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### **Credit Author Statement**

Conceived, designed the study, and wrote the first version of the manuscript: V.M. Conducted the systematic literature search: VM., F.D. and G.T.V. Final approval of eligible articles: All authors. Analysed the data: V.M. and F.D. Materials/analysis tools and expertise provided: M.M., A.B., P.C., A.L., J.B.M., G.T.V., and F.D. Wrote the paper: V.M. and F.D. Critical revision of the article: All authors. Integrity of the data analysis: G.T.V. and F.D. All authors have read and agreed to the published version of the manuscript.

# Does heart rate variability predict better executive functioning? A systematic review and meta-analysis

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2 The recent focus on the bidirectional heart-brain interactions in psychoneurophysiological research 3 has led to a variety of findings suggesting vagal activity is associated with cognition and, possibly, 4 specifically with executive functioning. This systematic review and meta-analysis aimed to provide 5 a better understanding of the association between vagally-mediated heart rate variability (HRV) 6 and executive functioning. We included 13 correlational studies. We found a small positive 7 association between vagally-mediated HRV and executive functioning (r = 0.19, 95%CI 0.15 to 0.23, p < 0.0001) using a quantitative synthesis of existing studies with random-effect models. 8 9 Conducting meta-regression analyses, we found that vagally-mediated HRV predicts cognitive 10 inhibition and cognitive flexibility more than working memory. In addition to the specific executive 11 function measured, this relationship is moderated by the HRV measurement used, and age. After 12 proposing a theoretical interpretation of the results, we emphasized the need for further research in 13 light of the methodological issues identified in the included studies, and we outline several aspects 14 to consider in future studies.

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Keywords: Autonomic nervous system, vagal tone, cognition, psychophysiology, embodied brain

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### Introduction

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19 Advances in cognitive neuroscience and psychophysiology on body-brain interactions (Bruineberg 20 & Rietveld, 2014; Kiverstein & Miller, 2015; Pezzulo & Cisek, 2016) has increasingly confirmed 21 the role of bodily signals in mental processes (Badcock et al., 2019; Damasio & Carvalho, 2013; 22 Seth, 2013). Accordingly, several peripheral factors, such as enteric microbiota (Cryan & Dinan, 23 2012), muscle mass (Pedersen, 2019), and the secretion of certain hormones (e.g., the link between 24 adrenal hormones and memory (McGaugh, 2013)), seem to influence cognitive processes. Recent 25 work on body-brain interactions has focused on the role of visceral signals and autonomic activity 26 in changing cerebral dynamics and cognition (Azzalini et al., 2019). Indeed, as cognitive 27 functioning worsens under conditions of autonomic dysfunctions, a promising physiological correlate of cognitive functioning is thus the autonomic nervous system functioning (Forte et al., 28 29 2019; Porges, 2007; Thayer et al., 2009). The autonomic nervous system is composed of the 30 sympathetic nervous system (mainly associated with physiological "flight or fight" responses) and 31 parasympathetic nervous system (depending on vagal activity, mainly related to energy 32 conservation, rest, and relaxation (Wehrwein et al., 2016)) which are associated with neural 33 dynamics (Sattin et al., 2020). 34 Bidirectional interactions between the autonomic and central nervous systems, primarily mediated 35 by the vagus nerve, are predicted by the neurovisceral integration model (Thayer et al., 2009). 36 According to this model, the functioning of the autonomic nervous system is an index of an 37 organism's self-regulatory capacities, promoting flexibility and adaptability in a changing 38 environment (Thayer & Lane, 2000). The primary marker of self-regulation is the vagal inhibition 39 of the heart, which can be assessed by recording the naturally occurring fluctuation in time intervals 40 between succeeding heartbeats over time, called heart rate variability (HRV, see Shaffer & 41 Ginsberg, 2017). Although heart-brain interaction can be measured by several methodologies such 42 as electrocardiogram heartbeat-evoked potentials (i.e., neural responses to heartbeats, see H.-D. 43 Park & Blanke, 2019) and psychological correlates of the phases of the cardiac cycle (Skora et al., 44 2022), HRV is a non-invasive index of cardiac control (Shaffer et al., 2014) widely adopted in 45 psychophysiological research (Quintana & Heathers, 2014). Frequently used HRV measurements 46 include the high-frequency band (HF) of the HRV power spectrum which coincides with 47 respiration (typically 0.15 to 0.4 Hz, called the respiratory band), the root mean of the square 48 successive differences (RMSSD), and respiratory sinus arrhythmia (RSA) which are associated 49 with vagal activity (McCraty & Shaffer, 2015). While HF is a marker of parasympathetic activity 50 (Shaffer & Ginsberg, 2017), lower frequencies (LF, 0.04 to 0.15 Hz) have been considered as a 51 marker of sympathetic activity, but not exclusively (as it seems to be also influenced by 52 parasympathetic activity, see Hayano & Yuda, 2019). The LF/HF ratio would thus reflect the 53 autonomic balance resulting from the hypothesis that the sympathetic and parasympathetic nervous 54 systems competitively regulate sinoatrial node firing (Billman, 2013). However, it is now generally 55 accepted that both branches of the autonomic nervous system can be simultaneously active 56 (Berntson & Cacioppo, 1999) making LF/HF ratio interpretation controversial (Billman, 2013; 57 Hayano & Yuda, 2019). Overall, vagally-mediated HRV is considered as the most relevant index 58 of self-regulatory abilities (Thayer et al., 2012). 59 Indeed, vagally-mediated resting-state HRV is associated with activity in several neural networks, 60 including brain areas involved in emotion processing (e.g., amygdala), visceral integration (e.g., 61 insular cortex), attentional and memory processes (e.g., prefrontal cortex, see Thayer et al., 2009). 62 For example, with respect to emotional processing, recent evidence shows that autonomic activity 63 may play a causal role in emotional responses, in which afferent signals from vagal activity precede 64 neural dynamics and correlate with the reported level of arousal (Candia-Rivera et al., 2022), and

65 may also be involved in emotional regulation through bodily feedback (e.g., in mice, see Klein et 66 al., 2021). Other recent studies suggested a role of cardiac activity in ventromedial prefrontal 67 activity influencing decision-making (Azzalini et al., 2021) and in measures of agency (the 68 experience of control and causing desired effects in the environment, see Herman & Tsakiris, 69 2020). Also, the cardiac cycle seems to be associated with the timing of action (Palser et al., 2021) 70 and the active processing of visual information (Kunzendorf et al., 2019). Together, these results 71 suggest that autonomic activity may have an ascending influence on brain, and thus cognitive, 72 processes. In line with this hypothesis, vagally-mediated resting-state HRV has been associated 73 with better performance on tasks assessing, for instance, emotion recognition (Quintana et al., 74 2012), heartbeat detection (Lischke et al., 2021), cognitive flexibility (Colzato et al., 2018), 75 cognitive inhibition (Ottaviani et al., 2019), working memory (Laborde et al., 2015), memory 76 retrieval (Gillie et al., 2014), memory discrimination (Feeling et al., 2021). A recent systematic 77 review further supports the association between HRV and cognitive functioning, highlighting that 78 vagally-mediated resting-state HRV seems to be specifically associated with executive functioning 79 (Forte et al., 2019). 80 Although HRV has been associated with several cognitive functions (e.g., memory and attention, 81 see Forte et al., 2019), it is rather considered as a marker of executive functions that may be 82 involved in other cognitive functions (such as the involvement of executive functions in memory, 83 see Feeling et al., 2021). Executive functioning can be defined as the control processes 84 implemented when the usual courses of action are no longer relevant in a given context (i.e., new, 85 unfamiliar, dangerous, or conflicting situations) allowing the person to adapt to new situations 86 (Diamond, 2013). According to Miyake's framework, the three main components of executive 87 functioning are task-switching, updating working memory, and response inhibition, playing a 88 crucial role in complex cognition and regulatory processes (Hsu et al., 2014; Miyake et al., 2000). 89

