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Bemused and Befuddled: Adiponectin Gene, Diet and Everyday Cognitive Complaints

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ABSTRACT: Vulnerability to everyday cognitive complaints constitutes a risk factor for physical and mental health, and depicts a complex interaction of environmental and biological factors. In the present study, we tested for a molecular genetic association between variants [rs266729 (-11377C>G in promoter) and rs1501299 (+276G>T in intron 2)] on the adiponectin gene (ADIPOQ), which relate to several pathologies, and susceptibility to everyday cognitive complaints (ECCs) as assessed by the cognitive failure questionnaire (CFQ) in a sample of N = 116 (n = 90 females, n = 26 males, mean age, M = 22.24, SD = 2.60) healthy participants of Nigerian descent. Moreover, we assessed whether dietary alcohol and vitamin D (as measured by food frequency questionnaire; FFQ) or psychological symptoms of depression, anxiety and stress (as measured by depression, anxiety and stress scale; DAS-21) correlate with CFQ scores. We found no significant associations between ADIPOQ variants and the CFQ. CFQ was however, positively and significantly related to alcohol intake as well as the depression, anxiety and stress symptoms. The *ADIPOQ* -11377C>G and +276G>T variants respectively, constitute non-significant protective and harmful factors for the susceptibility to everyday cognitive complaints.

Keywords: ADIPOQ, Cognitive complaint, Depression, Anxiety, Stress

Introduction

Cognitive functioning involving multiple mental abilities that include clear thinking, learning, and remembering (Fisher *et al.* 2019) is vital for performing everyday activities. These abilities are heterogeneous among all individuals and can be influenced substantially by genes – nearly half of the variance in general cognition are attributed to genetic factors (Haworth *et al.*, 2010; Mollon *et al.*, 2021) – or can be impacted by other non–genetic factors that contribute to task performance, such as diet, self–efficacy or mood (Steinberg *et al.*, 2013; Koekkoek *et al.*, 2014; Awofala and Ogundele, 2018; Ogundele *et al.*, 2022). Consequently, cognitive complaints which constitute cognitive errors in elderly (Stewart, 2012) and non-elderly adults (Stenfors *et al.*, 2014) and include frequent forgetfulness, and difficulties in concentrating, making decisions and thinking clearly, can be experienced during the performance of everyday task that a person is normally successful in executing. Thus, an individual's susceptibility to these everyday–task failures encompasses environmental, psychological and biological factors (Harris and Deary, 2011; Awofala and Ogundele, 2018; Koekkoek *et al.*, 2014).

Subjective perceptions of lapses in cognition have been implicated not only in alcohol intake (Awofala and Ogundele, 2018) but also self–efficacy for managing chronic diseases (Awofala *et al.*, 2021) and food consumption (Ogundele *et al.*, 2022) in cross–sectional studies. After rigorous control for known confounders, participants in the highest compared with the lowest quintile of alcohol intake had a significantly increased odds of cognitive complaints; the effect seen to be more pronounced in males when alcohol intake was doubled (Awofala and Ogundele, 2018). In addition, significant negative relationship of cognitive failures with self–efficacy was found among chronic disease patients (Awofala *et al.*, 2021). Finally, consumption of four different foods was significantly associated with cognitive complaints: meat product and sugary snacks were associated with increased cognitive complaints whereas consumption of cereal products and potatoes were associated with decreased levels of cognitive complaints (Ogundele *et al.*, 2022).

Studies exploring the psychological correlates of subjective cognitive complaints as assessed by cognitive failures have shown that higher perceptions of depression, anxiety, anger and stress, which are typically correlated with less effective cognitive functioning, are also associated with higher self-reported and observed cognitive failures (Mahoney *et al.*, 1998; Mecacci *et al.*, 2004; Schrier *et al.*, 2017; Santangelo *et al.*, 2021). Interestingly, the associations between cognitive failures and some of these psychological factors (specifically, depression and anger) were mediated by personal resilience (i.e., the capacity to thrive in the face of adversity, while maintaining relatively normal physical and psychological function over time) but not by coping style (i.e., the employment of adaptive or maladaptive coping strategies to tolerate, minimize, accept, or ignore stressful situations) (Santangelo *et al.*, 2021). These findings are in line with the social stress model (Aneshensel, 1992) which holds that individuals with negative affect states are more likely to be vulnerable to stress and to suffer from poor mental health because they have limited psychosocial coping resources.

