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

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1 Abstract

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.

15

16 Keywords: Autonomic nervous system, vagal tone, cognition, psychophysiology, embodied brain17

18 Introduction

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).

Bidirectional interactions between the autonomic and central nervous systems, primarily mediated by the vagus nerve, are predicted by the neurovisceral integration model (Thayer et al., 2009). According to this model, the functioning of the autonomic nervous system is an index of an organism's self-regulatory capacities, promoting flexibility and adaptability in a changing environment (Thayer & Lane, 2000). The primary marker of self-regulation is the vagal inhibition of the heart, which can be assessed by recording the naturally occurring fluctuation in time intervals 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).

Indeed, vagally-mediated resting-state HRV is associated with activity in several neural networks, including brain areas involved in emotion processing (e.g., amygdala), visceral integration (e.g., insular cortex), attentional and memory processes (e.g., prefrontal cortex, see Thayer et al., 2009).
For example, with respect to emotional processing, recent evidence shows that autonomic activity may play a causal role in emotional responses, in which afferent signals from vagal activity precede 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 Executive functioning, being relatively malleable (Hsu et al., 2014), could be influenced by vagal 90 activity, as vagally-mediated HRV is a marker of self-regulatory abilities (Thayer et al., 2012). Yet, 91 the magnitude, robustness, and mechanisms involved in the association between HRV and 92 executive functioning remain unclear. For instance, several methodological issues have been 93 identified to explain the inconsistency of the results such as the lack of control for sexual 94 dimorphism (likely to influence autonomic responses, see Koenig & Thayer, 2016), the high 95 variability of the data attributable to different methodological procedures and study designs, and 96 executive functions have not previously been assessed in detail (Forte et al., 2019). Moreover, 97 inhibition is considered as a common executive factor, underlying the performance in all executive 98 function tasks (Miyake & Friedman, 2012). As the neuro-integration visceral model (Thayer et al., 99 2009) predict that HRV is associated with executive functioning, if cognitive inhibition is the core 100 component of executive functions (Miyake & Friedman, 2012), then HRV might be more strongly 101 associated with some executive component rather than others. In the same way, some HRV 102 measurements have been described to reflect not only vagal activity but also sympathetic activity 103 (Berntson et al., 2005). If vagal activity is associated with executive functioning, then the HRV 104 measurements reflecting both vagal and sympathetic activity should be less predive of executive 105 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.

120

121 Materials & Methods

122 Throughout the meta-analytic process, we followed the recommendations of the Preferred 123 Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA, see Liberati et al., 2009; 124 Moher et al., 2009) statement and recent recommendations for conducting correlational meta-125 analyses (Quintana, 2015).

126 Systematic literature search

127 A systematic literature search was performed to identify studies reporting on vagally-mediated 128 resting-state HRV in association with executive functioning. Only studies assessing the three main 129 components of executive functioning (i.e., cognitive flexibility, updating in working memory, and 130 cognitive inhibition, see(Miyake et al., 2000)) either in a composite task or separately and that used 131 time- or frequency-domain measures or RSA to extract vagally-mediated HRV were included. A 132 broad search strategy (Supplementary material 1) was formulated and employed a combination of 133 keywords: (cognit* OR neuropsycholog* OR "executive function*" OR "cognitive inhibition" OR 134 "cognitive flexibility" OR "updating of working memory") AND (HRV OR "heart rate variability" 135 OR "vagal tone" OR "vagal activity") in PsycINFO, PubMed, Embase, ScienceDirect and

136 Cochrane library. The following constraints were applied to limit search results: (1) articles on 137 adults (>18 years), (2) written in English, and (3) original research articles (excluding reviews and 138 meta-analysis). Identical search terms were employed in all database searches. For some databases 139 (e.g. ScienceDirect) that have a limitation on the number of keywords used in the search equation, 140 we had to adapt the search equation to use all terms from the main equation. In addition, the 141 reference lists of included publications identified through database searches were screened for 142 additional relevant articles. Searches were conducted on July 9, 2021, to May 31, 2022 (for 143 additional articles). Two authors (Valentin Magnon, Guillaume Vallet) conducted the literature 144 searches, reviewed the abstracts, and based on the selection criteria, decide on d the suitability of 145 the articles for inclusion, and extracted the data. When necessary, disagreements were solved with a third author (Frédéric Dutheil). 146

147 Inclusion of eligible studies

148 We included only correlational studies in the current systematic review and meta-analysis to 149 control the issue of the variability of study designs and methodological procedures previously 150 identified (Forte et al., 2019). To be included, studies needed to report a correlation analysis 151 between vagally-mediated resting-state HRV (i.e., RMSSD, RSA, or HF) and performance on tasks 152 evaluating executive functioning in healthy adults. Studies reporting regression analyses were 153 included only if vagally-mediated resting-state HRV was the main predictor of executive 154 functioning as a dependant variable and if the effect size (ES) was stated. Procedures of extraction 155 of HRV from inter-beat interval data and analyses were carried out in accordance with the approved 156 recommended guidelines for assessing HRV variables in psychophysiological research (Laborde 157 et al., 2017; Quintana & Heathers, 2014; Task Force Report, 1996).

