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Executive functions in older adults with generalised anxiety disorder and healthy controls: Associations with heart rate variability, brain-derived neurotrophic factor, and physical fitness

Kristine Sirevåg[a,b], Silje Haukenes Stavestrand[a,b], Karsten Specht[b,c,d], Inger Hilde Nordhus[b], Åsa Hammar[e,f,g], Helge Molde[b], Jan Mohlman[h], Trygve Bruun Endal[a,i], Anne Halmøy[j,k], Eva Andersson[l,m], Trond Sjøbø[a], Hans M. Nordahl[i], Julian F. Thayer[n] and Anders Hovland[a,b,o]

[a]Solli DPS, Bergen, Norway; [b]Department of Clinical Psychology, University of Bergen, Bergen, Norway; [c]Mohn Medical and Imaging Visualization Centre, Haukeland University Hospital, Bergen, Norway; [d]Department of Education, UiT/The Arctic University of Norway, Tromsø, Norway; [e]Department of Biological and Medical Psychology, University of Bergen, Bergen, Norway; [f]Department of Clinical Sciences, Faculty of Medicine, Lund University, Lund, Sweden; [g]Office for Psychiatry and Habilitation, Psychiatry Research Skåne, Region Skåne, Sweden; [h]William Paterson University, Wayne, NJ, USA; [i]Department of Mental Health, Norwegian University of Science and Technology, Trondheim, Norway; [j]Department of Psychiatry, Haukeland University Hospital, Kronstad DPS, Bergen, Norway; [k]Department of Clinical Medicine, University of Bergen, Bergen, Norway; [l]The Swedish School of Sport and Health Sciences, Stockholm, Stockholm, Sweden; [m]Department of Neuroscience, Karolinska Institute, Stockholm, Sweden; [n]The Ohio State University, Columbus, OH, USA; [o]Helse Fonna Hospital Trust, Haugesund, Norway

ABSTRACT

Executive functions (EF) decline with age and this decline in older adults with generalised anxiety disorder (GAD) may be influenced by heart rate variability (HRV), brain-derived neurotrophic factor (BDNF), and physical fitness. Understanding these relationships is important for tailored treatments in this population. In this study, 51 adults with GAD (*M* age = 66.46, *SD*=4.08) and 51 healthy controls (*M* age = 67.67, *SD*=4.04) were assessed on cognitive inhibition (Stroop task), shifting (Trails part 4), flexibility (Wisconsin Card Sorting Test – Perseverative errors), working memory (Digit Span Backwards), IQ (Wechsler Abbreviated Scale of Intelligence), high frequency HRV, serum mature BDNF levels, and VO_2 max. Results indicated that participants with GAD exhibited better cognitive inhibition compared to controls, with no general reduction in EF. Cognitive inhibition was predicted by gender, HRV, and BDNF levels, while cognitive shifting was predicted by gender and IQ, and cognitive flexibility and working memory by IQ. The enhanced cognitive inhibition in GAD participants might stem from maladaptive use of this function, characteristic of GAD, or protection from EF decline due to normal HRV. Increased BDNF levels, possibly due to good fitness, or compensatory mechanisms related to the disorder, might also play a role. These findings highlight the complexity of EF and related mechanisms in GAD, highlighting the need for interventions that consider both cognitive and physiological factors for optimal outcomes.

KEYWORDS

Brain-derived neurotrophic factor; executive functions; generalized anxiety disorder; heart rate variability

Introduction

Anxiety disorders in older age are associated with a decline in cognitive functions (Kassem et al., 2017; Perna et al., 2016). The executive functions (EF) are cognitive functions involved in goal-directed systems giving us the ability to overcome habits, weigh benefits and costs, prioritize goals, decide strategically, and respond adaptively (Zainal & Newman, 2018), abilities that have been shown to decline with increasing age (Buckner, 2004). The verbal-linguistic content of worry, the key characteristic of generalised anxiety disorder (GAD; American Psychiatric Association, 2013) is associated with EFs such as cognitive inhibition, shifting/flexibility, and working memory (Eysenck & Derakshan, 2011; Hirsch & Mathews, 2012; Miyake et al., 2000). According to the Attentional Control Theory, which states that anxiety interferes with attentional control in managing cognitive tasks under stress, one would expect anxiety to have a negative effect on EF (Eysenck et al., 2007). In a large sampled study, Gulpers et al. (2022) found that high scores on the Generalized Anxiety Disorder – 7 scale (Spitzer et al., 2006) was associated with worse scores on processing speed and increased risk of cognitive impairment. Additionally, reduced EFs in older adults is associated with increased risk of falls (Hsu et al., 2012) and poorer treatment outcome of cognitive behavior therapy for GAD (Mohlman, 2013). Research show that EFs are related to

CONTACT Kristine Sirevåg kristine.sirevag@solli.no Solli DPS, Osvegen 15, Bergen, Norway.
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both psychophysiological and biological factors such as heart rate variability (HRV) and the Brain Derived Neurotrophic Factor (BDNF).

