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Sugar Rush or Sugar Crash? A Meta-Analysis of Carbohydrate Effects on Mood

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Abstract

The effect of carbohydrate (CHO) consumption on mood is much debated, with researchers reporting both mood improvements and decrements following CHO ingestion. As global consumption of sugar-sweetened products has sharply increased in recent years, examining the validity of claims of an association between CHOs and mood is of high importance. We conducted a systematic review and meta-analysis to evaluate the relationship between acute CHO ingestion and mood. We examined the time-course of CHO-mood interactions and considered the role of moderator variables potentially affecting the CHO-mood relationship. Analysis of 176 effect sizes (31 studies, 1259 participants) revealed no positive effect of CHOs on any aspect of mood at any time-point following their consumption. However, CHO administration was associated with higher levels of fatigue and less alertness compared with placebo within the first hour post-ingestion. These findings challenge the idea that CHOs can improve mood, and might be used to increase the public's awareness that the 'sugar rush' is a myth, inform health policies to decrease sugar consumption, and promote healthier alternatives.

Keywords: meta-analysis, carbohydrates, sugar, mood, acute

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1. Introduction

Over the last decades, consumption of sugar-sweetened soft drinks has increased dramatically. In the US alone, consumption of such drinks has increased by 135% from the 1970s to the early 2000s (Nielsen and Popkin, 2004). Similar findings have been reported in countries all over the world, including Germany, Spain and the United Kingdom (for a review, see Malik et al., 2010), with annual sales of energy drinks alone surpassing four billion EUR across Europe (490 million liters consumed; see Zucconi et al., 2013). Currently, soft drinks are a major contributor to daily energy intake, accounting for more than 7% of energy consumption and representing the largest single source of calories in people's diets (Block, 2004). The widespread appeal of sugar-sweetened and energy drinks is associated with the marketing of these products as a way of combating fatigue, increasing energy and promoting a euphoric feeling. As the main ingredient in such drinks is sugar, research has focused on understanding how sugar-sweetened drinks, and carbohydrates (CHOs) in general, might promote cognitive facilitation and emotional wellbeing (for reviews, see Benton, 2002; Benton and Donohoe, 1999; Gibson and Green, 2002; Smith et al., 2011; Sünram-Lea and Owen, 2017).

Several influential studies have suggested that CHO ingestion might have mood-boosting properties. It has been observed that, compared with healthy populations, individuals suffering from affective conditions (e.g., seasonal affective disorder and depression) tend to 'self-medicate' by increasing their daily consumption of CHO-rich meals and beverages (Wurtman and Wurtman, 2018, 1995, 1989). On the other hand, recent studies have suggested that, on top of the metabolic health concerns associated with high levels of sugar consumption (e.g., Malik et al., 2006; Vartanian et al., 2007), high long-term

consumption of CHOs has adverse effects on psychological wellbeing, even leading to higher rates of depression (Knüppel et al., 2017; Westover and Marangell, 2002). This ongoing debate has renewed the interest of researchers, media and the public in the relationship between sugar and mental wellbeing. As the trend for high consumption of sugary drinks shows no signs of abating, understanding the appeal of these products and the mental and physical health consequences of their consumption is of high priority.

Interestingly, despite researchers not having reached a consensus regarding the exact effects of sugar on mood, it seems that the public strongly believes in the idea that sugar improves mood (‘Why is sugar so addictive?’, 2013) and increases activity levels (especially in children; Furnham, 2018). Although it is difficult to pinpoint the exact pathways that have made the ‘sugar rush’ notion so widely influential in popular culture, the origins of this notion can be traced back to studies suggesting that consumption of CHOs may increase hyperactivity in children (Flora and Polenick, 2013; Rojas and Chan, 2005; Wolraich et al., 1995, 1994; Yu et al., 2016). Whereas it is generally accepted that children’s ‘sugar rush’ is a myth (for a meta-analysis, see Wolraich et al., 1995), there is less agreement about the effect of sugar on mood. The purpose of the present review is to address the assertion that consumption of CHOs can affect mood. We begin by reviewing the theory behind the supposed neurobiological substrates of CHO-mood interactions, as well as the criticism that this framework has received over the years. We then present the current state of the field by discussing studies supporting and rejecting the claim that CHOs can improve mood, as well as how methodological differences among these studies could help explain these conflicting findings. Finally, we present a meta-analysis where we investigate the relationship between acute CHO administration and mood, while also considering the effect of moderator variables.

1.1. Carbohydrates and Mood: Mechanisms and Evidence

The rationale behind the assertions that CHOs improve mood has a strong physiological basis. Consumption of pure CHOs is associated with an increase in neurotransmitter synthesis and uptake in the brain. Specifically, the availability of neurotransmitters such as glutamate, acetylcholine and gamma-aminobutyric acid appears to be modulated by exogenous glucose supply (for a review, see Messier, 2004). For example, in mice, even small doses of glucose have been found to increase acetylcholine synthesis and release in the hippocampus (Durkin et al., 1992) and facilitate cognitive performance (Kopf et al., 2001). Additionally, the effects of glucose on gamma-aminobutyric acid release are also accompanied by alterations in dopaminergic activity (Levin, 2000), further strengthening the assertion that glucose is an important precursor to neurotransmitter synthesis (also see Yeghiayan et al., 2004). The serotoninergic system in particular is susceptible to CHO manipulations, and it has been suggested that the supposed effects on mood are related to fluctuations in serotonin availability following CHO ingestion (for reviews, see Gibson, 2007; Markus, 2008; Spring et al., 1987). It is well-established that serotonin and mood are intrinsically related, with the serotoninergic system being implicated in the etiology of a number of mood disorders, including depression, mania, seasonal affective disorders, anxiety and aggression (for reviews, see Chaouloff et al., 1999; Jenkins et al., 2016; Marek et al., 2003; Sandyk, 1992). Studies manipulating levels of tryptophan (a precursor to serotonin) using tryptophan depletion protocols have found low mood, increased irritability and aggression in human volunteers. However, restoring tryptophan levels has been shown to have antidepressant qualities and can reduce levels of aggression in human volunteers (for reviews, see Jenkins et al., 2016; Young and Leyton, 2002).

It has been observed that both CHO administration and insulin injections in rats are followed by a marked increase in tryptophan (large neutral amino acid; LNAA) in the plasma as well as higher levels of serotonin and tryptophan concentrations in the brain (Fernstrom

and Wurtman, 1972, 1971). Similar findings have been reported in humans, with CHO consumption leading to higher tryptophan availability in the periphery (Fernstrom, 1990; Markus, 2007; Markus et al., 1999, 1998; Rosenthal et al., 1989), accompanied by increased levels of brain tryptophan and a surge in serotonin synthesis (Carpenter et al., 1998; Markus, 2008; Nishizawa et al., 1997; Williams et al., 1999). Whereas protein consumption has been found to decrease tryptophan availability (Fernstrom et al., 2013), ingestion of pure CHOs leads to a higher tryptophan:LNAA ratio, despite CHOs being devoid of tryptophan (Fernstrom and Wurtman, 1971; Markus, 2007). This is because insulin secretion following a meal high in CHOs results in all LNAAs except for tryptophan to be taken up by tissue (e.g., muscle) and, consequently, tryptophan levels remain high compared to other LNAAs (Cangiano et al., 1983; for a review, see Bellisle et al., 1998). As tryptophan competes with other amino acids to cross the blood brain barrier, such higher tryptophan:LNAA ratio increases tryptophan influx in the brain, resulting in higher brain tryptophan concentrations and increased serotonin synthesis (for reviews, see Gibson, 2007; Markus, 2008; Spring et al., 1987; Wurtman and Wurtman, 2018).

As such, the supposed effects of CHO on mood are posited to be related to the increase in serotoninergic activity following CHO ingestion. It should be noted that this serotonin surge (or, at the very least, the increase in tryptophan availability in the brain) is observed only when CHOs are consumed alone and not when ingested in combination with other macronutrients. Specifically, CHO meals and beverages containing as little as 5% protein do not increase tryptophan concentrations (Yokogoshi and Wurtman, 1986; for a review, see Benton and Donohoe, 1999). Some studies have failed to observe increases in tryptophan and serotonin availability following CHO ingestion (Teff et al., 1989), suggesting that the CHO-tryptophan relationship could be mediated by other factors, including CHO dose or the presence of protein in the stomach from a previous meal, which can attenuate the

effect. Although the real-life applicability of the CHO-serotonin-mood relationship has been challenged because meals typically contain enough protein to suppress a CHO-related increase in tryptophan (for reviews, see Benton, 2002; Benton and Donohoe, 1999; Benton and Nabb, 2003; Spring et al., 1987), the majority of commercially available soft drinks do not contain any macronutrients other than CHOs. Considering the global increase in the consumption of CHO-rich soft drinks, investigating the extent to which sugar affects mood is an important step in understanding and managing the appeal of these products.

Over the years, evidence has been accumulating in support of the premise that CHOs can improve mood. For instance, Benton and Owens (1993) found that an increase in blood glucose levels after the consumption of 50 g of CHOs is associated with decreased levels of tension (also see Smit et al., 2004). CHO administration has also been related to increased ratings of activation and arousal (Backhouse et al., 2007), higher alertness following a 2-hour fast (Owen et al., 2012), higher levels of subjective positive affect (Backhouse et al., 2005; Peacock et al., 2012), lower levels of confusion (Lieberman et al., 2002) and tension (Lieberman et al., 2002; Markus, 2007), higher levels of clear-headedness (Smit et al., 2004), and less fatigue (Markus, 2007; Reay et al., 2006). Furthermore, CHO ingestion has been shown to be related to increased calmness (Spring et al., 1982), particularly following a long period of fasting (i.e., overnight fast; Owen et al., 2012).

The literature on CHO effects on cognition suggests that CHOs can improve cognitive functioning, particularly under circumstances where participants are asked to perform cognitively demanding rather than easy tasks (Mantantzis et al., 2017; Scholey et al., 2009; Sünram-Lea et al., 2002). In a similar manner, studies have found the protective effects of CHOs on mood to be more robust when participants perform demanding physical and cognitive tasks. In fact, whereas participants in control groups experience higher levels of tiredness after performing a cognitively demanding task, consumption of CHOs seems to

protect subjective ratings of energy against a potential drop-off after high cognitive exertion (Benton and Owens, 1993; Owens et al., 1997). Additionally, exogenous energy supply in the form of CHOs has been shown to increase vigor and reduce fatigue under conditions of increased physical stress (Ali et al., 2017; Lieberman et al., 2002; Markus, 2007; Welsh et al., 2002) and cognitive demands (Owens et al., 1997; Smit et al., 2004). Therefore, it has been hypothesized that, similar to cognition, mood improvement following CHO administration is stronger when participants have to perform demanding cognitive or physical tasks (for a review, see Benton, 2002).

Furthermore, consumption of CHO-rich foods (i.e., meals with a high CHO-to-other-macronutrients ratio) has been found to have a protective effect against increases in subjective ratings of depression and performance-related declines in vigor, specifically in individuals prone to stress (Markus et al., 1999, 1998). Meals high in CHOs can also decrease levels of fatigue compared with meals high in protein (Lloyd et al., 1996). Additionally, whereas consumption of low-CHO diets over long periods increases depression, tension, anger and fatigue (Deijen et al., 1989), CHO-rich diets can lead to lower hypothalamic-anterior pituitary-adrenocortical axis stress response (Anderson et al., 1987; Blass, 1987; Drewnowski et al., 1992), suggesting that CHOs might have a protective effect against stress and depression (Dallman et al., 2003; Wurtman and Wurtman, 1995, 1989). Similarly, it has been found that self-reported levels of daily CHO intake are negatively associated with depression ratings (de Castro, 1987; for a review, see Soh et al., 2009). Researchers have hypothesized that the relationship between CHO-rich meals, serotonin and mood is so potent that CHO meals are consumed as ‘comfort foods’ by individuals suffering from mood or affective disorders in an effort to improve their mood (for a review, see Wurtman and Wurtman, 2018).

Despite the intuitive appeal of the serotoninergic hypothesis and the literature reporting CHO effects on several mood aspects, there are also studies investigating CHO-mood interactions that have reported conflicting findings. Over the last three decades, an increasing number of empirical reports have suggested that ingestion of CHOs does not lead to any pronounced increases in subjective mood and overall affect, but can even have detrimental effects on mood (Adan and Serra-Grabulosa, 2010; Brody and Wolitzky, 1983; Duckworth et al., 2013; Giles et al., 2012; Harte and Kanarek, 2004; Howard and Marczinski, 2010; Jones et al., 2012; Jones and Sünram-Lea, 2008; Meikle et al., 2004; Miller et al., 2013, 2014; O'Neal et al., 2013; Owen et al., 2013; Qin et al., 2017; Reid and Hammersley, 1998, 1995; Riby et al., 2004; Scholey et al., 2014, 2009; Scholey and Fowles, 2002; Scholey and Kennedy, 2004; Seo et al., 2014; Stollery and Christian, 2013; Sünram-Lea et al., 2011; Ullrich et al., 2015; van der Zwaluw et al., 2014; Zacchia et al., 1991). Researchers have acknowledged the complicated nature of the results and have challenged the reliability of CHO effects on mood (Benton, 2002; Boyle et al., 2018; van de Rest et al., 2017). Whereas CHO effects on cognition are strong and well-documented (Messier, 2004; Riby, 2004; Smith et al., 2011), the effects of CHO administration on mood are not as dependable, a finding that could be attributed to a number of factors including the diverse methodologies employed by researchers to assess CHO-mood interactions.