158 Data extraction and management

159 ES and sample sizes were extracted from eligible studies. When data were not provided, the 160 corresponding author of the publication was contacted. By using a digital data extraction sheet, the 161 following data were extracted if available: general information and identifying features of the study 162 (full reference, author names, the journal, and year of publication), descriptive data (sample 163 population, size, age, sex and body mass index as it was the most frequently controlled variable 164 provided), measures of executive functioning (neuropsychological test used and corresponding 165 executive component assessed, main outcomes, reaction times, error rate, accuracy or composite 166 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). 167

168 Study quality assessment

169 The risk of bias was defined as a measure of risk for a biased estimation of the association between 170 vagally-mediated HRV and executive functioning. As there are few reliable and validated tools 171 available to appropriately assess the risk of bias in included correlational studies, we relied on two 172 assessment tools for greater validity. Therefore, to assess the quality and possible risk of bias in 173 correlational studies, we used the National Institutes of Health (NIH) Quality Assessment Tool for 174 Observational Cohort and Cross-Sectional Studies (Ma et al., 2020; National Institutes of Health, 175 2014) in combination with the Strengthening the Reporting of Observational Studies in 176 Epidemiology (STROBE) guidelines (Vandenbroucke et al., 2007). The quality of a study was 177 considered poor, fair, or good when the study met less than 5, between 5 and 8, and more than 8 of 178 the NIH Quality Assessment Tool criteria, respectively (Supplementary material 2). As the 179 STROBE checklist is not strictly speaking a risk of bias assessment tool (Costa et al., 2011), it was 180 used to corroborate the NIH Quality Assessment Tool criteria.

181 Statistical analysis

Statistical analysis were performed with RStudio software version 3.6.3(RStudio Team, 2020), using the *meta*(Schwarzer, 2021), *metafor*(Viechtbauer, 2021), and *dmetar*(Harrer et al., 2021a) R packages. Raw ES were transformed to Fisher's *z* for variance stabilization (Harrer et al., 2021b). A random effects model(DerSimonian & Kacker, 2007; Higgins et al., 2009), where betweenstudies variance (τ 2) was estimated using a restricted maximum likelihood method as recommended for continuous outcomes(Veroniki et al., 2016), was used in the synthesis of individual ES into a summary ES.

In order to test whether a specific HRV measurement better predicted executive functioning than other measures and if a specific executive function was predicted more by vagally-mediated HRV than the others, we performed subgroup meta-analyses according to vagally-mediated HRV parameters (RMSSD *vs.* HF *vs.* RSA) then according to executive functions (cognitive functioning *vs.* cognitive inhibition *vs.* updating in working memory *vs.* global composite executive score) 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.

203 For all statistical analyses, the employed statistical significance threshold was set at p < 0.05. To 204 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 & 205 Thompson, 2002) were computed. I^2 values of ~25%, ~50%, and ~75% were interpreted as low, 206 207 moderate, and high heterogeneity between studies(Higgins et al., 2003). A Baujat plot (Baujat et 208 al., 2002) enabled the detection of ES which overly contribute to the heterogeneity in order to 209 remove them if heterogeneity > 50%. Furthermore, in order to identify potential ES outliers, outlier 210 diagnostics were performed (Viechtbauer & Cheung, 2010). Next, the conventional Egger's 211 regression test was applied (Egger et al., 1997) to investigate whether the presence of small-study 212 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 213 likelihood of a publication bias as well (Schmucker et al., 2014). Funnel plots traditionally illustrate 214 215 the distribution of ES estimates by their standard errors including an idealized funnel-shape 216 centered on the summary ES. Contour enhanced funnel plot superimposes key areas of statistical 217 significance (p = 0.1, p = 0.05, p = 0.01) to assess for risk of publication bias (indicated by over-218 representation of ES in areas of significance). When there is no publication bias, studies should 219 roughly follow the shape delineated by the funnel displayed in the plot and the data points should 220 form a roughly symmetrical, upside-down funnel(Harrer et al., 2021a). However, asymmetry of 221 the funnel plot can be caused by very different mechanisms, and should not be readily attributed to 222 publication bias(Doleman et al., 2020). Once the outliers were removed, the meta-analysis was 223 conducted again, along with subgroup analyses and meta-regressions.

224

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

All studies have been assessed as either fair (Capuana et al., 2014; Colzato & Steenbergen, 2017; Kaufmann et al., 2012; D. P. Williams et al., 2016) or good quality(Colzato et al., 2018; Hansen et al., 2003; Keen et al., 2020; Mathewson et al., 2010; Ottaviani et al., 2019; Spangler et al., 2018; Stenfors et al., 2016; P. G. Williams et al., 2019; Xing et al., 2020) based on the validated NIH Quality Assessment Tool (Fig. 2). This was further supported by the STROBE checklist according to which all studies presented overall good quality (scores $\geq 19/27$).

241

242 Characteristics of population

The total number of participants included was 998: 411 men (41%) and 587 women (59%). The proportion of men varied from 21% (Stenfors et al., 2016) to 100% (Hansen et al., 2003). The mean age of participants was 24.6 years old ranging from 18(Xing et al., 2020) to 48 years old (Stenfors et al., 2016). Nine studies were conducted on undergraduates students (Capuana et al., 2014; 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/m² 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 260et 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

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 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

271 for RMSSD (p < 0.01) and HF (p < 0.01). ES for RSA were larger than for RMSSD (p < 0.05). HF 272 did not differ from RMSSD (p = 0.42) and HF was marginally smaller than RSA (p = 0.09). 273 Another subgroup analysis based on executive functions indicated positive small ES for cognitive 274 inhibition (p < 0.001) and cognitive flexibility (p < 0.001), a negative ES for global executive 275 functioning (p < 0.05) and no significant ES for working memory (p = 0.16). ES significantly 276 differed across executive functions ($Q_b(3)$ = 19.86, p = 0.0002). ES for cognitive inhibition were 277 significantly larger than ES for global executive functioning (p < 0.001) and working memory (p278 < 0.001) whereas they did no differ from ES for cognitive flexibility (p = 0.78). Similarly, ES 279 estimates for cognitive flexibility were significantly larger than ES for global executive functioning 280 (p < 0.001) and working memory (p < 0.05). ES were also larger for working memory than for 281 global executive functioning (p < 0.01). The small number of ES (k = 4) and high heterogeneity $(I^2 = 92\%)$ for global executive functioning severely limits the interpretation of the results for this 282 283 subgroup. There was no evidence of an interaction term between HRV parameters and executive functions (F(3, 43) = 0.52, p = 0.67) (see all statistical details in Supplementary material 3). 284