Higher high-frequency (HF) HRV is associated with parasympathetic activation and is considered an expression of vagal activity and self-regulatory mechanism and adaptability (Magnon et al., 2022; Thayer & Lane, 2000). Furthermore, correlations, although small, between HF HRV and EF were found in a systematic review by Magnon et al. (2022). Specifically, stronger associations were found for HRV and cognitive inhibition and cognitive flexibility, and weaker or non-existing associations were found for HRV and working memory. The authors discuss that the cognitive process of inhibition and flexibility might rely more heavily on self-regulatory mechanisms involved in parasympathetic activity, and that working memory on the other hand is more affected by stress and sympathetic activation. Psychological stress, where challenges exceed the individual's ability to cope, is related to premature aging (Thayer et al., 2021), and thus one could hypothesize that the stress associated with GAD would be relevant. Also, an early study by Thayer et al. (1996) found that adults ($M = 35.6$ years, $SD = 10.2$) with GAD had significantly lower HRV when in an acute bout of worry and lower baseline HRV levels than healthy controls. The same results were found in a meta-analysis on anxiety disorders and HRV (Chalmers et al., 2014). In summary, it appears that higher HF HRV is associated with better cognitive inhibition and flexibility due to enhanced self-regulation via parasympathetic activity, while working memory is more affected by stress, and individuals with GAD tend to have lower HRV, particularly during acute worry and at baseline.

It is of importance to find means to improve EF. A low-cost intervention with important general health effects is physical exercise, which are associated with EF through physical fitness. There are robust findings showing that better physical fitness is related to increased EF in older adults (Berryman et al., 2013; Colcombe & Kramer, 2003; Kramer et al., 2006), and that reduced physical fitness is associated with a decline in EF in later life (Monteiro-Junior et al., 2022). Furthermore, several meta-analyses (Chen et al., 2020; Colcombe & Kramer, 2003; Xiong et al., 2021) have found that regular physical exercise is related to improved working memory, cognitive flexibility, and cognitive inhibition in healthy older adults, with small to medium effect sizes. Previous findings suggest that physical exercise influences EF through a mediating effect of physical fitness via neurophysiological mechanisms, including BDNF levels (Erickson et al., 2011).

Mature BDNF is a neurotrophin associated with synaptogenesis and neurogenesis and has been shown to exert protective effects on brain health (Sharma et al., 2023) which makes it a relevant mechanism to investigate when exploring cognitive functioning. BDNF is also related to the preservation of EF (Leckie et al., 2014) influenced by physical fitness (Inoue et al., 2020; Kaur et al., 2016). In a study of adolescents, BDNF was linked to the prediction of cognitive functioning through interaction with physical exercise (Lee et al., 2014). Also Alizadeh and Dehghanizade (2022), in an investigation of functional training on BDNF and cognitive functions in women with obesity, concluded that BDNF plays an important role in the interplay between physical exercise and the effect on the brain and its functions. Normalization of EF in a sample of patients with major depressive disorder was found after treatment with antidepressant medication, related to changes in BDNF levels (Wagner et al., 2019). The studies on the associations between BDNF and EF vary in methodology both related to cognitive outcome measures and whether BDNF is measured in serum or plasma. However, a general tendency toward improvement of EF as an interaction effect of physical exercise and BDNF levels in diverse populations has been found.

Despite this background, the knowledge on associations between EF, HRV, BDNF and physical fitness in older adults with GAD are scarce. To improve treatment outcome and adjust treatment according to the EF in this group, it is of importance to investigate these potential associations. The research background on cognitive inhibition shows both decreased (Hallion et al., 2017) and increased function (Price & Mohlman, 2007) associated with GAD, and thus we explore this hypothesis tentative. We furthermore expect the EF shifting, flexibility, and working memory to be reduced in older adults with GAD compared to healthy controls. Furthermore, we expect better EF to be predicted by higher HRV and better physical fitness independently of the diagnostic group. As the literature and previous research on BDNF and EF in the population of interest are scarce, these hypotheses are tentative.

Methods

Design

The current study is a part of the randomized controlled trial *Physical exercise augmented cognitive behavior therapy for older adults with generalized anxiety disorder* (the PEXACOG study, ClinicalTrials.gov NCT02690441; Stavestrand et al., 2019). The data for the current study is a part of the baseline measurements of the patient group and healthy control group in PEXACOG.

Participants

Inclusion criteria for the patient sample were: Age between 60 and 75 years and having a primary diagnosis of GAD as determined by the M.I.N.I. Neuropsychiatric Interview (Lecrubier et al., 1997; Sheehan et al., 1980) and Anxiety Disorders Interview Schedule for DSM-IV (ADIS-IV; DiNardo et al., 1994). The inclusion age criteria were the same for the healthy control group, in addition to not having a history of mental illness. Exclusion criteria for both participants with GAD and healthy controls were: (1) substance abuse; (2) use of benzodiazepines and antipsychotic medication; (3) changes in the dose of other psychotropic medication during the study; (4) medical conditions that preclude participation in physical testing/exercise; (5) severe major depression as determined by the M.I.N.I.; (6) life-time

history of psychosis and/or mania; (7) participation in other ongoing psychotherapy; (8) organic brain disease; (9) a score of 25 or less on the Mini Mental State Examination (MMS-E; Folstein et al., 1975), and (10) physical exercise of moderate intensity of 60 min or more of two or more sessions per week during an average week for the last three months.

Procedure

Participants met with a trained clinical psychologist twice for assessment of eligibility. If eligible, they signed a consent for participation and had a medical evaluation to ensure safety on participating in physical tests. The testing was distributed across two days (Refer to Figure 1). On the first test day, a trained test technician performed the neuropsychological testing with the participants. The second test day, participants underwent ECG for measuring HRV, blood samples for measuring serum BDNF levels, and a submaximal ergometer cycle test to estimate physical fitness (VO_2 max) levels.

