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Appetite Loss and Neurocognitive Deficits in Late-Life Depression

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Abstract

Objectives—Examine association of appetite loss symptoms to neurocognitive performance in late-life depression (LLD).

Methods—Cross-sectional data from individuals aged 60+ with Major Depressive Disorder (N = 322). Participants received clinical assessment of depression and neuropsychological testing. Factor analysis was used to characterize depression symptom factors, and composite scales were developed for episodic memory, psychomotor executive functions, verbal fluency, and working memory span.

Results—Factor analysis produced a five-factor solution: (1) Anhedonia/Sadness, (2) Suicidality/Guilt, (3) Appetite/Weight Loss, (4) Sleep Disturbance, and (5) Anxiety/Tension. In separate multivariate models for each neurocognitive domain and including all 5 depression factors, higher appetite-loss-related symptoms were associated with lower performance in episodic memory, psychomotor executive functions, and verbal fluency; results were significant with covariates of age, education, race, sex, age of depression onset, and illness burden. No other depression factors were associated with neurocognitive performance in these models. In an additional set of models, the Appetite factor mediated the association between global depression severity and neurocognitive performance.

Discussion—A factor of appetite and weight loss symptoms in LLD was uniquely associated with neurocognitive performance, in contrast to lack of association among other depression symptom factors.

Conclusion—Cognitive deficits are a major adverse outcome of LLD, and prominent appetite loss during acute depression may be a marker for these deficits, independent of overall depression severity. Research is needed to understand the mechanisms that may explain this association, and how it is related to the cognitive and symptomatic course of LLD.

Keywords

geriatric depression; late life depression; appetite loss; neuropsychological; cognitive

INTRODUCTION

Older adults with major depressive disorder (MDD) and comorbid neurocognitive dysfunction face more adverse outcomes than those with either condition alone (Steffens and Potter, 2008, Mehta *et al.*, 2003). Identifying and treating causes of neurocognitive dysfunction in late-life depression (LLD) is essential to reducing its illness burden; however, LLD is a heterogeneous condition and each symptom an individual experiences may not necessarily have an equal influence on neurocognition. In order to treat neurocognitive deficits effectively in LLD, it is important to identify the depression symptoms mostly closely associated with neurocognitive dysfunction, and use this knowledge to inform intervention strategies.

One approach to identifying depression symptoms with a unique contribution to neurocognitive deficits in LLD is to consider symptoms that are more prominent in aging and which plausibly contribute to neurocognitive dysfunction. From this perspective, appetite disturbance is a candidate symptom. First, appetite loss as a symptom among individuals with MDD is more common in those over 60 years of age than those younger (Hybels *et al.*, 2012). Second, there is a physiologic reduction in appetite and food intake with age, known as the anorexia of aging, which is exacerbated by depression symptoms (Chapman, 2007, Morley, 2001). Loss of appetite may contribute to neurocognitive dysfunction in several possible ways. Low food intake may lead to deficiency in micronutrients like vitamin D or iron, which are important to neurocognitive function (Yavuz *et al.*, 2012, Anastasiou *et al.*, 2014). Low food intake can lead to unintentional weight loss in older adults, which is a predictor of frailty and other conditions associated with cognitive impairment (Driscoll *et al.*, 2011). From a neural perspective, appetite-regulating neurohormones are highly expressed in brain regions associated with mood and neurocognition; thus, in theory, deficits in appetite and neurocognition in LLD could be influenced by a common aberrant circuit in the brain.