At the biological level, cognitive dysfunction has been hinted to be associated with decreased adiponectin levels (Teixeira *et al.*, 2012). Adiponectin is an insulin-sensitizer adipocytokine endowed with neuroprotective actions, and has been independently associated with delayed recall memory in middle-aged individuals (Cezaretto *et al.*, 2018) indicating that this adipocytokine could anticipate cognitive impairment, suggesting the biomarker could be useful in identifying individuals with increased risk for cognitive dysfunction before advanced age. Adiponectin gene (ADIPOQ) is located on chromosome 3q27 and has polymorphisms including +276G>T (rs1501299) and –11377C>G (rs266729) that influence the level and activity of adiponectin (Christodoulou *et al.*, 2020). The two ADIPOQ variants +276G>T and –11377C>G in intron 2 and the promoter region of chromosome 3, respectively, constitute few of the most widely known and studied single nucleotide polymorphisms (SNPs). Previous reports indicated that the two SNPs were significantly correlated with various metabolic disorders including diabetes, insulin resistance and coronary heart disease (Gable *et al.*, 2007; Liu *et al.*, 2018). Interestingly, both SNPs have been correlated with late onset of Alzheimer's disease (Yu *et al.*, 2015).

To sum up, so little is known about the genetic and environmental states associated with subjective perception of cognitive complaints. Additionally, no research has examined the role of adiponectin gene on cognitive failures. Consequently, the focus of the present study was to investigate the relationship between everyday cognitive complaints and ADIPOQ variants involving rs266729 and rs1501299. The other aim was to determine whether ECCs is associated with dietary factors involving alcohol and vitamin D as well as the psychological symptoms of depression, anxiety and stress in a Nigerian sample.

Materials and methods

Design: This was a cross-sectional design

Characteristics of the subjects and clinical evaluation: A total sampled population of 116 students from Tai Solarin University of Education, both sexes, aged 18 to 30 years without a previous diagnosis of chronic non–communicable diseases and serious illnesses, head trauma or impaired consciousness, were selected as previously described (Ogundele *et al.*, 2018). The participants signed informed consent to perform the clinical evaluation and for the use of their data for scientific research. The project was approved by the Health Research Ethics Committee (HREC) of Lagos University Teaching Hospital (LUTH) (Reference no. ADM/DCST/HREC/APP/800) and performed under the guidelines of the Declaration of Helsinki (World Medical Association, 2001).

All participants underwent an anthropometric assessment that consisted of collecting data from their height and weight. These anthropometric evaluations were performed using previously standardised procedures recommended by the World Health Organisation (De Onis and Habicht, 1996).

Cognitive complaints were measured everyday using the original CFQ (Broadbent *et al.*, 1982). The CFQ contains 25 items self–report measure of failures in attention, perception, memory and action (e.g. #6, "Do you forget whether you've turned off a light or a fire or locked the door?", and #21, "Do you start doing one thing at home and get distracted into doing something else (unintentionally)?"). Using a five-point Likert scale (ranging from "0 = never" to "4 = very often"), participants had to indicate how often each of the mentioned events happened to them in the past six months. Reliability in the current study was ($\alpha = 0.79$).

Participants also completed the short version of the Depression Anxiety Stress Scale (DASS-21; Lovibond and Lovibond, 1996). The scale contains 21 items with three main dimensional symptoms each containing a 7-item sub-scales that measure the frequency and severity of each symptom or trait in clinical and non-clinical sample: Depression (e.g. "I couldn't seem to experience any positive feeling at all"), Anxiety (e.g. "I felt scared without any good reason"), and Stress (e.g. "I found it difficult to relax"). Using a four-point Likert scale (ranging from "0 = Did not apply to me at all" to "3 = Applied to me very much or most of the time"), participants had to indicate how much the statement applied to them over the past week. Reliability in the current study was the following: Depression ($\alpha = 0.78$), Anxiety ($\alpha = 0.81$), and Stress ($\alpha = 0.73$).