Materials

Neuropsychological tests

The executive outcome measures cognitive inhibition and shifting were assessed with two tests from the Delis-Kaplan Executive Function System battery (D-KEFS; Delis et al., 2001). Condition three, the Stroop task (Stroop, 1935), of the Color-Word Interference Test (CWIT) was used to measure cognitive inhibition. In this task, participants are asked to scan color words that are typed with both congruent and incongruent colors. It is assumed that naming the ink of an incongruent color word is harder than to name the ink of a congruent color word. The performance on the Stroop task is measured in seconds used to complete the task, and hence a lower score indicates better cognitive inhibition than a higher score. Trail Making Test Condition Four (TMT; Delis et al., 2001) from D-KEFS was used to measure cognitive shifting, the ability to change attention when appropriate. In the task, participants are asked to draw a line between sequential numbers and letters, e.g., 1 – A – 2 – B – 3 – C and so forth. The performance on the TMT is measured in seconds used to complete the task, and a lower score indicates better cognitive shifting abilities than a higher score.

Working memory was measured by Numbers – Digit Span Backwards where the participants are asked to repeat an increasing number of digits, arranging them in a backward direction. A higher score indicates more numbers remembered in a backwards sequence, and hence a better working memory than a lower score. In addition, the Wisconsin Card Sorting Test: Computer Version 4 research edition (WCST; Heaton et al., 2003) perseverative errors measured cognitive flexibility as a response to changing conditions. In this task participants are asked to sort cards after specific rules, and as these rules changes, participants are demanded to change their strategy. Perseverative errors are the number of persistent errors the participant is doing based on the previous rules in the card sorting, and hence a higher score indicates more perseverative errors than a lower score.

We used the subtests Matrix reasoning and Vocabulary from the Wechsler Abbreviated Scale of Intelligence to obtain an estimate of total IQ (Wechsler, 2011).

Electrocardiogram for measure of heart rate variability (HRV)

HRV was measured by a three-lead electrocardiogram with an ambulatory monitoring system in a recording session that lasted for 14 minutes. The ECG sampling rate was 1,000 Hz, and the data were collected with Ambu® BlueSensor VLC ECG Electrodes. One electrode was placed in position midway between and below V1; the fourth intercostal space to the right of the sternum, and V2; the fourth intercostal space to the left of the sternum. The other electrode was placed at V4; the fifth intercostal space in line with the middle of the clavicle. The

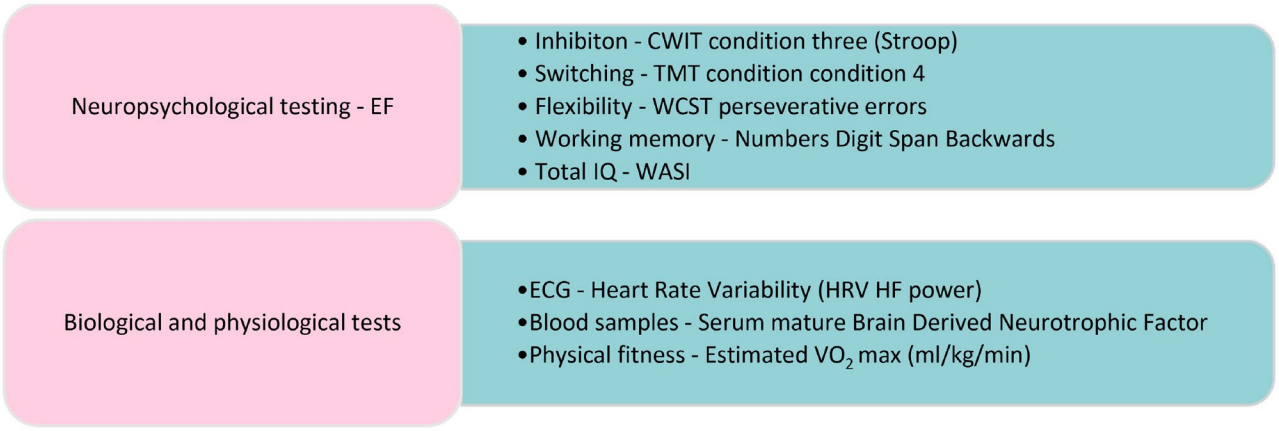

Figure 1. Overview of neuropsychological tests of EF, biological and physiological tests in the study.CWIT: Color-Word Interference Test (Stroop, 1935).TMT: Trail making test (Delis et al., 2001).Numbers Digit Span BackwardsWCST: Wisconsin Card Sorting Test (Heaton et al., 2003).WASI: Weschler Abbreviated Scale of Intelligence (Wechsler, 2011).

recordings were collected in a quiet room with a bench for supine ECG and a chair for sitting ECG. The test administrator was present during all recordings. The ECG procedure was seven minutes of laying down while recording, and then seven minutes of sitting recording, the two recordings were separated by one minute where the participant changed posture from supine to sitting. Processing and analysis of ECG data was done with Kubios HRV Scientific (Tarvainen et al., 2014). To obtain a stable and artefact-free recording the first and last minute of each seven-minute recordings were excluded from the analyses, resulting in two five-minutes recordings for analyses. In addition, the automatic beat correction in Kubios (Tarvainen et al., 2014) was used to correct for artifacts. A correlation analysis of HF HRV and the Root Mean Square of Successive Differences (RMSSD) was done for supine ($r = 0.727$, $p < .001$) and sitting ($r = 0.938$, $p < .001$) recordings.