Review of the existing literature found limited research investigating a direct association between appetite loss and neurocognitive performance in LLD. The most relevant study finding an association between appetite loss and neurocognition in LLD used principal component scores from the Hamilton Depression Rating Scale in a sample of early, midlife, and late age of onset of MDD (age range 30-89), finding: (1) greater weight loss and gastrointestinal symptoms in the late-onset group compared to the early onset group, and (2) higher scores on this component were correlated with lower scores on scales reflecting (a) learning memory and (b) executive functions (Charlton *et al.*, 2013). These findings concur with the rationale of the current study, which sought to test the unique association of appetite loss symptoms to neurocognitive performance in acute LLD, while accounting for clinical and demographic covariates that may also contribute to the association between depression symptoms and neurocognition. Given the heterogeneous nature of depression, we used factor analysis of two widely used clinical measures of depression, the 17-item Hamilton Depression Rating Scale and Montgomery-Åsberg Depression Rating Scale, to identify underlying symptom factors in LLD. Our hypothesis was that the depression symptom factor including appetite loss would be associated with neurocognitive performance in LLD in a multivariate model that includes competing symptom factors and

potential demographic and clinical covariates. Although we did not presume an appetite-related factor as the only factor associated with neurocognition, we also did not propose specific hypotheses regarding other factors.

Methods

Participants

All participants were enrolled in the Neurocognitive Outcomes of Depression in the Elderly Study (Steffens *et al.*, 2004), were 60 years or older, and had acute MDD at time of enrollment. Exclusion criteria included: (1) another major psychiatric illness, including bipolar disorder, schizophrenia, or dementia; (2) alcohol or drug abuse or dependence; and (3) primary neurologic illness, including dementia. Comorbid anxiety disorders (30% of sample) were not excluded, as long as MDD was the primary diagnosis. Individuals were screened and excluded for dementia at time of enrollment based on an established protocol that included review of a comprehensive clinical evaluation, consultation with referring physicians, and cognitive screening with the Mini-Mental State Examination (MMSE; Folstein *et al.*, 1975). Research was in accordance with the Helsinki Declaration (World Medical Association, 2013) and was approved by the Duke University Institutional Review Board.

Antidepressant Treatment

Participants were on multiple medications at study enrollment/time of neuropsychological assessment. Seventy percent of individuals were taking a selective serotonin reuptake inhibitor (SSRI); however, only 18% of patients were on SSRI alone. Other medications included tricyclic antidepressants (16%), monoamine-oxidase inhibitors (1%), and other/atypical antidepressants (e.g., bupropion, venlafaxine, mirtazapine, trazodone, duloxetine; 68%). Only 9% of individuals were on no antidepressant medication at the time of study enrollment.

Clinical Assessment

At enrollment, a geriatric psychiatrist interviewed each depressed participant and assessed depression symptoms with standardized clinical assessments including the 17-item Hamilton Rating Scale for Depression (HRSD17; Hamilton, 1960), and the Montgomery-Åsberg Depression Rating Scale (MADRS; Montgomery and Asberg, 1979, Montgomery and Asberg, 2000). We combined both scales for factor analysis because they capture a broader range of depression symptoms together than either scale alone (Heo *et al.*, 2007). Individuals included in factor analysis had complete data for both HRSD17 and MADRS.

Common factor analysis was performed with SAS Proc Factor (SAS Institute, 2012), using principal components extraction, varimax rotation to produce orthogonal factors, and factor scores from SAS Proc Score. Eigenvalues greater than 1.0 and a scree plot were used to determine number of factors. To facilitate interpretation, we weighted our consideration toward items with factor loadings ≥ 0.50 (see Table 1 for item loadings): Factor 1 was interpreted as Anhedonia and Sadness (Factor name: Anhedonia); Factor 2 was interpreted as Suicidality and Guilt (Factor name: Suicidality); Factor 3 was interpreted as Appetite and

Weight loss (Factor name: Appetite); Factor 4 was interpreted as Sleep Disturbance (Factor name: Sleep); and Factor 5 was interpreted as Anxiety and Tension (Factor name: Anxiety).

Neuropsychological Assessment

Participants completed neuropsychological testing at study enrollment, following standardized procedures. Similar to other studies of neurocognition in depressed older adults (Sheline *et al.*, 2006, Sheline *et al.*, 2010), we created *z*-scores for each neuropsychological measure of interest, derived from performances across all participants. We then created summed averages of the scores, grouped into rational constructs based on clinical and research literature. The Trail Making Test (Parts A and B) was reverse-scored prior to *z*-score conversion so that higher scores represented better performance for all variables. Cronbach's coefficient alpha (α) was computed for each domain.

