



Review

Prefrontal cortex asymmetry and psychological responses to exercise: A systematic review

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ABSTRACT

Background: Studies have shown a relationship between prefrontal cortex (PFC) activation asymmetry and psychological responses to exercise, so that a higher rest activation in left rather than right PFC has been associated with positive psychological responses to exercise such as an improved affect, anxiety and multidimensional arousal states.

Purpose: To review: 1) evidence that PFC activation asymmetry before exercise is associated with psychological responses to exercise; 2) protocols of PFC asymmetry determination.

Methods: A systematic review (SR) was performed on studies retrieved from the PubMed and Web of Science database up to 04-30-2019. Eligibility criteria were: 1) studies investigating participants submitted to aerobic exercises; 2) including cerebral activation measures through electroencephalography (EEG) before the exercise bout; 3) and psychological measures during or after the exercise bout; 4) original studies.

Results: A number of 1901 studies was retrieved from the databases and 1 study was manually inserted. Thereafter, 1858 studies were excluded during the screening stage so that 30 studies remained for the SR. After full reading, 22 studies were excluded and 8 studies composed the final SR. Methodological assessment revealed that 62.5% of the studies showed a low risk of bias, while 34.37% and 3.12% showed either an unclear or a high risk of bias, respectively. Protocols of PFC activation asymmetry used EEG at F3-F4-P3-P4 (3 studies), F3-F4 (2 studies), F3-F4-T3-T4 (1 study), F3-F4-F7-F8-T5-T6-P3-P4 (1 study) and Fp1-Fp2-Fz-F3-F4-F7-F8-Cz-C3-C4-T3-T4-T5-T6-Pz-P3-P4-Oz-O1-O2 (1 study) positions. Most studies (75%) found a higher left PFC activation associated with a greater affect ($n = 2$), energetic arousal ($n = 2$), lower anxiety ($n = 2$) as well as calmness and tired arousal, simultaneously ($n = 1$).

Conclusions: Although the heterogeneity of PFC asymmetry protocols, reviewed studies showed a low risk of bias, suggesting that a higher left PFC activation is associated with a positive psychological response to exercise.

1. Introduction

Studies have suggested that prefrontal cortex (PFC) asymmetric activation is associated with alterations in psychological responses such as depression, affect and anxiety, given that PFC plays a key role when inhibiting activation of different subcortical structures such as amygdala and hippocampus [1–3]. In a seminal study, Davidson and colleagues [4] identified an imbalance (i.e. asymmetry) in electroencephalogram (EEG) responses between the left and right PFC hemi-

spheres [5]. In this regard, an imbalance in favor of a higher activation in the right PFC (PFC_{RA}) was associated with impaired psychological responses such as reduced motivation and higher stress and anxiety, while a higher activation in the left PFC (PFC_{LA}) was associated with an improved psychological responses such as increased motivation and higher affect and resilient behavior [6]. Briefly, frontal activation asymmetry is characterized by a reduced EEG alpha band (8–13 Hz) in one PFC hemisphere, thereby suggesting a higher activation in this hemisphere [7–10]. Therefore, it has been theorized that individuals showing a PFC_{LA} rather than PFC_{RA} may experience more positive psy-

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chological responses to distinct contexts [5,6,11–13] including exercise [14,15], such as an increased affect [15], lowered anxiety [11,12] and enhanced energetic arousal [12,16].

In physical activity and health-scenario, it is important to note that the improved affect, anxiety, energetic and calmness arousal responses to exercise have been associated with exercise adherence [17–20]. Studies verified that individuals showing a greater affective valence, energetic or calmness arousal were more likely to adhere to a physical training program than those showing psychological responses in a different direction [18,21]. For example, a previous study verified that greater anxiety responses were associated with a low level of physical activity [22]. At least in sedentary, unfit and overweight/obese individuals, affect is inversely associated with exercise intensity so that the higher exercise intensity, the more unpleasant the exercise session [23–25]. Likewise, anxiety responses may play a role as an exercise modulator, as higher anxiety levels may lead individuals to perceive the exercise bout as more effortful than it really does [26,27]. Although future studies are required to closer investigate the exercise intensity-anxiety relationship, the overall suggestion is that higher exercise intensities are associated with an impaired affect [28,29] and anxiety response [26,27] to exercise.

The practice of regular exercise is an essential mean to promote healthy, as regular exercises are known to induce improvements in health markers such as body composition, oxygen consumption, inflammatory responses, and blood glucose concentrations [30–33]. Consequently, factors that improve the practitioners' adherence to regular exercises are of interest of health and exercise sciences researchers as well as healthcare professionals [34–36]. Assuming that most sedentary individuals such as obese, smokers or individuals with non-communicable diseases may tolerate only low levels of exercise, the promotion of positive psychological responses to exercise (i.e. an increased affect and energetic or calmness arousal and a reduced anxiety) may play a key role to improve adherence of these individuals to a regular exercise practice, since individuals experiencing negative sensations to exercise may be less willing to repeat the exercise session [34,37,38].

Some reviews have been designed to elucidate the relationship between PFC_{LA} and psychological responses to exercise [39,40], however there is a paucity of reviews that have systematically assessed results from original studies according to straightforward criteria suggested for systematic reviews [41]. For example, although Lattari and colleagues [39] have systematically reviewed the influence of cerebral activation on exercise-induced mood state responses [39], these authors included studies which assessed cerebral activation through different methodologies such as PFC activation asymmetry, absolute and relative power, and sLORETA, thus likely introducing a confounding factor to understand the relationship between PFC_{LA} and psychological responses to exercise. Interestingly, the authors concluded that exercise-derived psychological responses may be partially influenced by PFC activation, given the relationship between them [39]. Therefore, a systematic review of the evidence of a likely association between PFC activation asymmetry as assessed by EEG measures and an improved psychological response to exercise is yet to be provided.

The present study systematically reviewed data from the literature regarding PFC activation asymmetry and psychological responses to exercise. Specifically, we aimed to verify if PFC activation asymmetry as assessed by resting EEG measures may be associated with psychological responses to exercise such as affect, anxiety and multidimensional arousal states (energy, tension, calmness, and tiredness). Moreover, we further aimed to review the PFC activation asymmetry protocols.