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Executive functioning, being relatively malleable (Hsu et al., 2014), could be influenced by vagal activity, as vagally-mediated HRV is a marker of self-regulatory abilities (Thayer et al., 2012). Yet, the magnitude, robustness, and mechanisms involved in the association between HRV and executive functioning remain unclear. For instance, several methodological issues have been identified to explain the inconsistency of the results such as the lack of control for sexual dimorphism (likely to influence autonomic responses, see Koenig & Thayer, 2016), the high variability of the data attributable to different methodological procedures and study designs, and executive functions have not previously been assessed in detail (Forte et al., 2019). Moreover, inhibition is considered as a common executive factor, underlying the performance in all executive function tasks (Miyake & Friedman, 2012). As the neuro-integration visceral model (Thayer et al., 2009) predict that HRV is associated with executive functioning, if cognitive inhibition is the core component of executive functions (Miyake & Friedman, 2012), then HRV might be more strongly associated with some executive component rather than others. In the same way, some HRV measurements have been described to reflect not only vagal activity but also sympathetic activity (Berntson et al., 2005). If vagal activity is associated with executive functioning, then the HRV measurements reflecting both vagal and sympathetic activity should be less predive of executive functioning than other vagally-mediated HRV measurements. In the present study, we aimed to investigate this association in a systematic review and metaanalysis in order to contribute to a better understanding of how HRV might be related to executive functioning. The primary objective of this study was to synthesize studies in which the relationship between vagally-mediated HRV and executive functioning has been tested and to assess the magnitude of this relationship by addressing the methodological issues previously identified (control of sexual dysmorphism, heterogeneity in study design and population studied etc., see Forte et al., 2019). Secondary objectives included (1) testing whether a specific measurement of

vagally mediated HRV better predicted executive functioning than others, (2) testing whether a specific executive function was predicted more by vagally-mediated HRV than the others, (3) and determining possible moderators of this association such as sexual dimorphism, age, the year of publication and study quality. We addressed the primary and secondary objectives by conducting correlational meta-analyses and group comparisons, respectively. To address potential moderators of the presumed relationship between vagally-mediated resting-state HRV and executive functioning, we conducted meta-regression analyses.

#### **Materials & Methods**

- Throughout the meta-analytic process, we followed the recommendations of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA, see Liberati et al., 2009;
- Moher et al., 2009) statement and recent recommendations for conducting correlational meta-
- 125 analyses (Quintana, 2015).

# 126 Systematic literature search

A systematic literature search was performed to identify studies reporting on vagally-mediated resting-state HRV in association with executive functioning. Only studies assessing the three main components of executive functioning (i.e., cognitive flexibility, updating in working memory, and cognitive inhibition, see(Miyake et al., 2000)) either in a composite task or separately and that used time- or frequency-domain measures or RSA to extract vagally-mediated HRV were included. A broad search strategy (Supplementary material 1) was formulated and employed a combination of keywords: (cognit\* OR neuropsycholog\* OR "executive function\*" OR "cognitive inhibition" OR "cognitive flexibility" OR "updating of working memory") AND (HRV OR "heart rate variability" OR "vagal tone" OR "vagal activity") in PsycINFO, PubMed, Embase, ScienceDirect and

Cochrane library. The following constraints were applied to limit search results: (1) articles on adults (>18 years), (2) written in English, and (3) original research articles (excluding reviews and meta-analysis). Identical search terms were employed in all database searches. For some databases (e.g. ScienceDirect) that have a limitation on the number of keywords used in the search equation, we had to adapt the search equation to use all terms from the main equation. In addition, the reference lists of included publications identified through database searches were screened for additional relevant articles. Searches were conducted on July 9, 2021, to May 31, 2022 (for additional articles). Two authors (Valentin Magnon, Guillaume Vallet) conducted the literature searches, reviewed the abstracts, and based on the selection criteria, decide on d the suitability of the articles for inclusion, and extracted the data. When necessary, disagreements were solved with a third author (Frédéric Dutheil).

# **Inclusion of eligible studies**

We included only correlational studies in the current systematic review and meta-analysis to control the issue of the variability of study designs and methodological procedures previously identified (Forte et al., 2019). To be included, studies needed to report a correlation analysis between vagally-mediated resting-state HRV (i.e., RMSSD, RSA, or HF) and performance on tasks evaluating executive functioning in healthy adults. Studies reporting regression analyses were included only if vagally-mediated resting-state HRV was the main predictor of executive functioning as a dependant variable and if the effect size (ES) was stated. Procedures of extraction of HRV from inter-beat interval data and analyses were carried out in accordance with the approved recommended guidelines for assessing HRV variables in psychophysiological research (Laborde et al., 2017; Quintana & Heathers, 2014; Task Force Report, 1996).

# Data extraction and management

ES and sample sizes were extracted from eligible studies. When data were not provided, the corresponding author of the publication was contacted. By using a digital data extraction sheet, the following data were extracted if available: general information and identifying features of the study (full reference, author names, the journal, and year of publication), descriptive data (sample population, size, age, sex and body mass index as it was the most frequently controlled variable provided), measures of executive functioning (neuropsychological test used and corresponding executive component assessed, main outcomes, reaction times, error rate, accuracy or composite scores), HRV measurement (frequency- or time-domain, RMSSD, HF or RSA, the recording length and device used), results (correlation coefficient or regression effect size to be converted).

### Study quality assessment

The risk of bias was defined as a measure of risk for a biased estimation of the association between vagally-mediated HRV and executive functioning. As there are few reliable and validated tools available to appropriately assess the risk of bias in included correlational studies, we relied on two assessment tools for greater validity. Therefore, to assess the quality and possible risk of bias in correlational studies, we used the National Institutes of Health (NIH) Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies (Ma et al., 2020; National Institutes of Health, 2014) in combination with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines (Vandenbroucke et al., 2007). The quality of a study was considered poor, fair, or good when the study met less than 5, between 5 and 8, and more than 8 of the NIH Quality Assessment Tool criteria, respectively (Supplementary material 2). As the STROBE checklist is not strictly speaking a risk of bias assessment tool (Costa et al., 2011), it was used to corroborate the NIH Quality Assessment Tool criteria.

# **Statistical analysis**

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182 Statistical analysis were performed with RStudio software version 3.6.3(RStudio Team, 2020), 183 using the meta(Schwarzer, 2021), metafor(Viechtbauer, 2021), and dmetar(Harrer et al., 2021a) R 184 packages. Raw ES were transformed to Fisher's z for variance stabilization (Harrer et al., 2021b). 185 A random effects model(DerSimonian & Kacker, 2007; Higgins et al., 2009), where between-186 studies variance (τ2) was estimated using a restricted maximum likelihood method as recommended for continuous outcomes(Veroniki et al., 2016), was used in the synthesis of 187 188 individual ES into a summary ES. 189 In order to test whether a specific HRV measurement better predicted executive functioning than 190 other measures and if a specific executive function was predicted more by vagally-mediated HRV 191 than the others, we performed subgroup meta-analyses according to vagally-mediated HRV 192 parameters (RMSSD vs. HF vs. RSA) then according to executive functions (cognitive functioning 193 vs. cognitive inhibition vs. updating in working memory vs. global composite executive score) 194 respectively. 195 Meta-regressions were then conducted to test potential moderators which were defined a priori. 196 The vagally-mediated HRV parameters and the executive functions were included in the regression 197 model as two categorial predictors to test possible interaction terms. Permutation tests were also 198 conducted as they have been recommended to assess the robustness of the meta-regression 199 models(Higgins & Thompson, 2004). Age, sex distribution, the year of publication, and study 200 quality (indicated by NIH Quality Assessment scores) were tested as continuous predictors. The 201 Knapp-Hartung method(IntHout et al., 2014) and method of restricted maximum 202 likelihood(Langan et al., 2019) were used for meta-regression analyses.