Blood samples

Non-fasting serum BDNF samples were collected by a single venepuncture using Serum Separation Tubes (SST). The sample tube was set for clotting at room temperature for 60 min. The sample was then centrifuged at 3000 × g for 10 minutes at room temperature. The centrifuged samples were transferred to 1.5 ml microtubes (Eppendorf) and frozen at −30 °C. Within three months, the samples were transferred to long-term storage at −80 °C until final analysis at the Department of Biological and Medical Psychology, University of Bergen. The serum BDNF samples were analyzed using a Mature BDNF/proBDNF Combo Rapid ELISA kit (Biosensis®). The sensitivity for this kit was less than 2 pg/ml for BDNF determined as 150% of the blank value. BDNF analyses were run in duplicates, and results were averaged. The inter-assay variation for BDNF was 14.1 coefficients of variation (CV %). The BDNF values reported in this study are Mature BDNF.

Estimation of maximal oxygen uptake

The Ekblom-Bak ergometer cycle test (Ekblom-Bak et al., 2014) was used for estimating maximal oxygen uptake (VO_2 max) as a measure of physical fitness. The test procedure (Björkman et al., 2016) was performed on a stationary bike (Monark model 928) and included four minutes of cycling on a standardized low work rate of 30 watt with a pedal frequency of 60 rpm, followed by four minutes of cycling on a higher individually adjusted work rate at a pedal frequency of 60 rpm. Toward the end of the latter work level, the aim was a Rating of Perceived Extortion (RPE) of 12–16 on the Borg scale. Mean steady-state HR during the last minute on the low and high work rates, respectively was recorded by taking the mean of the observed HR at 3:15, 3:30, 3:45, and 4:00 min at each work rate. Maximal oxygen uptake was estimated with gender-specific equations (Björkman et al., 2016). The equation takes the increase in heart rate in relation to the increase in work rate, gender, age, and heart rate at lower and higher work rates into consideration.

Statistical analyses

All analyses were performed in R (Team, 2023) using the "robustbase", "siPlot" and "easystats" packages. Five participants, who did not complete any neuropsychological testing, were excluded from the analyses. The final sample consisted of $N = 102$. We fitted a robust multiple regression model (Field & Wilcox, 2017) using "MM" estimation ("lmrob: MM-type estimators for linear regression") with four outcome measures: Stroop task, TMT condition 4, WCST perseverative errors, and Digit span backwards in addition to the predictor variables diagnostic group (GAD vs. healthy control), HRV supine and HRV sitting, BDNF, physical fitness, gender, age, education, and IQ. For the outcome measure Wisconsin Card Sorting Test perseverative errors there was 2.9% missing data, and for the Digit Span Backwards test there was 2.9% missing data. Missing values for the other predictor variables were IQ 1%, VO2 max 2%, BDNF 2%, HRV sitting 8.8%, HRV supine 2.9%. The missing data mechanism was evaluated as missing at random and managed with multiple imputation. Normality checks and the residuals for the dependent variables can be seen in Appendix A and B, respectively. A correlation analysis between the outcome measures and predictors were done (Appendix C). We used propensity scoring (average treatment effect-weights based on PS scores) to remove potential selection bias (See Appendix D). In the analyses, age was applied as a categorical variable with two categories (Age: Older = 68–75 years, and Age: Younger = 60–67 years) to be able to detect age segment effects. Because of moderate multicollinearity of the two HRV measures on the Stroop task, we only included the sitting HRV measure in this model. Both HRV and BDNF was log transformed to achieve a more normal distribution of the data points on these variables. The Benjamini-Hochberg Procedure (Benjamini & Hochberg, 1995) was used to decrease risk of type I error when applying four statistical tests with the same predictors.

Results

Sample

The patient sample consisted of 51 persons (76.8% female) with a mean age of 66.27 ($SD = 4.15$) years, while the healthy control group consisted of 51 persons (78.4% female) with a mean age of 67.67 ($SD = 4.04$) years. Characteristics of the sample can be seen in Table 1.

Results on the neuropsychological measures

Table 2 refers to scores on the neuropsychological tests conducted in the study. For figures of the difference in mean scores for participants with GAD and the healthy control group, see Abstract D, Figure D1–D4.

Regression model

The model explained 12.2%, 17.3%, 25.9% and 16.5% of the total variance (adjusted R^2) in the Stroop task, TMT, WCST

Table 1. Participant characteristics.