1.2. Methodological Considerations

1.2.1. Time-course of CHO Effects

It is evident from the literature that vast methodological differences exist across studies. One of the main factors influencing the reliability of the CHO-mood relationship might be related to the time-course of CHO effects. The serotoninergic mechanism that is supposed to underlie CHO-mood interactions can provide us with a plausible timeframe

based on which we can infer the magnitude of the effects of CHOs at different time-points. Considering that a reliable increase in tryptophan availability and serotonin synthesis occurs beyond the first hour post-CHO consumption (Fernstrom and Wurtman, 1971; Markus, 2008; Wurtman et al., 2003), it can be expected that CHO effects would be particularly pronounced around the 1- to 2-hour mark. In line with this theory, some studies have reported beneficial effects of CHO on mood 60 minutes post-ingestion (e.g., Ali et al., 2017; Lieberman et al., 2002; Markus, 2007; Reay et al., 2006; Smit et al., 2004). However, mood-boosting effects of CHOs have been observed as early as 15, 30 and 45 minutes after consumption (Benton and Owens, 1993; Owen et al., 2012; Smit et al., 2004), suggesting that there might be additional, faster-acting mechanisms mediating the CHO-mood relationship other than the influence on the serotoninergic system. In fact, CHO ingestion has been associated with a cascade of physiological effects, including alterations in neural and peripheral metabolism, and increased synthesis of neurotransmitters other than serotonin (Korol and Gold, 1998; Riby, 2004), all of which could be plausibly related to mood enhancement.

1.2.2. CHO Type

Additionally, studies assessing the effects of CHO on cognition and mood have administered a wide variety of CHO types and doses, and have implemented different fasting intervals prior to CHO consumption to investigate the optimal conditions under which CHO effects are most prominent. Although the majority of studies in the area routinely administer glucose (Mantantzis et al., 2018, 2017; Scholey and Fowles, 2002; Sünram-Lea et al., 2001), a number of other reports have opted for sucrose (van der Zwaluw et al., 2014; Zacchia et al., 1991), fructose (Miller et al., 2013), galactose (Duckworth et al., 2013), and isomaltulose (Dye et al., 2010; Young and Benton, 2014). This methodological choice could influence the magnitude of CHO-mood interactions as considerable differences exist in the way that each CHO is metabolized and converted into energy (see Bantle et al., 1983; Rippe and

Angelopoulos, 2013). As different CHO types are metabolized in distinct ways and within different timeframes, this should be taken into consideration when examining the potentially time-sensitive relationship between CHO and mood outcomes.

1.2.3. CHO Dose

In a similar way, CHO dose is an important factor whose influence has been systematically examined in previous studies (e.g., Sünram-Lea et al., 2011). Although recent work has suggested that CHO dose should be determined based on individual differences in glucoregulatory capacity and the cognitive/behavioral domain being examined (e.g., Owen et al., 2010), results from a meta-analysis suggest that 25 g of CHO is sufficient to observe facilitation effects on cognitive outcomes in both young and older adults (Riby, 2004). Studies on glucose, in particular, have shown that its effects on cognitive indices follow an inverted U-shape dose-response curve, suggesting that below and above a certain threshold glucose either has no effect on behavior or can even lead to cognitive decrements (for a review, see Sünram-Lea and Owen, 2017). Although our knowledge of the moderating effects of CHO dose is limited to cognitive performance indices, it is possible that CHO effects on mood follow similar patterns. However, the selection of CHO doses in published reports is not always justified or adequately explained by researchers.

1.2.4. Fasting Interval

In addition, studies have used varied fasting intervals prior to CHO administration, ranging from no fasting (Reid and Hammersley, 1998) to 2-hour (Giles et al., 2012) and overnight fasting restrictions imposed (e.g., 12 hours; Owen et al., 2013; Scholey et al., 2014). However, the moderating effect of fasting duration on CHO effects is not yet clear. In fact, one of the few studies investigating how fasting intervals affect CHO effects on mood has found calmness and alertness to be differentially affected by CHOs under different

fasting restrictions (Owen et al., 2012). Specifically, whereas the CHO group's alertness ratings increased following a 2-hour fast, higher levels of calmness were found only for the CHO groups that were required to fast overnight. Although a 2-hour fast is usually the minimum requirement to observe CHO facilitation effects (for a meta-analysis, see Riby, 2004), a wide variety of fasting regimes is employed across studies measuring CHO effects on behavior and the moderating influence of such methodological decisions is not as yet clear.

1.2.5. Tasks Preceding Mood Assessment

The relationship between CHO administration and mood is further complicated by the use of different testing conditions and tasks preceding the evaluation of mood. A range of experimental paradigms have been employed to assess the effects of CHO on behavioral outcomes, with effects on mood assessed after cognitively (Scholey et al., 2014, 2009) and physically demanding tasks (Ali et al., 2017; Backhouse et al., 2007; O'Neal et al., 2013), stress-inducing procedures (Markus, 2007), and periods of inactivity during which participants are not asked to perform any tasks (Reid and Hammersley, 1998, 1995). This poses a problem for the investigation of mood effects as activity prior to mood assessment is likely to affect mood ratings. Furthermore, as the facilitation effects of CHOs are suggested to be more reliable in the cognitive domain (for a review, see Boyle et al., 2018), some studies assess mood as a variable of secondary importance, without appropriate justification as to why such measures are included and no a priori hypotheses with regards to expected mood outcomes. More importantly, the focus on cognitive outcomes means that sample sizes are selected based on the number of participants needed to observe CHO-related cognitive facilitation. It has been proposed that the effects of CHOs on mood are relatively small and observable only with large sample sizes (Benton and Owens, 1993; for a review, see Benton, 2002). As a result, studies assessing CHO effects on mood as a secondary outcome may not

be adequately powered to identify such effects, potentially increasing the number of false negatives in published reports. A more systematic review of the literature and meta-analytic attempts are urgently needed.

1.3. The Current Study

Overall, the research area of CHO-mood interactions is surprisingly complicated, owing to methodological differences identified across empirical reports. Our goal was to investigate the relationship between CHO consumption and mood by using synthesis methods to group and analyze results from all available studies assessing CHO-mood interactions. We set out to examine whether the assertion that CHOs improve mood is robust, or whether this perception is guided by a small number of influential studies reporting a positive relationship. There have been several reviews on the CHO-mood relationship (Benton, 2002; Benton and Donohoe, 1999; Benton and Nabb, 2003; Boyle et al., 2018; Gibson and Green, 2002; van de Rest et al., 2017) but this is the first attempt at using synthesis methods to deconstruct exactly how CHOs affect mood. The purpose of the present meta-analysis is to analyze all available data to see how different mood constructs are affected by CHOs and how methodological decisions can help us understand the discrepant nature of published findings. It should be noted that the diverse methodological choices of published studies complicate the use of synthesis methods and the grouping of effect sizes from different studies. This does not only relate to the type of CHOs used, the doses, or the timeframe of mood assessment following CHO ingestion, but also to the use of different mood assessment tools to investigate similar mood constructs (for a review of mood tests routinely used in nutritional research, see Polak et al., 2015).

Therefore, we will provide an overview of the methodologies used in studies assessing CHO-mood interactions and aim to systematically disentangle the effect of

moderating variables on the CHO-mood relationship. First, if the effects of CHOs are related to fluctuations in serotonin synthesis and availability, we expected that strong CHO-mood interactions would appear beyond the first hour post-CHO ingestion. As the serotoninergic system has been shown to affect depression, anxiety and aggression, we expected the effects to be more reliable for mood constructs related to these specific aspects of emotionality. However, if CHO effects on mood are related to other mechanisms, it is possible that stronger CHO-mood interactions would be obtained at earlier time-points and for different mood constructs (e.g., fatigue and alertness). Investigating the time-sensitivity of CHO-mood interactions will provide us with a better understanding of the time-course of CHO effects: do people experience a temporary 'sugar high' following CHO ingestion that fades within the first hour post-CHO consumption (e.g., Benton and Owens, 1993), or are the beneficial effects of CHOs more likely to appear hours after ingestion because of the influence of the serotoninergic system?

Second, if the suggestion that most individual studies are potentially underpowered to detect statistically significant CHO-related mood fluctuations is valid, we would not expect to see strong effects of CHO on mood in the reports included in this meta-analysis. However, the synthesis methods should allow us to examine how even small trends identified in individual studies can potentially be combined to provide a clear picture of how CHOs affect different aspects of mood. Finally, it was expected that the methodological differences between studies would lead to highly variable results as evidenced by high levels of heterogeneity in the meta-analyses.

2. Method

2.1. Search Strategy

A comprehensive literature search was conducted to identify empirical articles and original research addressing the CHO-mood relationship in the following databases: MedLine/PubMed, Scopus and Web of Science. Titles, abstracts and keywords were scanned in each database using the following search terms: *(carbohydrate* OR glucose OR dextrose OR galactose OR lactose OR sucrose OR fructose OR macronutrient* OR sugar* OR sweet*) AND (supplement* OR consume* OR admin* OR ingest* OR drink* OR eat*) AND (mood OR emotion* OR affect* OR alert* OR excite* OR elat* OR happy* OR happi* OR content* OR seren* OR relaxe* OR calm* OR fatigue* OR letharg* OR depress* OR sad* OR upset* OR stress* OR nervous* OR tense OR tension OR tired*) AND (random*) AND (placebo*).* The final literature search was completed on August 21st, 2017.

The asterisk symbol at the end of search terms is a wildcard character that permits the inclusion of all variations of words starting with the same letters. For example, the search term *content** would additionally retrieve words such as *contented, contentedness* and *contentment.* The literature search was further limited to peer-reviewed articles published in scholarly journals and written in English, and studies conducted with human participants, when the databases offered such options. A forward and backward literature search was also performed on all eligible articles and reviews to identify relevant studies not found during the initial literature search. The search terms relating to mood constructs were chosen based on the affect circumplex model outlined in Barrett and Russell (1999). A flowchart describing the literature search process is presented in Figure 1.

2.2. Inclusion and Exclusion Criteria

For a study to be included, the following criteria had to be met: 1) must be a randomized controlled trial, 2) must include a sample of healthy adults over the age of 18, 3) must investigate the acute effects of oral administration of CHO, 4) must measure mood

constructs using explicit mood assessment tests, and 5) CHO treatments must be compared with a no-CHO condition. As the goal of the present meta-analysis was to investigate the acute effects of CHO administration on mood, studies examining the effects of long-term (longitudinal) CHO supplementation or empirical reports investigating the relationship between participant-reported CHO consumption and mood were excluded. Although we were interested in how administration of pure CHOs affects mood, we also considered studies administering CHOs combined with other constituents in cases where a comparison was made with an appropriate placebo that would allow us to make inferences regarding the effects of CHOs. For example, we included studies that compared CHO-and-caffeine treatments with a placebo condition containing the same dose of caffeine but no CHOs (e.g., Wesnes et al., 2017). Additionally, studies not providing enough information to calculate effect sizes had to be excluded from this meta-analysis if the authors had no access to the data or did not respond to requests. Characteristics of included studies can be found in Table 1.

2.3. Mood Constructs

Reviewing all eligible articles, we found that most studies investigating CHO-mood interactions employed either the Bond-Lader Visual Analogue Scales (BL-VAS; Bond and Lader, 1974) or the Profile of Mood States (POMS; McNair et al., 1971). Both mood assessment scales are widely used in nutritional research and have been found to be particularly sensitive to nutritional manipulations (for a review, see Polak et al., 2015).

Bond-Lader VAS. The BL-VAS consists of 16 adjective antonym pairs (e.g., ‘alert’ – ‘drowsy’). Each of the two mood states (forming an antonym pair) is placed at the end of a 100-mm horizontal line. Participants are asked to indicate where their current subjective experience falls along the continuum. Ratings are calculated as distance from the negative antonym in millimeters. Ratings on the individual item scales are combined to calculate

composite mood scores to assess levels of ‘alertness’ (nine items), ‘calmness’ (five items), and ‘contentedness’ (two items).

POMS. The Profile of Mood States consists of 65 single items. Participants give their ratings on 5-point unipolar scales ranging from 0 (not at all) to 4 (extremely) to indicate their current subjective levels of affective experience for each item. Single-item ratings are grouped to create composite scores to evaluate both negative (i.e., ‘tension/anxiety’, ‘depression/dejection’, ‘anger/hostility’, ‘fatigue/inertia’, ‘confusion/bewilderment’) and positive (i.e., ‘vigor/activity’) aspects of mood.

As most eligible studies employed one of these two mood assessment tools, we used the composite mood constructs derived from the BL-VAS and the POMS as the outcome measures in the present meta-analysis. With many studies reporting discrepant findings regarding the effects of CHOs on different mood items, it is possible that different facets of positive and negative mood would be differentially affected by CHOs and the supposed serotonin surge that accompanies their consumption. The inclusion of mood constructs from both scales allowed for a more comprehensive investigation of CHO-mood interactions across a number of positive and negative mood aspects. Data from empirical reports using other mood assessment tools to investigate CHO-mood interactions were grouped with the mood scales from the BL-VAS and POMS if an overlap between constructs was identified. For example, in the meta-analysis of the POMS ‘tension/anxiety’ construct, studies measuring anxiety and stress using tools other than the POMS were additionally included (e.g., Stress and Arousal Questionnaire, and Positive and Negative Affect Schedule, Riby et al., 2004, and Ullrich et al., 2015, respectively). If a study provided multiple measures of similar mood constructs, only the mood measure closest to the mood construct of interest was included in the meta-analysis. The grouping of constructs from different scales was based on

research reporting associations between constructs and discussions among the authors. See Table 2 for a summary of the outcomes and mood constructs that were combined.

2.4. Effect Size Calculation

Effect sizes were calculated as standardized mean differences (SMDs) between CHO and inactive placebo. The mean difference between the two groups was divided by their pooled *SD* and further corrected for sample size-related biases using the Hedges and Olkin (1985) correction. To account for pre-treatment baseline differences in mood, effect sizes were calculated after adjusting for baseline mood levels or by using the change from baseline scores, if either was available in the included articles. If neither format was available, the authors were contacted and asked to provide this information. When the correlation between pre- and post-treatment mood ratings was not available, a default correlation coefficient of .5 was used to address the dependency of measurements arising from the within-subjects nature of the pre- and post-treatment scores (see Borenstein et al., 2009; Duke et al., 2013; Wampold et al., 1997). To assess the appropriateness of this default coefficient, we calculated the correlation between pre- and post-treatment mood ratings in one of the databases available (Jones et al., 2012), which produced an average coefficient of approximately .58 across all mood constructs.