For all statistical analyses, the employed statistical significance threshold was set at $p < 0.05$ . To
assess the observed variance and heterogeneity in the true ES between included studies, the
significance of Cochran's $Q$ (Cochran, 1954) and Higgins & Thompson's $I^2$ statistic(Higgins &
Thompson, 2002) were computed. $I^2$ values of $\sim 25\%$ , $\sim 50\%$ , and $\sim 75\%$ were interpreted as low,
moderate, and high heterogeneity between studies(Higgins et al., 2003). A Baujat plot (Baujat et
al., 2002) enabled the detection of ES which overly contribute to the heterogeneity in order to
remove them if heterogeneity > 50%. Furthermore, in order to identify potential ES outliers, outlier
diagnostics were performed (Viechtbauer & Cheung, 2010). Next, the conventional Egger's
regression test was applied(Egger et al., 1997) to investigate whether the presence of small-study
effects(Sterne et al., 2000) is likely (Egger's regression test: $p < 0.05$ ) or not. As a further model
diagnostic, variants of the funnel plot (including contour-enhanced) were created to investigate the
likelihood of a publication bias as well (Schmucker et al., 2014). Funnel plots traditionally illustrate
the distribution of ES estimates by their standard errors including an idealized funnel-shape
centered on the summary ES. Contour enhanced funnel plot superimposes key areas of statistical
significance ( $p = 0.1$ , $p = 0.05$ , $p = 0.01$ ) to assess for risk of publication bias (indicated by over-
representation of ES in areas of significance). When there is no publication bias, studies should
roughly follow the shape delineated by the funnel displayed in the plot and the data points should
form a roughly symmetrical, upside-down funnel(Harrer et al., 2021a). However, asymmetry of
the funnel plot can be caused by very different mechanisms, and should not be readily attributed to
publication bias(Doleman et al., 2020). Once the outliers were removed, the meta-analysis was
conducted again, along with subgroup analyses and meta-regressions.

225	Results
226	The searches resulted in a total of 16,675 studies. Based on the title, irrelevant articles and
227	duplicates were removed to obtain 1,306 articles that were then screened based on the abstract.
228	Then, 37 studies were assessed for eligibility. After full-text reading, 13 articles were included in
229	the present systematic review and meta-analysis (Fig. 1). In this meta-analysis, 13 studies yielding
230	52 ES were included (Capuana et al., 2014; Colzato et al., 2018; Colzato & Steenbergen, 2017;
231	Hansen et al., 2003; Kaufmann et al., 2012; Keen et al., 2020; Mathewson et al., 2010; Ottaviani
232	et al., 2019; Spangler et al., 2018; Stenfors et al., 2016; D. P. Williams et al., 2016; P. G. Williams
233	et al., 2019; Xing et al., 2020). Characteristics of studies are presented in Table 1.
234	Study quality
235	All studies have been assessed as either fair (Capuana et al., 2014; Colzato & Steenbergen, 2017;
236	Kaufmann et al., 2012; D. P. Williams et al., 2016) or good quality(Colzato et al., 2018; Hansen et
237	al., 2003; Keen et al., 2020; Mathewson et al., 2010; Ottaviani et al., 2019; Spangler et al., 2018;
238	Stenfors et al., 2016; P. G. Williams et al., 2019; Xing et al., 2020) based on the validated NIH
239	Quality Assessment Tool (Fig. 2). This was further supported by the STROBE checklist according
240	to which all studies presented overall good quality (scores $\geq$ 19/27).
241	
242	Characteristics of population
243	The total number of participants included was 998: 411 men (41%) and 587 women (59%). The
244	proportion of men varied from 21%(Stenfors et al., 2016) to 100%(Hansen et al., 2003). The mean
245	age of participants was 24.6 years old ranging from 18(Xing et al., 2020) to 48 years old(Stenfors
246	et al., 2016). Nine studies were conducted on undergraduates students (Capuana et al., 2014;
247	Colzato et al., 2018; Colzato & Steenbergen, 2017; Kaufmann et al., 2012; Keen et al., 2020;

Spangler et al., 2018; D. P. Williams et al., 2016; P. G. Williams et al., 2019; Xing et al., 2020), 248 one study (Mathewson et al., 2010) on young participants recruited at the university, 249 250 another(Ottaviani et al., 2019) on young adults recruited from the general population and one 251 study(Hansen et al., 2003) on male sailors from the Royal Norwegian Navy. Only one 252 study(Stenfors et al., 2016) was conducted on middle-aged working adults. Only six studies reported body mass index(Colzato et al., 2018; Colzato & Steenbergen, 2017; Keen et al., 2020; 253 254 Ottaviani et al., 2019; Spangler et al., 2018; P. G. Williams et al., 2019). The mean body mass index was 23.7 kg/m<sup>2</sup> ranging from 17.2 to 44.0(P. G. Williams et al., 2019). Only two studies 255 256 reported anxiety levels(Colzato et al., 2018; Colzato & Steenbergen, 2017), and only one reported 257 education level(Stenfors et al., 2016). Despite six studies controlling for smoking(Colzato et al., 2018; Mathewson et al., 2010; Ottaviani et al., 2019; Spangler et al., 2018; D. P. Williams et al., 258 259 2016; P. G. Williams et al., 2019), five for coffee consumption (Mathewson et al., 2010; Ottaviani 260 et al., 2019; Spangler et al., 2018; D. P. Williams et al., 2016; P. G. Williams et al., 2019), three 261 for alcohol intake (Ottaviani et al., 2019; Spangler et al., 2018; P. G. Williams et al., 2019), two 262 for the medication (Capuana et al., 2014; Ottaviani et al., 2019), those data were seldomly reported. Participants were asked to not use those substances 2 to 6 hours before the experiment, as well as 263 264 to refrain from engaging in moderate or vigorous physical activity(Ottaviani et al., 2019; D. P. 265 Williams et al., 2016; P. G. Williams et al., 2019). 266 Meta-analysis on the association between vagally-mediated HRV and executive functioning 267 The meta-analysis revealed a small positive correlation between vagally-mediated HRV and executive functioning (r = 0.15, 95% CI 0.09 to 0.21, p < 0.0001, k = 52), with a  $I^2$  of 65%. A 268 269 subgroup analysis showed significant differences between HRV parameters (p < 0.05). A moderate positive ES estimate were observed for RSA (p < 0.001) while a small positive ES were revealed 270

for RMSSD (p < 0.01) and HF (p < 0.01). ES for RSA were larger than for RMSSD (p < 0.05). HF did not differ from RMSSD (p = 0.42) and HF was marginally smaller than RSA (p = 0.09). Another subgroup analysis based on executive functions indicated positive small ES for cognitive inhibition (p < 0.001) and cognitive flexibility (p < 0.001), a negative ES for global executive functioning (p < 0.05) and no significant ES for working memory (p = 0.16). ES significantly differed across executive functions ( $Q_b(3) = 19.86$ , p = 0.0002). ES for cognitive inhibition were significantly larger than ES for global executive functioning (p < 0.001) and working memory (p < 0.001) whereas they did no differ from ES for cognitive flexibility (p = 0.78). Similarly, ES estimates for cognitive flexibility were significantly larger than ES for global executive functioning (p < 0.001) and working memory (p < 0.05). ES were also larger for working memory than for global executive functioning (p < 0.01). The small number of ES (p = 0.05) for global executive functioning severely limits the interpretation of the results for this subgroup. There was no evidence of an interaction term between HRV parameters and executive functions (p = 0.52, p = 0.67) (see all statistical details in Supplementary material 3).