Dietary intake information was obtained using a food frequency questionnaire with items that were previously validated (Mulligan *et al.*, 2014). The alcohol intake (in gramme) and vitamin D (in microgramme) composition were analysed using feta software as previously described (Mulligan *et al.*, 2014).

Extraction and quantification of genetic material: Genomic deoxyribonucleic acid (DNA) was extracted from dried blood spots samples using Zymo Research (ZR) DNA Card Extraction Kits following manufacturer's protocol and recommendations. Purified DNA was used for genotyping. The genotyping reaction was performed with SNP-specific polymerase chain reaction using single-base primer extension technology (Sequenom MassARRAY Genotyping System (Sequenom, San Diego, CA, USA) based on the method described by Yue and colleagues (Yu *et al.*, 2015). The two SNPs achieved genotyping efficiencies > 92% and minor allelic frequencies (MAF) > 10%.

Data analysis: The CFQ and DAS–21, respectively, as measures of everyday cognitive complaints and psychological symptoms of depression, anxiety and stress were assessed for internal consistencies using Cronbach's alpha reliability coefficient. Variables (as continuous measures) are presented as means and standard deviations and were compared between male and female participants using independent sample t–test. We tested associations between CFQ and the dietary and psychological parameters involving alcohol and vitamin D intakes, and depression, anxiety and stress factors using Pearson product–moment correlation coefficient. Finally, to comprehensively analyse the association between genotyped ADIPOQ SNPs and everyday cognitive complaints, we adopted three genetic models: the additive effect model, the dominant effect model, and the recessive effect model. In these models, we assumed that each SNP marker locus has two alleles, **A** and **a**, with A being the high–risk allele, while a is the low–risk allele. The three models are depicted mathematically in linear regression models as follows:

(i) Additive model: $$y = \beta_0 + \beta \times \#\text{minor alleles}$$
$$\text{AA} = 0,\ \text{Aa} = 1,\ \text{aa} = 2$$

(ii) Dominant model: $$y = \beta_0 + \beta \times (\text{G} \neq \text{AA})$$
$$\text{AA} = 0,\ \text{Aa} = 1,\ \text{aa} = 1$$

(iii) Recessive model: $$y = \beta_0 + \beta \times (\text{G} == \text{aa})$$
$$\text{AA} = 0,\ \text{Aa} = 0,\ \text{aa} = 1$$

As genotype data were available for 92 participants, a complete case genotype analysis was adopted. All statistical analysis was performed using R Statistical Software (version 4.2.1; R Foundation for Statistical Computing, Vienna, Austria).

Results

The sample characteristics and the distribution of the study variables are presented in Table 1. The sample was 77.6% females and showed a significantly lower average height as compared with the male counterparts (mean height, m: 1.63 ± 0.07 vs. 1.72 ± 0.08, $p<0.001$). Male and female participants did not differ in terms of age (mean age, yr: 21.85 ± 2.37 vs. 22.10 ± 2.92, $p=0.25$) and weight (weight, kg: 59.43 ± 7.02 vs. 59.24 ± 13.26, $p=0.92$). Of

note, females showed a lower ECCs when compared to their male participants, however, this did not reach a statistical significance (Mean ECCs: 44.96 ± 17.72 vs. 47.04 ±14.33, p=0.20). Other comparisons involving psychological symptoms and dietary factors between gender groups were not significant.
By applying Pearson correlation, we found modest and positively significant correlations between ECCs and depression (r=0.30, p<0.001), anxiety (r=0.30, p<0.001), stress (r=0.31, p<0.001), and alcohol (r=0.48, p<0.01) but vitamin D (r= –0.08, p=0.47).

Table 1: Descriptive and correlational statistics for the study variables.