2. Methods

This study was conducted according to recommendations for systematic reviews elaboration of the PICO (Population, Intervention,

Comparison, and Outcome) criteria [42]. In addition, the methodological quality was conducted according to the Cochrane Handbook [41] and reported in accordance with the PRISMA statement [43]. This systematic review was registered on the PROSPERO platform (International prospective register of systematic reviews; Process CRD42017079461).

2.1. Eligibility criteria

PICO criteria were used for eligibility procedures so that studies involving healthy participants submitted to aerobic exercise interventions were considered. Furthermore, original studies reporting the relationship between resting PFC activation asymmetry as assessed by EEG technique (i.e. PFC_{LA} and PFC_{RA}) and psychological responses to exercise (i.e. affect, anxiety and multidimensional arousal states) were considered as eligible.

2.2. Electronic search

Searches were made on the PubMed and Web of Science databases to include articles published up to 30-04-2019, by using “((((Frontal*[Text Word]) OR Prefrontal*[Text Word]) AND Alpha[Text Word]) OR Asymmetr*[Text Word]) AND exercise[MeSH Terms])” or “ALL FIELDS: (Frontal* Alpha Asymmetr*) OR ALL FIELDS: (Prefrontal* Alpha Asymmetr*) AND TOPIC: (exercise) Refined by: DOCUMENT TYPES: (ARTICLE)” as truncated keywords.

2.3. Studies selection

After the initial search, studies were checked for duplicates by using the Mendeley Desktop software (v1.17.11, 2008–2016). Thereafter, two researchers (RS and RP) independently assessed the studies by reading title and abstract, in order to select them according to eligibility criteria. Researches experienced with SR (CB or HC) decided disagreements.

2.4. Data extraction and synthesis

Outcomes were independently extracted by two researchers (RA and RP) to a spreadsheet containing: authors/publication year, sample size, age, maximum or peak oxygen consumption (VO_{2MAX} and VO_{2PEAK}), design, exercise model, psychological scales, and EEG results.

2.5. Methodological aspects

The risk of bias was independently analyzed by two researchers (FOP and TMS), according to the Cochrane Handbook for Systematic Reviews of Interventions [41]. Firstly, procedures were conducted according to the blinding of assessed studies, such as blinding of authors and affiliations name, article's title and journal published (RA). Secondly, inclusion criteria were the random sequence generation (selection bias), blinding of participants and personnel (performance bias), blinding of outcome assessment (detection bias), incomplete outcome data (attrition bias) and selective reporting (reporting bias). Importantly, criteria such as random sequence generation, blinding of participants and personnel were assessed only in crossover designs, as these criteria are incompatible with cross-sectional studies. Hence, this bias yielded no risk of influencing outcomes in cross-sectional studies (indicated as green circles in Fig. 2). Hence, selection bias was assessed by selecting only crossover design studies and an experienced researcher (HJ CJ) decided disagreements between researches. Figures were designed through the software Review Manager 5.3.

3. Results

3.1. Search results and study characteristics

Initially, the search resulted in 1901 studies (1298 retrieved from PubMed, 603 retrieved from Web of Science and 1 study manually inserted). Afterward, 14 duplicates and 1858 studies which did not meet the PICO criteria (i.e. reviews, studies with animal model, and studies either without exercise intervention or without EEG PFC activation asymmetry protocol) were excluded, thus remaining 30 studies for screening. Scrutiny of these 30 studies resulted in 22 studies excluded, as they did not match the purpose in the present review. Consequently, 8 studies meeting eligible criteria of methodological assessment were included in the final SR (Fig. 1). Overall, these reviewed studies assessed 328 healthy male and female participants, from 14.7 to 26.5 years old, with a VO_{2MAX} or VO_{2PEAK} from 37.9 to 54.9 mL.kg⁻¹.min⁻¹, as shown in Table 1.

The present review analyzed cross-sectional (50%) and crossover designed-studies (50%) that used a bicycle (37.5%) or treadmill (62.5%) as an ergometer. These studies assessed psychological responses to exercise through different scales. For example, 25% of the studies applied the State Anxiety Inventory, a Likert questionnaire [44]. In contrast, 62.5% of the studies assessed multidimensional arousal states through the Activation-Deactivation Adjective Check List (AD-ACL), a questionnaire proposed to assess tiredness-energy and calmness-tension dimensions through Energy (General Activation), Tiredness (Deactivation-Sleep), Tension (High Activation) and Calmness (General Deactivation) subscales [45]. In this regard, AD-ACL questionnaire conceptualizes multidimensional arousal states as high

energetic arousal (high pleasantness and high activation), high tense arousal (low pleasantness and high activation), tiredness (low pleasantness and low activation) and calmness (high pleasantness and low activation) [45].

Moreover, 25% of the studies assessed pleasure and displeasure through the Feeling Scale [46] and 12.5% of the studies assessed the perceived arousal by using the Felt Arousal Scale [47].

PFC asymmetry protocols recorded EEG data at F3 and F4 (100% of the studies), P3 and P4 (62.5% of the studies), T3 and T4 or T5 and T6 (25% of the studies) and Pz, Oz, O1 and O2 (12.5% of the studies) positions, according to the 10–20 EEG system. Most recorded EEG signal for 8 min (75% of the studies), while a smaller part recorded EEG for the 4 min (25% of the studies) preceding the exercise bout. Studies applying an 8 min protocol (n = 6) either sampled EEG intermittently with 8 trials of 1 min (n = 4) or continuously (n = 2). In this regard, three studies using intermittent EEG measures maintained participants with closed eyes (n = 3) while one (n = 1) with opened eyes. In contrast, studies using continuous EEG sampling either oriented participants (n = 1) to vary between opened and closed eyes (4 vs 4 min, respectively) or maintained participants exclusively with closed eyes (n = 1). Studies applying a 4 min protocol (n = 2) sampled EEG data intermittently (4 trials of 1 min), while participants maintained their eyes closed. Table 2 shows these data.

