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# Examining HPA-axis functioning as a mediator of the relationship between depression and cognition across the adult lifespan

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## Abstract

**Background—**Altered HPA-axis functioning and cognition are common features in depression, and it has been hypothesized that altered HPA-axis functioning leads to worsened cognition in depression. While associations between cognition and HPA-axis functioning in depression have been shown previously, this work has not examined HPA-axis functioning as a potential mediator of cognition. The current study uses mediation models to examine indirect effects of depression on processing speed, executive functioning, and memory as a function of HPA-axis across the adult lifespan.

**Methods—**38 individuals with a depression diagnosis and 50 healthy controls aged 18–86 underwent comprehensive neuropsychological testing and at-home diurnal salivary cortisol collection. Depression was assessed via structured clinical interviews and rating scales. Factor analyses were used to derive cognitive composite scores. Area under the curve (AUC) was calculated to estimate cortisol exposure throughout the day.

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**Results—**Multivariate linear regressions adjusting for age and sex revealed that depression was associated with higher cortisol levels and slower processing speed compared to healthy controls. Bootstrapped mediation analyses revealed a significant suppression effect of AUC on the relationship between depression and processing speed.

**Limitations—**The cross-sectional nature of the study and limited heterogeneity of our sample limit the interpretation and generalizability of the results.

**Conclusions—**Various studies have inferred that poorly modulated HPA-axis is one mechanism of cognitive alterations in depression, however, results of mediation models did not support this conclusion for processing speed. Longitudinal work is needed and alternative mechanisms should be considered to inform interventions to target cognitive alterations in depression.

### Keywords

depression; cortisol; memory; speeded processing; cognition; HPA-axis

## Introduction

The hypothalamic pituitary adrenal axis (HPA-axis) is a system that regulates the neuroendocrine response to stress through a feedback loop that normally inhibits cortisol production by binding to glucocorticoid receptors in the brain. Disrupted neuroendocrine functioning is a common feature of depressive disorders (Stetler & Miller, 2011) that may mediate the cognitive alterations in depression (i.e., processing speed, executive functioning, memory; Rock et al., 2013). Altered HPA-axis functioning in depression is characterized by a pattern of hyperactivity and a resistant or sluggish feedback loop. Diurnal cortisol patterns may include a greater post-awakening response coupled with elevated afternoon and evening levels (Stetler & Miller, 2011). Prolonged stimulation and release of glucocorticoid receptors may lead to dendritic atrophy (Herbert et al., 2006) in the prefrontal cortex and hippocampus–brain regions involved in processing speed, executive functioning, and memory functioning. Altered HPA-axis functioning is associated with altered cognition in individuals with depression (Egeland et al., 2005; Gomez et al., 2006; Gomez et al., 2009; Hinkelmann et al., 2009). However, the extent to which HPA-axis functioning has a direct role in the cognitive sequelae associated with depression is unclear. Elucidating the role of cortisol in the cognitive profiles observed in depression is important for informing future work given, for example, evidence for both HPA axis functioning and cognition as predictors of poor treatment response (Morimoto et al., 2012; Holland et al., 2013).

To date, the studies that have examined the relationship between HPA-axis functioning and cognition in adults with depression have only tested direct, but not indirect associations. Specifically, for individuals with depression, higher cortisol levels are associated with slower processing speed (Gomez et al., 2006; Hinkelmann et al., 2009), poorer executive functioning (Egeland et al., 2005; Gomez et al., 2006; Hinkelmann et al., 2009), and lower performance on memory measures (Egeland et al., 2005; Gomez et al., 2006; Gomez et al., 2009; Hinkelmann et al., 2009). In contrast, not all studies have found significant associations between cortisol and cognition in depression (Belanoff et al., 2001; Vythilingam et al., 2004). Inconsistencies in the literature may be due, in part, to common

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comorbidities or characteristics of depression that may contribute to altered cortisol or cognition. For example, subtypes of depression that show distinct patterns of altered HPA-axis functioning may act as potential confounds, such as HPA-axis hyperactivity in psychotic depression (Schatzberg et al., 2014; Keller et al., 2017).

The relationship between cortisol and cognition may be particularly important in the context of aging and late life depression. In observational studies, older adults show a flatter diurnal slope (Halbreich et al., 1984; Deuschle et al., 1997) as well as exaggerated cortisol production/poor suppression in HPA-axis challenge studies (i.e., psychological and pharmacological manipulation; Otte et al., 2005). In addition, alterations in cognitive functioning are more pronounced in mid and late life depression, likely for a variety of reasons (Lockwood et al., 2002; Murri et al., 2014). ~~The~~ HPA-axis dysfunction is one proposed mechanism for cumulative cognitive difficulties and increased risk of cognitive decline and dementia in these individuals (Butters et al., 2008; Du & Pang, 2015).

Of note, later onset depression (i.e., first episode during older age) may reflect a distinct subtype of depression, in comparison to depression with an early onset (typically in the late teens/early 20s), in which there is more variable hippocampal morphology and cognitive profiles (Hickie et al., 2005; Ballmaier et al., 2008; Yeh et al., 2011; Geerlings & Gerritsen, 2017). Further, salient cognitive deficits in late onset depression may be linked to underlying vascular or Alzheimer's type neurodegenerative processes (Naismith et al., 2012; Sexton et al., 2012; Bora et al., 2013; Taylor et al., 2013). Most work fails to control for age of depression onset, either statistically or through exclusionary criteria (Reppermund et al., 2007; Gomez et al., 2009; Hinkelmann et al., 2009), including studies with null findings related to HPA-axis functioning and cognition in late life depression (O'Brien et al., 2004; Köhler et al., 2010). Further, Comijs et al., (2010) found no significant interactive association of blood serum cortisol levels and self-reported clinically elevated depression on processing speed, learning, and memory in a large sample of older adults. Thus, studies that have failed to control for late onset depression, coupled with samples that have prevalent medical comorbidities such as diabetes (Yokoyama et al., 2015; Joseph & Golden, 2017) and age-related cognitive decline, may contribute to the varying directionality of findings of HPA-axis functioning in samples that include older adults with depression. As such, the heterogeneity of limitations seen across studies makes it difficult to draw specific conclusions about the HPA-axis functioning and risk for cognitive decline and dementia.