### Sensitivity analyses

The Egger's test was significant (p = 0.01). Furthermore, the chi-square Q-statistic (Cochran's Q test for heterogeneity) exceeded the level of significance ( $Q_{51} = 146.1$ , p < 0.0001) assuming that variation in ES estimates was not caused by sampling error alone. Therefore, 65 % of the variance in ES estimates was due to true variation among studies rather than mere sampling error. Since it assumes that more than half of the variation was due to true ES differences(Higgins & Thompson, 2002), outlier diagnostics were performed. Six ES from 4 studies(Hansen et al., 2003; Keen et al., 2020; Stenfors et al., 2016; Xing et al., 2020) were distributed outside of the idealized funnel-shape centered on the summary ES (Fig. 3) and were removed from further analyses. The meta-analysis

295 conducted without outliers confirmed a positive correlation between vagally-mediated HRV and 296 executive functioning (r = 0.19, 95% CI 0.15 to 0.23, p < 0.0001, k = 46; Fig. 4) with low heterogeneity between true ES ( $I^2 < 25$  %). As such, this new model was retained as the most 297 298 robust analyses (Table 2). 299 Significant differences between HRV parameters (Fig. 5) were revealed by subgroup analysis 300  $(Q_b(2)=13.13, p=0.0014)$ . Moderate positive ES estimates were observed for RSA  $(k=8, \beta=1.0014)$ 301 0.40, 95% CI 0.25 to 0.54, SE = 0.07, p < 0.0001), while small positive ES were revealed for 302 RMSSD  $(k = 20, \beta = 0.21, 95\%)$  CI 0.15 to 0.26, SE = 0.03, p < 0.0001) and HF  $(k = 18, \beta = 0.14, \beta = 0.14)$ 303 95% CI 0.09 to 0.19, SE = 0.03, p < 0.0001). ES estimates for RSA were larger than for HF ( $\beta$  = 304 0.26, 95% CI 0.10 to 0.41, SE = 0.08, p = 0.0018) and for RMSSD ( $\beta = 0.19$ , 95% CI 0.03 to 0.35, 305 SE = 0.08, p = 0.0164). ES for RMSSD did not differ from ES for HF ( $\beta = 0.06$ , 95% CI -0.01 to 306 0.14, SE = 0.04, p = 0.08). Similarly, subgroup analysis based on executive functions (Fig. 5) 307 revealed significant differences between subgroups ( $Q_b(3)$ = 19.37, p = 0.0002) indicating positive 308 small ES for cognitive inhibition (k = 24,  $\beta = 0.21$ , 95% CI 0.16 to 0.26, SE = 0.03, p < 0.0001), 309 cognitive flexibility (k = 10,  $\beta = 0.23$ , 95 % CI 0.16 to 0.30, SE = 0.03, p < 0.0001) and working 310 memory (k = 11,  $\beta = 0.08$ , 95 % CI 0.02 to 0.15, SE = 0.03, p = 0.008). There was only one ES 311 estimate for global cognitive functioning composite score severely limiting the interpretation of 312 the results for this subgroup (k = 1,  $\beta = 0.41$ , 95 % CI 0.19 to 0.64, SE = 0.11, p = 0.0007). ES 313 estimates for cognitive inhibition and cognitive flexibility were larger than for working memory ( $\beta$ 314 = 0.13, 95 % CI 0.05 to 0.21, SE = 0.04, p = 0.0019;  $\beta = 0.14, 95 \%$  CI 0.05 to 0.23, SE = 0.05, p = 0.0019;  $\beta = 0.0019$ ;  $\delta = 0.0019$ 315 = 0.0027 respectively). No differences in ES estimates were observed between cognitive inhibition 316 and cognitive flexibility ( $\beta = 0.01$ , 95% CI -0.07 to 0.10, SE = 0.04, p = 0.75). Further exploratory 317 analyses did not reveal an interaction between executive functioning component and vagallymediated HRV measurements (F(2, 38) = 0.67, p = 0.52). 318

# Impact of other possible moderators on effect size

- A Meta regression analysis model revealed that age negatively influenced ES ( $\beta = -0.005, 95 \%$  CI
- -0.008 to -0.002, SE = 0.001, p = 0.005) while there was no evidence that the proportion of males
- in the sample had a significant effect on effect size ( $\beta = 0.0001$ , 95% CI -0.002 to 0.003, SE =
- 323 0.001, p = 0.94). BMI did not influence effect size either ( $\beta = 0.01$ , 95 % CI -0.04 to 0.07, SE =
- 324 0.03, p = 0.65). In addition, meta-regression analysis revealed that neither study quality ( $\beta = -0.03$ ,
- 325 95 % CI -0.09 to 0.03, SE = 0.03, p = 0.34) nor year of publication ( $\beta = -0.003$ , 95 % CI -0.01 to
- 326 0.01, SE = 0.01, p = 0.63) influenced effect size (Fig 6).

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### Discussion

- 329 The objective of the present systematic review and meta-analysis was to provide a better
- understanding of how HRV might be related to executive functioning. A small positive correlation
- was revealed between vagally-mediated HRV and executive functioning. This finding supports the
- 332 association between vagally-mediated HRV and executive functioning predicted by the
- 333 neurovisceral integration model(Thayer et al., 2009). The vagus nerve might be the
- 334 psychophysiological pathway to the activity of the prefrontal cortex and the anterior cingulate
- 335 cortex involved in the regulation of inhibitory/self-regulatory abilities and thus executive
- functioning(Thayer et al., 2012). The relationship between vagally mediated HRV and executive
- 337 functioning appears to depend on the HRV parameter assessed, the executive function measured,
- and the age of the participants.

#### Moderating effect of vagally-mediated HRV parameters

- 340 Interestingly, while all vagally-mediated HRV parameters correlated with executive functioning,
- 341 the association between RSA and executive functioning was moderate while the correlation

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between HF or RMSSD and executive functioning was significantly smaller. From a theoretical standpoint, one possible explanation is that RSA may be a reliable index of self-regulatory abilities. RSA reflect the respiration-driven increasing and decreasing of the heart, via the vagus nerve, made possible by the baroreflex (Karemaker, 2009; Shaffer & Ginsberg, 2017). As such, it reflects the adjustment of the heart rate by the vagus nerve according to respiration rate. Under the right circumstances (spontaneous breathing), RSA may index the adaptation of the vagus nerve to an external factor, i.e. respiration rate, and thus the self-regulatory capacities of the vagus nerve. In this hypothesis, RSA would not reflect vagal activity as such (usually assessed by the power spectrum density of HF band or RMSSD) but rather how well vagal activity is regulated by the vagus nerve in accordance with respiration rate. Previously, a review suggested that RSA is essential in self-regulation as it plays a primary role in the regulation of energy exchange by synchronizing respiratory and cardiovascular processes during metabolic and behavioral change(Grossman & Taylor, 2007). However, it was noted that, under certain circumstances (longer exhalations allowing greater acetylcholine metabolism), slower respiration rates can produce higher RSA amplitudes that are not mediated by changes in vagal firing(Shaffer & Ginsberg, 2017). As none of the articles included in the present systematic meta-analysis manipulated respiration rate, RSA in those articles should reflect vagally-mediated changes in heart rate. Supporting the importance of changes in vagal activity rather than vagal activity as such, the vagal tank theory (Laborde et al., 2018) suggests that vagal reactivity to, and recovery from, a specific extern event (beyond the influence of respiration rate such as undertaking a cognitively engaging task) are relevant to index self-regulatory abilities.

