision making, based on the evaluation of rewards and potential costs. Based on their results, Kato et al. [39] suggested that intermittent exposure to several odours (i.e., citral, green and menthol) of neutral pleasantness leads to positive feelings and as such mitigates MF-related effects on cognitive performance. With this suggestion they emphasized the importance of positive feelings and affective valence as a mediating mechanism of MF-counteracting properties of odours.

Besides caffeine, multiple other nutritional interventions were evaluated. Kennedy et al. [60] used a nutritional supplement with added guarana (Berocca Boost®) and found an improvement in speed (~ 30 ms in favour of the intervention) and accuracy (approximately 11% more accurate) on performing the Rapid Visual Information Processing task, while attenuating the subjective feelings of MF. While it might seem that guarana could be a good countermeasure against MF, it should be noted that the used supplement also contained 40 mg of caffeine. Given the mix of guarana and caffeine, and the high risk of bias within this study, no conclusion on the use of guarana alone against MF could be drawn and subsequently these results could also be interpreted as additional evidence for the use of caffeine as a MF countermeasure. Two studies [13, 14] investigated the ability of creatine supplementation to counteract MF due to its cognitive function improvement properties [73]. They both found an increase in the performances of their cognitive tasks [13, 14], but Van Cutsem et al. [13] did not find an effect of creatine on the evaluated sport-specific visuomotor performance (i.e., badminton-related reaction time) in a mentally fatigued state. Van Cutsem et al. [13] argued that the occurrence of MF could be (partly) linked to a drop in the brain's phosphocreatine concentration; as such, creatine supplementation might be able to increase brain energy resources and postpone the drop in phosphocreatine and subsequently also the emergence of MF. Further evidence is, however, necessary to substantiate this mechanism. Besides creatine supplementation, cocoa flavanols were, based on their positive impact on subjective and behavioural markers of MF [53], proven effective to counteract MF. This can presumably be explained by their capacity to improve the endothelial function with an increase in blood flow, possible glucose uptake, cerebral oxygenation and ultimately cognition [74]. However, the link between MF and oxygenation is an underexplored mechanism. Kennedy et al. [57] explored the use of orally administered capsules filled with a certain dose of essential oils (Mentha spicata and M. piperita) and their effects on brain function. They found an increase in performance in a visual sustained attention task at 1 h and 3 h after the highest dose, and an attenuated subjective feeling of fatigue with both doses. Two studies explored the use of chicken essence in countering MF [48, 58]. Chicken essence is rich in amino acids and the dipeptides carnosine and anserine [75, 76]. These have shown to be effective in elderly subjects and patients with mild cognitive impairment, with clinical efficacy against the cognitive decline [77]. Also, several amino acids (e.g., tyrosine, which is a precursor of dopamine) seem to improve cognitive performance [74, 78]. Both Nagai et al. [48] and Yamano et al. [58] showed that consuming chicken essence in the morning for a 7-day period is effective in reducing the feeling of fatigue when performing cognitive tasks and improves task performance. Therefore, it seems that chicken essence is a useful countermeasure for MF; however, it should be noted that both studies were supported by the same company that also provided the chicken essences (and which are commercially available). A non-sponsored study or one investigating the active components of chicken essence might therefore be of added value to confirm the usefulness of chicken essence in overcoming MF.

Interventions other than nutritional ones may also have a positive effect on MF through physiological mechanisms. The pharmacological intervention modafinil is perhaps a logical one to combat MF given its action as a modulator of dopaminergic and adrenergic pathways [65, 79] (see Colzato and Mourits [80] for more information on the mechanisms of action of modafinil). However, it should be noted that modafinil is a banned drug in competition, which limits its use outside a scientific setting but which could be useful in the military [81] and certain occupational settings. In specific situations (e.g., when sleep deprived), modafinil is known to increase attention and vigilance and reduce reaction time and general fatigue [65, 81], while possibly influencing the effort-related decision-making pathways [71, 82]. Additionally, it is also suggested that it has fewer side effects and a longer-lasting effect in comparison with caffeine [65]. However, despite the theoretical advantages of modafinil on MF, Rattray et al. [62] only found improved performance on a cognitive task evaluating executive functioning and not on cycling endurance performance following an MF-inducing task. Additionally, they also found higher heart rates and disrupted sleep patterns in the intervention group, which are important side effects of modafinil.