Most studies (75%) reported an association between PFC asymmetry and psychological responses to exercise, as participants eliciting a PFC_{LA} also showed an improved affective response (n = 2), energetic arousal (n = 2) and lowered anxiety (n = 2) when compared to those eliciting a PFC_{RA}. However, a single study (n = 1) reported an association between PFC_{LA} and calmness as well as between PFC_{LA} and tiredness arousal. Most studies (75% of the studies) assessed psychological

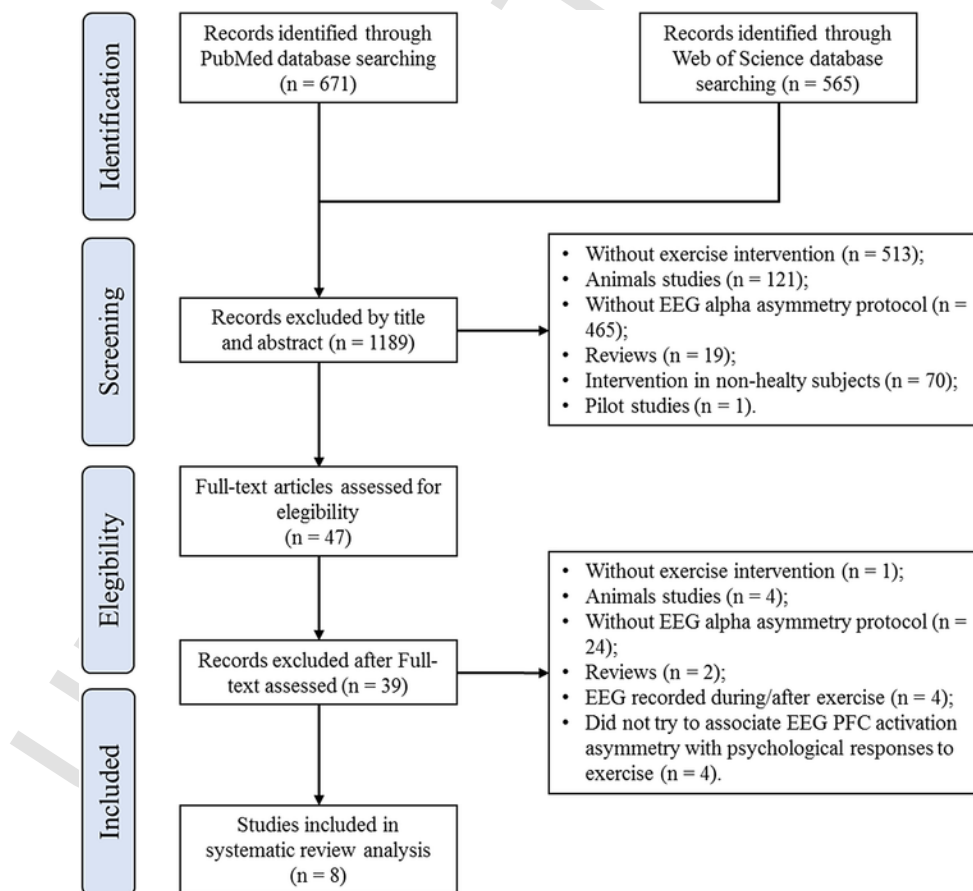


Fig. 1. PRISMA Flow chart of study selection and eligibility criteria.

Table 1
Sample characteristics of selected studies.

Authors	Sample size	Age (years)	Mean VO_{2MAX}/VO_{2PEAK} ($mL \cdot kg^{-1} \cdot min^{-1}$)
Petruzzello; Landers [11]	19 male	22.7 ± 2.4	VO_{2MAX} - 54.9 ± 8.4
Petruzzello; Tate [12]	20 (15 male, 5 female)	22.6 ± 3.3	VO_{2MAX} - 47.8 ± 8.6
Hall; Ekkekakis; Van Landuyt; Petruzzello [13]	42 (23 male, 19 female)	22.4 ± 2.2	No information
Petruzzello; Hall; Ekkekakis [16]	69 (38 male, 31 female)	21.4 ± 2.9	VO_{2MAX} - Male = 49.9 ± 7.2, Female = 45.2 ± 6.1
Hall; Ekkekakis; Petruzzello [61]	30 (17 male, 13 female)	Male (24.4 ± 4.1) Female (23.2 ± 2.8)	VO_{2MAX} - Male = 51.5 ± 7.0, Female = 47.3 ± 4.0
Schneider et al. [15]	98 (54 male, 44 female) (PFC_{LA} 56, PFC_{RA} 42)	14.7 ± 0.4	VO_{2PEAK} - PFC_{LA} = 38.6 ± 8.4, PFC_{RA} = 39.1 ± 8.3
Hall; Ekkekakis; Petruzzello [14]	30 (16 male, 14 female)	Male = 21.5 ± 2.5, Female = 21.2 ± 2.0	VO_{2MAX} - Male = 56.6 ± 7.3, Female = 47.7 ± 7.6
Lattari et al. [39]	20 male	26.5 ± 3.8	VO_{2MAX} - 37.9 ± 6.6

PFC_{LA} = predominant left PFC activation; PFC_{RA} = predominant right PFC activation

responses after the exercise bout so that only two studies (25% of the studies) measured psychological responses during the exercise. In this regard, while one study verified that PFC activation asymmetry was correlated with affective responses to exercise bouts performed at or below the ventilatory threshold (VT) intensity, the other verified no association in a self-selected intensity at 50% VO_{2MAX} . When psychological measures were obtained after the exercise bout, most studies ($n = 5$) observed an association between PFC activation asymmetry and psychological responses to exercise below the VO_{2MAX} intensity, while some ($n = 2$) reported similar results when investigating different intensities comprising intensities <VT and >VT. Additionally, a single study investigating walking as an exercise mode reported no association between PFC activation asymmetry and psychological responses. Table 2 shows these data.

3.2. Risk of bias

Regarding the selection, detection, attrition and reporting bias, three studies showed an unclear risk of selection bias because they did not clarify how randomization was conducted. Additionally, considering cross-sectional studies are considered as having a low risk of bias, given it is impossible to use random sequence generation in this kind of study, risk of bias identification was further unclear. All studies presented an unclear risk of detection bias as none reported if and how the blinding outcome assessment was conducted. In contrast, one study presented a high risk of bias, given the attrition bias derived from the absence of fitness level assessment in two participants (due to technical problems when measuring cardiopulmonary responses to exercise, the authors of these studies estimated rather than determining the exercise intensity at 75% VO_{2MAX}). Figs. 2 and 3 depict the bias risk outcomes of the reviewed studies.