Although calculating effect sizes using change from baseline scores provides a more powerful analysis as it removes individual variability in subjective mood ratings, in some cases only final values were available and, therefore, effect sizes were calculated based on that information alone. In the meta-analyses, effect sizes calculated using change from baseline scores and final values are presented together as there is no statistical reason to present them separately (Deeks et al., 2008). An effort was made to calculate effect sizes using statistics appropriate for each study design (i.e., *t*-tests for within-subjects designs, *M*s

and *SD*s for between-subjects designs) but this was not always possible because of insufficient information in the published articles. Authors were contacted to provide the appropriate statistics but in cases of no replies or data being unavailable effect sizes were calculated based on the information reported in the published article.

If multiple mood assessment ratings were taken over the course of a single study visit (multiple assessment time-points), composite scores were created to address the dependency of measures (i.e., same participants providing measures on multiple outcomes). We used previously published recommendations on calculating the mean effect size and variance of the composite scores (Borenstein et al., 2009). The mean effect size of the composite score ($\bar{Y}$) was calculated as the average of the effect sizes of the outcomes and the variance of the composite score as:

$$V_{\bar{Y}} = \left(\frac{1}{m}\right)^2 \left(\sum_{j=1}^{m} V_i + \sum_{j \neq k} (r_{jk} \sqrt{V_j} \sqrt{V_k})\right)$$

where *m* = number of outcomes combined, *V* = variance and *r* = correlation coefficient for each combination of outcomes. When the correlation between outcomes was unknown, a default conservative coefficient of .5 was assumed. The actual correlation coefficient was used for studies whose authors provided us with data. For studies giving participants multiple CHO treatments at intervals throughout a single experimental session (e.g., 10 g every 10 minutes), we calculated effect sizes only for the final mood measurement, after all individual doses had been consumed. If a study provided participants with different types of CHO, only one CHO type was included in the meta-analysis. This was done for within-participants studies to address the dependency of measures, but not for between-participants designs where different participants were assigned to different treatments.

2.5. Analytic Strategy

Analyses were performed in R using the 'metafor' package (Viechtbauer, 2010). Meta-analyses were conducted using random-effects models with Hedges *g*-corrected SMDs as the measure of effect size and 95% CIs. Mixed-effects models were used to evaluate the effect of moderators only when heterogeneity (Cochran's *Q* and I^2 statistics) was significantly high. Both random- and mixed-effects models were estimated using restricted maximum likelihood estimation. The Knapp and Hartung (2003) adjustment was employed to account for the uncertainty in the estimation of residual heterogeneity. As the presence of outliers can significantly affect the strength and validity of meta-analyses (Viechtbauer and Cheung, 2010), studies were excluded from the pooled effect size estimate if their standardized residual *z* value was above the ± 2.5 threshold (see Camfield et al., 2014). We only present random- and fixed-effects models for meta-analyses of mood items where at least three studies were available. As one of the main goals of this meta-analysis was to examine the time-course of CHO effects on mood, we assessed how the CHO-mood relationship changes over time by running separate meta-analyses for three time windows covering immediate (0-30 minutes), short-term (31-60 minutes) and long-term (61+ minutes) effects of CHO consumption. If a study involved taking multiple mood measurements within the same time window (e.g., mood measured at 10 and 20 minutes post-CHO consumption), composite scores were created using the method described earlier. Moderator variables included CHO dose (higher or lower than 25 g), CHO type (e.g., glucose, sucrose, fructose etc.), fasting interval (e.g., less or more than 2 hours before CHO administration), and the nature of the activity preceding mood assessment (e.g., physical task, cognitive task, rest). Two raters coded the moderator variables independently (all Cohen's κs > .889). Coding differences were discussed among the raters and the authors until an agreement was reached.

To assess the impact of publication bias in our analysis (the 'file drawer problem'; Rosenthal, 1979), we created funnel graphs by plotting effect sizes against the standard error

of the estimates and visually inspected them for signs of asymmetry that could be interpreted as an indication of publication bias. It should be noted that funnel plot asymmetry is not always a sign of publication bias and it can also be associated with other factors, including chance (for a review, see Egger et al., 1997). Begg's adjusted rank correlation (Begg and Mazumdar, 1994) and Egger's test (Egger et al., 1997) were employed to provide a quantitative index of publication bias. Similar to the visual examination of funnel plots, these statistical tests are not infallible as they are low-powered and are more appropriate when (a) heterogeneity is low ($I^2 < 50\%$), (b) there are at least 10 studies included in each meta-analysis, with at least one study reporting statistically significant findings, and (c) the ratio of extreme variance across studies is greater than four (see Ioannidis and Trikalinos, 2007).

3. Results

Of the 5757 studies identified in the literature search stage, 51 met the inclusion criteria and were considered relevant to the present meta-analysis. However, 20 studies had to be excluded at the final stage because of data/information not being available or authors not replying to data requests, leaving 31 studies ($N = 1259$) available for the meta-analysis (see Figure 1). Separate meta-analyses are presented for each of the three time windows, as specified in the method section.

Separate forest plots are presented for each mood construct. In the plots, we present the effect sizes and 95% CIs for all available studies assessing mood at each of the three time windows, as well as the pooled effect size estimate, calculated separately for each time window. Results in the forest plots are presented such that 'favors CHO' or 'favors Pla' means that participants in the CHO or placebo group experienced more positive outcomes compared to the other group with regards to a particular mood construct. For example, if for the 'fatigue' construct the pooled effect size estimate favors placebo, it should be interpreted

as participants in the placebo group experiencing less fatigue (i.e., more positive outcomes) compared with the CHO group. Heterogeneity and publication bias statistics are presented in Table 3 and Table 4, respectively. It should also be noted that most of the random-effects models presented do not meet the criteria to ensure the robustness of the asymmetry tests (Ioannidis and Trikalinos, 2007) and, therefore, results on publication bias should be interpreted with caution.

3.1. Bond-Lader VAS

Alertness. Effect sizes and 95% CIs for the three time windows are presented in Figure 2. In all three time windows (0-30, 31-60 and 61+ minutes), alertness was lower for CHO than placebo. This difference was significant for the second time window (12 studies; p = .020), though not for the first (eight studies; p = .194). For the 61+ time window, eight studies were found to be relevant. However, Sihvola et al. (2013) had to be excluded as it was found to be an outlier (z = 2.55) leaving seven studies in the analysis. No effects of CHO on alertness were found for this time window (p = .343). Heterogeneity for all time windows was low and, therefore, no moderator analyses were conducted. No evidence of publication bias was found across the three alertness time windows.

Calmness (Figure 3). Seven studies were included in the meta-analysis of the 0-30 minutes time window. No evidence of increased calmness following CHO consumption was found (p = .391). For the 31-60 minutes meta-analysis, nine studies were included. CHOs were shown to increase calmness compared with placebo but the effect was not significant (p = .201). For the 61+ minutes time window, four studies were included. The meta-analysis showed no evidence of increased calmness with either CHOs or placebo (p = .813). Heterogeneity was not significantly high and no evidence of publication bias was found.

Contentedness (Figure 4). In all three time windows, contentedness was higher for CHO than placebo. However, the difference was not significant in any of the time windows (0-30 minutes: seven studies, $p = .313$; 31-60 minutes: eight studies, $p = .600$; 61+ minutes: five studies, $p = .199$). Although Begg's test did not show evidence of publication bias for any time windows, Egger's test suggested significant publication bias for the 61+ time window. It should be noted that only five studies were included in the meta-analysis of the 61+ time window and so the results of Egger's test could be influenced by the low number of studies.

3.2. POMS

Anger (Figure 5). For the 0-30 time window, three studies were included in the analysis. No evidence of fluctuations in anger was identified within the first 30 minutes post-CHO ingestion ($p = .580$). As there were only two studies available for the 31-60 time window, a meta-analysis was not conducted and the results will not be discussed. For the 61+ time window, eight studies were included in the model. Anger levels did not change as a result of ingestion of CHOs or placebo during this time window ($p = .837$). No evidence of high heterogeneity or publication bias was found.

Confusion (Figure 6). No effects of CHOs were found in any of the three time windows. Confusion was lower in placebo compared with CHOs during the first two time windows, but the difference was not significant (0-30 minutes: three studies, $p = .096$; 31-60 minutes: four studies, $p = .435$). For the 61+ time window, seven studies were found to be relevant. Similar to the previous time windows, confusion did not seem to be affected by CHO administration compared with placebo ($p = .927$). Heterogeneity was low and no evidence of bias was obtained.

Depression (Figure 7). Depression levels did not appear to be affected by CHO or placebo consumption at any time-point. Depression was slightly lower with CHOs during the first and third time window, but the difference was not significant (0-30 minutes: three studies, $p = .694$; 61+ minutes: nine studies, $p = .742$). A pattern of lower levels of depression for placebo compared with CHO was obtained during the 31-60 time window, but the observed difference failed to reach significance (three studies, $p = .158$). Heterogeneity was not statistically significant and no evidence of bias was identified.

Fatigue (Figure 8). For the 0-30 time window, 10 studies were initially available. However, the Young and Benton (2013) study had to be excluded as it was found to be an outlier (z value = 5.07), leaving nine studies in the analysis. The meta-analysis showed that participants receiving CHO reported significantly higher levels of fatigue compared with placebo across these studies ($p = .011$). For the 31-60 time window, nine studies were identified. Although a similar pattern to the 0-30 time window was observed (i.e., higher fatigue in the CHO group), the difference between CHO and placebo was not significant ($p = .201$). For the 61+ time window, 13 studies were available. In contrast to the previous time windows, a pattern of slightly lower fatigue with CHO treatments was found an hour after CHO ingestion, but this was not significant ($p = .404$). Whereas no heterogeneity was found for the first two time window, studies included in the 61+ time window showed significantly high levels of heterogeneity and moderator analyses were conducted to assess the influence of methodological discrepancies among these studies. Separate analyses were run for each moderator variable described in the method section. CHO dose, CHO type and fasting interval did not influence fatigue self-reports (all Fs < 1.67, all ps > .236). However, a trend was found for the type of task preceding mood assessment ($F(3, 9) = 3.14$, $p = .080$). Although this trend was not significant, further analysis revealed that CHO groups reported significantly less fatigue compared with placebo only after performing physically demanding

tasks (b = 0.474, 95% CIs [0.04, 0.91], p = .037), and not after a cognitive task (p = .578) or a period of inactivity/rest (p = .517). A trend was also found for CHO groups to show lower levels of fatigue following a stress-inducing task (p = .078), but only one study using a stressful task was included in the meta-analysis of fatigue at 61+ minutes.

Tension (Figure 9). For the 0-30 time window, seven studies were identified. Results showed that CHO treatments led to lower tension compared with placebo, but the effect was not significant (p = .089). For the 31-60 time window, six studies were included in the analysis. Tension levels did not seem to be sensitive to CHO or placebo treatments during this time window (p = .794). For the final time window (61+ minutes), nine studies were identified as relevant. Similar to the previous time window, tension levels did not seem to fluctuate as a result of CHO or placebo administration (p = .605). No evidence of high heterogeneity or publication bias was found.

Vigor (Figure 10). Both for the 0-30 and 31-60 time windows, there were only two studies available for each meta-analysis and, therefore, the results of the random-effects models are not presented. For the 61+ time window, nine studies were found and included in the meta-analysis. Consumption of CHOs did not have an appreciable effect on levels of vigor (p = .260). Heterogeneity was not significantly high and no evidence of publication bias was found.

3.3. Overall Mood

We combined all available effect sizes from each individual study to create a composite score representing the effect of CHO on overall mood (see Figure 11). For example, for studies using the BL-VAS mood assessment tool, we grouped the effect sizes from the ‘alertness’, ‘calmness’ and ‘contentedness’ mood constructs to calculate an overall mood score. As in previous analyses, a positive effect size is construed as CHOs having a

beneficial effect on mood, while a negative effect size should be interpreted as evidence that CHOs worsen overall mood compared with placebo. The calculation of effect sizes and variances was done based on the procedure described earlier. If data on overall mood were available, we used that score instead of combining individual effect sizes from different mood items (e.g., Adan and Serra-Grabulosa, 2010; Miller et al., 2014).

For the 0-30 time window, 17 studies were initially available. However, the Young and Benton (2013) study had to be excluded as it was found to be an outlier (*z* value = 4.42), leaving 16 studies in the analysis. No effect of CHO was found on overall mood ($p = .667$). For the 31-60 time window, 16 studies were included in the analysis. CHOs did not affect overall mood during this time window ($p = .219$). For the 61+ time window, 19 studies were included in the model. Although a marginal trend of better overall mood was found after CHO consumption, this effect failed to reach significance ($p = .051$). No evidence of high heterogeneity was found for this construct. Although no publication bias was found for the 0-30 and 31-60 time windows, Begg's and Egger's tests revealed trends of publication bias for the 61+ time window ($p = .058$ and .089, respectively).

4. Discussion

Although several reviews have been published to investigate the complex relationship between CHO and mood, no research has attempted to systematically deconstruct CHO-mood interactions and assess the influence of moderator variables. In light of studies presenting conflicting findings regarding the effects of CHOs on different aspects of mood at different time-points, the aim of this study was to assess the immediate (0-30 minutes), short-term (31-60 minutes), and long-term (61+ minutes) effects of acute CHO consumption on a number of positive and negative mood constructs. The methodological differences among eligible studies were also reviewed and used in the analysis as moderator variables when

heterogeneity was high. Overall, our meta-analysis provides no evidence of mood facilitation following CHO ingestion at any time-point following consumption. In fact, CHO consumption was related to decreased alertness and higher levels of fatigue within the first hour post-ingestion. Despite the methodological differences between studies, the effect sizes were relatively homogeneous across all mood constructs and time windows. High heterogeneity was found for fatigue at 61+ minutes, which was partially explained by the nature of the task preceding mood assessment.