	GAD			Healthy controls		
	Total	Female	Male	Total	Female	Male
Sample number (%)	51	40 (78.4)	11 (21.6)	51	40 (78.4)	11 (21.6)
Age total, *M* (*SD*)	66.46 (4.08)	66.05 (4.06)	67.09 (4.55)	67.67 (4.04)	67.28 (3.86)	69.09 (4.57)
Age, younger, *n*	32	26	6	29	24	5
Age, older, *n*	19	14	5	22	16	6
Years of education, *M* (*SD*)	15.10 (3.47)	14.08 (2.89)	15.18 (2.40)	16.05 (2.96)	15.26 (2.71)	16.46 (2.46)
Duration of symptoms in years, *M* (*SD*)	16.16 (17.86)	16.49 (18.39)	14.72 (16.25)	N/A	N/A	N/A
Years of employment, *M* (*SD*)	37.38 (7.33)	35.99 (7.23)	42.18 (5.67)	40.78 (6.18)	39.95 (6.11)	43.82 (5.69)
Years out of work, *M* (*SD*)	3.52 (4.76)	3.80 (5.18)	2.53 (2.64)	3.01 (3.41)	2.82 (2.98)	3.73 (4.80)
PSWQ, *M* (*SD*)	61.59 (8.08)	61.85 (7.83)	60.64 (9.27)	29.80 (5.95)	30.90 (5.96)	25.82 (4.00)
MMS-E score, *M* (*SD*)	29.20 (1.11)	29.20 (1.18)	29.18 (0.87)	29.53 (0.67)	29.45 (0.71)	29.82 (0.41)
MINI – depression, %						
Ongoing	5.9	5.0	9.1	0	0	0
Recurrent	35.3	40.0	18.2	0	0	0
Previous	29.4	22.5	54.5	0	0	0
MINI – panic disorder, %						
With agoraphobia	5.9	5.0	9.1	0	0	0
Lifetime	13.7	10.0	27.3	0	0	0
MINI – social phobia, %						
Not generalized	2.0	0	9.1	0	0	0
Generalized	7.8	10.0	0	0	0	0
MINI – generalized anxiety disorder, %	90.2	87.5	100	0	0	0
WASI total IQ, *M* (*SD*)	111.16 (10.03)	109.69 (10.46)	116.36 (6.25)	115.65 (9.53)	114.85 (9.74)	118.55 (8.50)
BDNF ng/ml log transformed, *M* (*SD*)	3.46 (0.24)	3.51 (0.23)	3.29 (0.23)	3.32 (0.22)	3.36 (0.17)	3.19 (0.34)
HRV HF Power log transformed – sitting	4.91 (1.42)	4.88 (1.50)	5.08 (1.07)	4.80 (1.14)	4.75 (1.16)	5.02 (1.12)
HRV HF Power log transformed – supine	4.73 (1.39)	4.63 (1.40)	5.08 (1.33)	4.50 (1.13)	4.50 (1.12)	4.50 (1.23)
Estimated VO_2 max – ml/kg/min, *M* (*SD*)	28.20 (5.94)	26.88 (4.82)	32.90 (7.32)	30.11 (4.99)	29.28 (4.65)	33.03 (5.28)
Body Mass Index (BMI)	25.09 (3.66)	24.85 (3.27)	25.93 (4.91)	24.55 (2.94)	23.87 (2.51)	26.96 (3.18)

PSWQ: Penn State Worry Questionnaire (Meyer et al., 1990); MMS-E: Mini Mental State Examination (Folstein et al., 1975); MINI: M.I.N.I. Neuropsychiatric Interview (Lecrubier et al., 1997); WASI: Wechsler (2011) abbreviated scale of intelligence (RANGE).

Table 2. Scores on the neuropsychological tests for participants with GAD and healthy controls.

	GAD			Healthy controls		
	Total	Female	Male	Total	Female	Male
CWIT condition 1, *M* seconds (*SD*)	31.47 (5.19)	30.50 (4.79)	35.00 (5.27)	31.14 (5.32)	30.13 (4.43)	34.82 (6.78)
CWIT condition 2, *M* seconds (*SD*)	21.96 (3.32)	21.60 (3.14)	23.27 (3.74)	22.94 (3.95)	22.95 (4.00)	22.91 (3.96)
CWIT condition 3, *M* seconds (*SD*)	55.96 (10.77)	55.20 (10.99)	58.73 (9.90)	59.08 (10.44)	57.10 (8.73)	66.27 (13.21)
CWIT condition 4, *M* seconds (*SD*)	61.37 (10.96)	61.05 (11.46)	62.55 (9.27)	66.84 (13.32)	65.43 (13.26)	72.00 (12.84)
TMT condition 1, *M* seconds (*SD*)	24.67 (5.73)	23.60 (5.05)	28.55 (6.61)	23.24 (4.58)	22.15 (3.28)	27.18 (6.40)
TMT condition 2, *M* seconds (*SD*)	38.55 (9.96)	37.00 (8.52)	44.18 (12.98)	35.06 (9.05)	34.98 (9.85)	35.36 (5.56)
TMT condition 3, *M* seconds (*SD*)	41.10 (14.27)	39.08 (11.80)	48.46 (19.99)	39.24 (14.93)	38.55 (13.97)	41.73 (18.55)
TMT condition 4, *M* seconds (*SD*)	96.53 (34.79)	92.53 (32.56)	111.09 (40.23)	88.45 (22.69)	84.83 (19.14)	101.64 (30.00)
TMT condition 5, *M* seconds (*SD*)	21.33 (5.60)	20.53 (5.12)	24.27 (6.51)	22.61 (8.21)	22.65 (8.93)	22.46 (5.09)
WCST perseverative response, *M* (*SD*)	14.25 (11.25)	17.47 (12,38)	16.46 (6.28)	17.64 (11.79)	19.41 (12.49)	11.36 (5.71)
WCST perseverative errors, *M* (*SD*)	15.74 (9.69)	15.87 (10.63)	15.27 (5.66)	15.68 (9.81)	16.95 (10.42)	11.18 (5.53)
WCST categories complete, *M* (*SD*)	4.84 (1.76)	4.87 (1.76)	4.73 (1.85)	4.76 (1.79)	4.72 (1.85)	4.91 (1.64)
Numbers Digit Span Forward, *M* (*SD*)	8.53 (1.59)	8.63 (1.58)	8.18 (1.66)	8.23 (1.61)	8.21 (1.61)	8.33 (1.73)
Numbers Digit Span Backward, *M* (*SD*)	7.75 (1.61)	7.88 (1.70)	7.27 (1.19)	7.92 (1.80)	7.80 (1.81)	8.44 (1.74)
Numbers Digit Span Sequence, *M* (*SD*)	7.57 (1.77)	7.55 (1.74)	7.63 (1.96)	7.83 (1.77)	7.80 (1.84)	8.00 (1.50)