4. Discussion

The present review systematically analyzed the evidence regarding the relationship between PFC activation asymmetry and psychological responses to exercise such as affect, anxiety and multidimensional

arousal states. Outcomes of this review reinforced the notion that PFC activation asymmetry may be associated with improved psychological responses to exercise [7–10]. The overall suggestion was that PFC_{LA} , as indicated by a lower EEG alpha band over the left PFC, may be related to an increased affect and energetic arousal, and a lower anxiety during exercise. In contrast, PFC_{RA} may be related to an impaired psychological response to exercise such as lower energetic arousal and affect, and higher anxiety.

It is important to highlight that one single study observed that PFC_{LA} correlated simultaneously with tiredness and calmness, even though tiredness is considered as a state of low arousal and affect. In this regard, according to studies by Thayer who developed the AD-ACL questionnaire [45], “calm tiredness” is an exhaustive physical demand-derived pleasant state caused by simultaneous tiredness and calmness sensations. For example, although some individuals may experience a tiredness sensation when performing an exhaustive exercise bout, they may also experience a pleasant sensation with a low arousal level due to the cessation of a such stressful exercise [48,49].

The likely mechanism of the PFC asymmetry involves the activation of cortical areas linked to subcortical structures such as hippocampus and amygdala. Briefly, the left dorsolateral (dlPFC) is associated with memory formation, positive emotion and approach goals, while the left ventromedial (vmPFC) is associated with a non-emotional memory, approach motivation and affective down-regulation. In contrast, right dlPFC is related to memory retrieval, negative emotion and withdraw goals, while the right vmPFC is related to emotional memory, withdraw motivation and stress reaction initiation [6]. Therefore, one may argue that activation in different PFC areas activation is related to different sensations evoked from hippocampus and amygdala. Actually, functional magnetic resonance imaging (fMRI) studies suggested a PFC-inhibited hippocampus and amygdala activity, as the amygdala is associated with phobias and negative emotions and hippocampus plays a role when integrating contextual information of a given situation [10,50,51]. It has been suggested that PFC exerts control over these structures through an asymmetric activation of its hemispheres. For example, the higher the PFC_{LA} , the higher the inhibition over amygdala and increased hippocampus activation. Somehow, the higher resilience to overcome unpleasantness sensations may occur due to a higher PFC_{LA} . However, when considering PFC_{RA} , amygdala and hippocampus become more and less activated, respectively, thereby inducing to negative thoughts such as hesitation and reduced resilience [6].

The present review highlights important methodological aspects for studies correlating PFC activation asymmetry and psychological responses. A previous review [39] had challenged the association between EEG data and psychological responses to exercise, as the authors highlighted that the EEG technique may be unreliable to this proposal. However, it is important to note that this earlier review neither selected studies according to PFC EEG measures nor discussed the exercise-induced affective valence and anxiety responses [39]. The present review systematically analyzed evidence from studies assessing PFC EEG measures obtained before the exercise bout, in order to verify the possible relationship between PFC activation asymmetry and psychological responses to exercise such as affective valence, anxiety and multidimensional arousal states. We accessed methodological aspects concerning EEG measures protocols and the relationship between PFC asymmetry and psychological responses to different exercise modes. In this regard, most reviewed studies included different EEG positions (P3, P4, T3, T4, T5, T6, Pz, Oz, O1 and O2) in addition to measures of PFC areas. Two prior studies [52,53] had found a relationship between alpha asymmetry (i.e. left to right) measured in temporal and parietal cortical areas (T3, T4, P3, and P4) and anxiety during exercise. In addition, others [54–57] had proposed an association between activation in parietal and temporal cortical regions and arousal as measured by the Felt Arousal Scale. However, according to other studies [3,6,58–60],

Table 2
Characteristics and results of selected studies.

Authors	Design	Exercise	Exercise model	Results	PFC _{LA} association	PFC _{RA} association	Psychological scale	EEG derivations and measurement protocol
Petruzzello; Landers [11]	Cross-sectional	Treadmill	30 min at 75% of VO _{2MAX} .	PFC asymmetry was significantly related to anxiety (pre-to-post exercise reduced anxiety in PFC _{LA} but not in PFC _{RA} group).	↓ Anxiety	↑ Anxiety	State Anxiety Inventory	 <p>EEG sampled in 8 × 1 minute trials with open eyes</p>
Petruzzello; Tate [12]	Crossover	Bicycle	1) 30 min as a control session (without exercise); 2) 55% of VO _{2MAX} for 30 min; 3) 70% of VO _{2MAX} for 30 min.	At 70% of VO _{2MAX} PFC _{LA} was associated with an increase in positive affect and a decrease in state anxiety after the exercise. PFC _{RA} was associated with an increase in anxiety (Obs. Arousal state not reported).	↑ Positive Affect, ↓ Anxiety	↓ Positive Affect, ↑ Anxiety	AD ACL and State Anxiety Inventory	 <p>EEG sampled in 8 × 1 minute trials with closed eyes (with a 2 minutes interval between 4 and 5 trials)</p>

Table 2 (Continued)

Authors	Design	Exercise	Exercise model	Results	PFC _{LA} association	PFC _{RA} association	Psychological scale	EEG derivations and measurement protocol
Hall; Ekkekakis Van Landuyt; Petruzzello [13]	Cross-sectional	Walking	10 min in self-selected treadmill performed.	PFC asymmetry was unable to be associated with psychological responses in short walking exercise bout.	Could not be associated with any psychological response	Could not be associated with any psychological response	AD ACL	 <p>EEG sampled in 4 × 1 minute trials with closed eyes.</p>
Petruzzello; Hall; Ekkekakis [16]	Cross-sectional	Treadmill	30 min at the 75% VO _{2MAX} .	PFC _{LA} rather than PFC _{RA} was associated with greater energetic arousal after the exercise bout.	↑ Energetic Arousal	↓ Energetic Arousal	AD ACL	 <p>EEG sampled in 8 × 1 minute trials with closed eyes.</p>

Table 2 (Continued)