In line with the serotoninergic hypothesis of CHO effects on mood, we expected a positive effect of CHO ingestion on mood ratings beyond the first hour post-CHO consumption. Interestingly, no facilitation effects of CHO were found compared with placebo during the time window where a CHO-related serotoninergic surge is posited to occur (i.e., 61+ minutes). This was the case for all mood constructs, including depression, tension and anger, on which one would expect the supposed CHO-related increase in serotoninergic activity to have the strongest effect (Benton and Owens, 1993; Chaouloff et al., 1999; Markus, 2008; Wurtman and Wurtman, 2018). Interestingly, a marginal trend of CHO-related facilitation was found for the overall mood construct calculated for each individual study. It should be noted that some of the effect sizes included in this construct originated from studies that selectively reported only CHO-mood associations that were statistically significant (e.g., Lieberman et al., 2002; Sihvola et al., 2013). To illustrate, although Lieberman et al. (2002) used the full version of the POMS (six subscales), they only provided data on Confusion/Bewilderment and Vigor/Activity, while no data were available for the remaining four subscales of the POMS. Therefore, we had to calculate the overall mood score using only the statistically significant associations reported in the published report, which are not necessarily indicative of the actual overall mood effect found in the study. The trend of high publication bias found in the analysis of this construct further supports the assertion that the

results of the overall mood meta-analysis could be affected by selective reporting. We urge readers to take this into consideration when attempting to interpret the marginal positive effect of CHO administration on overall mood.

Considering that no beneficial effects of CHOs on mood were identified, our meta-analysis calls into question the existence of a mood-boosting mechanism (serotonin-based or otherwise) related to CHO consumption. In fact, the validity of the CHO-serotonin mechanism and, by extension, the CHO-mood relationship has received criticism and has been difficult to replicate in experimental settings (for reviews, see Benton, 2002; Boyle et al., 2018; van de Rest et al., 2017). Interestingly, even in studies that have found CHO to influence serotoninergic activity, it is suggested that this effect is observable only under specific conditions (e.g., stress; Markus, 2007), and for clinical populations rather than healthy individuals (for a review, see Wurtman and Wurtman, 2018), calling into question the validity of the CHO-mood relationship for the general population.

The present meta-analysis also examined the effect of CHOs on mood at earlier time windows (0-30 and 31-60 minutes post-CHO consumption). With a number of studies uncovering mood effects as early as 15 minutes post-ingestion (e.g., Benton and Owens, 1993), we wanted to assess whether the effects of mood are stronger during earlier time-points. This would allow us to investigate the time-course of CHO effects and the influence of other mechanisms through which CHOs could potentially affect mood (e.g., mood improvement because of a rapid increase in energy availability). However, similar to the results obtained from the 61+ time window, CHOs did not seem to lead to improvements in any mood constructs (including overall mood) during the earlier time windows. In fact, the only significant effects identified in our meta-analysis speak against CHO-related facilitation and suggest that, compared with placebo, CHO leads to mood decrements. Specifically, CHO consumption was related to greater fatigue and less alertness, 0-30 minutes and 31-60

minutes post-ingestion, respectively. It should be noted that the decreased alertness observed in the meta-analysis could be related to the sedative effect of tryptophan/serotonin, but the timeframe in which this effect was observed (i.e., 31-60 minutes) does not corroborate this theory. Although small trends of decreased tension as well as increased calmness and contentedness were observed within the first hour following CHO administration, they failed to reach significance. In line with recent reviews (Boyle et al., 2018; van de Rest et al., 2017) CHOs do not seem to improve any aspect of mood at any time-point after their consumption, challenging the notion that CHOs could offer a temporary 'high' (for a meta-analysis dispelling the 'sugar rush' myth in children, see Wolraich et al., 1995).

Previous studies have shown that, similar to CHO-cognition interaction, the effects of CHO ingestion on mood are stronger when participants have to perform difficult cognitive or physical tasks (e.g., Backhouse et al., 2007; Lieberman et al., 2002; Markus, 2007; Owens et al., 1997; Reay et al., 2006). Additionally, methodological choices such as dose, type of CHO and fasting intervals have been shown to affect the magnitude of the CHO facilitation effect and could, theoretically, affect the CHO-mood relationship as well (Riby, 2004; Smith et al., 2011; Sünram-Lea and Owen, 2017). Therefore, one of the predictions of this meta-analysis was that methodological differences across studies would lead to significant heterogeneity in the results. Although our goal was to evaluate the influence of such moderators on CHO-mood interactions, our results turned out to be not heterogeneous enough to justify conducting moderator analyses for most mood constructs and time windows. Significant heterogeneity was found for fatigue at 61+ minutes, but our pre-specified moderators failed to account for the heterogeneity obtained. The only moderator variable that approached significance was the nature of the task preceding mood evaluation. Specifically, we found that CHOs can alleviate fatigue only under physically demanding conditions (e.g., strenuous physical exercise), but not under high cognitive load or periods of inactivity. These findings

are in line with studies that have found positive effects of CHOs on mood after exercise (e.g., Ali et al., 2017; Backhouse et al., 2005), but do not support previous work showing that CHOs can improve mood under high cognitive demands (Benton and Owens, 1993; Owens et al., 1997; Smit et al., 2004). Overall, the homogeneity of the results points to little variance across studies with regards to the effects of CHO on mood, suggesting that the influence of methodological variables is not as pronounced as previously thought (for a review, see Benton, 2002).

4.1. Limitations and Recommendations

Although our results are consistent with the interpretation that CHOs do not affect mood, limitations of the present meta-analysis should be considered when attempting to generalize our findings to broader contexts. First, we examined the effects of CHOs on mood in samples of healthy adults. The literature on CHO-mood interactions has also investigated the effect of CHOs in clinical populations (e.g., depression and obesity; Wurtman and Wurtman, 2018, 1995, 1989), participants with high sensitivity to stress (Markus et al., 1998), and women during the luteal phase of the menstrual cycle (for a review, see Benton, 2002). Interestingly, researchers have also coined the term ‘carbohydrate-craving’ depression to describe a clinical population showing excessive CHO intake as a means of ‘self-medicating’ to improve mood (Wurtman and Wurtman, 1995). It is possible that mood in clinical or subclinical populations exhibiting emotional disturbances could be more sensitive to CHO manipulations. Further meta-analytic attempts focusing on examining the effects of CHO on mood in these populations could shed light on this topic, and, potentially, the neurobiological or behavioral mechanisms behind CHO-mood interactions.

Second, our meta-analysis included studies that provided participants with CHO in isolation to other macronutrients or nutraceutical constituents. In recent years, because of the

sharp increase in the consumption of energy drinks, research has also focused on the synergistic effects of CHO with other psychoactive constituents such as caffeine. These studies have found the effects of CHO-caffeine combinations to go beyond the facilitation observed when either of these constituents is administered alone (e.g., Kennedy and Scholey, 2004; Scholey et al., 2014, 2009; Scholey and Kennedy, 2004; Sünram-Lea et al., 2012). However, the effects of energy drink consumption on mood are not clear and more investigations and meta-analytic attempts are warranted. Furthermore, other studies have examined the effects of CHO combined with macronutrients such as protein and fiber (Benton et al., 2001; Lloyd et al., 1996; Qin et al., 2017; Sihvola et al., 2013) or by creating experimental diets controlling for the content of CHO compared with other constituents (Dye et al., 2000; Markus et al., 1998) to examine CHO-mood interactions. Although the purpose of our meta-analysis was to investigate how pure CHO administration can affect mood, it would be interesting to discover whether CHO interactions with other nutrients could more prominently affect mood and emotionality.

A factor that should also be considered when examining CHO-mood interactions is the role of individual differences in glucose regulation. Studies have shown that glucoregulatory capacity and changes in blood glucose levels following CHO ingestion are related to the strength of the glucose facilitation effect on behavior. For example, poorer glucose regulatory control has been associated with greater susceptibility to cognitive facilitation following CHO administration (Owen et al., 2013). In terms of mood, it has been reported that participants who experience high levels of blood glucose levels following CHO ingestion tend to report less tension compared with those who exhibit lower glucose concentrations (Benton and Owens, 1993). At the same time, reductions in glucose concentration in the periphery after strenuous cognitive performance have been associated with increased tiredness (Owens et al., 1997). In the present meta-analysis, we have not

examined the moderating role of glucoregulatory capacity or blood glucose levels in CHO-mood interactions. Because of the low number of studies that have formally assessed glucoregulatory control using an appropriate oral glucose tolerance test (the 'gold standard'; World Health Organization, 2006), it would be difficult to accurately examine the role of glucoregulation in this meta-analysis. Although using blood glucose levels as another potential moderator would have been an interesting addition, the levels of heterogeneity found across the analyses of all mood constructs and time windows were not sufficiently high to justify conducting further moderator analyses. Therefore, considering the homogeneous nature of our results, incorporating this factor in our meta-analysis would not have conferred any additional benefits with regards to the interpretation of the results.

Based on the evidence presented in this meta-analysis, recommendations can be made to improve both the quality of future work in the field and assist in further meta-analytic attempts. First, we recommend that open and reproducible science practices should be followed by all researchers in the field. This would lead to less selective reporting and greater transparency of the research process. In the present meta-analysis, 20 out of the 51 eligible studies had to be excluded at the final stage because of no responses from authors or data being unavailable, a fact that needs to be taken into account when assessing the results of the present meta-analysis (see the Appendix for a list of these studies). Data being freely available for other researchers to use would greatly facilitate research synthesis by increasing the number of studies included in such meta-analyses, which would provide more accurate estimation of the true nature of a studied effect.

With regards to the research area itself, several methodological issues should be considered when assessing CHO-mood interactions to facilitate the comparison of studies and the interpretation of their results when grouped. Methodological decisions regarding sample size should be justified and accompanied by appropriate power analysis to ensure that studies

are adequately powered to detect mood fluctuations following nutraceutical interventions. What is evident from the present meta-analysis is that studies investigating CHO-mood interactions test varied numbers of participants (see Table 1), not always accompanied by power analyses. Similarly, justifications should be provided when deciding on dosage, types of CHO, fasting intervals and even mood assessment tools to allow researchers to critique and assess the appropriateness of such decisions and measures. A common issue with the CHO-mood research area is related to the fact that mood is primarily assessed as an outcome of secondary importance compared to cognitive outcomes, which are thought to be more strongly affected by CHO manipulations (for a meta-analysis, see Riby, 2004). This also means that no a priori hypotheses are made regarding CHO effects on mood, and statistical results are rarely presented if CHOs do not have a statistically significant effect on mood. Providing more detailed descriptions and presenting all available results would facilitate future meta-analytic efforts and increase confidence in the field and its reporting standards. In fact, researchers investigating CHO- and nutrition-related changes in behavior have called for greater detail in the description of nutraceutical intervention protocols and the methodological justifications presented by researchers, to allow for more accurate comparisons across different studies (Gilsenan et al., 2009).

5. Conclusions

As the public consumes sugar-sweetened energy drinks to cope with fatigue and negative mood, our goal was to understand whether this pervasive perception holds under scrutiny. Overall, our meta-analysis does not provide support for the supposed CHO-mood relationship and casts doubt on how the neurobiological mechanisms implicated translate into observable mood outcomes. Interestingly, the only evidence uncovered in the present work points to a detrimental effect of CHO on mood constructs such as alertness and fatigue, suggesting that the idea of a positive CHO-mood relationship is unsubstantiated. In the last

couple of decades, consumption of sugar-sweetened soft drinks has seen a sharp increase, leading to a renewed interest by researchers and the public in understanding how CHOs affect physical and mental health. Our results can be used to increase the public's awareness of the effects of sugar consumption, and inform public health policies aimed at decreasing sugar consumption and promoting healthy alternatives.

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Declarations of interest

None

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Appendix

List of Studies Excluded at the Final Stage of the Meta-Analysis Because of Relevant Data or Information Not Being Available

Authors	Journal	Notes
Backhouse et al., 2005	*Medicine and Science in Sports and Exercise*	- *FS*: Main effect of treatment (across all time-points). Better mood with CHO than Pla
Backhouse et al., 2007	*Scandinavian Journal of Medicine and Science in Sports*	- *FAS:* Treatment × Time interaction. Higher activation for CHO compared with Pla at 75 and 90 minutes - *FS:* No effects
Benton and Owens, 1993 (**Experiment 1**)	*Journal of Psychosomatic Research*	- *Tired/Energetic:* Glucose led to lower levels of energy compared with placebo in females - *Relaxed/Tense:* Glucose led to lower tension compared with placebo when subjects were tested in the morning
Benton and Owens, 1993 (**Experiment 2**)	*Journal of Psychosomatic Research*	- *Tired/Energetic:* No effects - *Relaxed/Tense:* No effects
Benton and Owens, 1993 (**Experiment 3**)	*Journal of Psychosomatic Research*	- *Tired/Energetic:* No effects - *Relaxed/Tense:* No effects
Duckworth et al., 2013	*Appetite*	- *FAS:* No effects - *FS:* No effects
Harte and Kanarek, 2004	*Nutritional Neuroscience*	- *POMS:* No effects

Meikle et al., 2004	*Human Psychopharmacology: Clinical and Experimental*	- *Stress and Arousal Questionnaire:* No effects
Owens et al., 1997 (**Experiment 1**)	*Physiology & Behavior*	- *Tired/Energetic:* No effects - *Relaxed/Tense:* No effects
Owens et al., 1997 (**Experiment 2**)	*Physiology & Behavior*	- *Tired/Energetic:* No effects - *Relaxed/Tense:* No effects
Owens et al., 1997 (**Experiment 3**)	*Physiology & Behavior*	- *Tired/Energetic:* No effects - *Relaxed/Tense:* No effects
Peacock et al., 2012	*Appetite*	- *FS:* Treatment × Time interaction. Higher ratings in CHO compared with 'water' and 'no fluids' condition at 65, 75, 100, 110 and 145 minutes
Pivonka and Grunewald, 1990	*Journal of the American Dietetic Association*	- *SSS:* Participants reported higher sleepiness after CHO compared with Pla - *POMS:* No effects - *VAMS*: No effects
Qin et al., 2017	*Physiology & Behavior*	- *FS:* No effects
Scholey and Fowles, 2002	*Neurobiology of Learning and Memory*	- *POMS:* No effects
Scholey and Kennedy, 2004	*Psychopharmacology*	- *POMS:* No effects
Scholey et al., 2009	*Psychopharmacology*	- *VAS:* No effects
Seo et al., 2014	*Journal of the International Society of Sports Nutrition*	- *POMS-SF:* No effects
Smit et al., 2004 (**Experiment 2**)	*Nutritional Neuroscience*	- *VAS:* No effects
Smit et al., 2004 (**Experiment 3**)	*Nutritional Neuroscience*	- *Tense:* Treatment × Time interaction. Lower levels of

			tension with CHO compared with no-CHO energy drink at 73 minutes - *Jittery:* CHO led to lower scores compared with no-CHO energy drink at 50 minutes post-treatment

Note. FS = Feeling Scale; FAS = Felt Arousal Scale; POMS-SF = short form of the Profile of Mood States; SSS = Stanford Sleepiness Scale; VAS = Visual Analogue Scales; VAMS = Visual Analogue Mood Scales.