CWIT: Color-Word Interference Test; TMT: Trail Making Test; WCST: Wisconsin Card Sorting Test.

perseverative errors and Digit span backwards, respectively. Results from the total model is shown in Table 3. For an overview of differences between groups on predictor variables, please refer to Appendix D for Propensity Scoring for each outcome measure.

Group differences

Within the predictor model, the effect of diagnostic group on the Stroop task was significant (β = −4.66, 95% CI [−8.46 to −0.86], $t(93)$ = −2.43, p = .017), with a moderate effect size (d = −.50). Participants with GAD used significantly less time than healthy controls on the Stroop task. There were no significant differences between groups on the other outcome measures.

Predictive factors of the Stroop task

Within the predictor model, the effect of HRV sitting was significant (β = −2.25, 95% CI [−3.57 to −.94], $t(93)$ = −3.41, p = .001), with a moderate/large effect size (d = −0.71). Higher HRV was associated with faster completion of the Stroop task. BDNF significantly predicted performance on the Stroop task (β = 9.56, 95% CI [1.83–17.30], $t(93)$ = 2.46, p = .016), with a moderate effect size (d = .51). Higher BDNF levels were associated with longer time spent on the Stroop task. Gender had a significant effect on the Stroop task (β = −8.87, 95% CI [−14.29 to −3.46], $t(93)$ = −3.25, p = .002) with a moderate effect size (d = −0.67). Male participants used significantly longer time on the Stroop task than female participants.

Table 3. Multiple regression model with predictors of the outcome measures cognitive inhibition, shifting, flexibility and working memory.

	Stroop			TMT			WCST pers. err.			Digit span backwards		
Predictors	*Estimates*	*CI*	*p*	*Estimates*	*CI*	*p*	*Estimates*	*CI*	*p*	*Estimates*	*CI*	*p*
(Intercept)	61.86	22.61–101.11	**.002**	157.19	55.42–258.95	**.003**	84.58	47.00–122.16	**<.001**	−3.69	−10.49–3.11	.284
Participant	−4.66	−8.46 – −0.86	**.017***	1.63	−5.56–8.82	.653	0.78	−2.60–4.15	.649	0.13	−0.55–0.80	.711
Gender	−8.87	−14.29 – −3.46	**.002***	−19.23	−29.94 – −8.51	**.001***	2.17	−2.77–7.11	.385	0.13	−0.65–0.91	.745
Age	2.59	−1.16–6.34	.173	−3.21	−13.15–6.73	.523	−1.05	−4.42–2.31	.536	−0.47	−1.17–0.22	.179
Education	−0.12	−1.02–0.77	.786	−0.22	−2.14–1.70	.820	−0.60	−1.28–0.09	.086	0.05	−0.10–0.20	.486
lnBDNF	9.56	1.83–17.30	**.016***	7.66	−12.78–28.11	.458	−8.03	−16.36–0.30	.059	0.66	−0.79–2.11	.367
IQ	−0.21	−0.49–0.07	.144	−0.63	−1.03 – −0.23	**.003***	−0.35	−0.56 – −0.14	**.002***	0.08	0.03–0.14	**.004***
HRV sitting	−2.25	−3.57 – −0.94	**.001***	−0.49	−5.16–4.18	.836	−0.36	−2.10–1.39	.687	0.16	−0.22–0.55	.401
VO2max	0.28	−0.13–0.69	.175	0.57	−0.41–1.55	.253	0.38	−0.17–0.93	.177	−0.00	−0.07–0.06	.910
HRV supine				−4.29	−8.61–0.03	.051	−1.11	−2.92–0.71	.228	−0.37	−0.72 – −0.02	**.039**
Observations	102			102			102			102		
R^2/R^2 adjusted	0.191/0.122			0.247/0.173			0.325/0.259			0.239/0.165		

Significant values at <.05 before correcting for multiple comparisons are bolded.
*Significant values after the Benjamini-Hochberg Procedure for multiple comparisons are marked with an asterisk.

Table 4. Correlation analysis.