Authors	Design	Exercise	Exercise model	Results	PFC _{LA} association	PFC _{RA} association	Psychological scale	EEG derivations and measurement protocol
Hall; Ekkekakis; Petruzzello [61]	Cross-sectional	Treadmill	Maximal incremental test.	PFC _{LA} rather than PFC _{RA} was associated with tiredness and calmness arousal after strenuous exercise performance.	↑ Tiredness and Calmness Arousal	↓ Tiredness and Calmness Arousal	AD ACL	 <p>EEG sampled in 4 × 1 minute trials with closed eyes</p>
Schneider; Graham; Grant; King; Cooper [15]	Crossover	Bicycle	30 min in cycle-ergometer; 80% to VT or heavy intensity (above VT).	PFC _{LA} elicited more positive affect than PFC _{RA} at 80% VT (reported at an exercise bout performed before a heavy exercise bout).	↑ Positive Affect	↓ Positive Affect	Feeling Scale	 <p>EEG sampled in 8 consecutive minutes with open (4 min) and closed eyes (4 min)</p>

Table 2 (Continued)

Authors	Design	Exercise	Exercise model	Results	PFC _{LA} association	PFC _{RA} association	Psychological scale	EEG derivations and measurement protocol
Hall; Ekkekakis; Petruzzello [14]	Crossover	Treadmill	1) 20% below the VT for 15 min; 2) at the VT for 15 min; 3) 10% above the VT for 15 min.	The results show that PFC _{LA} was able to be associated with greater energetic arousal after exercise than those whose PFC _{RA} , it is worth noting that PFC _{LA} was related to greater aerobic fitness. It was also identified that there was no systematic influence of exercise intensity in this study.	↑ Energetic Arousal	↓ Energetic Arousal	AD ACL	 <p>EEG sampled in 8 × 1 minute trials with closed eyes</p>
Lattari et al. [39]	Crossover	Bicycle	3 sessions: a) 50% PVO _{2MAX} ; b) self-selected intensity; c) without exercise (control).	PFC asymmetry could not be associated with any psychological response.	Could not be associated with any psychological response	Could not be associated with any psychological response	Feeling Scale and Felt Arousal Scale	 <p>EEG sampled in 8 consecutive minutes with closed eyes</p>

VT = Ventilatory threshold; PVO_{2MAX} = Maximum power at VO_{2MAX}; PFC = Prefrontal cortex; PFC_{LA} = Predominant left PFC activation; PFC_{RA} = Predominant right PFC activation; ↑ = Higher; ↓ = Lower; AD ACL = Activation deactivation adjective check list; EEG = Electroencephalogram.

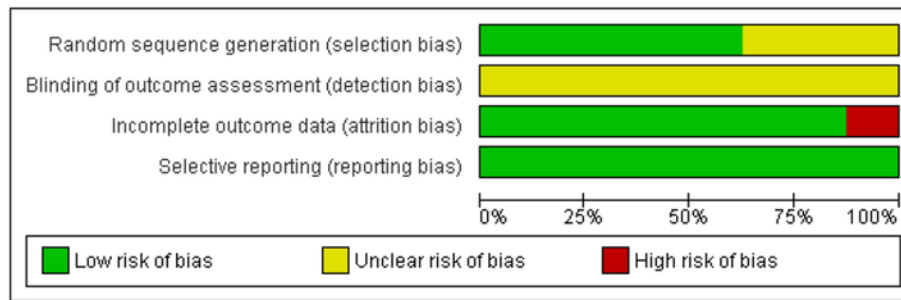


Fig. 2. Risk of bias graph. The colors represent risk of bias judged (green - low risk, yellow - unclear risk and red - high risk). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

	Random sequence generation (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)
Petruzzello & Landers (1994)	+	+	?	+	+
Petruzzello & Tate (1997)	?	+	?	+	+
Hall, Ekkekakis, Van Landuyt & Petruzzello (2000)	+	+	?	+	+
Petruzzello, Hall & Ekkekakis (2001)	+	+	?	-	+
Hall, Ekkekakis & Petruzzello (2007)	+	+	?	+	+
Schneider, Grahamc, Grant, King & Cooper (2009)	?	+	?	+	+
Hall, Ekkekakis & Petruzzello (2010)	?	+	?	+	+
Lattari et al. (2016)	+	+	?	+	+

Fig. 3. Individual risk of bias of selected studies. The colors and symbols represent risk of bias judged (green or "+" - low risk, yellow or "?" - unclear risk and red or "-" - high risk). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

frontal areas such as F3 and F4 positions rather than parietal and temporal ones have been suggested to reflect emotional responses to different conditions, including exercises [14,16,61]. In theory, F3 and F4 positions have been suggested to reflect activation in dlPFC regions [62,63].

Importantly, we observed a strong level of evidence indicating that PFC_{LA} may predict an improved psychological response to exercise such as an increased affect and energetic arousal, and reduced anxiety. In fact, most studies, excepting two [13,39], observed a PFC asymmetry ability in predicting psychological responses in moderate exercise intensity. In this sense, moderate exercise intensities have been suggested as a "point of affective responses variability", as some individuals may show a positive affect while others, a negative one [21]. Therefore, one may argue that PFC activation asymmetry may be a neurophysiological marker associated with a greater affective responses variability so that

an imbalance in favor of a higher activation in PFC_{RA} may increase the likelihood of aversive feelings during exercise at this intensity.

4.1. Methodological considerations and future perspectives

There was a paucity of studies meeting PICO criteria, as several cerebral asymmetry studies failed to meet inclusion criteria such as availability of EEG measures before the exercise bout [64–70] and association between PFC activation asymmetry and psychological responses [71–73]. Therefore, we selected studies reporting PFC asymmetry data as suggested elsewhere [74], thus improving the reliability of outcomes in this review. Consequently, studies investigating cortical asymmetry through other imaging techniques such as Near-Infrared Spectroscopy (NIRS) [75–77] could not have been included in the present review, as comparisons between EEG and NIRS may be considered as inadequate. Future original researches are encouraged to compare PFC activation asymmetry accessed through different imaging techniques such as EEG and NIRS.

Furthermore, PFC activation measures before rather than after or during the exercise bout should be obtained, given the influence of exercise-induced interoception responses in cerebral responses. Additionally, results of the present review suggest that future cortical asymmetry studies may include F3 and F4 positions together with other frontal cortex regions such as FC1, FC2, FC3, thus likely providing a broad PFC activation asymmetry scenario as used in other research fields [78–80]. Importantly, this topic may benefit from studies reporting the blinding outcome assessment, as most studies have not attempted to accomplish this aspect. Moreover, new research teams with different orientations are encouraged to promote new knowledge on this topic, as most studies (75%) included in this systematic review were published by a single research group.