285

286 Sensitivity analyses

The Egger's test was significant (p = 0.01). Furthermore, the chi-square Q-statistic (Cochran's Q 287 288 test for heterogeneity) exceeded the level of significance ($Q_{51} = 146.1, p < 0.0001$) assuming that 289 variation in ES estimates was not caused by sampling error alone. Therefore, 65 % of the variance 290 in ES estimates was due to true variation among studies rather than mere sampling error. Since it 291 assumes that more than half of the variation was due to true ES differences(Higgins & Thompson, 292 2002), outlier diagnostics were performed. Six ES from 4 studies (Hansen et al., 2003; Keen et al., 293 2020; Stenfors et al., 2016; Xing et al., 2020) were distributed outside of the idealized funnel-shape 294 centered on the summary ES (Fig. 3) and were removed from further analyses. The meta-analysis

conducted without outliers confirmed a positive correlation between vagally-mediated HRV and 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 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 ($k=8, \beta=$ 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 ($k = 18, \beta = 0.14$, 303 95% CI 0.09 to 0.19, SE = 0.03, p < 0.0001). ES estimates for RSA were larger than for HF (β = 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 (β 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 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

319 Impact of other possible moderators on effect size

A Meta regression analysis model revealed that age negatively influenced ES (β = -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 (β = 0.0001, 95% CI -0.002 to 0.003, SE = 0.001, *p* = 0.94). BMI did not influence effect size either (β = 0.01, 95 % CI -0.04 to 0.07, SE = 0.03, *p* = 0.65). In addition, meta-regression analysis revealed that neither study quality (β = -0.03, 95 % CI -0.09 to 0.03, SE = 0.03, *p* = 0.34) nor year of publication (β = -0.003, 95 % CI -0.01 to 0.01, SE = 0.01, *p* = 0.63) influenced effect size (Fig 6).

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328 Discussion

329 The objective of the present systematic review and meta-analysis was to provide a better 330 understanding of how HRV might be related to executive functioning. A small positive correlation 331 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 336 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, 338 and the age of the participants.

339 Moderating effect of vagally-mediated HRV parameters

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

between HF or RMSSD and executive functioning was significantly smaller. From a theoretical 342 343 standpoint, one possible explanation is that RSA may be a reliable index of self-regulatory abilities. 344 RSA reflect the respiration-driven increasing and decreasing of the heart, *via* the vagus nerve, made 345 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 346 347 circumstances (spontaneous breathing), RSA may index the adaptation of the vagus nerve to an 348 external factor, i.e. respiration rate, and thus the self-regulatory capacities of the vagus nerve. In 349 this hypothesis, RSA would not reflect vagal activity as such (usually assessed by the power 350 spectrum density of HF band or RMSSD) but rather how well vagal activity is regulated by the 351 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 352 353 synchronizing respiratory and cardiovascular processes during metabolic and behavioral 354 change(Grossman & Taylor, 2007). However, it was noted that, under certain circumstances 355 (longer exhalations allowing greater acetylcholine metabolism), slower respiration rates can 356 produce higher RSA amplitudes that are not mediated by changes in vagal firing(Shaffer & 357 Ginsberg, 2017). As none of the articles included in the present systematic meta-analysis 358 manipulated respiration rate, RSA in those articles should reflect vagally-mediated changes in heart 359 rate. Supporting the importance of changes in vagal activity rather than vagal activity as such, the 360 vagal tank theory (Laborde et al., 2018) suggests that vagal reactivity to, and recovery from, a 361 specific extern event (beyond the influence of respiration rate such as undertaking a cognitively 362 engaging task) are relevant to index self-regulatory abilities.

363 Moderating effect of specific executive functions

364 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, vagally-365 366 mediated HRV correlated more with cognitive inhibition and cognitive flexibility than with 367 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 goal-368 369 directed tasks involving adaptive psychological regulation and flexible cognitive processes 370 (involving cognitive inhibition and cognitive flexibility), whereas tasks inducing mental stress (i.e., 371 working memory tasks) are associated with decreased vagal-mediated HRV(G. Park et al., 2014). 372 More precisely, working memory would require more cognitive engagement resulting in 373 sympathetic predominance to manage mental stress(Duschek et al., 2009). In contrast, tasks 374 involving cognitive inhibition or cognitive flexibility require greater self-regulatory effort associated with parasympathetic activity (G. Park et al., 2014; Segerstrom & Nes, 2007). The 375 376 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 377 378 to this theory, the autonomic nervous system has evolved to promote the focus of attention 379 (sympathetically-driven) in threatening situations and cognitive flexibility processes 380 (parasympathetically-driven) in secure situations to favor social cognition and increase the odds of 381 survival. Taken together, these findings suggest that the adaptability of the vagal inhibitory cardiac 382 control is directly related to adaptative cognitive processes, mainly cognitive inhibition and 383 flexibility.