	1.	2.	3.	4.	5.	6.	7.	8.	9.	10.
1. Participant	–	−0.147	0.138	0.003	−0.051	**0.915****	**0.726****	**0.315****	**0.221****	**0.737****
2. Stroop	−0.147	–	**0.252***	−0.010	−0.025	−0.180	−0.021	−0.071	0.066	−0.089
3. TMT	0.138	**0.252***	–	**0.233***	−0.139	0.128	−0.008	−0.061	**0.274****	0.134
4. WCST pers.err.	0.003	−0.010	**0.233***	–	**−0.201***	−0.018	−0.102	−0.138	0.082	−0.028
5. Digit span backwards	−0.051	−0.025	−0.139	**−0.201***	–	−0.093	0.038	−0.134	−0.126	−0.029
6. PSWQ	**0.915****	−0.180	0.128	−0.018	−0.093	–	**0.683****	**0.306****	**0.233***	**0.713****
7. MDD	**0.726****	−0.021	−0.008	−0.102	0.038	**0.683****	–	**0.216***	0.121	**0.545****
8. PD	**0.315****	−0.071	−0.061	−0.138	−0.134	**0.306****	**0.216***	–	−0.067	**0.343****
9. SAD	**0.221****	0.066	**0.274****	0.082	−0.126	**0.233***	0.121	−0.067	–	0.124
10. GAD problem	**0.737****	−0.089	0.134	−0.028	−0.029	**0.713****	**0.545****	**0.343****	0.124	–

**$p < .01$; *$p < .05$.

Predictive factors of TMT

Performance on the TMT was significantly predicted by gender and IQ. The effect of gender was significant (β = −19.23, 95% CI [−29.94 to −8.51], $t(92)$ = −3.56, p = .001), with a moderate effect size (d = −0.74). Female participants performed significantly better than male participants. The effect of IQ was significant (β = −0.63, 95% CI [−1.03 to −.23], $t(92)$ = −3.10, p = .003) with a moderate effect (d = −0.65). A higher IQ score was associated with better performance on the TMT.

Predictive factors of WCST perseverative errors

The amount of perseverative errors on the WCST was significantly predicted by total IQ (β = −0.35, 95% CI [−0.56 to −0.14], $t(92)$ = −3.27, p = .002), with moderate effect size (d = −0.65). Higher IQ was associated with less perseverative errors on the WCST.

Predictive factors of Digit span backwards

Within the predictor model, performance on the Digit span backwards test was predicted by IQ and HRV. The effect of IQ on the task was significant (β = 0.08, 95% CI [0.03–0.14], $t(92)$ = 2.99, p = .004), with a moderate effect size of d = 0.62. Higher IQ was associated with a higher number of digits remembered on the Digit span backwards test. The effect of HRV on Digit span backwards test was significant (β = −0.37, 95% CI [−0.72 to −0.02], $t(92)$ = −2.10, p = .004), with a moderate effect size of d = −0.44. After correcting for multiple analyses, the predictive value of HRV was no longer significant.

Post hoc correlation analysis

Our prediction models explained between 12.2% and 25.9% of the variance in the EF measures chosen. This indicates that there are other important contributing factors of EF that were not investigated in this study. Such factors could be duration of symptoms, diverse symptom levels or how much the symptoms are reported being a problem for the individual, and comorbid conditions such as depression and other anxiety disorders. A post hoc correlation analysis (refer to Table 4) between the outcome measures of the regression model and symptom level (PSWQ), symptoms of depression (M.I.N.I. Major Depressive Disorder (MDD)), symptoms of panic disorder (M.I.N.I. Panic Disorder (PD)), symptoms of social anxiety disorder (M.I.N.I. Social Anxiety Disorder (SAD)) and perceived problems with having GAD-symptoms (last item of the GAD-7) was done to investigate these potential associations.

The correlation analysis revealed a positive significant association between TMT and symptoms of social anxiety (r = 0.274, p = .006). There were no other significant associations between any of the four outcome variables and chosen potential predictors.

Discussion

Participants with GAD performed significantly better than the healthy controls on cognitive inhibition, as measured by the Stroop task. There were no significant differences between the groups on the other outcome measures.

Performance on the Stroop task was significantly and positively predicted by having GAD, higher HRV, and being female, and was negatively correlated with higher levels of BDNF. Better performance on the TMT was significantly predicted by being female and having a higher IQ. WCST perseverative errors and Digit Span Backwards were significantly predicted by higher IQ.

In contrast to previous studies that have found both impaired (Hallion et al., 2017) and intact (Liu et al., 2021) cognitive inhibition in younger samples with GAD, our results showed that older adults with GAD had better cognitive inhibitory abilities than healthy controls. This result is in line with Price and Mohlman (2007) who have hypothesized that increased cognitive inhibition can be construed as worrying in the service of inhibiting strong negative arousal in GAD, consistent with the avoidance theory of GAD (Sibrava & Borkovec, 2006). According to this model, worry is a verbal-linguistic process that contributes to supress and avoid the emotional content and imagery associated with anxiety. One could therefore assume that people with GAD develop an increased, however maladaptive, ability to apply cognitive inhibition. Older adults have often experienced GAD symptoms for several years (mean duration in our sample was 16.16 ($SD = 17.86$) years), and thus would have had more time to develop a maladaptive pattern than younger adults. Considering the Attentional Control Theory, one would expect worry to impair the performance on the Stroop task (Eysenck et al., 2007) as the task increase the cognitive load on the individual and the worry could represent a distractor. On the other hand, worry and anxiety could increase focus and vigilance through heightened activation. In line with this, Moser et al. (2013) describes a compensatory attentional effort when facing cognitive tasks that is activated as a result of the cognitive load of worry.