5. Conclusion

Summarizing, results of this review may suggest that resting PFC activation asymmetry, as indicated by a PFC_{LA} as measured by EEG alpha band, may predict improved psychological responses to exercise such as increased affect and energetic arousal and reduced anxiety during and after aerobic exercise.

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Authors' contribution

Through the document declared the participation of all authors involved research. In addition, all statements contained within the work

are based on scientific evidence. We are also aware that if necessary, reviews should be carried out in order to improve the work in question. Finally, I am aware of all the procedures proposed by Physiology and Behavior if the work in question is accepted for publication.

Declaration of Competing Interest

The authors have no conflict of interests.

References

- [1] A.W. Toga, P.M. Thompson, Mapping brain asymmetry, *Nat. Rev. Neurosci.* 4 (2003) 37–48.
- [2] I.H. Gotlib, EEG Alpha Asymmetry, Depression, and Cognitive Functioning, 1998.
- [3] R.J. Davidson, Cerebral asymmetry and emotion: conceptual and methodological conundrums, *Cognit. Emot.* 7 (1993) 115–138.
- [4] R.J. Davidson, G.E. Schwartz, C. Saron, J. Bennett, D.J. Goleman, Frontal versus parietal EEG asymmetry during positive and negative affect, *Psychophysiology* 16 (1979) 202–203.
- [5] R.J. Davidson, What does the prefrontal cortex “do” in affect: perspectives on frontal EEG asymmetry research, *Biol. Psychol.* 67 (2004) 219–233.
- [6] T. Meyer, T. Smeets, T. Giesbrecht, C.W.E.M. Quaedflieg, F.T.Y. Smulders, E.H. Meijer, H.L.G.J. Merckelbach, The role of frontal EEG asymmetry in post-traumatic stress disorder, *Biol. Psychol.* 108 (2015) 62–77.
- [7] R.J. Davidson, Affective style, psychopathology, and resilience: brain mechanisms and plasticity, *Am. Psychol.* 55 (2000) 1196–1214.
- [8] J.B. Henriques, R.J. Davidson, Left frontal hypoactivation in depression, *J. Abnorm. Psychol.* 100 (1991) 535–545.
- [9] G.E. Schwartz, R.J. Davidson, F. Maer, Right hemisphere lateralization for emotion in the human brain: interactions with cognition, *Science (80-)* 190 (1975) 286–288.
- [10] R.J. Davidson, Affective style and affective disorders: perspectives from affective neuroscience, *Cognit. Emot.* 12 (1998) 307–330.
- [11] S.J. Petruzzello, D.M. Landers, State anxiety reduction and exercise: does hemispheric activation reflect such changes?, *Med. Sci. Sports Exerc.* 26 (1994) 1028–1035.
- [12] S.J. Petruzzello, A.K. Tate, Brain activation, affect, and aerobic exercise: an examination of both state-independent and state-dependent relationships, *Psychophysiology* 34 (1997) 527–533.
- [13] E.E. Hall, P. Ekkekakis, L.M. Van Landuyt, S.J. Petruzzello, Resting frontal asymmetry predicts self-selected walking speed but not affective responses to a short walk, *Res. Q. Exerc. Sport* 71 (2000) 74–79.
- [14] E.E. Hall, P. Ekkekakis, S.J. Petruzzello, Predicting affective responses to exercise using resting EEG frontal asymmetry: does intensity matter?, *Biol. Psychol.* 83 (2010) 201–206.
- [15] M. Schneider, D. Graham, A. Grant, P. King, D. Cooper, Regional brain activation and affective response to physical activity among healthy adolescents, *Biol. Psychol.* 82 (2009) 246–252.
- [16] S.J. Petruzzello, E.E. Hall, P. Ekkekakis, Regional brain activation as a biological marker of affective responsivity to acute exercise: influence of fitness, *Psychophysiology* 38 (2001) 99–106.
- [17] D.M. Williams, Exercise, affect, and adherence: an integrated model and a case for self-paced exercise, *J. Sport Exerc. Psychol.* 30 (2008) 471–496.
- [18] M. Lacharité-Lemieux, J.-P. Brunelle, L.J. Dionne, Adherence to exercise and affective responses: comparison between outdoor and indoor training, *Menopause* 22 (2015) 731–740.
- [19] H. Hawley-Hague, M. Horne, D.A. Skelton, C. Todd, Review of how we should define (and measure) adherence in studies examining older adults' participation in exercise classes, *BMJ Open* 6 (2016), e011560.
- [20] G.L. Stonerock, J.A. Blumenthal, Role of counseling to promote adherence in healthy lifestyle medicine: strategies to improve exercise adherence and enhance physical activity, *Prog. Cardiovasc. Dis.* 59 (2017) 455–462.
- [21] N.M. Schutte, I. Nederend, J.J. Hudziak, M. Bartels, E.J.C. de Geus, Heritability of the affective response to exercise and its correlation to exercise behavior, *Psychol. Sport Exerc.* 31 (2017) 139–148.
- [22] C.T. Belem da Silva, F. Schuch, M. Costa, V. Hirakata, G.G. Manfro, Somatic, but not cognitive, symptoms of anxiety predict lower levels of physical activity in panic disorder patients, *J. Affect. Disord.* 164 (2014) 63–68.
- [23] M.A. Ladwig, A. Matthew, M. Hartman, P. Ekkekakis, Affect-based exercise prescription, *ACSM's Health Fit. J.* 21 (2017) 10–15.
- [24] E.A. Rose, G. Parfitt, Exercise experience influences affective and motivational outcomes of prescribed and self-selected intensity exercise, *Scand. J. Med. Sci. Sports* 22 (2012) 265–277.
- [25] P. Ekkekakis, E. Lind, S. Vazou, Affective responses to increasing levels of exercise intensity in normal-weight, overweight, and obese middle-aged women, *Obesity* 18 (2010) 79–85.
- [26] A.J. Knicker, I. Renshaw, A.R.H. Oldham, S.P. Cairns, Interactive processes link the multiple symptoms of fatigue in sport competition, *Sports Med.* 41 (2011) 307–328.
- [27] W.P. Morgan, Psychological components of effort sense, *Med. Sci. Sports Exerc.* 26 (1994) 1071–1077.
- [28] E.S. Decker, P. Ekkekakis, More efficient, perhaps, but at what price? Pleasure and enjoyment responses to high-intensity interval exercise in low-active women with obesity, *Psychol. Sport Exerc.* 28 (2017) 1–10.
- [29] B.R. Ramalho Oliveira, B.F. Viana, F.O. Pires, M. Júnior Oliveira, T.M. Santos, Prediction of affective responses in aerobic exercise sessions, *CNS Neurol Disord - Drug Targets* 14 (2015) 1214–1218.