Interventions with non-invasive brain stimulation techniques were also evaluated to perhaps positively impact MF via a physiological mechanism, possibly by altering the threshold required for an action potential within the nervous system [83, 84]. Three studies used a magnetic-based intervention during the MF-inducing task [38, 41, 49]. Ishihara et al. [38] used a general magnetic field to combat MF, but failed to show differences in MF exposure after the task. Li and colleagues [41] used a more targeted magnetic stimulation on acupuncture points and did find a significant difference in reaction time between the control and study group post-task in favour of the study group. This observation was confirmed by Yang et al. [85] and as such it is assumed that magnitopuncture is an adequate countermeasure against MF. However, it is important to note that the study of Yang et al. [85] did not include a control group, which lowers the quality of the study and puts their conclusions into question. Also, it remains unclear whether participants were blinded for the intervention in the study of Li et al. [41]; therefore, the conclusions should be read with caution. Penna et al. [49] used tDCS in order to counter the decrements due to MF in swimming performance. By stimulating the left temporal lobe, the excitability of the insular cortex would increase and therefore influence the awareness of subjective feelings (e.g., subjective feeling of physical exertion) playing a role during exercise. Unfortunately, they were unable to prove that MF negatively affected swimming performance, which makes it difficult to give a conclusive answer regarding the effectiveness of tDCS and MF-related decrements in physical performance. Despite the absence of an effect of MF on swimming performance, the effectiveness of tDCS to counteract MF could still be evaluated. Penna et al. [49] observed a greater fatigue perception and a drop in cognitive performance due to prolonged performance on the mentally fatiguing task (i.e., a Stroop task). However, no difference in perceived fatigue or cognitive performance was found between the brain stimulation and sham condition. The inability of tDCS to counteract MF while performing a prolonged cognitive task could be due to the stimulated area not being related to cognitive performance. It would therefore be interesting to see if the stimulation of other regions known to impact cognitive function would be more successful in order to make a firm conclusion regarding the use of tDCS as a MF countermeasure [12, 86].

4.1.2 Behavioural and Psychological Countermeasures

Eleven studies used a behavioural and/or psychological countermeasure against MF. One of the most-used behavioural countermeasures was the application of auditory stimuli. Guo et al. [20] used instrumental folk music, while Jacquet et al. [40] let the participants themselves select the songs. The choice to use music as a countermeasure is a reasonable one as music has the potential to improve cognitive and physical performance [21, 22, 87], most plausibly via its beneficial effects on affective valence and motivation [87]. Motivation and mental fatigue are two psychobiological states that can be dissociated from each other [88] but that have clearly been shown to impact one another [37, 89–91]. Indeed, in the study of Guo et al. [20], they found that the intervention group maintained their performance through the MF task while listening to music. Also, the subjective feeling of MF was significantly lower in comparison with the control groups [20]. Two other studies [26, 45] used binaural beats as auditory stimuli because of the positive effect of binaural beats on mind wandering and cognitive flexibility [64, 92], two actions which play a role in MF. Therefore, influencing these two processes might combat the decrements in performance due to MF. Indeed, both studies found a positive effect of binaural beats in reducing the effect of MF. Axelsen et al. [26] even observed a slight increase of 3.8% on cognitive performance after using binaural beats to counter the negative effects of MF, possibly mediated by less mind wandering. However, it should be noted that in the study of Lim et al. [45], this was combined with a mechanical massage chair. The combination of binaural beats and mechanical massage could have reinforced each other. Also the mechanical massage alone was found to positively impact the recovery from MF, a finding that is also confirmed by the study of Mizuno et al. [47] where they implemented a massage provided by a mild stream function while bathing. They suggested that this could be related to the stress-alleviating effect of mild-stream bathing, which could also underly the positive effect of listening to music [93, 94], sitting next to a pellet stove [54] and exposure to a natural environment [55, 95] on MF. Therefore, potentially, similar brain mechanisms (e.g., increase in dopamine) might play a role in both creatine/caffeine and non-nutritional countermeasures (such as music and massage).