The relatively improved performance on the Stroop task could be associated with protective factors such as relatively heightened self-regulatory ability through increased HRV. Higher HRV was associated with better performance on the Stroop task in the current study. Similar results have been found in a meta-analysis with younger adults (mean age 24.6; Magnon et al., 2022) and a study of adults with a mean age of 75 years (Mahinrad et al., 2016). Another perspective is introduced in a study by Fishback et al. (2020) who found positive associations between GAD and cognitive control, and that this association is related to higher HRV. According to this study, the persistent worry among persons with better cognitive control is related to a positive belief in worries utility. Furthermore, the high HRV was related to a belief that worry would distract the person with GAD from even more emotional content. These results relate to our findings that participants with GAD have better performance on the Stroop task, and that higher HRV was related to better performance on the Stroop task. This supports the notion that inhibition is a cognitive process dependent on self-regulatory mechanisms. HRV can be increased by physical exercise. Indirectly our results could thus support using physical exercise to enhance EF. Our findings are not suitable to conclude that physical exercise is beneficial for the HRV in older adults with GAD, or how it is related to psychological treatment, which therefore would be a question for further research.

Higher BDNF levels were significantly associated with longer time taken on the Stroop task. There are suggestions that elevated BDNF levels might be related to neurodegeneration which is triggering a compensatory BDNF repair mechanism in older adults (Dols et al., 2015), however, at an early stage, one would not find differences in cognitive function. Dols et al. (2015) argue that this change would be more visible on measures of atrophy than function at this stage. We did not find an interaction effect between group and BDNF levels on cognitive inhibition, however this could be due to low statistical power of the study. One could still hypothesize that increased BDNF levels in older adults generally, and in GAD specifically, reflect a less efficient brain functioning, and that this could affect cognitive functions.

Women performed better than men on the Stroop task in this study. This is in line with previous findings (e.g. Mekarski et al., 1996). In the current study, 78% of participants were women. This is representative of the uneven prevalence of GAD across gender (Vesga-López et al., 2008), with a larger proportion of women having GAD than men. Therefore, our results could also have been skewed by uneven groups. According to Christidi et al. (2015), the cognitive shifting task TMT is not significantly affected by demographic variables such as gender. However, we found that women performed better on the TMT than men.

In our predictive model, cognitive flexibility, as measured by WCST perseverative errors and working memory as measured by Digit Span Backwards were significantly predicted by total IQ. For both, better performance on the cognitive tasks was related to higher IQ scores. Regarding cognitive flexibility and IQ, our findings are contradictory to a meta-analysis that concluded that the WCST perseverative errors was unrelated to intelligence (Kopp et al., 2019). The association between IQ and working memory has shown to be inconclusive, with some studies finding stronger associations than others (Ackerman et al., 2005; Alloway & Alloway, 2010). Our results suggest that the impact of IQ on executive functioning might vary depending on cognitive domain. In addition, IQ may have indicated an absence of cognitive decline in our sample.

In addition to the finding that participants with GAD performed better than healthy controls on cognitive inhibition, our results generally indicate that older adults with GAD do not have reduced EF compared to healthy older adults. HRV levels were not reduced in patients with GAD compared to healthy controls, contrary to findings by Thayer et al. (1996). Their sample was younger than ours, and one could speculate that our results are related to higher age. In a study by Geovanini et al. (2020) one found a U-shaped relationship between age and HRV, where parasympathetic measures of HRV tended to increase after 60 years. There is evidence to argue for a compensatory mechanism to preserve EF at the same level as in younger individuals (Cabeza et al., 2002; Cabeza et al., 2004), and HRV might play a role in this. Hence, as our sample is above 60 years one could speculate whether their HRV have increased as a result of age itself.

In addition, our participants with GAD had lower VO_2 max than the healthy controls, but compared to international reports of physical fitness, they were in relatively good physical shape (Peterman et al., 2020), which might limit the generalizability of these findings. In the predictive model, VO_2 max was not a significant predictor of any of the outcome measures. However, physical fitness may have potentially increased the participants resilience (Casaletto et al., 2022) by protecting EF through neurobiological mechanisms. Future research is needed to clarify these associations in our study population.

Limitations

Our relatively small sample limits the possibility to perform more complex analyses on the data such as two-way and three-way interaction effect analyses or mediation analyses that would be necessary to answer questions that came up as a part of the results and discussion in the study. Future research should aim at this increased complexity in research questions and analyses.

Implications and conclusions

Overall, our findings indicate that older adults with GAD do not exhibit significantly reduced EF compared to healthy peers. Moreover, interventions targeting EF should consider individual differences such as gender and IQ, while promoting factors like physical fitness that may enhance cognitive outcomes. The study reveals intricate relationships influencing EF in older adults with GAD. While GAD may not lead to significant reductions in EF compared to healthy controls, factors like gender, IQ, HRV, BDNF levels, and physical fitness play complex roles in shaping executive functioning outcomes in this population. These findings highlight the importance of understanding the underlying mechanisms of EF in GAD and developing targeted interventions to enhance cognitive functioning in affected individuals, in line with proposals from previous research (De Vito et al., 2022; Mohlman, 2020).

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Ethics statement

The Regional Ethical Committee in Norway has approved the study (reference number 2015/2189, approved 2015.11.15). The study was carried out in according to the Declaration of Helsinki. All participants signed a written informed consent before being enrolled in the study. Procedures for ensuring safety during physical testing, and in case of unwanted findings during neuropsychological testing was developed and used when needed.

Disclosure statement

No potential conflict of interest was reported by the author(s).

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ORCID

Kristine Sirevåg http://orcid.org/0000-0002-2349-2306

Data availability statement

The data that support the findings of this study are available on request from the corresponding author, KS. The data are not publicly available due to privacy or ethical restrictions.

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