- [30] W.M. Valencia, M. Stoutenberg, H. Florez, Weight loss and physical activity for disease prevention in obese older adults: an important role for lifestyle management, *Curr. Diab. Rep.* 14 (2014) 539.
- [31] V.A. Catenacci, H.R. Wyatt, The role of physical activity in producing and maintaining weight loss, *Nat. Clin. Pract. Endocrinol. Metab.* 3 (2007) 518–529.
- [32] F.G.S. Toledo, B.H. Goodpaster, The role of weight loss and exercise in correcting skeletal muscle mitochondrial abnormalities in obesity, diabetes and aging, *Mol. Cell. Endocrinol.* 379 (2013) 30–34.
- [33] A.A. Ascensão, J.F. Magalhães, J.M. Soares, R.M. Ferreira, M.J. Neuparth, H.J. Appell, J.A. Duarte, Cardiac mitochondrial respiratory function and oxidative stress: the role of exercise, *Int. J. Sports Med.* 26 (2005) 258–267.
- [34] P. Ekkekakis, S. Vazou, W.R. Bixby, E. Georgiadi, The mysterious case of the public health guideline that is (almost) entirely ignored: call for a research agenda on the causes of the extreme avoidance of physical activity in obesity, *Obes. Rev.* 17 (2016) 313–329.
- [35] S.H. Backhouse, P. Ekkekakis, S.J.H. Biddle, A. Foskett, C. Williams, Exercise makes people feel better but people are inactive: paradox or artifact?, *J. Sport Exerc. Psychol.* 29 (2007) 498–517.
- [36] H.H. Lee, J.A. Emerson, D.M. Williams, The exercise-affect-adherence pathway: an evolutionary perspective, *Front. Psychol.* 7 (2016) 1–11.
- [37] M. Kopp, M. Steinlechner, G. Ruedl, L. Ledochowski, G. Rumpold, A.H. Taylor, Acute effects of brisk walking on affect and psychological well-being in individuals with type 2 diabetes, *Diabetes Res. Clin. Pract.* 95 (2012) 25–29.
- [38] E.S. Everson, A.J. Daley, M. Ussher, Does exercise have an acute effect on desire to smoke, mood and withdrawal symptoms in abstaining adolescent smokers?, *Addict. Behav.* 31 (2006) 1547–1558.
- [39] E. Lattari, E. Portugal, H. Moraes, S. Machado, T.M. Santos, A.C. Deslandes, Acute effects of exercise on mood and EEG activity in healthy young subjects: a systematic review, *CNS Neurol. Disord. Drug Targets* 13 (2014) 972–980.
- [40] P. Ekkekakis, Illuminating the black box: investigating prefrontal cortical hemodynamics during exercise with near-infrared spectroscopy, *J. Sport Exerc. Psychol.* 31 (2009) 505–553.
- [41] J.P. Higgins, D.G. Altman, P.C. Gøtzsche, et al., The Cochrane Collaboration's tool for assessing risk of bias in randomised trials, *BMJ* 343 (2011) d5928.
- [42] E. Tacconelli, Systematic reviews: CRD's guidance for undertaking reviews in health care, *Lancet Infect. Dis.* (2010) [https://doi.org/10.1016/S1473-3099\(10\)70065-7](https://doi.org/10.1016/S1473-3099(10)70065-7).
- [43] A. Liberati, D.G. Altman, J. Tetzlaff, C. Mulrow, Ioannidis JP, A. Clarke, P.J. Devereaux, J. Kleijnen, D. Moher, Annals of internal medicine academia and clinic the PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions, *Ann. Intern. Med.* 151 (2009) W65–W94.
- [44] C. Spielberger, R. Gorsuch, R. Lushene, P.R. Vagg, G. Jacobs, Manual for the State-Trait Anxiety Inventory (Form Y1 – Y2), 1983.
- [45] R.E. Thayer, Activation-deactivation adjective check list: current overview and structural analysis, *Psychol. Rep.* 58 (1986) 607–614.
- [46] C.J. Hardy, W.J. Rejeski, Not what, but how one feels: the measurement of affect during exercise, *J. Sport Exerc. Psychol.* 11 (1989) 304–317.
- [47] S. Svebak, S. Murgatroyd, Metamotivational dominance. A multimethod validation of reversal theory constructs, *J. Pers. Soc. Psychol.* 48 (1985) 107–116.
- [48] R.E. Thayer, *Calm Energy: How People Regulate Mood with Food and Exercise*, Oxford University Press, New York, NY, US, 2001.
- [49] R.E. Thayer, *The Biopsychology of Mood and Arousal*, Oxford University Press, 1989.
- [50] J.M. Spielberg, G.A. Miller, S.L. Warren, A.S. Engels, L.D. Crocker, B.P. Sutton, W. Heller, Trait motivation moderates neural activation associated with goal pursuit, *Cogn. Affect. Behav. Neurosci.* 12 (2012) 308–322.
- [51] J.M. Spielberg, G.A. Miller, A.S. Engels, J.D. Herrington, B.P. Sutton, M.T. Banich, W. Heller, Trait approach and avoidance motivation: lateralized neural activity associated with executive function, *Neuroimage* 54 (2011) 661–670.
- [52] S.H. Boutcher, D.M. Landers, The effects of vigorous exercise on anxiety, heart rate, and alpha activity of runners and nonrunners, *Psychophysiology* 25 (1988) 696–702.
- [53] J. Wiese, M. Singh, L. Yeudall, Occipital and parietal alpha power before, during and after exercise, *Med. Sci. Sports Exerc.* 15 (1983).
- [54] R. Davidson, A. Tomarken, Laterality and emotion: an electrophysiological approach, *Handb. Neuropsychol.* (1989).
- [55] W. Heller, Neuropsychological mechanisms of individual differences in emotion, personality, and arousal, *Neuropsychology* 7 (1993) 476–489.
- [56] A.J. Tomarken, R.J. Davidson, Frontal brain activation in repressors and nonrepressors, *J. Abnorm. Psychol.* 103 (1994) 339–349.
- [57] A.J. Tomarken, R.J. Davidson, J.B. Henriques, Resting frontal brain asymmetry predicts affective responses to films, *J. Pers. Soc. Psychol.* 59 (1990) 791–801.
- [58] A.J. Tomarken, R.J. Davidson, Frontal brain activation in repressors and nonrepressors, *J. Abnorm. Psychol.* 103 (1994) 339–349.
- [59] R.J. Davidson, Anterior cerebral asymmetry and the nature of emotion, *Brain Cogn.* 20 (1992) 125–151.
- [60] J.J.B. Allen, J.A. Coan, M. Nazarian, Issues and assumptions on the road from raw signals to metrics of frontal EEG asymmetry in emotion, *Biol. Psychol.* (2004) <https://doi.org/10.1016/j.biopsycho.2004.03.007>.
- [61] E.E. Hall, P. Ekkekakis, S.J. Petruzzello, Regional brain activity and strenuous exercise: predicting affective responses using EEG asymmetry, *Biol. Psychol.* 75 (2007) 194–200.
- [62] M. Conson, D. Errico, E. Mazzarella, M. Giordano, D. Grossi, L. Trojano, Transcranial electrical stimulation over dorsolateral prefrontal cortex modulates processing