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Table 1

Characteristics of the Studies Included in the Meta-Analysis.

Study	*N* (F) [1]	Mean age [2]	Design	Fast	CHO type	CHO dose	CHO compared with	Mood assessment	Time windows (minutes)	Task preceding mood assessment	Notes
Adan and Serra-Grabulosa, 2010	36 (18)	21.1	Between, double-blind	Overnight	Glucose	75 g	Water	VAS	0-30, 31-60, 61+	Cognitive	*SD*s calculated from *SEM* as: $SEM \times \sqrt{n}$
Ali et al., 2017	9 (0)	32.7	Within, not blinded	Overnight	CHO [3]	7.5% CHO, 1.5 mL/kg every 12.5% of exercise completed	AS	FAS, FS, POMS	61+	Physical	Only final mood measurement considered because of multiple doses
Brody and Wolitzky, 1983	39 (-)	18.7	Between, participants blind to treatment conditions	Overnight	Sucrose	100 g	AS	NIMH	0-30, 61+	Rest	*SD*s were imputed based on note in the article that *SD*s amounted to 1/3 of the means
Giles et al., 2012	48 (31)	20.1	Between, double-blind	2 hours	Glucose	50 g	AS	POMS	31-60, 61+	Cognitive	
Giles et al., 2018	105 (74)	22.5	Between, double-blind	2 hours	CHO	38 g	AS	POMS	0-30, 61+	Cognitive	Combined effect sizes from told/not told groups

Green et al., 2001	26 (-)	18-40 range	Within, participants aware of treatment for 'told' conditions	Overnight	Glucose	50 g	AS	VAS	31-60	Cognitive	Combined effect sizes from told/not told groups
Howard and Marczinski, 2010	32 (18)	20.1	Between, participants blind to treatment conditions	2 hours	Glucose	29.3 g for a 78-kg ppt	No drink	MFRS	31-60	Cognitive	Glucose drink compared to a 'no drink' condition
Jones and Sünram-Lea, 2008	28 (-)	20.0	Between, participants blind to treatment conditions	2 hours	Glucose	25 g	AS	BL-VAS	0-30	Cognitive	Mood measurements in the morning and the afternoon. Effect sizes calculated for morning session only
Jones et al., 2012	18 (13)	19.0	Within, participants blind to treatment conditions	Overnight	Glucose	40 g	AS	BL-VAS	0-30, 31-60, 61+	Rest, Cognitive	
Lieberman et al., 2002	143 (0)	21	Between, double-blind	2 hours	Maltodextrin	CHO 6%: 2.1 g/kg (36 mL/kg) CHO 12%: 4.2 g/kg (36 mL/kg)	AS	POMS	61+	Physical	Effect sizes calculated for final treatment only (2-h after previous meal)
Markus, 2007	37 (29)	18-25 range	Within, double-blind	Overnight	CHO	40 g × 2	AS	POMS	61+	Rest, Stress	Effect sizes calculated for post-stress mood scores

											only. Mood during rest was assessed retrospectively, after the stressor was introduced.
Mets et al., 2011	24 (12)	21-35 range	Within, double-blind	No restrictions	CHO (glucose + sucrose)	26 g	No drink	KSS	31-60, 61+	Driving	Glucose drink compared to a 'no drink' condition
Miller et al., 2013	36 (25)	23.3	Between, double-blind	3 hours	Glucose, fructose	25 g	AS	Likert	0-30	Cognitive	
Miller et al., 2014	24 (16)	20.7 (for full sample, *n* = 48)	Between, double-blind	3 hours	Glucose	25 g	AS	Likert	0-30	Cognitive (computer game)	Effect size calculated for the 'inclusion' group. Only the 'overall mood' construct was available for analysis
O'Neal et al., 2013	36 (13)	23	Within, double-blind	At least 2 and no more than 4 hours	CHO	6% CHO (mean 847 mL): three aliquots at time 0, 20 & 40 mins	AS	POMS	61+	Physical	
Owen et al., 2012	30 (-)	20	Within, double-blind	2 hours, overnight	Glucose	25 g, 60 g	AS	BL-VAS	0-30, 31-60	Rest, Cognitive	Composite scores combining different fasting and

											dose conditions
Owen et al., 2013	24 (-)	20	Within, double-blind	Overnight	Glucose	25 g, 60 g	AS	BL-VAS	31-60	Cognitive	
Reay et al., 2006	27 (10)	21.9	Within, double-blind	Overnight	Glucose	25 g	AS	VAS	31-60, 61+	Cognitive	*SD*s calculated from *SEM* as: $SEM \times \sqrt{n}$. Composite scores combining multiple mood assessment measurements falling within the same time window
Reid and Hammersley, 1995	38 (-)	18-55 range	Between, participants blind to treatments	Overnight	Sucrose	40 g	AS	POMS	0-30, 31-60, 61+	Rest	
Reid and Hammersley, 1998	45 (45)	33.2	Between, not blinded	No restrictions	Sucrose	40 g	AS	POMS	0-30, 31-60	Rest	Effect sizes calculated only for normal weight participants (45 out of 90)
Riby et al., 2004	20 (-)	68.8	Within, no information provided	Overnight	Glucose	25 g	AS	Stress and Arousal Questionnaire	0-30, 31-60	Cognitive	
Scholey et al., 2014	114 (71)	34.8	Between, double-blind	Overnight	Glucose	25 g, 60 g	AS	BL-VAS, Stress and	0-30, 31-60	Rest, Cognitive	Mistakes were found in the *SD*s of the

								Fatigue, STAI			published article and imputed values were used instead.
Sihvola et al., 2013	10 (7)	26 (median), 22-40 range	Within, Investigators blind to treatments. Control drink had different appearance to CHO drink	Overnight	CHO	76 g	AS	KSS, m-POMS	61+		Effect sizes calculated only for KSS. No m-POMS data available
Stollery and Christian, 2013	30 (12)	20.7	Between, participants aware of treatment for 'told' conditions	Overnight	Glucose	50 g	AS	Stress and Arousal Questionnaire	0-30	Cognitive	Effect sizes calculated only for group that was told nothing regarding the constituents of drink consumed
Sünram-Lea et al., 2011	30 (24)	20	Within, double-blind	Overnight	Glucose	15 g, 25 g, 50 g, 60 g	AS	BL-VAS	31-60	Cognitive	Composite scores combining different doses
Ullrich et al., 2015 (**Experiment 1**)	17 (0)	28.5	Within, double-blind	2 hours	Glucose	25 g	AS	PANAS	61+	Cognitive	
van der Zwaluw et al., 2014	43 (27)	77.7	Within, participants blind to	Overnight	Glucose, Sucrose	Glucose: 50 g, Sucrose: 100g	AS	s-POMS	0-30, 61+	Rest, Cognitive	Effect sizes calculated only for glucose

			treatment conditions								
Welsh et al., 2002	10 (5)	24.3	Within, double-blind	Overnight	CHO	6% CHO, 5mL/kg at intervals (approximately 128 g of CHO)	AS	POMS	61+	Physical	Only final mood measurement considered because of multiple doses
Wesnes et al., 2017	24 (18)	22.5	Within, double-blind	Overnight (breakfast provided before testing)	CHO in energy drink	27 g	Energy drink without CHO	POMS, BL-VAS	61+	Cognitive	CHO + caffeine energy drink compared with caffeine-only drink (no CHO)
Young and Benton, 2013	112 (-)	21.8	Between, participants blind to treatment conditions	Overnight	Glucose	39 g	AS	POMS: Fatigue	0-30	Rest	Study not included in the meta-analysis as the only available effect size was an outlier
Zacchia et al., 1991 (**Experiment 1**)	44 (0)	22	Between, double-blind	Overnight	Sucrose	35 g, 100 g	AS	POMS, STAI, SSS	31-60, 61+	Cognitive	Effect sizes calculated only for the 'sober' condition. Composite scores for doses and multiple mood assessments within a single time window

Note. [1] Only the number of participants assigned to treatment groups of interest to the meta-analysis are presented (i.e., CHO and placebo/control). The '-' sign means that either no information on gender was present in the articles or that no information regarding the gender composition of the treatment groups of interest was available. [2] For studies not reporting the mean age of the sample, we present the age range provided in the published article. [3] CHO type was unspecified or a combination of different CHOs.

AS = Artificial Sweetener; BL-VAS: Bond-Lader Visual Analogue Scales; FS = Feeling Scale; FAS = Felt Arousal Scale; MFRS = Mental Fatigue Rating Scale; KSS = Karolinska Sleepiness Scale; STAI = Stress and Anxiety Inventory; PANAS = Positive and Negative Affect Schedule; m-POMS = modified version of the Profile of Mood States; s-POMS = short form of the Profile of Mood States; SSS = Stanford Sleepiness Scale; VAS = Visual Analogue Scales (not taken from Bond & Lader, 1974).

Table 2

Mood Constructs Assessed in the Meta-Analysis and Combinations of Mood Outcomes Derived from Different Mood Assessment Tests

Mood constructs assessed	Combined with
Bond-Lader VAS	
Alertness	Activation, arousal, drowsiness, sleepiness, stimulation
Calmness	Composed
Contentedness	Elation, happy, pleasure
Profile of Mood States	
Anger/Hostility	-
Confusion/Bewilderment	Clearheaded
Depression/Dejection	-
Fatigue/Inertia	Energetic, tired
Tension/Anxiety	Stress
Vigor/Activity	-

Table 3

Number of Studies Available and Heterogeneity Statistics for Each Random-Effects Model, Assessed Separately for Different Mood Constructs and Time Windows

Mood constructs	Time window											
	0-30 minutes				31-60 minutes				61+ minutes			
	k	*Q*	I^2	*p*	*k*	*Q*	I^2	*p*	*k*	*Q*	I^2	*p*
Bond-Lader VAS												
Alertness	8	4.73	0.00%	.693	12	8.09	0.00%	.705	7	4.31	0.00%	.635
Calmness	7	4.83	0.00%	.566	9	2.39	0.00%	.966	4	5.50	43.94%	.139
Contentedness	7	2.62	0.00%	.855	8	5.22	0.00%	.634	5	1.93	0.00%	.748
Profile of Mood States												
Anger/Hostility	3	1.58	0.00%	.454	2	-	-	-	8	3.66	0.00%	.820
Confusion/Bewilderment	3	0.20	0.00%	.903	4	1.83	0.00%	.609	7	7.39	29.76%	.286
Depression/Dejection	3	1.35	0.00%	.508	3	0.06	0.00%	.971	9	10.32	24.89%	.243
Fatigue/Inertia	9	2.08	0.00%	.979	9	4.60	0.00%	.799	13	31.25	61.87%	**.002**
Tension/Anxiety	7	1.29	0.00%	.972	6	3.70	0.00%	.593	9	6.40	0.00%	.603
Vigor/Activity	2	-	-	-	2	-	-	-	9	14.38	43.54%	.072
Overall Mood	16	5.85	0.00%	.982	16	5.98	0.00%	.980	19	27.89	34.12%	.064

Note. Random-effects models were not conducted for mood constructs that had fewer than three studies available. *P* values are presented in bold if heterogeneity is significant.

k = number of studies included in the model; *Q* = Cochran's test of heterogeneity; I^2 = measure of heterogeneity; *p* = significance of Cochran's *Q* statistic.

Table 4

Publication Bias Tests (P-Values) for Random-Effects Models, Presented Separately for Each Mood Construct and Time Window

Mood constructs	Time window					
	0-30 minutes		31-60 minutes		61+ minutes	
	Begg	*Egger*	*Begg*	*Egger*	*Begg*	*Egger*
Bond-Lader VAS						
Alertness	.720	.345	.737	.561	.562	.181
Calmness	.239	.087	.761	.967	.333	.149
Contentedness	.381	.122	.548	.671	.083	**.003**
Profile of Mood States						
Anger/Hostility	1.00	.413	-	-	.905	.997
Confusion/Bewilderment	.333	.585	.333	.654	.773	.684
Depression/Dejection	1.00	.541	1.00	.867	.477	.809
Fatigue/Inertia	.761	.951	.477	.688	1.00	.887
Tension/Anxiety	.239	.277	.469	.791	.359	.767
Vigor/Activity	-	-	-	-	.920	.957
Overall Mood	1.00	.793	.757	.726	.058	.089

Note. P values in bold indicate significant publication bias.