Variable	Total N = 116	Female n = 90	Male n = 26	*P*	*Correlation with ECCs*
	Mean ± SD	Mean ± SD	Mean ± SD		
Age, yr.	22.24 ± 2.60	22.10 ± 2.92	21. 85 ± 2.37	0.25	
Height, m	1.66 ± 0.08	1.63 ± 0.07	1.72 ± 0.08	< 0.001	
Weight, kg	59.37 ± 12.10	59.24 ± 13.26	59.43 ± 7.02	0.92	
ECCs	45.54 ± 16.77	44.96 ± 17.72	47.04 ±14.33	0.20	
Depression	4.67 ± 4.01	4.5 ± 4.06	5.33 ± 3.87	0.43	0.30*
Anxiety	5.98 ± 4.55	6.04 ± 4.60	5.72 ± 4.43	0.79	0.30*
Stress	7.20 ± 4.02	7.08 ± 4.13	7.67 ± 3.61	0.59	0.31*
Alcohol, g	5.24 ± 14.36	3.46 ± 8.19	11.61 ± 25.92	0.13	0.48*
Vitamin D, mcg	4.85 ± 5.74	5.19 ± 6.29	4.36 ± 3.65	0.84	-0.08

ECCs= Everyday cognitive complaints, N= Number of individuals. *P <0.01

The population from which the two SNPs rs1501299 and rs266279 were drawn was in Hardy-Weinberg equilibrium (HWE) > 0.5 (Table 2). The distributions of genotypes of these SNPs with respect to ECCs are reported in Table 2. G–allele carriers, as compared to TT genotype carriers in rs1501299, reported significantly lower ECC scores (43.42 ± 3.12 vs. 49.00 ± 4.44, t=5.99, p<0.0001). However, C–allele carriers, as compared to GG genotype carriers in rs266729, showed significantly higher ECC scores (44.49 ± 2.48 vs. 33.00 ± 0.10, t= –6.52, p<0.0001). General Linear Models showed that the two *ADIPOQ* SNPs did not predict ECCs in the dominant, recessive and additive models (p>0.05) after controlling for age, body–height, alcohol and gender.

Table 2: Associations of SNPs with ECCs in three genetic models

					Trait		Genetic Models					
SNP	Chr.	Genotypes	M/m	HWE P	ECCs	*t* test *P*	Recessive β (95% CI)	*P*	Dominant β (95% CI)	*P*	Additive β (95% CI)	*P*
rs15 0129 9	3	GG:33 GT:41 TT:16	G/T	0.68	41.94 ± 2.97 44.61 ± 2.71 49.00 ± 4.44	< 0.0001	5.58 (-3.78, 14.94)	0.25	3.90 (-3.54, 11.34)	0.31	3.38 (-1.62, 8.39)	0.19
rs26 6729	3	CC:72 GC:19 GG:1	C/G	1.00	44.50 ± 2.11 44.47 ± 3.56 33.00 ± 0.00	< 0.0001	-11.49 (-45.63, 22.64)	0.52	-0.60 (-9.20, 8.00)	0.89	-1.14 (-9.11, 6.83)	0.78

ECCs according to genotypes. Data are means ± SE. All *P* values were two sided. βs and 95% CI were calculated using linear regression with genotypes as independent variables. Chr., chromosome.

Discussion

We have undertaken the first (though relatively small) study of the role of adiponectin gene on ECCs. We adopted three genetic models to comprehensively analyse this role and assess the validity and consistency of our findings. In addition, we assessed whether psychological factors (depression, anxiety and stress) and dietary intakes (alcohol and vitamin D) correlate with ECCs. Albeit, our results indicated that ADIPOQ +276G>T and –11377C>G respectively represent non–putative risk factors for people with high and low ECCs, yet, we found ECCs to be positively and significantly related to all the psychological factors as well as the dietary variable but vitamin D intake.

We have previously shown that ADIPOQ +276G>T and –11377C>G variants, respectively, were significantly associated with increased and decreased serum adiponectin levels (Christodoulou *et al.*, 2020) in young European population. They were also respectively implicated in a decreased susceptibility to emotional eating behaviour (Awofala *et al.*, 2020) and an increased probability of being obese using several obesity measures (Ogundele *et al.*, 2018) in young Nigerian population. However, our present results are not supportive of a protective (+276G>T) or susceptible (–11377C>G) role of the variants on the risk of ECCs. This conclusion is supported by our earlier findings that +276G>T showed no significant relationship to psychological factors in young Nigerian population (Awofala *et al.*, 2020). Thus, the overall conclusion that +276G>T and –11377C>G variants are not significantly associated with ECCs in this young Nigerian population is particularly interesting and suggests that different genetic variants and /or pathways other than the ones analysed in this study may contribute to the phenotype.