# Moderating effect of specific executive functions

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The results suggest that the adaptability and flexibility of the vagus nerve might directly relate to the corresponding executive functions. Indeed, regarding the executive functions tested, vagallymediated HRV correlated more with cognitive inhibition and cognitive flexibility than with updating in working memory, however, all associations were small. In support of this idea, it has been proposed that vagally-mediated HRV is particularly associated with performance on goaldirected tasks involving adaptive psychological regulation and flexible cognitive processes (involving cognitive inhibition and cognitive flexibility), whereas tasks inducing mental stress (i.e., working memory tasks) are associated with decreased vagal-mediated HRV(G. Park et al., 2014). More precisely, working memory would require more cognitive engagement resulting in sympathetic predominance to manage mental stress(Duschek et al., 2009). In contrast, tasks involving cognitive inhibition or cognitive flexibility require greater self-regulatory effort associated with parasympathetic activity (G. Park et al., 2014; Segerstrom & Nes, 2007). The polyvagal theory proposes an evolutionary point of view to interpret the role of the autonomic nervous system in cognitive functioning according to contextual cues (Porges, 2007). According to this theory, the autonomic nervous system has evolved to promote the focus of attention (sympathetically-driven) in threatening situations and cognitive flexibility processes (parasympathetically-driven) in secure situations to favor social cognition and increase the odds of survival. Taken together, these findings suggest that the adaptability of the vagal inhibitory cardiac control is directly related to adaptative cognitive processes, mainly cognitive inhibition and flexibility.

# **Moderating effect of age**

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The relationship between vagally-mediated HRV and executive functioning may however be influenced by several factors, including age. Specifically, age negatively predicted the strength of this relationship in the studied population ranging from 18 to 66 years old. Middle-aged adults seem to have some difficulties with certain executive functioning tasks (Ferguson et al., 2021). Concurrently, vagally-mediated HRV seems to decrease linearly with age and then the reverse with an increase in those above 60 years old(Geovanini et al., 2020). Concomitant vagal and executive declines support the direct association between vagal activity and prefrontal brain areas involved in executive functioning, which may play a role in cognitive aging (Thayer et al., 2021). In line with the bidirectional heart-brain axis hypothesis, the reverse vagal increase observed after 60 years old might be the physiological compensation mechanism underpinning the greater cerebral activation observed in the prefrontal cortex in older people to achieve equivalent cognitive performances to those of younger adults(Cabeza et al., 2002, 2004). However, the cerebral integration of cardiac information seems to decline with age(Khalsa et al., 2009; Murphy et al., 2018). The insular cortex is a key area in the cerebral integration of visceral signals including those from the cardiovascular system(Aleksandrov & Aleksandrova, 2015; Craig, 2009; Damasio & Carvalho, 2013). Aging is associated with grey matter loss in the insular cortex(Resnick et al., 2003) possibly explaining the decreased strength of the heart-brain bidirectional interactions with age. It has previously been reported that substantial sex differences existed in vagally-mediated HRV(Koenig & Thayer, 2016). Specifically, women seem to have lower total power in the spectral density than men and, while women show less power in the very-low and LF bands, they show greater power in the HF band than men. Interestingly, despite greater vagal activity in women, there was no evidence of sex differences in the association between vagally-mediated HRV and executive functioning in the present meta-analysis; suggesting that the physiological mechanisms underlying heart-brain interactions might be similar in men and women.

### **Limitations and current challenges**

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Interpretations of the current results must be nuanced as the present systematic meta-analysis is not without limitations. First, the nature of this meta-analysis is correlational, thus no causal conclusions can be drawn. In addition, despite a large number of included effect sizes, there were only eight ES estimates for updating in working memory and one for global executive functioning limiting the interpretations of the results for those subgroups. Furthermore, we conducted the metaanalyses only on published articles, so they are theoretically exposed to a possible publication bias. The few studies conducted on aging populations were not included as older people have very different profiles due to developmental trajectories which could have generated heterogeneity between studies. For instance, as far as vagal activity is concerned, some data indicate that older individuals can linearly maintain high HRV (Tan et al., 2019), others suggest that HRV decreases with age before increasing around 65 years old as a U shape developmental trajectory (Almeida-Santos et al., 2016) while others rapport linear decline in HRV with age (Reardon & Malik, 1996). A meta-analysis inherits also the limitations and biases of the individual studies investigated. Indeed, several methodological issues were identified in the included studies through the systematic review process, despite good overall methodological quality following recommendations for conducting research on HRV(Laborde et al., 2017; Quintana & Heathers, 2014), with the length of the recording (5-6 min.) adequate for short-term HRV recording(Li et al., 2019; Shaffer & Ginsberg, 2017) and the accuracy of the recording devices validated and reliable, especially when the recording occurs at rest (for the validation of the Polar H7, see Hernández-Vicente et al., 2021; for a general review see Ishaque et al., 2021). While several studies use ECG 430

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to assess the relationship (through correlations) between heart rate variability and cognitive variables, the directionality of the observed effect remains uncertain. The potential causality in this relationship could be further investigated with other methodologies that require the recording of brain oscillations through electroencephalography (EEG) in addition to the heart activity recording within a framework of mutual influence (Candia-Rivera, Catrambone, et al., 2021). Nonetheless, the small summary ES may reflect that some of the included studies are underpowered. Only two studies (Spangler et al., 2018; Xing et al., 2020) have conducted a priori power analysis (Cohen, 2013). Another main issue was that several factors likely to influence either cardiovascular functioning or cognitive functioning or both were not always controlled. Besides age and sex distribution which were always reported, the most controlled and reported variable was body mass index(Colzato et al., 2018; Colzato & Steenbergen, 2017; Keen et al., 2020; Ottaviani et al., 2019; Spangler et al., 2018; P. G. Williams et al., 2019) followed by smoking(Colzato et al., 2018; Mathewson et al., 2010; Ottaviani et al., 2019; Spangler et al., 2018; D. P. Williams et al., 2016; P. G. Williams et al., 2019) and caffeine intake(Mathewson et al., 2010; Ottaviani et al., 2019; Spangler et al., 2018; D. P. Williams et al., 2016; P. G. Williams et al., 2019). However, some lifestyle factors that may influence executive functioning or HRV were not considered in the studies included in this review, such as diet(Martínez-Lapiscina et al., 2013; Millman et al., 2021), sleep quality(Bourdillon et al., 2021; Rana et al., 2018) and sedentariness(Magnon, Vallet, et al., 2018, 2021; Zaffalon Júnior et al., 2018) recognized as a risk factor independent of physical inactivity(Magnon, Dutheil, et al., 2018; Panahi & Tremblay, 2018). Finally, it is recommended that cognitive function is evaluated by two different measures (Hebben & Milberg, 2009) whereas only one test has often been used to assess a specific executive function in the included studies. Moreover, certain tests might not be the most appropriate for the studied population. For instance, since the 2-back version of the n-back induced a relatively low cognitive engagement level in a young population compared to the 3-back version (Herff et al., 2014), the difficulty might not be high enough for undergraduates students (Dong et al., 2015). The heterogeneity between studies in cognitive measurements might also explain the small effect size of the overall association between HRV and executive performance. One can imagine that if the same tests were used to assess a specific executive function, the association between HRV and executive functioning would have been stronger than the one observed in the present study. Nonetheless, the results of this systematic review and meta-analysis are in line with the neurovisceral integration model (G. Park & Thayer, 2014; Thayer et al., 2009) and embodied cognitive sciences (Badcock et al., 2019; Pezzulo & Cisek, 2016; Seth, 2013) suggesting that visceral information may underpin executive functioning to some extent. From a clinical perspective, if the heart-brain axis interactions are further empirically supported, breathing exercises are efficient, cheap and simple to increase vagally-mediated HRV (Magnon, Dutheil, et al., 2021; Van Diest et al., 2014) which could possibly enhance cognitive functioning (De Couck et al., 2019; Zaccaro et al., 2018) and thus could be used as a way to prevent cognitive difficulties associated with chronic pathologies and aging.