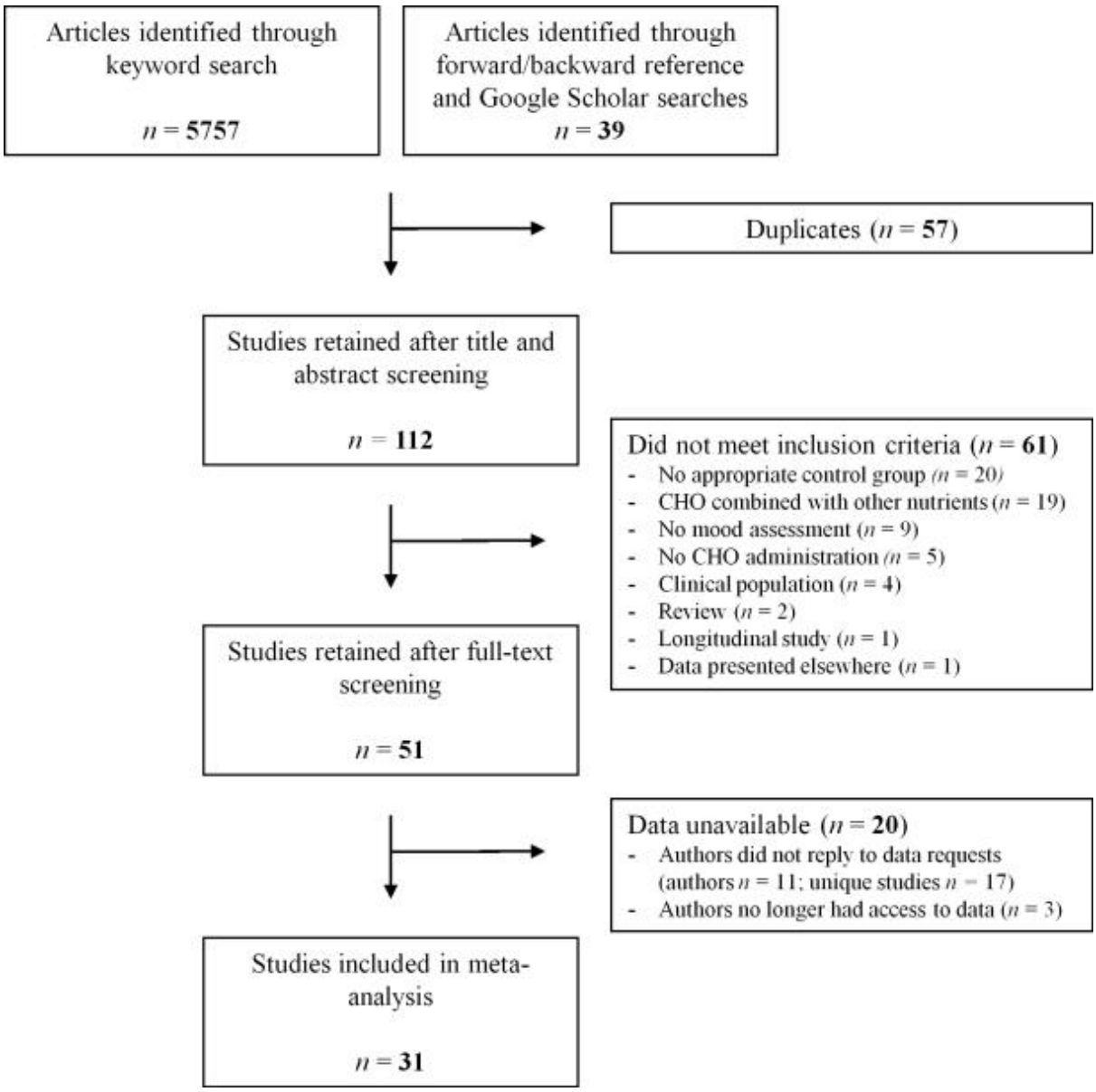

Figure 1. Literature search flowchart.

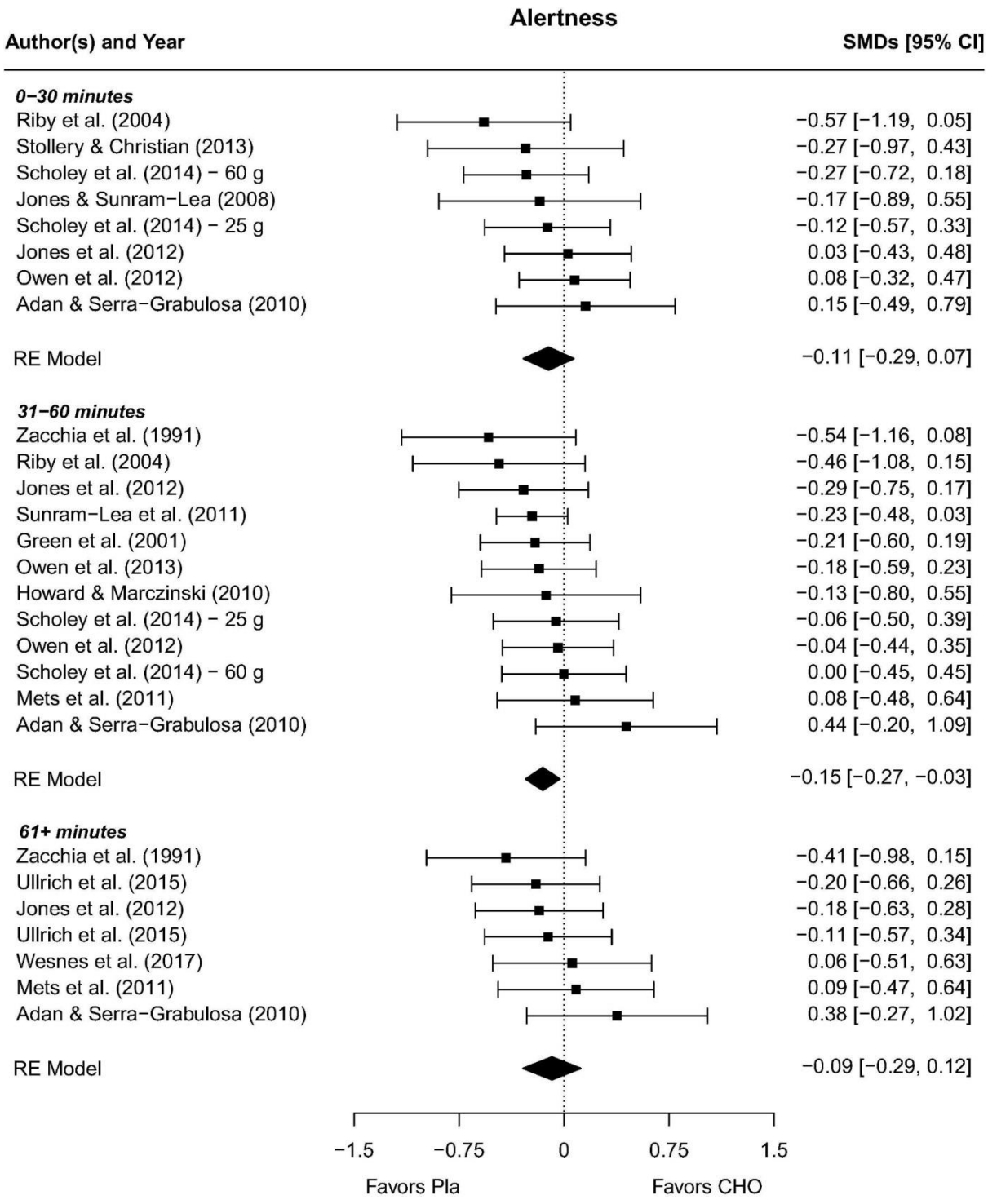

Figure 2. Forest plot of alertness effect sizes with 95% confidence intervals.

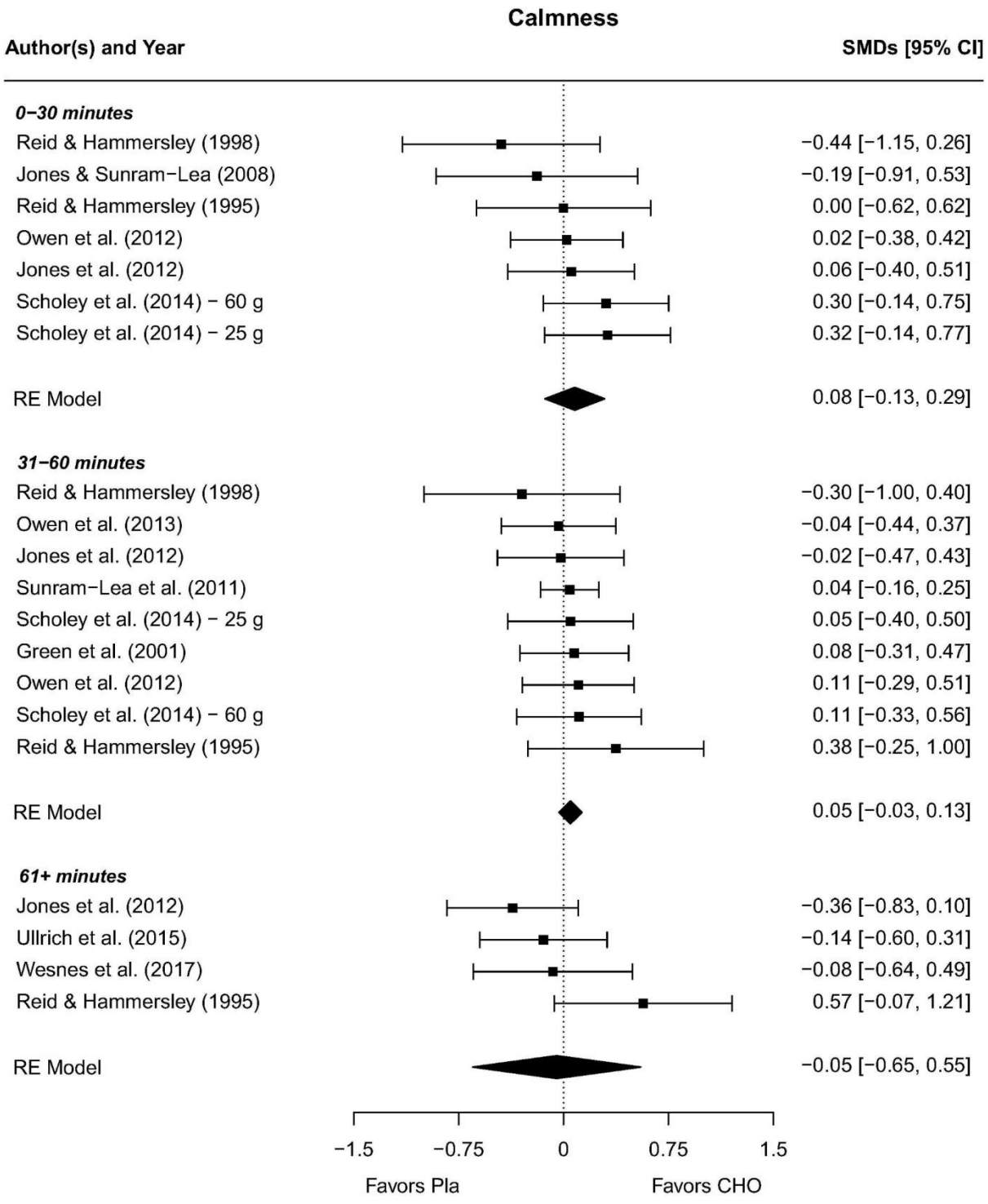

Figure 3. Forest plot of calmness effect sizes with 95% confidence intervals.

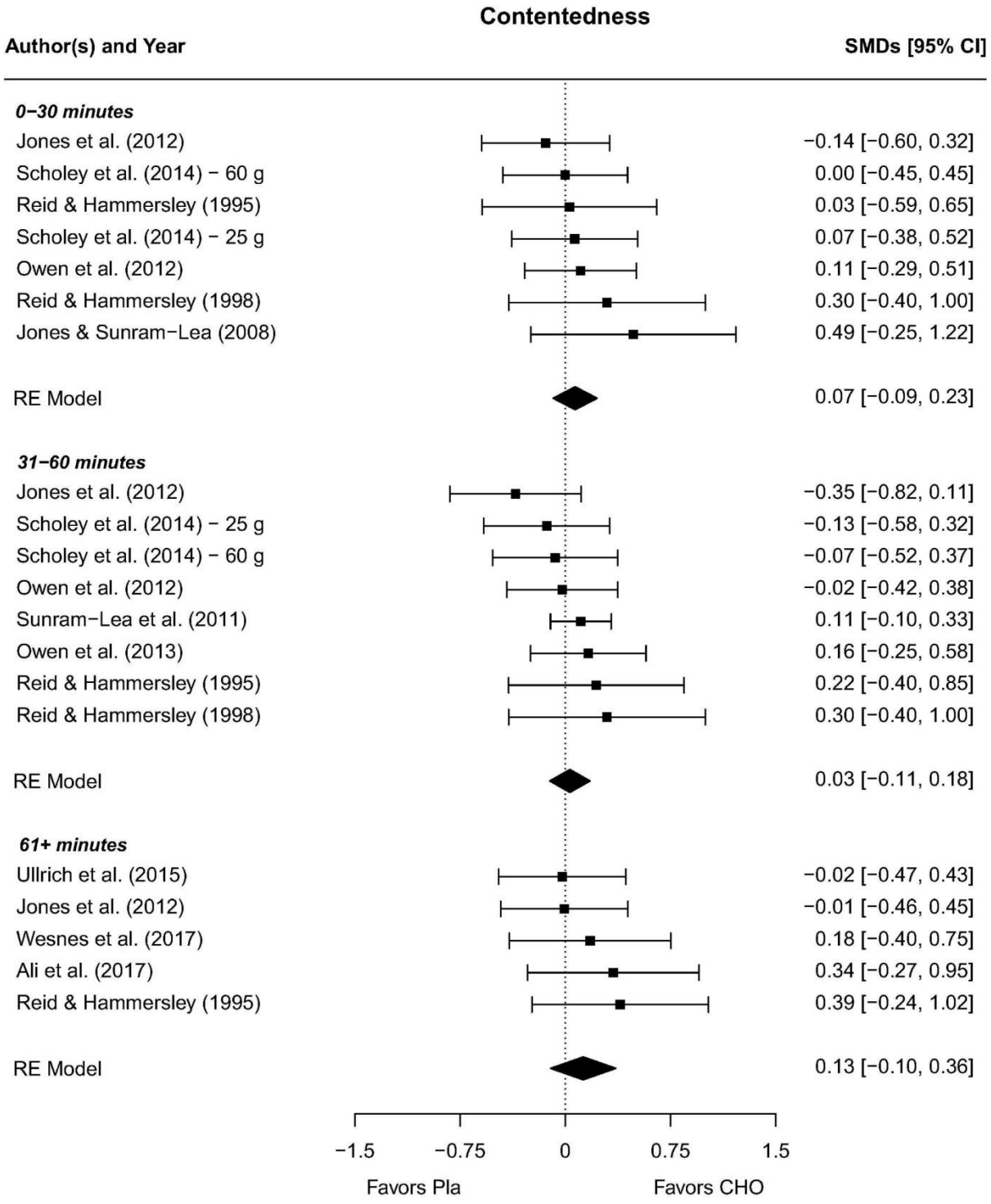

Figure 4. Forest plot of contentedness effect sizes with 95% confidence intervals.