Findings from our study are strengthened by the consistent positive associations of ECCs with psychological symptoms of depression, anxiety and stress, and the dietary intake of alcohol. Higher perceptions of depression, anxiety and stress symptoms have been typically correlated with poor cognitive performance (Del Brutto *et al.*, 2015), decreased cognitive function (Perin *et al.*, 2022) and elevated self–reported and observed cognitive failures (Mahoney *et al.*, 1998; Mecacci *et al.*, 2004; Schrier *et al.*, 2017; Santangelo *et al.*, 2021) in several populations of diverse age groups. More so, previous early researches have indicated that cognitive performance deteriorates in direct relationship to the severity and duration of alcohol use disorders (Oscar-Berman *et al.*, 1997; Parsons and Nixon, 1998; Beatty *et al.*, 2000). Recently, an analysis of a large sample involving 20,965 participants in a United Kingdom cohort study exploring the relationships between self-reported alcohol consumption and brain iron levels, measured using magnetic resonance imaging, revealed that moderate alcohol consumption was associated with higher iron levels in the brain which represents a potential biomarker for alcohol-related cognitive decline (Topiwala *et al.*, 2022). Interestingly, research from our lab has shown that high alcohol intake was associated with higher odds of subjective cognitive complaints (SCCs), a relationship that remained even after adjustment for life style and cardiovascular risk factors suggesting that either of these factors may not fully explain the relationship between SCCs and alcohol intake (Awofala and Ogundele, 2018).

It is particularly noteworthy that this study failed to find any evidence of a significant association between dietary vitamin D and ECCs. Our results are in line with previous studies examining relationships between vitamin D and cognitive functions in both observational (Maddock *et al.*, 2017) and experimental studies (Dean *et al.*, 2011; Stein *et al.*, 2011; Rossom *et al.*, 2012). A recent study examining the role of vitamin D on cognitive performance among healthy volunteers in rural India revealed that vitamin D has no significant effect on cognitive performance (Menesgere *et al.*, 2022).

Our findings should be interpreted with caution as it has few limitations. First, the cross–sectional design and the non–probabilistic sampling technique adopted may limit the generalisability of our results. Second, the sample size of the study was not large enough to allow for adequate data stratification for subgroup analysis. Third, because the present study used the genotyping data from a population of Yoruba descent in Nigeria, similar studies on other ethnic populations should be performed in the future. Finally, we only analysed associations between genetic variants in the adiponectin pathway and ECCs, more ECCs–association studies should be called up on genetic variants in other important biological pathway genes that are likely relevant to cognitive functioning.

Overall, our findings are not supportive of a role of adiponectin gene in ECCs but indicate a direct association of ECCs with dietary alcohol and psychological symptoms of depression, anxiety and stress.

References

Aneshensel CS. Social stress: Theory and research. Ann Rev Sociol, 1:15-38. 1992.

Awofala AA, Ogundele OE: Association between alcohol intake and subjective cognitive complaints in southwest Nigeria: a cross-sectional observational study. Alexandria J Med. 54(3):251-256. 2018.

Awofala A, Ogundele O, Awofodu A, Ojo F, Oladapo F, Adewole A: Validation of the Self-Efficacy for managing chronic disease scale in Nigeria: Impact on patients' cognitive capacity. Covenant J Phys Life Sci, 9(2): 1–14. 2021.

Beatty WW, Tivis R, Stott HD, Nixon SJ, Parsons OA: Neuropsychological deficits in sober alcoholics: influences of chronicity and recent alcohol consumption. Alcohol Clin Exp Res, 24(2):149-154. 2000.