Axelsen et al. [26] also evaluated the potential benefits of on-the-spot mindfulness in the recovery from MF. Mindfulness is a behavioural therapy that provides training in self-regulation in a systematic way [92], which might be appropriate for countering MF [96]. Self-regulation is the ability to exert control over one's own behaviour. It is defined as the ability to overcome urges and habitual reactions, such as emotions and impulses. Importantly, self-regulation is regarded as a capability based on a limited capacity of internal resources. By engaging in activities that require self-regulation, such as cognitive tasks used to induce MF, this internal reserve of resources is being drained (i.e., being mentally fatigued). By training to improve this self-regulation capacity, it is suggested that future self-regulation activities will cost fewer internal resources [96–98]. This was the case in the study of Axelsen et al. [26], but only for the experienced mindfulness group, the novice mindfulness group performed even worse on the cognitive task compared with the control group. Since mindfulness was new to the novice mindfulness group, and thus requiring a certain level of self-regulatory resources, this impaired performance might be explained by the cognitive task (i.e., trying mindfulness for the first time) requiring extra self-regulatory resources and even aggravating the emergence of MF. Therefore, it can be concluded that mindfulness could be a helpful recovery strategy for MF, but only after a certain period of training [99]. Another long-term countermeasure against MF could be brain endurance training [25, 100]. The possible mechanism behind this is that the ability to tolerate a certain amount of mental exertion is trainable and as such could prevent/postpone the occurrence of MF. Although this is still a relatively unknown field, the first studies seem rather promising [25, 99, 100].

Loch and colleagues [46] evaluated the recovery effect of a 20-min powernap on MF but failed to find a significant effect. This led them to the conclusion that a period of rest with mental recovery strategies might be enough to recover from MF. This is exactly what Hayashi et al. [27] did, but in contrast to Loch et al. [46], they introduced this 20-min rest period during the MF task and compared it with a 20-min nap. They found that a short nap was more successful in maintaining subjective alertness and kept performance at a higher level and subjective feeling of MF at a lower level than a moment of rest. This could indicate that a nap is more useful as a countermeasure during the MF task compared with after the MF task. However, given the heterogeneity in duration and the type of MF task and MF markers, it is difficult to formulate a final conclusion on this matter. The use of a mid-task break also seems to be a countermeasure worth looking further into, as previously published research already provided promising results by making use of tasks shorter than 30 min [101, 102]. The choice of activity during this break of course seems to be of importance. Gao et al. [103] stated that implementing a mid-task 15-min cycling exercise led to an improved reaction time and response accuracy. However, it should be noted that they compared this to a group without a break. On the other hand, given the benefits of physical activity regarding executive functioning [104], Jacquet et al. [40] and Oberste et al. [59] investigated the effect of light physical aerobic exercise after the MF task to counter the negative consequences due to MF. They both found a positive effect or no negative effect of their intervention, meaning that a physical activity to recover from a mentally fatiguing task is useful. An explanation for the effectivity of this countermeasure can be found in the dopamine-releasing effect of physical activity, which also strengthens the theory that adenosine and dopamine may play an important mechanistic role in the MF-associated decrease in performance [17, 104, 105].

A last non-physiological countermeasure is the use of motivation against MF. In the study of Hopstaken et al. [37], it was found that by adding a time-based reward towards the end of the task, participants could restore task engagement and performance despite staying subjectively mentally fatigued. This is in accordance with the results of Herlambang et al. [90] and Brown and Bray [106], who used monetary incentives to overcome MF, but it should be taken into account that both studies might be biased due to their study design. However, it is clear that motivation may be an effective countermeasure for MF if introduced in a proper way [88, 91, 107, 108].