Episodic Memory—This domain included CERAD (Welsh *et al.*, 1994) Word List Learning (total correct of 3 trials), CERAD Word List Delayed Recall (total correct), Logical Memory I and II subtests from the Wechsler Memory Scale-Revised (total correct; Wechsler, 1987), and total correct on the Benton Visual Retention Test (Sivan, 1992). Cronbach's α was 0.80.

Psychomotor-Executive Function—This domain included the Symbol-Digit Modalities Test (total completed; Smith, 1982) and Parts A and B of the Trail Making Test (time to complete; Reitan, 1992). Cronbach's α was 0.79.

Verbal Fluency—This domain included 1-minute Animal Naming and the Controlled Oral Word Association Test (Benton and Hamsher, 1988). Total correct responses was the index of performance for both tasks. Cronbach's α was 0.83.

Working Memory Span—This domain included the Forward and Backward subtests of Digit Span, from the Wechsler Adult Intelligence Scale-Third Edition (Wechsler, 1997), and Ascending Digit Span (Sair *et al.*, 2006). Total correct responses was the index of performance for each task. Cronbach's α was 0.84.

Illness Burden

Illness burden was assessed with the Cumulative Illness Rating Scale-Geriatric (CIRS-G; Miller *et al.*, 1992), which rates 12 organ systems on a 5-point scale, ranging from 0 (No problem or impairment) to 4 (Extremely severe). Ratings were obtained by the treating psychiatrists.

Statistical Methods

Statistical analysis included examination of descriptive statistics and demographic variables, bivariate correlations to characterize associations of interest, and multivariate regression models to formally test the relationship between depression factor scores and neurocognition. Regression models were based on simultaneous entry. We estimated one model for each neurocognitive domain score, in which the neurocognitive domain score was the dependent variable, and each of the depression factor scores were entered as an

independent variable in the model. In addition, each model included covariates that have been associated with neurocognitive performance in the context of aging and/or depression: age, years of education, sex, race (white/non-white), age of depression onset (< or ≥ 60), and illness burden (CIRS-G) score. A p -value < 0.05 was chosen as an indicator of statistical significance for both the bivariate and multivariate analyses.

RESULTS

Descriptive statistics for demographic and clinical characteristics are shown in Table 2.

Depression Symptom Factors

Higher severity on the Appetite symptom factor were associated with greater age, $r(320) = 0.23$, $p < 0.01$; and fewer years of education, $r(320) = -0.12$, $p = 0.03$. Caucasian race was associated with higher severity on the Anxiety factor, $r(320) = 0.16$, $p = 0.04$. The remaining depression symptom factors had no significant associations with these demographic variables. Later age of depression onset was associated with greater severity on the symptom factors of Anhedonia, $r(320) = 0.11$, $p = 0.05$, and Appetite, $r(320) = 0.19$, $p < 0.01$. Greater illness burden was associated with higher severity on the Anxiety depression symptom factor, $r(320) = 0.13$, $p = 0.02$.

Depression Symptoms and Neurocognition

Correlations between depression symptom factors and neurocognitive domains are presented in Table 3. Pearson correlations indicated that higher symptom severity on the Appetite factor was associated with lower performance across all four neurocognitive domains: episodic memory, $r(314) = -0.28$, $p < 0.01$; psychomotor executive functions, $r(304) = -0.26$, $p < 0.01$; verbal fluency, $r(318) = -0.21$, $p < 0.01$; and working memory, $r(290) = -0.12$, $p = 0.04$. Higher symptom severity on the Anhedonia factor was associated with lower memory performance, $r(314) = -0.11$, $p = 0.04$. Higher symptoms on the Suicidality factor were associated with lower episodic memory performance ($r = -0.11$, $p = 0.04$), but was not associated with the performance in the other neurocognitive domains. There were no significant associations between neurocognitive performance and depression-symptom factors of Sleep, Suicidality, and Anxiety. In addition to the depression symptom factors, a higher combined MADRS-HRSD17 global depression score was significantly associated with lower performance in the domains of episodic memory, $r(314) = -0.17$, $p < 0.01$; psychomotor executive functions, $r(304) = -0.16$, $p < 0.01$; and verbal fluency, $r(318) = -0.15$, $p < 0.01$, but was not significantly associated with working memory span. Individuals with comorbid anxiety were not significantly different from other participants with respect to neurocognitive performance.