#### **Further recommendations**

- In order to address the identified methodological issues and to ensure a greater methodological validity of studies investigating the association between vagally-mediated HRV and executive functioning, we suggest nine recommendations below organized in order of importance.
- 1. **ECG or validated non-invasive recording devices**. It is recommended to prioritize ECG when possible as it is the gold standard to accurately record inter-beat interval values. Interestingly, EEG in complement of ECG can be used to assess the brain and heartbeat oscillations respectively within a framework of mutual influence that may allow for causality assessment (e.g. physiological modeling approaches, see Candia-Rivera, Catrambone, et al., 2021). When other recording devices are used, we recommend to cite

- articles validating their accuracy and reliability as non-standardized recording devices can cloud interpretation and generalizability of findings (Nelson et al., 2020).
- 2. **Definition of the HRV measurement used in relation to the research question**. Since there is an ongoing debate about the theoretical interpretation of several HRV indices (Berntson et al., 2005; Hayano & Yuda, 2019; Karemaker, 2009), the theoretical definition of the HRV index measured should be defined *a priori* and clearly stated as well as its relevance for the research question. Furthermore, the formula for calculation of the HRV index and the data analysis software used should be indicated. For instance, the calculation of the HF band is not always reported, yet it can be expressed in many units such as m<sup>2</sup>, Hz, normalized units (n.u.), and in the percentage of the total power (Tarvainen et al., 2014).
  - 3. **Power analysis**. Conducting a power analysis can be difficult for pilot and exploratory studies that investigate a new research question that was not previously addressed since there are no studies on which the power analysis can be based on. However, when previous studies addressing similar research questions exists, a power analysis can be conducted easily using free software such as Gpower (Faul et al., 2009) or the *pwr* R package (Champely et al., 2020) ensuring sufficient sample size.
  - 4. **Homogeneity of the sample**. The target population should be as homogeneous as possible to control for the possible influence of variables such as prior cardiovascular illnesses (e.g. arrhythmia, heart failure), severe inflammation (e.g. arthritis), or a neurological (head trauma, epilepsy, etc.), physiological (hypo- or hyperthyroidism, type 2 diabetes) or neurodevelopmental disorder (autism, dyslexia, etc.). In addition, several lifestyle factors should be controlled and reported when possible: age, sex distribution, the body mass index, caffeine, alcohol, nicotine, medication, other substances consumption, anxiety level,

depression level, education level, physical activity level, sedentary time, diet, sleep quality
(Quintana & Heathers, 2014).

- 5. **Instructions priors to the experimental session**. It is recommended to give prior instructions to refrain the participants from engaging in any behaviors that might affect variables of interest before the experimental session (6 hours before if possible).
  - 6. **10 minutes of rest before baseline HRV.** We recommend that the participant rest 10 minutes before baseline to ensure resting state HRV is assessed, which is rarely implemented.
  - 7. **Resting, Reactivity, and Recovery**. Even if resting HRV has been the most investigated parameter in relation to executive functioning, certain associations might reveal themselves only when considering vagal reactivity (e.g., Calkins et al., 2007). As such, it is recommended to assess during at least 5 minutes (Malik et al., 1996) vagally-mediated HRV before (rest), during (reactivity) and after (recovery) a cognitive task (Laborde et al., 2018).
  - 8. **Neuropsychological tests.** The neuropsychological tests to assess executive functioning used must be valid, reliable, and sensitive. We recommended the use of standardized tests commonly recognized among researchers in cognitive psychology or neuropsychology, as well as, using ideally two different measures to evaluate one cognitive function (Hebben & Milberg, 2009).
  - 9. **Control of respiration.** When RSA or HF is assessed, we recommended to do so in a resting state without manipulating respiration rate (spontaneous breathing) or by controlling for respiratory rate. It was suggested that, under certain circumstances, respiration rate changes can produce large-scale shifts in RSA magnitude without affecting vagal tone (Shaffer & Ginsberg, 2017).

These recommendations can also be applied when studying the role of the heart-brain relationship beyond executive functioning, as it is studied in many other cognitive domains (see Zahn et al., 2016). For example, recent studies have addressed the long-standing debate about the role of bodily activity in emotion (Pace-Schott et al., 2019), attempting to propose an answer by showing that autonomic cardiac activity could play a leading and causal role in initiating emotional states (Candia-Rivera, Catrambone, et al., 2021). Interestingly, rather than investigating the role of heartbrain interaction in emotion, other studies have recently examined the role of a pre-existing emotional state in the involvement of heart-brain interaction in cognition. For example, induced sadness influences the association between HRV and cognitive inhibition (Hoffmann et al., 2022). Beyond emotional processing, other studies focused on the interplay between heart and brain in perception, showing that cardiac activity might influence the attention afforded to external signals and the preparation of an appropriate course of action (Skora et al., 2022). In a broader way, autonomic activity has also been studied in relation to consciousness generation (Candia-Rivera, Annen, et al., 2021), leading to the hypothesis that ascending bodily signals into neural systems could a switch for consciousness (Sattin et al., 2020).

### Conclusion

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In this first systematic review and meta-analysis of studies reporting data on a potential link between vagally-mediated HRV and executive functioning, we provide some evidence that 1) vagally-mediated HRV is associated with executive functioning; 2) RSA may be more strongly associated with executive functioning than RMSSD and HF; 3) vagally-mediated HRV correlates more with cognitive flexibility and cognitive inhibition than with updating in working memory; 4) age negatively moderates the relationship between vagally-mediated HRV and executive functioning. Our results are in line with the neurovisceral integration model suggesting that visceral

information may underpin executive functioning to some extent. Several methodological issues which may account for the small associations observed in the present meta-analysis were identified and discussed. Future quality studies addressing these methodological issues would be necessary to refine the conclusions drawn from these initial results.