4.2 Practical Application of Countermeasures

Given the wide variety in all discussed countermeasures, it may be difficult to decide which countermeasure could be useful, effective and easy to use within a setting where MF could emerge and where it is undesired. For example, during a long game or ride with no possibility to take a break, an easy-to-consume nutritional countermeasure could be the preferred option to counteract MF. On the other hand, when competing in a tournament with multiple rounds (e.g., judo, badminton), behavioural interventions such as listening for 20 min to music could specifically be of added value to deal with MF [26, 45]. If an individual knows there will be a cognitively demanding period within days, countermeasures such as creatine [13, 14] or chicken essence [48, 58] seem to be good candidates, but are of course more time consuming and require some planning. If MF is likely to occur within hours, the most appropriate countermeasure would be a 5 mg.kg^{-1} of body mass dose of caffeine [11, 44, 61], a caffeine-maltodextrin mix [12], cocoa flavanols [53] or one of the other countermeasures used by the research groups of Kennedy, Reay and Scholey [50, 51, 53, 57, 60]. These are all nutritional-based countermeasures that are easy and fast to use. However, one should be aware of the possible side effects of the mentioned countermeasures. For example, using higher doses of caffeine might lead to gastrointestinal distress [74], which might be unwanted in multiple situations (e.g., endurance performance), but also cause tremors [65], which could be a disadvantage for sport- and work-specific psychomotor performance. Regarding the other countermeasures, further research is needed to exclude undesirable side effects and to pinpoint the most advantageous dosage.

If there is no time to anticipate MF, countermeasures during the mentally demanding activity could be of use. Depending on the situation one might choose to use odours in overcoming the negative effects of MF [39, 52]. However, given the volatility of odours, their use is only possible in situations where one stays in the same place (e.g., table tennis [5], driving a car [109] or esports [110, 111]) or where the odour can be sprayed on clothing or the body [112]. In addition, the use of non-invasive brain stimulation techniques in counteracting MF [38, 41, 49] is also a possibility. This kind of countermeasure might, however, be impractical due to the required equipment. One of the most practical interventions in overcoming MF is the use of motivational stimuli [37]. The difficulty there is finding the adequate motivational determinants as this is very individually dependent [108, 113].

To recover from MF, different countermeasures have also been identified. The use of 20 min of binaural beats [26, 45] and long-term mindfulness [26] are promising countermeasures for athletes as these require no extra material or supplements and are easy to implement in a training regimen. Besides that, activities enhancing dopamine release [45, 47, 54, 55] can be easy to conduct after a MF task. However, as with motivation, it is a question of finding the adequate countermeasure for each individual.

4.3 Limitations and Future Perspectives for Research

The field of MF research in sport science lacks homogeneity in the methodological inducement of MF. There is no consensus on the gold standard method to induce MF; discussions on the optimal length and intensity of the cognitive challenge and on the most valid behavioural, subjective and (neuro)physiological markers of MF are still ongoing. Without a doubt, these discussions are of major importance to further unravel MF and the mechanism(s) behind it. The degree of MF induced by a certain task depends on the skill of the performer/participant, on the way it cognitively engages the performer/participant, the motivational level, etc. Moreover, the most valid marker of MF, be it a behavioural, subjective and/or (neuro) physiological one, will differ in each specific situation. As such, this challenging field of research will, most probably, keep on struggling with standardization issues. This does not need to be a major issue if study results are interpreted while taking into account these possible methodological differences and their impact on MF and on the observed efficacy of the evaluated MF countermeasure. Throughout the present review, however, it was clear that methodological differences exist, which complicated the comparison of the efficacy of each of the evaluated MF countermeasures. Specifically, the heterogeneity in MF inducement methods and in the employed MF markers resulted in the inability to execute any type of meta-analyses that would have been of added value.