The results of the multivariate regression models are presented in Table 4. The Appetite factor was the only depression symptom factor that significantly predicted neurocognitive performance in the multivariate models. Higher Appetite scores were a significant predictor of lower neurocognitive performance in the domains of episodic memory, psychomotor executive functions, and verbal fluency, but were not a significant predictor of working memory span.

In a final set of models, we examined whether Appetite-related depression symptoms mediate the relationship between overall depression symptom severity and cognition. In a first step, individual neurocognitive domains were the dependent variables in separate models, with the total MADRS/HRSD17 score as an independent variable along with the demographic covariates and illness burden. In these models, higher total depression severity was associated with worse performance in the domains of episodic memory, $B = -0.60$, $t(308) = -2.53$, $p = 0.01$, and psychomotor executive function, $B = -0.40$, $t(298) = -2.62$, $p < 0.01$. In a second step, we added the Appetite factor to each individual model and found that total depression severity was no longer significantly associated with episodic memory or psychomotor-executive function; rather, lower performance was associated with greater severity on the Appetite factor in the domains of episodic memory, $B = -9.47$, $t(307) = -2.76$, $p = 0.01$, and psychomotor executive functions, $B = -5.66$, $t(297) = -2.47$, $p = 0.01$. Together, these two sets of models suggest that the significant association of global depression symptom severity to episodic memory and psychomotor-executive functions was fully mediated by symptom severity attributable to the Appetite factor.

DISCUSSION

The current study found that individuals with higher symptoms of appetite loss and weight loss in the context of LLD had worse performance in the neurocognitive domains of episodic memory, psychomotor executive functions, and verbal fluency, controlling for other depression factors reflecting Sadness/Anhedonia, Sleep Disturbance, Suicide/Guilt, and Anxiety/Tension, and also controlling for participant demographics and illness burden. In contrast, we found that other depression symptom factors were not associated with neurocognitive performance. Consistent with previous findings (Charlton *et al.*, 2013), we found that depression symptoms related to appetite and weight loss appear most strongly associated with neurocognitive deficits in LLD compared to other depression symptoms, and we extend this previous work by demonstrating that: (1) the associations are not explained by common demographic and clinical factors, (2) they appear factorially consistent across two widely used measures of depression severity (HARDS17 and MADRS), and (3) they are independent of overall depression severity.

The current study was not designed to directly address mechanistic questions about how appetite loss might be associated with neurocognitive deficits in LLD, but a discussion of potential mechanisms is important to the interpretation of our results and to suggest future directions of research. A possible explanation for the association between appetite loss and cognitive deficits in LLD would be that appetite loss is part of a larger pattern of unmotivated and anergic behavior in depression, which contributes to a common pathway of decreased reward experience in eating and insufficient mental effort for neuropsychological tests. This explanation is suggested by studies finding greater neurocognitive deficits in melancholic depression (Austin *et al.*, 1999), which includes symptoms of appetite and weight loss in its taxonomy (American Psychiatric Association, 2000). In the current study, however, factor analysis found that anhedonic and vegetative symptoms were more strongly associated with depression symptom factors other than appetite loss, and that these factors were not associated with neurocognitive performance. We note that factor analytic studies of the MADRS or HARDS-17 separately have found appetite and weight loss to load on a

vegetative factor with sleep disturbance (Onega and Abraham, 1997, Parker *et al.*, 2003), whereas anhedonia and sadness loaded on a common factor as in the current study; thus, anhedonia does not appear to typically aggregate psychometrically with appetite loss symptoms in LLD. Prior findings that melancholic depression is associated with greater neurocognitive deficits may reflect the presence of appetite loss in the taxonomic classification, but additional research would be useful to reconcile taxonomic and psychometric classification of depression symptoms and their associations with neurocognition.