- [63] M. Mondino, F. Thiffault, S. Fecteau, Does non-invasive brain stimulation applied over the dorsolateral prefrontal cortex non-specifically influence mood and emotional processing in healthy individuals?, *Front. Cell. Neurosci.* 9 (2015) 399.
- [64] V. Bond Jr, A. Osby, T. Obisesan, K. Kumar, S. Pemminati, V.R. Gorantla, Y.A. Volkova, R.M. Millis, Effects of aerobic exercise on frontal EEG asymmetry, coherence and mood: a pilot study, *J. Clin. Diagnostic. Res.* 12 (2018) CC05–CC10.
- [65] E.K. Broelz, P. Enck, A.M. Niess, P. Schneeweiss, S. Wolf, K. Weimer, The neurobiology of placebo effects in sports: EEG frontal alpha asymmetry increases in response to a placebo ergogenic aid, *Sci. Rep.* (2019) <https://doi.org/10.1038/s41598-019-38828-9>.
- [66] M. Woo, S. Kim, J. Kim, S.J. Petruzzello, B.D. Hatfield, The influence of exercise intensity on frontal electroencephalographic asymmetry and self-reported affect, *Res. Q. Exerc. Sport* 81 (2010) 349–359.
- [67] M. Woo, S. Kim, J. Kim, S.J. Petruzzello, B.D. Hatfield, Examining the exercise-affect dose-response relationship: does duration influence frontal EEG asymmetry?, *Int. J. Psychophysiol.* 72 (2009) 166–172.
- [68] S. Schneider, C.D. Askew, J. Diehl, A. Mierau, J. Kleinert, T. Abel, H. Carnahan, H.K. Struder, EEG activity and mood in health orientated runners after different exercise intensities, *Physiol. Behav.* 96 (2009) 709–716.
- [69] H. Moraes, A. Deslandes, H. Silveira, P. Ribeiro, M. Cagy, R. Piedade, F. Pompeu, J. Laks, The effect of acute effort on EEG in healthy young and elderly subjects, *Eur. J. Appl. Physiol.* 111 (2011) 67–75.
- [70] S. Ohmatsu, H. Nakano, T. Tominaga, Y. Terakawa, T. Murata, S. Morioka, Activation of the serotonergic system by pedaling exercise changes anterior cingulate cortex activity and improves negative emotion, *Behav. Brain Res.* 270 (2014) 112–117.
- [71] J.B. Crabbe, J.C. Smith, R.K. Dishman, Emotional & electroencephalographic responses during affective picture viewing after exercise, *Physiol. Behav.* 90 (2007) 394–404.
- [72] S. Schneider, C.D. Askew, T. Abel, A. Mierau, H.K. Strueder, Brain and exercise: a first approach using electrotopography, *Med. Sci. Sports Exerc.* 42 (2010) 600–607.
- [73] T. Vogt, S. Schneider, V. Bruemmer, H.K. Strueder, Frontal EEG asymmetry: the effects of sustained walking in the elderly, *Neurosci. Lett.* 485 (2010) 134–137.
- [74] R.A. Hicks, P.A. Hall, W.R. Staines, W.E. McLroy, Frontal alpha asymmetry and aerobic exercise: are changes due to cardiovascular demand or bilateral rhythmic movement?, *Biol. Psychol.* 132 (2018) 9–16.
- [75] G. Tempest, G. Parfitt, Self-reported tolerance influences prefrontal cortex hemodynamics and affective responses, *Cogn. Affect. Behav. Neurosci.* 16 (2016) 63–71.
- [76] G.D. Tempest, R.G. Eston, G. Parfitt, Prefrontal cortex haemodynamics and affective responses during exercise: a multi-channel near infrared spectroscopy study, *PLoS ONE* 9 (2014), e95924.
- [77] G. Tempest, G. Parfitt, Imagery use and affective responses during exercise: an examination of cerebral hemodynamics using near-infrared spectroscopy, *J. Sport Exerc. Psychol.* 35 (2013) 503–513.
- [78] T. Meyer, C.W.E.M. Quaedflieg, K. Weijland, K. Schruers, H. Merckelbach, T. Smeets, Frontal EEG asymmetry during symptom provocation predicts subjective responses to intrusions in survivors with and without PTSD, *Psychophysiology.* (2018) <https://doi.org/10.1111/psyp.12779>.
- [79] E. Gordon, D.M. Palmer, N. Cooper, EEG alpha asymmetry in schizophrenia, depression, PTSD, panic disorder, ADHD and conduct disorder, *Clin. EEG Neurosci.* 41 (2010) 178–183.
- [80] H. Wahbeh, B.S. Oken, Peak high-frequency HRV and peak alpha frequency higher in PTSD, *Appl. Psychophysiol. Biofeedback* 38 (2013) 57–69.