384 Moderating effect of age

385 The relationship between vagally-mediated HRV and executive functioning may however be 386 influenced by several factors, including age. Specifically, age negatively predicted the strength of 387 this relationship in the studied population ranging from 18 to 66 years old. Middle-aged adults 388 seem to have some difficulties with certain executive functioning tasks(Ferguson et al., 2021). 389 Concurrently, vagally-mediated HRV seems to decrease linearly with age and then the reverse with 390 an increase in those above 60 years old(Geovanini et al., 2020). Concomitant vagal and executive 391 declines support the direct association between vagal activity and prefrontal brain areas involved 392 in executive functioning, which may play a role in cognitive aging (Thayer et al., 2021). In line with 393 the bidirectional heart-brain axis hypothesis, the reverse vagal increase observed after 60 years old 394 might be the physiological compensation mechanism underpinning the greater cerebral activation 395 observed in the prefrontal cortex in older people to achieve equivalent cognitive performances to 396 those of younger adults(Cabeza et al., 2002, 2004). However, the cerebral integration of cardiac 397 information seems to decline with age(Khalsa et al., 2009; Murphy et al., 2018). The insular cortex 398 is a key area in the cerebral integration of visceral signals including those from the cardiovascular 399 system(Aleksandrov & Aleksandrova, 2015; Craig, 2009; Damasio & Carvalho, 2013). Aging is 400 associated with grey matter loss in the insular cortex (Resnick et al., 2003) possibly explaining the 401 decreased strength of the heart-brain bidirectional interactions with age. It has previously been 402 reported that substantial sex differences existed in vagally-mediated HRV(Koenig & Thayer, 403 2016). Specifically, women seem to have lower total power in the spectral density than men and, 404 while women show less power in the very-low and LF bands, they show greater power in the HF 405 band than men. Interestingly, despite greater vagal activity in women, there was no evidence of sex 406 differences in the association between vagally-mediated HRV and executive functioning in the 407 present meta-analysis; suggesting that the physiological mechanisms underlying heart-brain408 interactions might be similar in men and women.

409 Limitations and current challenges

410 Interpretations of the current results must be nuanced as the present systematic meta-analysis is not 411 without limitations. First, the nature of this meta-analysis is correlational, thus no causal 412 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 413 414 limiting the interpretations of the results for those subgroups. Furthermore, we conducted the meta-415 analyses only on published articles, so they are theoretically exposed to a possible publication bias. 416 The few studies conducted on aging populations were not included as older people have very 417 different profiles due to developmental trajectories which could have generated heterogeneity 418 between studies. For instance, as far as vagal activity is concerned, some data indicate that older 419 individuals can linearly maintain high HRV (Tan et al., 2019), others suggest that HRV decreases 420 with age before increasing around 65 years old as a U shape developmental trajectory (Almeida-421 Santos et al., 2016) while others rapport linear decline in HRV with age (Reardon & Malik, 1996). 422 A meta-analysis inherits also the limitations and biases of the individual studies investigated. 423 Indeed, several methodological issues were identified in the included studies through the 424 systematic review process, despite good overall methodological quality following 425 recommendations for conducting research on HRV(Laborde et al., 2017; Quintana & Heathers, 426 2014), with the length of the recording (5-6 min.) adequate for short-term HRV recording(Li et al., 427 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-428 429 Vicente et al., 2021; for a general review see Ishaque et al., 2021). While several studies use ECG

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430 to assess the relationship (through correlations) between heart rate variability and cognitive 431 variables, the directionality of the observed effect remains uncertain. The potential causality in this 432 relationship could be further investigated with other methodologies that require the recording of 433 brain oscillations through electroencephalography (EEG) in addition to the heart activity recording 434 within a framework of mutual influence (Candia-Rivera, Catrambone, et al., 2021). Nonetheless, 435 the small summary ES may reflect that some of the included studies are underpowered. Only two 436 studies (Spangler et al., 2018; Xing et al., 2020) have conducted a priori power analysis(Cohen, 437 2013). Another main issue was that several factors likely to influence either cardiovascular 438 functioning or cognitive functioning or both were not always controlled. Besides age and sex 439 distribution which were always reported, the most controlled and reported variable was body mass 440 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; 441 442 Mathewson et al., 2010; Ottaviani et al., 2019; Spangler et al., 2018; D. P. Williams et al., 2016; 443 P. G. Williams et al., 2019) and caffeine intake(Mathewson et al., 2010; Ottaviani et al., 2019; 444 Spangler et al., 2018; D. P. Williams et al., 2016; P. G. Williams et al., 2019). However, some 445 lifestyle factors that may influence executive functioning or HRV were not considered in the 446 studies included in this review, such as diet(Martínez-Lapiscina et al., 2013; Millman et al., 2021), 447 sleep quality(Bourdillon et al., 2021; Rana et al., 2018) and sedentariness(Magnon, Vallet, et al., 448 2018, 2021; Zaffalon Júnior et al., 2018) recognized as a risk factor independent of physical 449 inactivity(Magnon, Dutheil, et al., 2018; Panahi & Tremblay, 2018). Finally, it is recommended 450 that cognitive function is evaluated by two different measures (Hebben & Milberg, 2009) whereas 451 only one test has often been used to assess a specific executive function in the included studies. 452 Moreover, certain tests might not be the most appropriate for the studied population. For instance, 453 since the 2-back version of the n-back induced a relatively low cognitive engagement level in a

454 young population compared to the 3-back version (Herff et al., 2014), the difficulty might not be 455 high enough for undergraduates students(Dong et al., 2015). The heterogeneity between studies in 456 cognitive measurements might also explain the small effect size of the overall association between 457 HRV and executive performance. One can imagine that if the same tests were used to assess a 458 specific executive function, the association between HRV and executive functioning would have 459 been stronger than the one observed in the present study. Nonetheless, the results of this systematic 460 review and meta-analysis are in line with the neurovisceral integration model(G. Park & Thayer, 461 2014; Thayer et al., 2009) and embodied cognitive sciences (Badcock et al., 2019; Pezzulo & Cisek, 462 2016; Seth, 2013) suggesting that visceral information may underpin executive functioning to some 463 extent. From a clinical perspective, if the heart-brain axis interactions are further empirically 464 supported, breathing exercises are efficient, cheap and simple to increase vagally-mediated 465 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 466 467 cognitive difficulties associated with chronic pathologies and aging.