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563	Data availability statement
564	The data supporting the conclusions of this article are available at: <a href="https://osf.io/fuhwt">https://osf.io/fuhwt</a>
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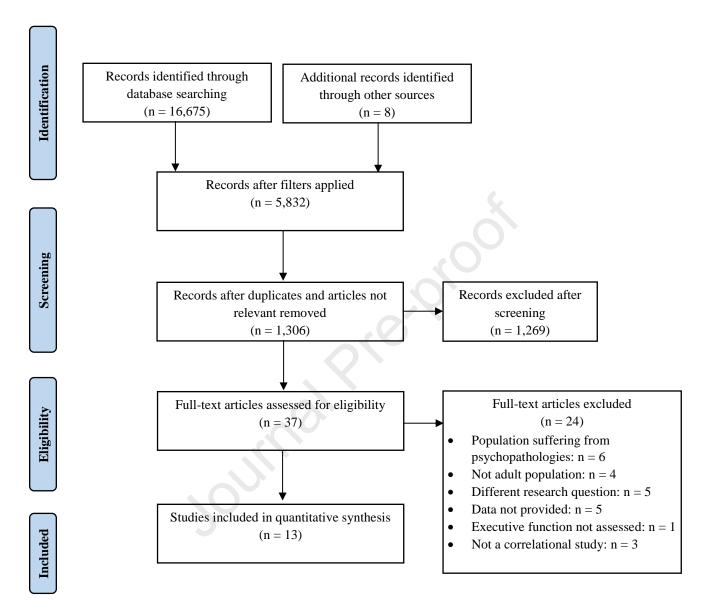


Fig. 1. PRISMA Flow Diagram depicting the study selection process.

**Table 1**Summary characteristics of included studies.

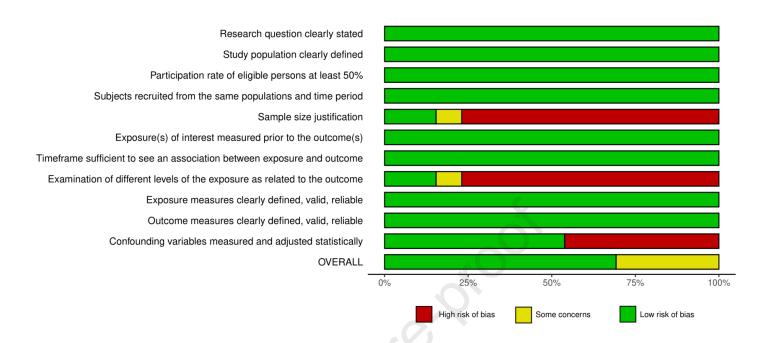
	Quality		Population					<b>Executive functioning</b>		HR	V record	ding	
Study	NIH (Strobe)	Type	n	Age*	Men/Women	BMI*	Function	Assessment	Outcomes	Pearson' r	Index	Length	Device
								Stroop task	Accuracy score	0.39			
								Stroop task (Incentive)	Accuracy score	0.51			
<b>C</b>	Fair	I I a da mana da aka		21.1			Camitina	Memory Stroop task	Accuracy score	0.57			
Capuana et al., 2014	Fair (23)	Undergraduate students	17	21.1 [18-26]	6/11	-	Cognitive inhibition	Memory Stroop task (Incentive)	Accuracy score	0.54	RSA	5 min	ECG
								Repeat Stroop task	Accuracy score	0.19			
								Repeat Stroop task (Incentive)	Accuracy score				
Colzato & Steenberge n, 2017	Fair	Undergraduate		21.2		22.17	Cognitive	Stop-change task: 0 ms delay stop - change.	Reaction time	-0.23		) 5 min.	Polar H7
	(20)	students	88	[18-33]	50/38	[18-30]		Stop-change task: 300 ms delay stop – change.	Reaction time	-0.18	RMSSD		
						Olli		Task switching: short delay response - stimulus	Reaction time	-0.294			
								Task switching: long delay response - stimulus	Reaction time	HF eaction time -0.252	HF		
Colzato et	Good	Undergraduate	dergraduate on 22.1 20/60 23.4 Cognitive Task switching Overall index	-0.168		5 min.	Polar H7						
al., 2018	(20)	students		(2.5)		(3.7)	flexibility	Task switching: short delay	Reaction time	-0.295		<b>-</b> 0	
								response - stimulus Task switching: long delay response - stimulus	Reaction time	-0.246	RMSSD		
								Task switching	Overall index	-0.156			
Hansen,		Male sailors						2 hools tools	Correct responses	0.23			
Johnsen, & Thayer, 2003	Good (19)	from the Royal Norwegian		-	- UWM	2-back task	Error rate Miss responses	0.22 -0.24	RMSSD	5 min.	AMS		
	(19)	Navy						Continuous performance test	Error rate	-0.23			

	Quality			Populat	ion			<b>Executive functioning</b>		Pearson'	HR	HRV recording		
Study	NIH (Strobe)	Туре	n	Age*	Men/Women BMI*		Function	Assessment	Outcomes	rearson r		Length	Device	
Kaufmann et al., 2012	Fair (20)	Undergraduate students	34	26.3 (6.1) [18-44]	16/18	-	Cognitive inhibition	Visual P300 spelling matrix	Accuracy score Accuracy score Accuracy score	0.51 0.24 0.40	RSA RMSSD HF	5 min.	ECG	
Keen, Tan, & Abbate, 2020	Good (23)	Undergraduate students	92	20.32 (2.28)	25/67	25.66 (6.52)	Global executive functioning	Berg Card Sorting Test	Completion speed Correct responses	-0.40 -0.40	RMSSD	5 min.	AMS	
				30.6				C	Total errors	0.41				
Mathewson et al., 2010	Good (21)	Young adults	76	(11) [18-55]	33/43	<u>-</u>	Cognitive inhibition	Pictorial Stroop task	Reaction times	-0.245	RSA	6 min.	ECG	
Ottaviani et al., 2019	Good (22)	Young adults	50	24.2 (4.0) [19-40]	19/31	22.5 [< 30]	Cognitive flexibility Cognitive inhibition	Rule Shift Card Hayling Sentence Completion Test	Reaction times Reaction times Reaction times	-0.42 -0.28 -0.30 -0.29	RMSSD HF RMSSD HF	5 min.	Bodygu ard 2	
Spangler et al., 2018	Good (20)	Undergraduate students	83	18.9 (1.4)	23/60	22.85 (3.22)	Cognitive inhibition	Stroop task	Accuracy score Reaction time SD of reaction times	0.26 -0.08 -0.11	RMSSD	5 min.	ECG	
						JOJIN	Cognitive flexibility	Trail Making Test b	Completion speed	-0.246				
							UWM UWM	2-back task 2-back task	Accuracy score Reaction time	0.119 -0.076				
							Cognitive inhibition	Stroop task	Reaction time	-0.247	RMSSD			
							Cognitive inhibition	Stroop-shifting task	Reaction time	-0.222				
Stenfors et al., 2016	Good (20)	Working adults	119	48.0 (10.5)	94/25	-	UWM UWM	Reading span Letter Digit Substitution test	Span score Accuracy score	0.027 0.177		5 min.	ECG	
ui., 2010		adaits		[25-66]			Cognitive flexibility	Trail Making Test b	Completion speed	0.035				
							UWM UWM	2-back task 2-back task	Accuracy score Reaction time	-0.014 0.040				
							Cognitive inhibition	Stroop task	Reaction time	-0.111	HF (Hz)			
							Cognitive inhibition	Stroop-shifting task	Reaction time	-0.085				
							UWM	Reading span	Span score	-0.01				