Based on the present systematic review, two important research avenues can be distinguished to advance this field of research; a practical and a mechanistic line. In terms of the practical research avenue, as stated by a recent systematic review [114], it would be interesting to gather more insight on the optimal dosage and timing of each of the evaluated MF countermeasures. Regarding caffeine, it is clear that a dosage of 5 $mg.kg^{-1}$ of body mass has been proven to be effective to counter MF. While for creatine, because the two included studies used a different dose (i.e., 20 g/day [13] and 8 g/day [14]) and different periods of supplementation (i.e., 7 days [13] and 5 days [14]), additional research to find the optimal design for application is needed. This would be important not only for creatine, but also for the other included MF countermeasures in the present systematic review; dosage and timing studies to evaluate the minimal dosage and timing that is needed to effectively counteract MF are necessary. In addition, before proceeding to dosage and timing studies, the usefulness of multiple countermeasures needs to be confirmed in replication studies [43, 50, 53].

From a mechanistic perspective, it would be worthwhile to see the mechanistic pathways that are suggested to be in place for some MF countermeasures confirmed. This could be attained via studies that incorporate outcome measures that are able to give insight into these mechanistic pathways (e.g., electroencephalography, near infrared spectroscopy) or via studies that evaluate the effectiveness of other interventions that we know counteract MF via the same mechanistic pathway, to eventually confirm the presence of that particular mechanistic pathway. For example, modafinil is thought to counteract MF via its impact on dopaminergic activity; the importance of this impact on dopaminergic activity to counteract MF could be further substantiated by evaluating the ability of methylphenidate (i.e., a dopamine reuptake inhibitor) to counteract MF [115].

To end, no countermeasure totally resolved MF, and therefore it would be interesting to see if the combination of different types of countermeasures (e.g., caffeine and music) would lead to better results in countering MF. The combination of the mechanistic pathways through which different countermeasures are suggested to positively impact MF could work synergistically in the sense that the positive impact of these different countermeasures could enhance each other, or could even reinforce one another.

5 Conclusion

Mental fatigue is known to impair physical and/or cognitive performance. The purpose of this review was therefore to create an overview of possible MF countermeasures and to discuss the underlying mechanisms and the practical application of these MF countermeasures, to eventually be able to use them across multiple contexts (e.g., sporting, occupational or military contexts). A total of 33 studies investigated a specific type of countermeasure for MF and its negative effects on sport performance or on cognitive performance. In general, a vast majority of the included countermeasures had a positive effect on behavioural and subjective markers of MF. Unfortunately, only 19 of the included studies used (neuro)physiological outcome measures, which hindered drawing a definitive conclusion on the effect of the employed countermeasures on (neuro)physiological markers of MF. The most investigated countermeasures with the most reliable evidence seem to be the use of caffeine before and/or during the occurrence of MF and the use of a noticeable and pleasant odour during the MF task. In addition, the use of strategies (e.g., rewards) to increase motivation, seems to be a promising psychological method to counteract MF. To provide in-detail practical guidelines for the real-life application of MF countermeasures, more research has to be performed on the underlying mechanisms and the optimal dosage and timing of application/intake.

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Compliance with ethical standards Matthias Proost, Jelle Habay, Jonas De Wachter, Kevin De Pauw, Ben Rattray, Romain Meeusen, Bart Roelands and Jeroen Van Cutsem declare that the systematic review complies with all ethical standards.

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Authorship contribution The design of the search strategy was performed by MP, and subsequently revised by JH, JDW, BaRo and JVC. Screening on title and abstract was done by MP and JH, while full-text screening was conducted by four authors, i.e., MP, JH, BaRo and JVC. Data analysis was first conducted by MP and JH and was later revised and updated by MP. RoB assessment was performed by MP who also designed the RoB figures. MP wrote the first draft of the manuscript which was later altered by JH, JDW, KDP, BeRa, RM, BaRo and JVC. All authors read, revised and approved the final manuscript.

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