A potential downstream consequence of appetite loss in LLD with respect to neurocognitive function is nutritional deficiency from low food intake. Several studies have found levels of specific nutrients to be lower in depressed older adults compared to nondepressed elderly, including iron, vitamin D, vitamin B-12, and folate (Stewart and Hirani, 2010, Hoogendijk *et al.*, 2008, Kim *et al.*, 2008). Thus, deficient micronutrient intake may contribute to neurocognitive dysfunction, but at this point research does not indicate what duration and severity of undernutrition would be necessary to produce cognitive dysfunction-- not to mention which specific nutrients would be most influential. Unfortunately, we do not have measures of body weight at study enrollment, and even so, an accurate estimate of weight loss due to acute depression would likely require an objective estimate of weight that predates the onset of depression and study enrollment. These mechanistic questions are best answered in the context of longitudinal studies.

Cognitive deficits in LLD may be consequence of comorbid medical illness, especially those that involve inflammatory processes. LLD has high comorbidity for cardiovascular disease and type II diabetes, both of which are associated with inflammation (Szczepanska-Sadowska *et al.*, 2010). A number of inflammatory agents present in these conditions are also associated with neurocognitive dysfunction (Mcafoose and Baune, 2009), and it is also the case that presence of many of these inflammatory agents is associated with appetite loss (Andreasson *et al.*, 2007). We attempted to control for illness comorbidities by including the CIRS-G in our multivariate models, and did not find this to be associated with neurocognitive performance. It appears unlikely that general illness burden explains the relationship between appetite loss and neurocognitive dysfunction, but we did not directly assess inflammatory markers, which may provide a more specific indicator of illness response.

A homeostatic explanation for our findings would be that appetite loss in LLD reflects an abnormality in processes regulating food intake and energy balance, which may also extend to neurocognitive function. For instance, leptin and insulin are two hormones that can suppress appetite and which are also associated with both depression and neurocognition (Paz-Filho *et al.*, 2010, Hendrickx *et al.*, 2005, Young *et al.*, 2006); however, they have a complex relationship with each other as well as with other hormones, in addition to having potentially different levels of sensitivity based on body weight, sex, and age (Kmieć, 2011). Food intake and energy homeostasis are part of a complex system of multiple central and peripheral messengers involving cognitive, emotional, and hedonic/motivational regions of the brain (Lenard and Berthoud, 2008); thus, more research is necessary to understand how these plausible but complex mechanisms may affect neurocognition in LLD.

The clinical significance of this study is that appetite loss has been identified as a potential marker for neurocognitive deficits in LLD. Effect sizes for correlations between the appetite factor and neurocognitive domains were small, explaining 1-2% of the variance in neurocognitive performance; however, in combination with other risk factors, clinicians could identify classes of patients who may benefit from more extensive evaluation and treatment of potentially reversible factors.