468 **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.

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

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articles validating their accuracy and reliability as non-standardized recording devices can cloud interpretation and generalizability of findings (Nelson et al., 2020).

480 2. Definition of the HRV measurement used in relation to the research question. Since 481 there is an ongoing debate about the theoretical interpretation of several HRV indices 482 (Berntson et al., 2005; Hayano & Yuda, 2019; Karemaker, 2009), the theoretical definition 483 of the HRV index measured should be defined a priori and clearly stated as well as its 484 relevance for the research question. Furthermore, the formula for calculation of the HRV 485 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^2 , 486 487 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 488 489 studies that investigate a new research question that was not previously addressed since 490 there are no studies on which the power analysis can be based on. However, when previous 491 studies addressing similar research questions exists, a power analysis can be conducted 492 easily using free software such as Gpower (Faul et al., 2009) or the pwr R package 493 (Champely et al., 2020) ensuring sufficient sample size.

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4. Homogeneity of the sample. The target population should be as homogeneous as possible
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depression level, education level, physical activity level, sedentary time, diet, sleep quality
(Quintana & Heathers, 2014).

- 503 5. **Instructions priors to the experimental session**. It is recommended to give prior 504 instructions to refrain the participants from engaging in any behaviors that might affect 505 variables of interest before the experimental session (6 hours before if possible).
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 6. 10 minutes of rest before baseline HRV. We recommend that the participant rest 10
 507 minutes before baseline to ensure resting state HRV is assessed, which is rarely
 508 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).
- 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).
- 520 9. Control of respiration. When RSA or HF is assessed, we recommended to do so in a
 521 resting state without manipulating respiration rate (spontaneous breathing) or by controlling
 522 for respiratory rate. It was suggested that, under certain circumstances, respiration rate
 523 changes can produce large-scale shifts in RSA magnitude without affecting vagal tone
 524 (Shaffer & Ginsberg, 2017).

525 These recommendations can also be applied when studying the role of the heart-brain relationship 526 beyond executive functioning, as it is studied in many other cognitive domains (see Zahn et al., 527 2016). For example, recent studies have addressed the long-standing debate about the role of 528 bodily activity in emotion (Pace-Schott et al., 2019), attempting to propose an answer by showing 529 that autonomic cardiac activity could play a leading and causal role in initiating emotional states 530 (Candia-Rivera, Catrambone, et al., 2021). Interestingly, rather than investigating the role of heart-531 brain interaction in emotion, other studies have recently examined the role of a pre-existing 532 emotional state in the involvement of heart-brain interaction in cognition. For example, induced 533 sadness influences the association between HRV and cognitive inhibition (Hoffmann et al., 2022). 534 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 535 536 and the preparation of an appropriate course of action (Skora et al., 2022). In a broader way, 537 autonomic activity has also been studied in relation to consciousness generation (Candia-Rivera, 538 Annen, et al., 2021), leading to the hypothesis that ascending bodily signals into neural systems 539 could a switch for consciousness (Sattin et al., 2020).

540 Conclusion

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

548 information may underpin executive functioning to some extent. Several methodological issues 549 which may account for the small associations observed in the present meta-analysis were identified 550 and discussed. Future quality studies addressing these methodological issues would be necessary 551 to refine the conclusions drawn from these initial results.

Journal Pre-proof

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- 554 Author contributions. Conceived, designed the study, and wrote the first version of the
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- 556 of eligible articles: All authors. Analysed the data: V.M. and F.D. Materials/analysis tools and
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- 563 Data availability statement
- 564 The data supporting the conclusions of this article are available at: <u>https://osf.io/fuhwt</u>
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Fig. 1. PRISMA Flow Diagram depicting the study selection process.

Table 1

Summary characteristics of included studies.

	Quality			Populat	tion			Executive functioning	5	Pearson'	HR	V record	ding					
Study	NIH (Strobe)	Туре	n	Age*	Men/Wome	n BMI*	Function	Assessment	Outcomes	r	Index	Length	Device					
								Stroop task	Accuracy score	0.39								
								Stroop task (Incentive)	Accuracy score	0.51								
Canuana et	Fair	Vair Undergraduate 23) students		21.1			Cognitive	Memory Stroop task	Accuracy score	0.57								
al., 2014	(23)		17	[18-26]	6/11	-	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	0.31								
Colzato &	Fair	Undergraduate		21.2		22.17	Cognitive	Stop-change task: 0 ms delay stop -	Reaction time	-0.23								
Steenberge n, 2017	(20)	students	students	students	students	students	students	88	[18-33]	50/38	[18-30]	inhibition	Stop-change task: 300 ms delay stop – change.	Reaction time	-0.18	RMSSD	5 min.	Polar H7
			Task switching: short delay Reaction time -0.294 response - stimulus Task switching: long HF delay Reaction time -0.252 response - stimulus ndergraduate 90 22.1 30/60 23.4 Cognitive Task switching Overall index -0.168 students 90 (2.5) 30/60 (2.7) floribility Task switching Start 5															
		Undergraduate						Task switching: long delay response - stimulus	Reaction time	-0.252	HF							
Colzato et	Good			ndergraduate 90	90 $\frac{22.1}{(2.5)}$	30/60	23.4	Cognitive	Task switching	Overall index	-0.168		5 min.	Polar H7				
ul., 2010	(20)	students		(2.3)		(3.7)	nexionity	delay	Reaction time	-0.295								
								Task switching: long delay response - stimulus	Reaction time	-0.246	RMSSD							
								Task switching	Overall index	-0.156								
Hansen,		Male sailors						2 book took	Correct responses	0.23								
Johnsen, & Thayer, 2003	Good (19)	from the Royal Norwegian	n the Royal orwegian 53		$153 \frac{23}{[18-34]}$	53/0	-	UWM	WM	Error rate Miss responses	0.22 -0.24	RMSSD	5 min.	AMS				
		Navy	53				Continuous performance test		Error rate	-0.24 -0.23								