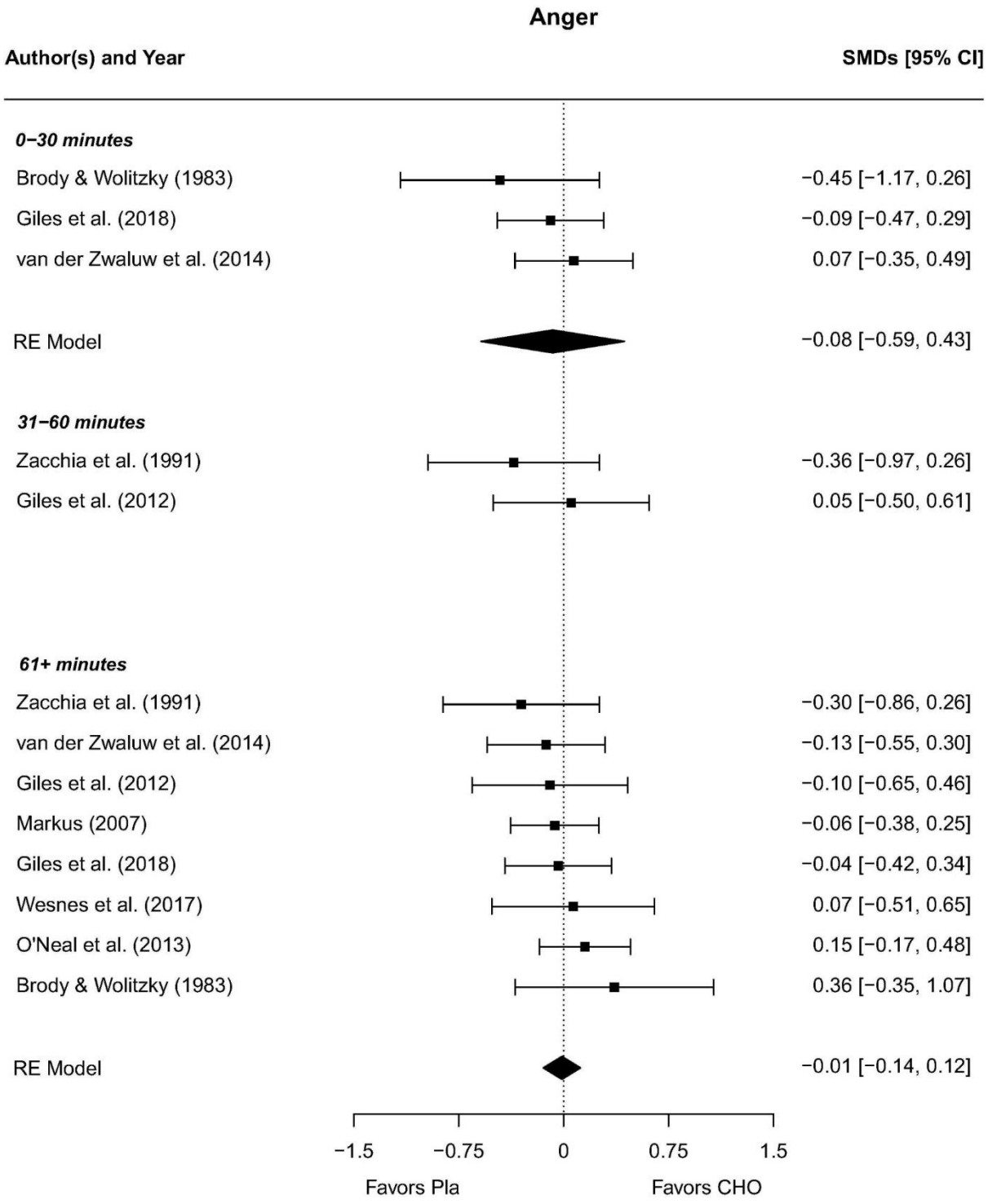

Figure 5. Forest plot of anger effect sizes with 95% confidence intervals. RE model is not presented for the 31-60 time window as only two studies were included.

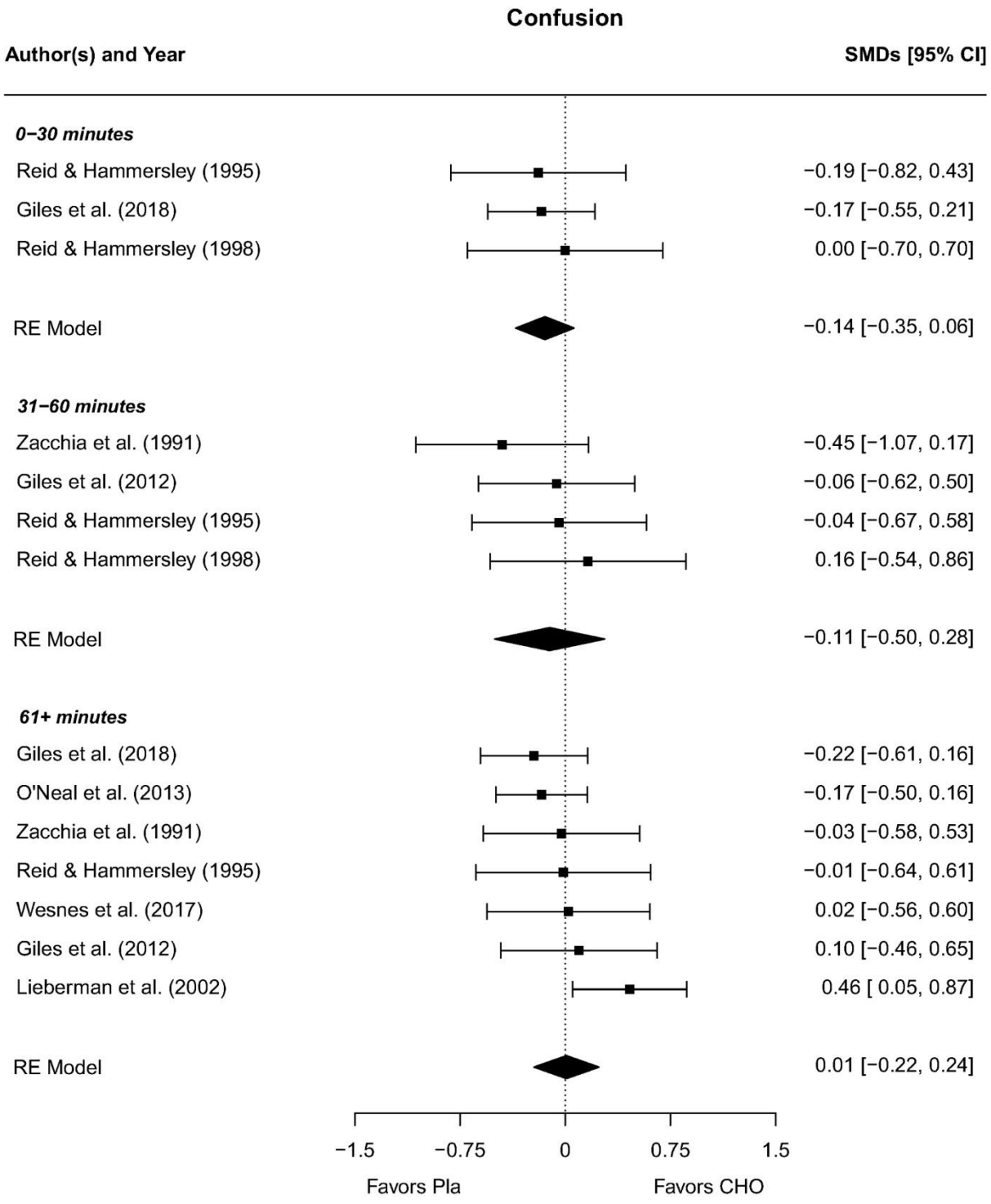

Figure 6. Forest plot of confusion effect sizes with 95% confidence intervals.

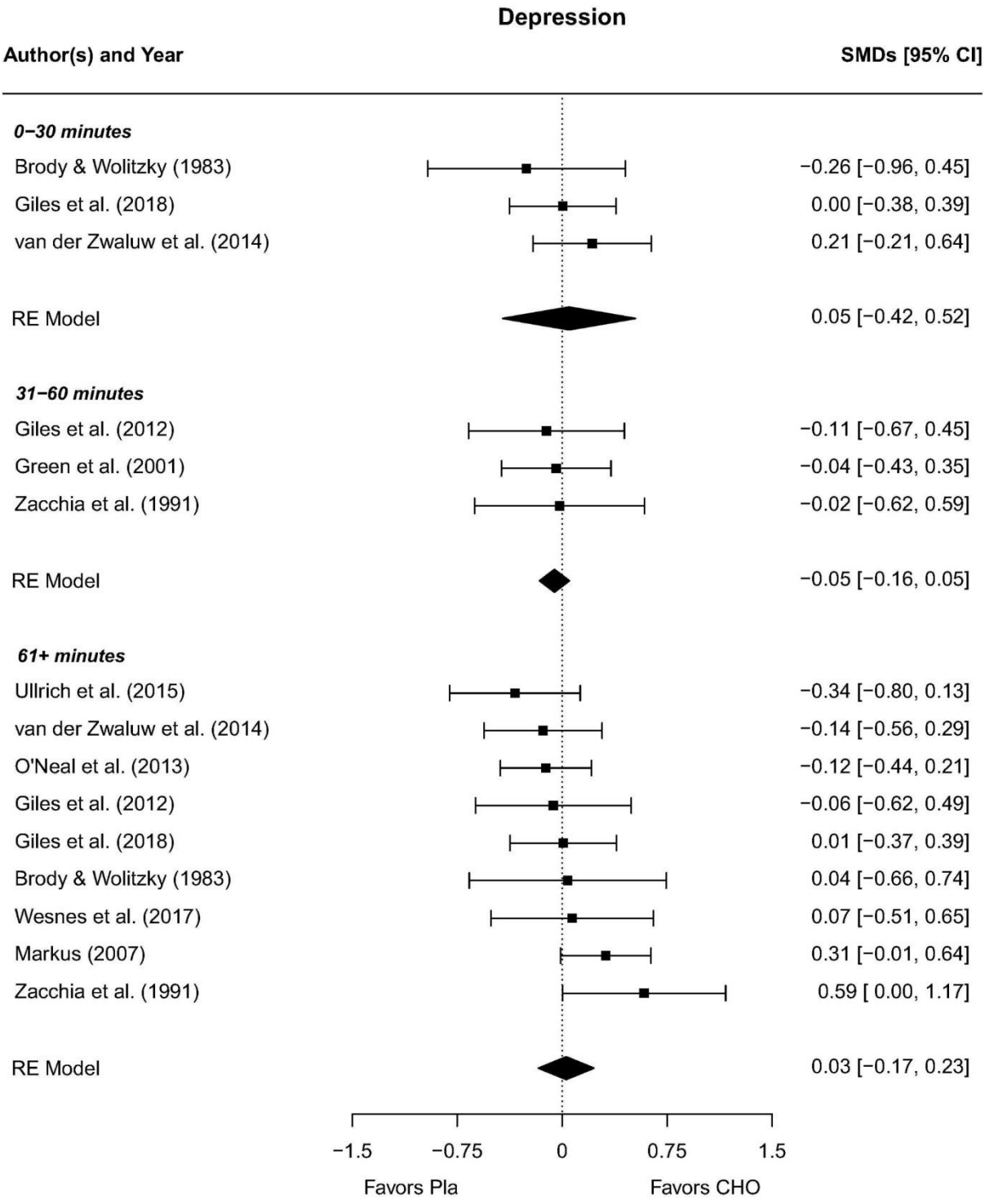

Figure 7. Forest plot of depression effect sizes with 95% confidence intervals.