The current study has some potential limitations to the generalizability of our findings. We have already discussed the lack of an objective assessment of weight or body mass index. Because our study design was cross-sectional, it lacked the ability to track changes in mood, appetite, weight, and cognition over time, which limits insight into causal mechanisms. We also studied a sample of individuals who are ambulatory and healthy enough to participate in a research study. The relationships among appetite loss, depression, and cognition may be different among less healthy individuals, and a sample of elders in assisted care would make a useful comparison group, given higher rates of medical comorbidity, malnutrition, and cachexia. Another limitation is that participants were enrolled in a naturalistic treatment study designed to optimize individual treatment response, and as a group were treated with several different psychotropic medications and combinations thereof. In this respect, our sample is more similar to the general population of depressed older adults treated in their community than are samples from single-agent trials. Most individuals were taking an SSRI, and in general this class of drugs is found to improve appetite in depressed individuals rather than the opposite (Thomas *et al.*, 2003). Although we are constrained in our ability to analyze potential effects of single anti-depressant agents, or specific reported side effects, we believe it unlikely that medication differences would have a systematic effect on the relationship between neuropsychological performance and appetite loss, given research suggesting that most antidepressant medications have small-to-nonexistent effects on neurocognitive performance (Siepmann *et al.*, 2003, Podewils and Lyketsos, 2002). Finally, it would be useful to examine neurocognitive performance in a nondepressed comparison group with a comparable assessment of symptoms related to appetite and weight loss, as this was unavailable in the current study.

CONCLUSION

In conclusion, symptoms related to appetite loss had a unique and stronger association to neurocognitive deficits in acute LLD than other depression symptoms. Additional research is needed to understand the clinical and biological factors that explain this association, and how it is related to the neurocognitive and symptomatic course of LLD.

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Table 1

Item loading of MADRS/HRSD17 items for rotated 5-factor solution

MADRS/HRSD17 scale item	Factor				
	Anhedonia	Suicide	Appetite	Sleep	Anxiety
M7-Lassitude	0.77	0.09	0.17	−0.00	0.05
H7-Work/activities	0.73	0.05	0.15	0.03	0.14
M8-Inability to feel	0.69	0.28	0.17	0.12	0.03
M1-Apparent sadness	0.59	0.43	0.21	0.13	0.07
M6-Concentration	0.58	0.01	0.05	0.07	0.29
M2-Reported sadness	0.57	0.50	0.04	0.11	0.15
H13-General somatic	0.54	0.10	0.10	0.08	0.25
H8-Retardation	0.51	0.16	0.27	0.24	−0.13
M10-Suicidal thoughts	0.19	0.81	0.05	0.01	0.10
H3-Suicide	0.13	0.79	0.12	0.03	0.08
M9-Pessimistic thoughts	0.22	0.58	−0.01	0.06	0.29
H1-Depressed mood	0.45	0.58	−0.01	0.13	0.12
H2-Guilt	0.03	0.55	0.16	0.10	0.10
M5-Reduced appetite	0.15	0.21	0.87	0.13	0.12
H16-Loss of weight	0.11	0.18	0.83	0.01	0.05
H12-Gastrointestinal	0.12	0.18	0.82	0.13	0.21
M4-Reduced sleep	0.11	0.12	0.09	0.89	0.07
H5-Middle insomnia	0.06	0.15	−0.00	0.79	0.13
H6-Delayed insomnia	0.10	−0.02	0.10	0.75	0.05
H4-Initial insomnia	0.16	0.04	0.10	0.63	0.11
H10-Anxiety-psychic	0.03	0.20	0.12	0.02	0.79
M3-Inner tension	0.13	0.16	0.10	0.04	0.77
H11-Anxiety somatic	0.19	−0.02	0.03	0.20	0.65
H9-Agitation	0.06	0.09	0.22	0.14	0.51
H14-Loss libido	0.35	0.10	−0.09	0.09	0.08
H17-Loss insight	0.15	−0.17	0.46	0.06	0.18
H15-Hypochondriasis	0.23	0.21	0.06	0.00	0.47
Eigenvalue	3.81	3.12	2.69	2.63	2.59
Variance explained	14.11%	11.55%	10.00%	9.70%	9.60%

Note. MADRS (M) = Montgomery-Åsberg Depression Rating Scale. HRSD17 (H) = Hamilton Rating Scale for Depression-17 item version. Numbers following M or H reflect item number for respective original scale.