Journal Pre-proof													
	Quality			Populat	tion		Executive functioning			Pearson'	HRV recording		
Study	NIH (Strobe)	Туре	n	Age*	Men/Women	BMI*	Function	Assessment	Outcomes	r	Index	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 Total errors	-0.40 -0.40 0.41	RMSSD	5 min.	AMS
Mathewson et al., 2010	Good (21)	Young adults	76	30.6 (11) [18-55]	33/43	-	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
				48.0		ourt	Cognitive flexibility UWM UWM Cognitive inhibition Cognitive inhibition UWM	Trail Making Test b 2-back task 2-back task Stroop task Stroop-shifting task Reading span	Completion speed Accuracy score Reaction time Reaction time Span score	-0.246 0.119 -0.076 -0.247 -0.222 0.027	RMSSD		
Stenfors et al., 2016	Good (20)	Working adults	119	(10.5) [25-66]	94/25	-	UWM Cognitive flexibility UWM UWM Cognitive inhibition Cognitive inhibition UWM	Letter Digit Substitution test Trail Making Test b 2-back task 2-back task Stroop task Stroop-shifting task Reading span	Accuracy score Completion speed Accuracy score Reaction time Reaction time Span score	0.177 0.035 -0.014 0.040 -0.111 -0.085 -0.01	HF (Hz)	5 min.	ECG

					J	ournal Pre-proof						
Quality		Population				Executive functioning			- Doorson'	HRV recording		
NIH (Strobe)	Туре	n	Age*	Men/Women	BMI*	Function	Assessment	Outcomes	r earson r	Index	Length	Device
						UWM	Letter Digit Substitution test	Accuracy scor	e 0.013			
			10.25					Accuracy scor	e 0.093			
Fair	Undergraduate	104	(1.4)	56/18		Cognitive	Modified Flenker teck	Reaction time	-0.105	UЕ	5 min	ECG
(19)	students	[104 [1	[18-25]	5]	_	inhibition	Woullied Failker task	SD of reaction times	ⁿ -0.313	III	5 mm.	LCO
						Global	Delis-Kaplan	Composite				
Good	Undergraduate		27.5		25.4	executive	Executive Function	score	0.39			
(24)	students	79	(6.5)	25/54	(5.5)	functioning	System	50010		HF	5 min.	ECG
(21)	students		[20-45]		[17-44]	UWM	WAIS: Working	Composite	0.14			
							Memory Composite	score	0.11			
Good (21)	Undergraduate students	132	18 (0.77)	50/82	-	Cognitive inhibition	Go/No-Go	Accuracy scor	e -0.01	RSA	5 min.	ECG
	Quality NIH (Strobe) Fair (19) Good (24) Good (21)	Quality NIH (Strobe)TypeFair (19)Undergraduate studentsGood (24)Undergraduate studentsGood (21)Undergraduate students	Quality NIH (Strobe)TypenFair (19)Undergraduate students104Good (24)Undergraduate students79Good (21)Undergraduate students132	Quality NIH (Strobe)TypenAge*Fair (19)Undergraduate students10419.25 (1.4) [18-25]Good (24)Undergraduate students7927.5 (6.5) [20-45]Good (21)Undergraduate students13218 (0.77)	Quality NIH (Strobe)TypenAge*Men/WomenFair (19)Undergraduate students10419.25 (1.4) [18-25]56/48Good (24)Undergraduate students7927.5 (6.5) [20-45]25/54Good (21)Undergraduate students13218 (0.77)50/82	Quality NIH (Strobe)TypenAge*Men/WomenBMI*Fair (19)Undergraduate students10419.25 (1.4) [18-25]56/48-Good (24)Undergraduate students7927.5 (6.5) [20-45]25/5425.4 (5.5) [17-44]Good (21)Undergraduate students13218 (0.77)50/82-	Journal Pre-proofQuality NIH (Strobe)TypenAge*Men/WomenBMI*FunctionFair (19)Undergraduate students10419.25 (1.4) [18-25]56/48-Cognitive inhibitionFair (19)Undergraduate students10427.5 (6.5) [20-45]56/48-Global executive functioning UWMGood (21)Undergraduate students7927.5 (6.5) [20-45]25/5425.4 (5.5) [17-44]Global executive functioning UWM	Quality NIH (Strobe)TypenAge*Men/WomenBMI*FunctionExecutive functioningNIH (Strobe)TypenAge*Men/WomenBMI*FunctionAssessmentEUUU19.25 (1.4) (18-25]56/48-Cognitive inhibitionModified Flanker taskFair (19)Undergraduate students10419.25 (1.4) (18-25]56/48-Cognitive inhibitionModified Flanker taskGood (24)Undergraduate students7927.5 (6.5) (20-45]25/5425.4 (5.5) (17-44]Global executive functioning (17-44]Delis-Kaplan Executive Function functioning UWMGood (21)Undergraduate students13218 (0.77)50/82-Cognitive inhibitionGo/No-Go	Quality NIH (Strobe)TypenAge*Men/WomenBMI*FunctionAssessmentOutcomesStrobeTypenAge*Men/WomenBMI*FunctionAssessmentOutcomesUWMLetter Digit Substitution testAccuracy scortFair (19)Undergraduate students10419.25 (1.4) [18-25]56/48 (1.4)-Cognitive inhibitionModified Flanker task SD of reaction timesAccuracy scort Reaction time SD of reaction timesGood (24)Undergraduate students7927.5 (6.5) [20-45]25.4 (5.5) [17-44]Global executive functioning UWMDelis-Kaplan Executive Function SystemComposite scoreGood (21)Undergraduate students13218 (0.77)50/82-Cognitive inhibitionGo/No-GoAccuracy scort	Num (Strobe) Population Executive functioning Pearson' of the team of the team of t	Nume result Journal Pre-proof Quality (Strobe) Type n Age* Men/Women BMI* Function Assessment Outcomes r Index (Strobe) Type n Age* Men/Women BMI* Function Assessment Outcomes r Index (Strobe) Undergraduate (19) 104 19.25 (1.4) 56/48 (18-25] $-$ Cognitive inhibition Modified Flanker task (Cognitive inhibition Accuracy score 0.093 (0.013 $ -$	Nume result (Stroke)PopulationExecutive functioning Executive functioningPearson'HRV recordNIH (Stroke)TypenAge*Men/WomenBMI*FunctionAssessmentOutcomes r' IndexLengthStroke) $Type$ nAge*Men/WomenBMI* $TuderLetter DigitSubstitution testAccuracy score0.013r'IndexLengthFair(19)Undergraduatestudents104\frac{19.25}{(1.4)}[18-25]56/48(1.4) CognitiveinhibitionCognitiveinhibitionAccuracy score0.093SD of reactiontimesHF5 min.Good(24)Undergraduatestudents79\frac{27.5}{(6.5)}[20-45]25/4\frac{25.4}{(5.5)}[17-44]GlobalexecutivefunctioningWAIS: WorkingMemory CompositeMemory Compositescore0.39scoreHF5 min.Good(21)Undergraduatestudents13218(0.77)50/82 CognitiveinhibitionGo/No-GoAccuracy score-0.01RSA5 min.$