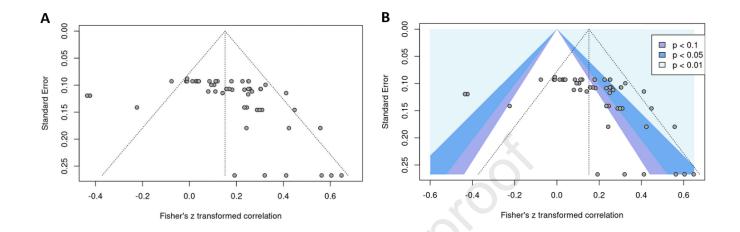
	Quality		Population Executive functioning					Pearson' HR		IRV recording			
Study	NIH (Strobe)	Type	n	Age*	ge* Men/Women BMI*		Function	Assessment	Outcomes		Index	Length	Device
							UWM	Letter Digit Substitution test	Accuracy score	0.013			
Williams,				10.25		_			Accuracy score	0.093			_
Thayer, & Koenig, 2016	Fair (19)	Undergraduate students	e 104	19.25 (1.4) [18-25]	56/48	-	Cognitive inhibition	Modified Flanker task	Reaction time	-0.105 -0.313	HF	5 min.	ECG
								Wodified Flanker task	SD of reaction times		ш	J IIIII.	LCO
Williams et al., 2019	Good (24)	Undergraduate	79	27.5 (6.5)	25/54	25.4 (5.5)	Global executive functioning	Delis-Kaplan Executive Function System	Composite score	0.39	HF	5 min.	ECG
ai., 2019	(24)	students		[20-45]		[17-44]	UWM	WAIS: Working Memory Composite	Composite score	0.14			
Xing, Lü, & Wang, 2020		Undergraduate students	132	18 (0.77)	50/82	-	Cognitive inhibition	Go/No-Go	Accuracy score	-0.01	RSA	5 min.	ECG

*Note*: **N**: sample size, **NIH**: national institutes of health, **SD**: standard deviation, **BMI**: body mass index, **UWM**: updating in working memory, **WAIS**: wechsler adult intelligence scale, **HRV**: heart rate variability, **RMSSD**: root mean square of successive differences, **HF**: high frequency band spectrum of heart rate variability (0.15-0.40 Hz), **RAS**: respiratory sinus arrhythmia, **ECG**: electrocardiogram, **AMS**: ambulatory monitoring system **NA**.: data not available.

<sup>\*</sup> mean, (SD) or [Range].



**Fig. 2**. Summary bias risk of included articles using the NIH Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies.

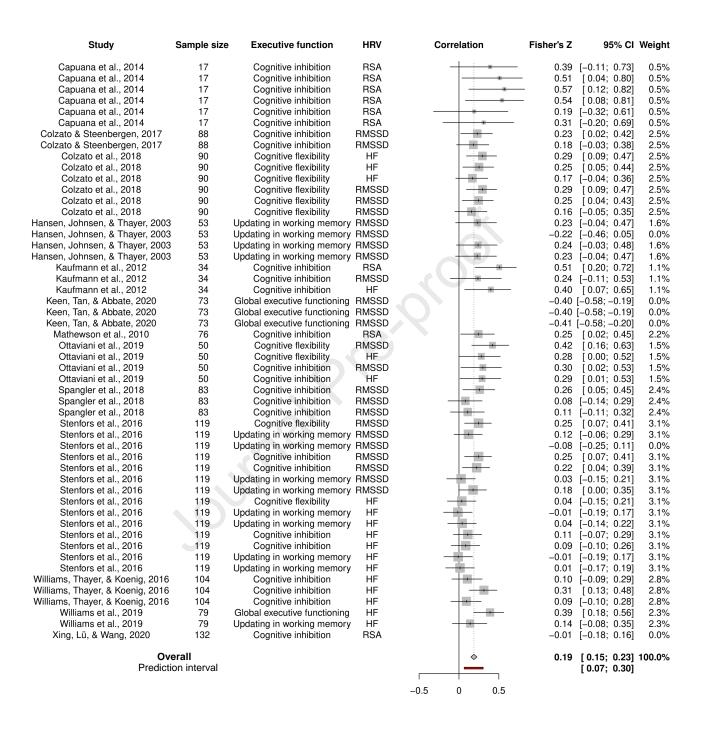


**Fig. 3**. Funnel plots A and B (contour-enhanced) illustrate the individual effect sizes on the horizontal axis and corresponding standard errors on the vertical axis for the initial model. Visual inspection of plots may indicate possible asymmetry emphasized by 6 studies outside of the idealized funnel-shape centered on the summary effect size (A) including 4 in high significance (p < 0.01; B).

**Table 2**Sensitivity analysis describing the initial meta-analysis model and the model characteristics after outliers removal (as recommended by Harrer et al., 2021b).

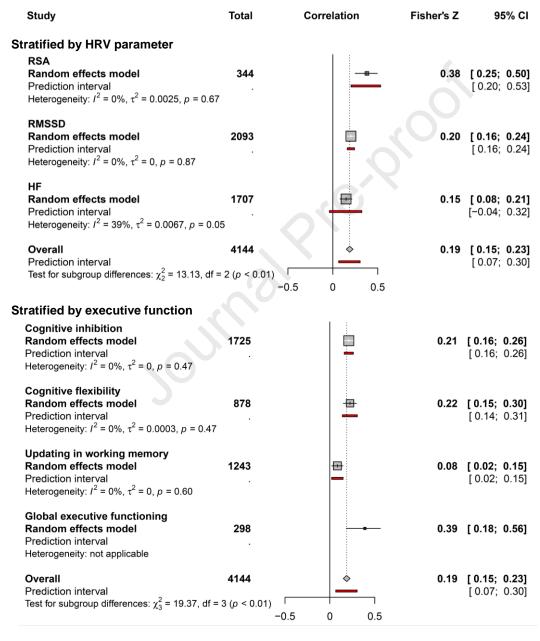
Analysis	k	ES	95 % CI	p	$I^2$	95 % CI
Initial model	52	0.15	0.09- 0.21	< 0.0001	65 %	53-74
Influential cases removed	46	0.19	0.15- 0.23	< 0.0001	21%	0-46

Note: CI: confidence interval, ES: summary effect size, p: p-value,  $I^2$ : Higgins & Thompson's  $I^2$  statistic reflecting the variance in effect size estimates due to true variation among studies. k: number of effect sizes included in meta-analysis.



**Fig. 4**. The relationship between vagally-mediated HRV and executive functioning. Fisher's Z point estimates are depicted by filled grey squares, with square sizes indicating the relative weight of each study's effect size estimates in the analysis with influential cases removed. Each line corresponds to the ES between an HRV index and a cognitive measure. The filled diamond reflects the overall summary effect size (Fisher's Z = 0.19, 95% CI 0.15 to 0.23, p < 0.0001,  $I^2 = 21$  %) and

the red line describes the prediction interval. The absence of a filled grey square means the effect size estimate was excluded from the model following sensitivity analysis.



**Fig. 5**. The relationship between vagally-mediated HRV and executive functioning by HRV parameter and by executive function.

*Note*: **HF**: high frequency band spectrum of heart rate variability (0.15-0.40 Hz), **HRV**: heart rate variability, **RMSSD**: root mean square of successive differences, **RSA**: respiratory sinus arrhythmia.

Variables		Coefficient (95% CI) p	o-value
Age, years	0	-0.005 (-0.008 to -0.002)	0.001
Sex, %men	þ	0.000 (-0.002 to 0.003)	0.94
BMI, kg/m2	$\rightarrow$	0.01 (-0.04 to 0.07)	0.65
Quality, NIH score ——————		-0.03 (-0.09 to 0.03)	0.34
Year of publication	-	0.00 (-0.01 to 0.01)	0.63
-0.09	0	0.09	

**Fig. 6**. Visual representation of meta-regression models describing the impact of possible moderators on effect size. The solid black lines in plots represent the standard deviation of the regression coefficient ( $\beta$ ; corresponding to the white circle).

*Note*: Age and sex distribution were included in the same regression model because they negatively correlated (r = -0.52, p < .001).