Table 2

Demographic Data

N = 322	
Sex (% female)	65%
Race (% Caucasian)	85%
Age of depression onset (% > age 60)	22%

	Mean (SD)
Age	69.00 (6.72)
Education	14.42 (3.17)
MADRS	24.11 (7.71)
HRSD17	17.74 (6.70)
Age of Depression Onset	41.07 (20.77)
CIRS-G	4.79 (3.07)

Note. M = male, F = female. MADRS = Montgomery-Åsberg Depression Rating Scale. HDRS-17 = Hamilton Depression Rating Scale-17 item. CIRS-G = Cumulative Illness Rating Scale-Geriatric.

Table 3

Pearson correlations between neurocognitive composites and depression symptom factors.

Neurocognitive composite	Factor				
	Anhedonia	Suicide	Appetite	Sleep	Anxiety
Memory (n = 316)	−0.11 <i>p</i> = 0.04	0.02 <i>p</i> = 0.77	−0.28 <i>P</i> < 0.01	0.00 <i>p</i> = 0.96	−0.02 <i>p</i> = 0.78
Executive functions (n = 306)	−0.09 <i>p</i> = 0.12	−0.00 <i>p</i> = 0.96	−0.26 <i>P</i> < 0.01	0.03 <i>p</i> = 0.63	−0.06 <i>p</i> = 0.33
Verbal fluency (n = 320)	−0.07 <i>p</i> = 0.16	−0.05 <i>p</i> = 0.38	−0.21 <i>P</i> < 0.01	0.00 <i>p</i> = 0.95	−0.03 <i>p</i> = 0.66
Working memory span (n = 292)	−0.02 <i>p</i> = 0.74	−0.07 <i>p</i> = 0.24	−0.12 <i>P</i> < 0.04	−0.02 <i>p</i> = 0.79	−0.03 <i>p</i> = 0.59

Note. Executive functions = Psychomotor Executive Functions, as referenced in text. Variation in sample size of composite is due to missing data on individual scales across sample.

Table 4
Regression coefficients for depression symptom factors and covariates on neurocognitive performance

	Memory			Psychomotor/Exec			Verbal fluency			Working memory		
	B	η^2	p	B	η^2	p	B	η^2	p	B	η^2	p
Anhedonia	-4.76	0.00	0.14	-3.81	0.00	0.12	-1.17	0.00	0.44	-0.53	0.00	0.81
Suicidality	-1.89	0.00	0.55	-2.46	0.00	0.23	-2.30	0.01	0.13	-3.18	0.01	0.15
Appetite	-11.40	0.02	<0.01	-6.94	0.02	<0.01	-3.33	0.01	0.03	-2.31	0.00	0.33
Sleep	0.11	0.00	0.97	1.62	0.00	0.43	0.98	0.00	0.51	-0.60	0.00	0.79
Anxiety	-1.57	0.00	0.63	-2.29	0.00	0.27	-0.44	0.00	0.77	-1.93	0.00	0.39
Age	-3.06	0.06	<0.01	-2.54	0.10	<0.01	-0.57	0.01	0.02	-0.90	0.01	0.02
Education	9.46	0.15	<0.01	5.52	0.12	<0.01	4.09	0.14	<0.01	4.65	0.10	<0.01
Sex	15.50	0.01	0.03	-5.62	0.00	0.21	0.59	0.00	0.86	-1.01	0.00	0.83
Race	36.90	0.03	<0.01	34.74	0.06	<0.01	18.10	0.04	<0.01	28.15	0.05	<0.01
Age onset	14.04	0.01	0.10	-0.78	0.00	0.89	5.80	0.00	0.15	1.35	0.00	0.82
CIRS-G	1.50	0.00	0.16	-0.79	0.00	0.24	-0.44	0.00	0.38	-0.62	0.00	0.40
F	19.55			21.94			13.66			8.07		
R ²	0.41			0.45			0.33			0.24		
Model p			<0.01			<0.01			<0.01			<0.01

Note. For Sex, female = 1. For Race, Caucasian = 1. For Age of first depression onset, < 60 = 1. SA = Sadness and Anhedonia. SG = Suicide and Guilt. AW = Appetite and Weight Loss. SD = Sleep Disturbance. AT = Anxiety and Tension.