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.

* 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	р	I^2	95 % CI
Initial model	52	0.15	0.09-	< 0.0001	65 %	53-74
		0.15	0.21	< 0.0001	05 /0	35-14
Influential cases	46	0.10	0.15-	< 0.0001	21%	0.46
removed		0.19	0.23	< 0.0001	2170	0-40

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.

Study	Sample size	Executive function	HRV	Correlation	Fisher's Z	95% CI	Weight
Capuana et al., 2014	17	Cognitive inhibition	RSA		0.39	[-0.11: 0.73]	0.5%
Capuana et al., 2014	17	Cognitive inhibition	RSA		0.51	[0.04: 0.80]	0.5%
Capuana et al., 2014	17	Cognitive inhibition	RSA		0.57	[0.12: 0.82]	0.5%
Capuana et al. 2014	17	Cognitive inhibition	RSA		0.54	[0.08: 0.81]	0.5%
Capuana et al. 2014	17	Cognitive inhibition	RSA		0.19	[-0.32; 0.61]	0.5%
Capuana et al. 2014	17	Cognitive inhibition	BSA		0.31	[-0.20; 0.69]	0.5%
Colzato & Steenbergen 2017	88	Cognitive inhibition	RMSSD		0.23	[0.02:0.42]	2.5%
Colzato & Steenbergen, 2017	88	Cognitive inhibition	RMSSD		0.18	[-0.03; 0.38]	2.5%
Colzato et al., 2018	90	Cognitive flexibility	HF	<u> </u>	0.29	[0.09: 0.47]	2.5%
Colzato et al., 2018	90	Cognitive flexibility	HE		0.25	[0.05: 0.44]	2.5%
Colzato et al., 2018	90	Cognitive flexibility	HE		0.17	[-0.04; 0.36]	2.5%
Colzato et al., 2018	90	Cognitive flexibility	RMSSD		0.29	[0.09: 0.47]	2.5%
Colzato et al., 2018	90	Cognitive flexibility	RMSSD		0.25	[0.04: 0.43]	2.5%
Colzato et al., 2018	90	Cognitive flexibility	RMSSD		0.16	[-0.05; 0.35]	2.5%
Hansen, Johnsen, & Thaver, 2003	53	Updating in working memory	RMSSD		0.23	[-0.04; 0.47]	1.6%
Hansen, Johnsen, & Thaver, 2003	53	Updating in working memory	RMSSD		-0.22	[-0.46: 0.05]	0.0%
Hansen, Johnsen, & Thaver, 2003	53	Updating in working memory	RMSSD		0.24	[-0.03: 0.48]	1.6%
Hansen, Johnsen, & Thaver, 2003	53	Updating in working memory	RMSSD		0.23	[-0.04: 0.47]	1.6%
Kaufmann et al., 2012	34	Cognitive inhibition	RSA		0.51	[0.20: 0.72]	1.1%
Kaufmann et al., 2012	34	Cognitive inhibition	RMSSD		0.24	[-0.11; 0.53]	1.1%
Kaufmann et al., 2012	34	Cognitive inhibition	HF		0.40	[0.07: 0.65]	1.1%
Keen, Tan, & Abbate, 2020	73	Global executive functioning	RMSSD		-0.40	[-0.58: -0.19]	0.0%
Keen, Tan, & Abbate, 2020	73	Global executive functioning	RMSSD		-0.40	[-0.58: -0.19]	0.0%
Keen, Tan, & Abbate, 2020	73	Global executive functioning	RMSSD		-0.41	[-0.58: -0.20]	0.0%
Mathewson et al., 2010	76	Cognitive inhibition	RSA		0.25	[0.02: 0.45]	2.2%
Ottaviani et al., 2019	50	Cognitive flexibility	RMSSD		0.42	[0.16: 0.63]	1.5%
Ottaviani et al., 2019	50	Cognitive flexibility	HF		0.28	[0.00: 0.52]	1.5%
Ottaviani et al., 2019	50	Cognitive inhibition	RMSSD		0.30	[0.02: 0.53]	1.5%
Ottaviani et al., 2019	50	Cognitive inhibition	HF	,	0.29	[0.01: 0.53]	1.5%
Spangler et al., 2018	83	Cognitive inhibition	RMSSD	· · · · ·	0.26	[0.05: 0.45]	2.4%
Spangler et al., 2018	83	Cognitive inhibition	RMSSD		0.08	[-0.14; 0.29]	2.4%
Spangler et al., 2018	83	Cognitive inhibition	RMSSD		0.11	[-0.11; 0.32]	2.4%
Stenfors et al., 2016	119	Cognitive flexibility	RMSSD	— · ·	0.25	[0.07; 0.41]	3.1%
Stenfors et al., 2016	119	Updating in working memory	RMSSD		0.12	[-0.06; 0.29]	3.1%
Stenfors et al., 2016	119	Updating in working memory	RMSSD		-0.08	[-0.25; 0.11]	0.0%