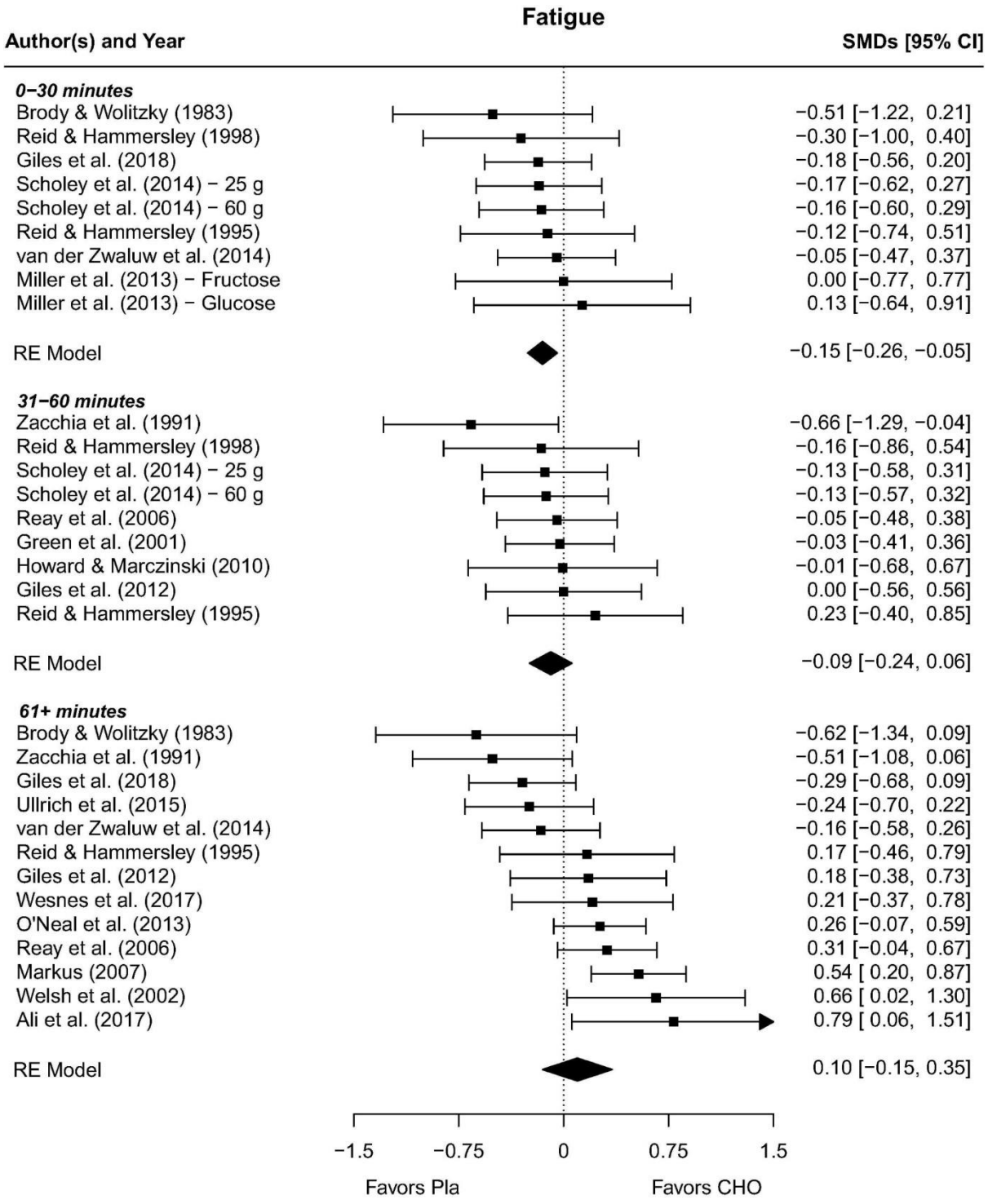

Figure 8. Forest plot of fatigue effect sizes with 95% confidence intervals.

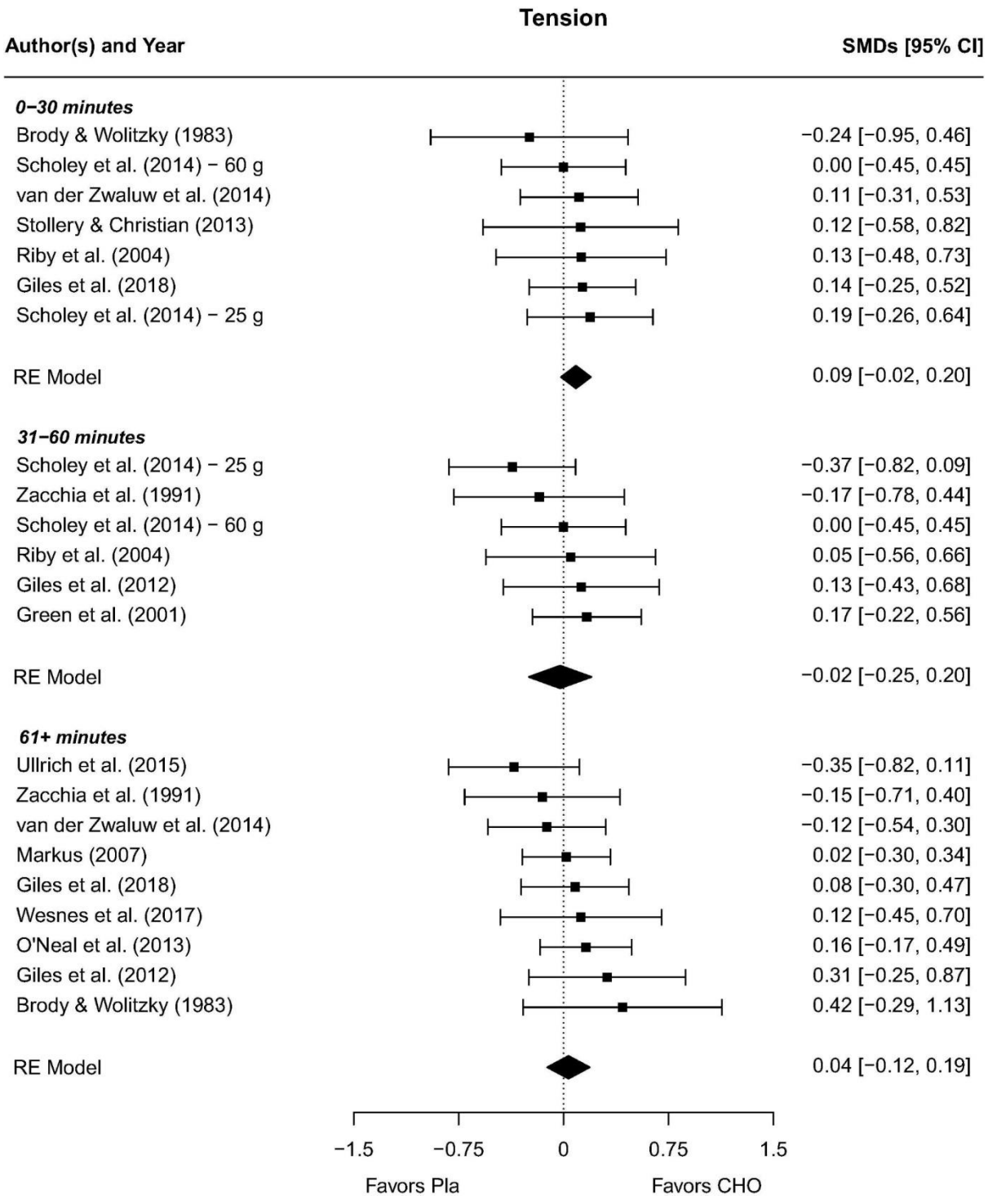

Figure 9. Forest plot of tension effect sizes with 95% confidence intervals.

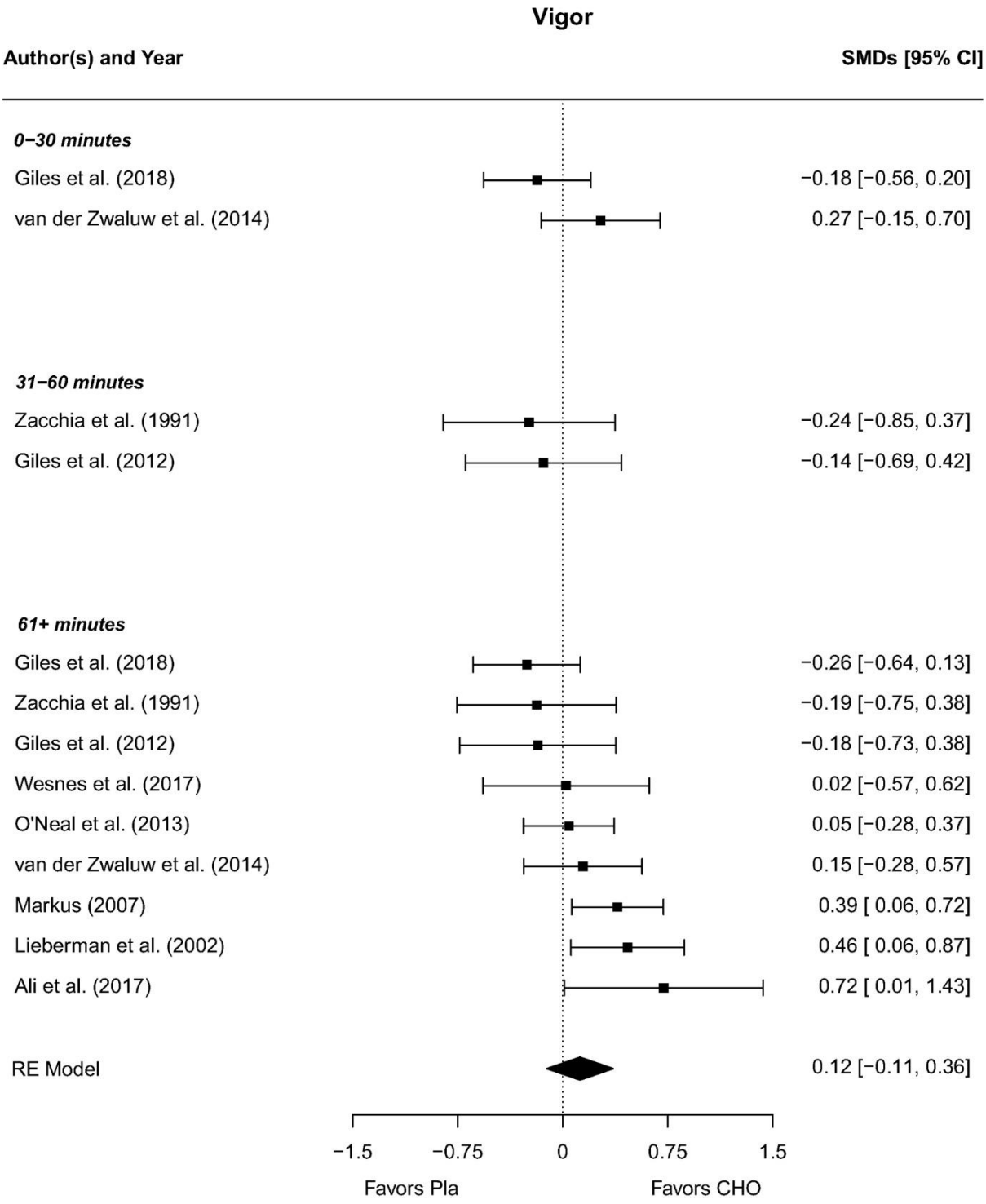

Figure 10. Forest plot of vigor effect sizes with 95% confidence intervals. RE models are not presented for the 0-30 and 31-60 time windows as only two studies were available for each time window.

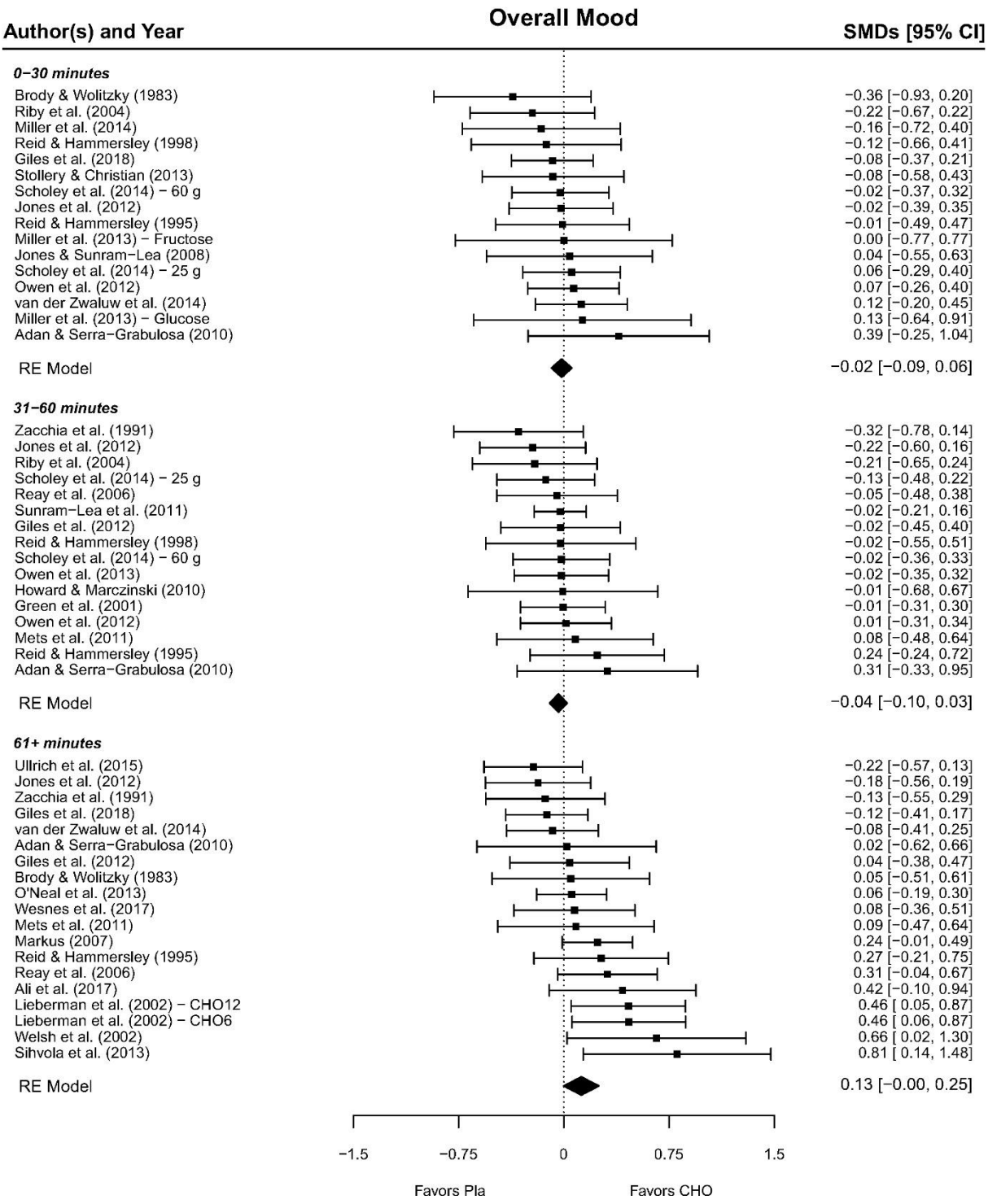

Figure 11. Forest plot of overall mood effect sizes with 95% confidence intervals.