Broadbent DE, Cooper PF, FitzGerald P, Parkes KR: The cognitive failures questionnaire (CFQ) and its correlates. Br J Clin Psychol, 21(1):1-6. 1982.

Cezaretto A, Suemoto CK, Bensenor I, Lotufo PA, de Almeida-Pititto B, Ferreira SR: Association of adiponectin with cognitive function precedes overt diabetes in the Brazilian Longitudinal Study of Adult Health: ELSA. Diabetol Metab Syndr, 10(1):1-8. 2018.

Christodoulou A, Ierodiakonou D, Awofala AA, Petrou M, Kales SN, Christiani DC, Mantzoros CS, Christophi CA: Variants in ADIPOQ gene are linked to adiponectin levels and lung function in young males independent of obesity. PLoS One. 15(1):e0225662. 2020.

Dean AJ, Bellgrove MA, Hall T, Phan WM, Eyles DW, Kvaskoff D, McGrath JJ: Effects of vitamin D supplementation on cognitive and emotional functioning in young adults--a randomised controlled trial. PLoS One. 6(11):e25966. 2011.

De Onis M, Habicht JP: Anthropometric reference data for international use: recommendations from a World Health Organization Expert Committee. Am J Clin Nutr, 64(4):650-658. 1996.

Fisher GG, Chacon M, Chaffee DS: Theories of cognitive aging and work: In: Work across the lifespan. Academic Press. pp. 17-45, 2019.

Gable DR, Matin J, Whittall R, Cakmak H, Li KW, Cooper J, Miller GJ, Humphries SE, HIFMECH investigators: Common adiponectin gene variants show different effects on risk of cardiovascular disease and type 2 diabetes in European subjects. Ann Hum Genet, 71(4):453-466. 2007.

Harris SE, Deary IJ: The genetics of cognitive ability and cognitive ageing in healthy older people. Trends Cogn Sci, 15(9):388-394. 2011.

Haworth CM, Wright MJ, Luciano M, Martin NG, de Geus EJ, van Beijsterveldt CE, Bartels M, Posthuma D, Boomsma DI, Davis OS, Kovas Y: The heritability of general cognitive ability increases linearly from childhood to young adulthood.. Mol Psychiatry. 15(11):1112-1120. 2010.

Koekkoek PS, Rutten GE, Biessels GJ. Cognitive disorders in diabetic patients. Hand Clin Neurol, 126:145-166. 2014.

Kanu JS, Qiu S, Cheng Y, Li R, Kou C, Gu Y, Bai Y, Shi J, Li Y, Liu Y, Yu Y: Associations between three common single nucleotide polymorphisms (rs266729, rs2241766, and rs1501299) of ADIPOQ and cardiovascular disease: a meta-analysis. Lipids Health Dis, 17(1):1-21. 2018.

Lovibond PF, Lovibond SH: Depression Anxiety and Stress Scales. Behaviour Research and Therapy. 1996.

Maddock J, Zhou A, Cavadino A, Kuźma E, Bao Y, Smart MC, Saum KU, Schöttker B, Engmann J, Kjærgaard M, Karhunen V. Vitamin D and cognitive function: A Mendelian randomisation study. Sci Rep. 7(1):1-8. 2017.

Mahoney AM, Dalby JT, King MC: Cognitive failures and stress. Psychol Rep, 82(3 suppl):1432-1434. 1998.

Mecacci L, Righi S, Rocchetti G: Cognitive failures and circadian typology. Pers Individ Dif. 37(1):107-113. 2004.

Menesgere A, Giridhar V, Bota R, Ravindranath V: Role of Vitamin D on cognitive performance among healthy volunteers of SANSCOG cohort. Clin Nutr Open Sci. 2022.

Mollon J, Knowles EE, Mathias SR, Gur R, Peralta JM, Weiner DJ, Robinson EB, Gur RE, Blangero J, Almasy L, Glahn DC: Genetic influence on cognitive development between childhood and adulthood. Mol Psychiatry. 26(2):656-665. 2021.