Stenfors et al., 2016	119	Cognitive inhibition	RMSSD		0.25	[0.07; 0.41]	3.1%
Stenfors et al., 2016	119	Cognitive inhibition	RMSSD		0.22	[0.04; 0.39]	3.1%
Stenfors et al., 2016	119	Updating in working memory	RMSSD		0.03	[-0.15; 0.21]	3.1%
Stenfors et al., 2016	119	Updating in working memory	RMSSD		0.18	[0.00; 0.35]	3.1%
Stenfors et al., 2016	119	Cognitive flexibility	HF		0.04	[-0.15; 0.21]	3.1%
Stenfors et al., 2016	119	Updating in working memory	HF		-0.01	[-0.19; 0.17]	3.1%
Stenfors et al., 2016	119	Updating in working memory	HF		0.04	[-0.14; 0.22]	3.1%
Stenfors et al., 2016	119	Cognitive inhibition	HF	-+	0.11	[-0.07; 0.29]	3.1%
Stenfors et al., 2016	119	Cognitive inhibition	HF		0.09	[-0.10; 0.26]	3.1%
Stenfors et al., 2016	119	Updating in working memory	HF		-0.01	[-0.19; 0.17]	3.1%
Stenfors et al., 2016	119	Updating in working memory	HF		0.01	[-0.17; 0.19]	3.1%
Williams, Thayer, & Koenig, 2016	104	Cognitive inhibition	HF		0.10	[-0.09; 0.29]	2.8%
Williams, Thayer, & Koenig, 2016	104	Cognitive inhibition	HF		0.31	[0.13; 0.48]	2.8%
Williams, Thayer, & Koenig, 2016	104	Cognitive inhibition	HF		0.09	[-0.10; 0.28]	2.8%
Williams et al., 2019	79	Global executive functioning	HF		0.39	[0.18; 0.56]	2.3%
Williams et al., 2019	79	Updating in working memory	HF	+=-	0.14	[-0.08; 0.35]	2.3%
Xing, Lü, & Wang, 2020	132	Cognitive inhibition	RSA		-0.01	[-0.18; 0.16]	0.0%
Ove	erall			\$	0.19	[0.15; 0.23]	100.0%
Predicti	on interval					[0.07; 0.30]	
						_	
				-0.5 0 0.5			

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.

Study	Total	Correlation	Fisher's Z	95% CI
Stratified by HRV parameter				
RSA Random effects model Prediction interval Heterogeneity: $I^2 = 0\%$, $\tau^2 = 0.0025$, $p = 0.6$	344		0.38	[0.25; 0.50] [0.20; 0.53]
RMSSD Random effects model Prediction interval Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.87	2093	- 5	0.20	[0.16; 0.24] [0.16; 0.24]
HF Random effects model Prediction interval Heterogeneity: l^2 = 39%, τ^2 = 0.0067, p = 0	1707 .05		0.15	[0.08; 0.21] [-0.04; 0.32]
Overall Prediction interval Test for subgroup differences: χ_2^2 = 13.13, di	4144 f = 2 (p < 0.01	-0.5 0 0.5	0.19	[0.15; 0.23] [0.07; 0.30]
Stratified by executive function				
Cognitive inhibition Random effects model Prediction interval Heterogeneity: $I^2 = 0\%$, $\tau^2 = 0$, $p = 0.47$	1725		0.21	[0.16; 0.26] [0.16; 0.26]
Cognitive flexibility Random effects model Prediction interval Heterogeneity: $I^2 = 0\%$, $\tau^2 = 0.0003$, $\rho = 0.4$	878 7	₽	0.22	[0.15; 0.30] [0.14; 0.31]
Updating in working memory Random effects model Prediction interval Heterogeneity: $I^2 = 0\%$, $\tau^2 = 0$, $p = 0.60$	1243		0.08	[0.02; 0.15] [0.02; 0.15]
Global executive functioning Random effects model Prediction interval Heterogeneity: not applicable	298		0.39	[0.18; 0.56]
Overall Prediction interval Test for subgroup differences: χ_3^2 = 19.37, df	4144 = 3 (<i>p</i> < 0.01)	-0.5 0 0.5	0.19	[0.15; 0.23] [0.07; 0.30]

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-va	alue
Age, years	0	-0.005 (-0.008 to -0.002) 0.0	001
Sex, %men	4	0.000 (-0.002 to 0.003) 0.	94
BMI, kg/m2		- 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	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 (β ; 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).