Mulligan AA, Luben RN, Bhaniani A, Parry-Smith DJ, O'Connor L, Khawaja AP, Forouhi NG, Khaw KT: A new tool for converting food frequency questionnaire data into nutrient and food group values: FETA research methods and availability. BMJ Open. 4(3):e004503. 2014.

Ogundele OE, Adekoya KO, Osinubi AA, Awofala AA, Oboh BO: Association of adiponectin gene (ADIPOQ) polymorphisms with measures of obesity in Nigerian young adults. Egypt J Med Hum Genet. 19(2):123-127. 2018.

Ogundele OE, Awofala AA, Awofodu AD, Ojo FT: Food Intake in Relation to Obesity and Subjective Cognitive Complaints: A Cross-sectional Study from Nigeria. J Sains Kesihatan Malays. 20(2), 69-76. 2022.

Oscar-Berman M, Shagrin B, Evert DL, Epstein C: Impairments of brain and behavior: the neurological effects of alcohol. Alcohol Res Health, 21(1):65. 1997.

Parsons OA: Neurocognitive deficits in alcoholics and social drinkers: a continuum? Alcohol Clin Exp Res, 22(4):954-961. 1998.

Parsons OA, Nixon SJ: Cognitive functioning in sober social drinkers: a review of the research since 1986. J Stud Alcohol, 59(2):180-190. 1998.

Rossom RC, Espeland MA, Manson JE, Dysken MW, Johnson KC, Lane DS, LeBlanc ES, Lederle FA, Masaki KH, Margolis KL: Calcium and vitamin D supplementation and cognitive impairment in the women's health initiative. J Am Geriatr Soc,. 60(12):2197-205. 2012.

Santangelo G, Baldassarre I, Barbaro A, Cavallo ND, Cropano M, Maggi G, Nappo R, Trojano L, Raimo S: Subjective cognitive failures and their psychological correlates in a large Italian sample during quarantine/self-isolation for COVID-19. Neurol Sci, 42(7):2625-2635. 2021.

Schrier E, Geertzen JH, Dijkstra PU: Subjective cognitive dysfunction in rehabilitation outpatients with musculoskeletal disorders or chronic pain. Eur J Phys Rehabil Med, 53:582-589. 2017.

Stein MS, Scherer SC, Ladd KS, Harrison LC: A randomized controlled trial of high-dose vitamin D2 followed by intranasal insulin in Alzheimer's disease. J Alzheimers Dis, 26(3):477-84. 2011.

Steinberg SI, Negash S, Sammel MD, Bogner H, Harel BT, Livney MG, McCoubrey H, Wolk DA, Kling MA, Arnold SE: Subjective memory complaints, cognitive performance, and psychological factors in healthy older adults. Am J Alzheimers Dis Other Demen, 28(8):776-783. 2013.

Stenfors CU, Marklund P, Magnusson Hanson LL, Theorell T, Nilsson LG: Are subjective cognitive complaints related to memory functioning in the working population? BMC Psychol, 2(1):1-4. 2014.

Stewart R. Subjective cognitive impairment. Curr Opin Psychiatry, 25(6):445-450. 2012.

Teixeira AL, Diniz BS, Campos AC, Miranda AS, Rocha NP, Talib LL, Gattaz WF, Forlenza OV. Decreased levels of circulating adiponectin in mild cognitive impairment and Alzheimer's disease. Neuromolecular Med, 15(1):115-121. 2013.

Topiwala A, Wang C, Ebmeier KP, Burgess S, Bell S, Levey DF, Zhou H, McCracken C, Roca-Fernández A, Petersen SE, Raman B, Husain M, Gelernter J, Miller KL, Smith SM, Nichols TE. Associations between moderate alcohol consumption, brain iron, and cognition in UK Biobank participants: Observational and mendelian randomization analyses. PLoS Med, 19(7):e1004039. 2022.

World Medical Association. World Medical Association Declaration of Helsinki. Ethical principles for medical research involving human subjects. Bull World Health Organ. 79(4):373. 2001.

Yu Z, Li W, Hou D, Zhou L, Deng Y, Tian M, Feng X. Relationship between adiponectin gene polymorphisms and late-onset Alzheimer's disease. PloS One, 10(4):e0125186. 2015.