While the literature to date supports an association between HPA-axis functioning as measured by free cortisol and cognition in individuals with depression, this finding has also been shown in individuals without depression and from various diagnostic groups (Fiocco et al., 2006; O'Hara et al., 2007; Beluche et al., 2010; Geerlings et al., 2015), as the negative effects of increased glucocorticoids on cognition is not a depression-specific phenomenon. For example, this phenomenon has been shown in individuals with Cushing's disease (Starkman et al., 2001) and individuals with trauma history (Nemeroff, 2016). Thus, mediation models may elucidate whether there is an indirect effect of depression on cognition via cortisol. In addition, controlling either statistically or via strict inclusion/exclusion criteria for factors that may otherwise influence cognition and/or cortisol is necessary to avoid confounded results.

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The current study examines independent and interactive effects of depression and age on HPA-axis functioning using diurnal cortisol measurements and neuropsychological testing. Processing speed, auditory learning and memory, and aspects of executive functioning are measured among individuals with early-onset depression (i.e., <35 years) and those with no history of depression personally or in first-degree relatives across the adult lifespan. We predict that both a diagnosis of depression and increased age will be positively associated with cortisol levels. There will be an interactive association of depression and age on cortisol such that the positive association between age and cortisol will be significantly greater in individuals with depression compared to healthy controls. Further, we test the indirect effect of depression on cognition via cortisol as measured by area under the curve (AUC). We predict that cortisol will mediate associations between a diagnosis of depression and lower cognition.

## Methods

Participants include 38 adults with Major Depressive Disorder (MDD) and 50 healthy controls (HC) between the ages of 18 and 86. Participants were recruited from outpatient clinics, participant databases, and community outreach for enrollment in depression studies conducted in Ann Arbor, Michigan. The study was approved by the University of Michigan Institutional Review Board and conducted in accordance with the 1975 Declaration of Helsinki, as revised in 2008.

For inclusion in the study, participants had to have greater than 10 years of formal education, an IQ above 70, and English language proficiency at or above the 5$^{th}$ grade level. Exclusion criteria for the study included a history of moderate to severe head injury or minor head trauma with loss of consciousness > 3 minutes; history of dementia, stroke, epilepsy, or other neurological disorder; diagnosis of schizophrenia, bipolar disorder, or psychotic depression; history of alcohol or substance dependence or current alcohol or substance abuse; learning disability; untreated diabetes or other medical instability (e.g. acute, terminal, or worsening major medical condition); major medical treatment such as chemotherapy or radiation; cortisol modifying medications; current or recent (3 months) pregnancy; and substantial suicide risk. Individuals with bipolar disorder were excluded, as the HPA-axis alterations manifest differently in bipolar vs. unipolar depression (Daban et al., 2005). Healthy control participants additionally could not have a personal or first-degree family member with a history of any psychiatric illness. Upon enrollment, the Structured Clinical Interview for the Diagnostic Statistical Manual, Fourth Edition (SCID-IV; First et al., 1995) was administered by Ph.D. level faculty or postdoctoral fellow to evaluate psychiatric history including diagnostic criteria for current MDD and relevant exclusionary criteria (e.g., history of manic episodes, onset of depression ≥ 35). The 17-item Hamilton Depression Rating Scale (HDRS; Hamilton, 1960) was used to assess severity of current depressive symptoms, and a cut-off score of 13 was used to ensure at least moderate symptoms of depression. A proportion of participants with MDD had current antidepressant use ($n$ = 22).

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## Neuropsychological Battery

Participants completed a comprehensive neuropsychological battery administered by trained research assistants. Neuropsychological tests included the California Verbal Learning Test, Second Edition (CVLT-II; Delis et al., 1987), Trail Making Test Parts A & B (TMT-A, TMT-B; Army Individual Test Battery, 1944), Controlled Oral Word Association Test (COWAT; Ruff et al., 1996), Wisconsin Card Sorting Task (WCST; Heaton et al., 1993) and the Parametric Go/No-Go Test (PGNG; Langenecker et al., 2007). The details of the larger battery are reported in Langenecker et al. (2005) and Considine et al. (2011).

## Salivary Cortisol

Participants were provided oral and written instructions to self-collect (at home) salivary cortisol at 8:00am, 12:00pm, 4:00pm, and 9:00pm across one day using the Salivette synthetic swab (Sarstedt AG, Nümbrecht, Germany), including phone call reminders. Samples were not collected on the same day as neuropsychological testing. Participants were instructed to avoid eating, drinking fluids other than water, smoking, or brushing their teeth at least 30 minutes prior to sample collection. This Salivary Cortisol assay is a competitive immunoassay run on the Siemen Centaur automated analyzer using chemiluminescent technology. Cortisol in the participant sample competes with acridinium ester-labeled cortisol in the Lite Reagent for binding to polyclonal rabbit anti-cortisol antibody in the Solid Phase Reagent. The polyclonal rabbit anti-cortisol antibody is bound to monoclonal mouse anti-rabbit antibody, which is covalently coupled to paramagnetic particles in the Solid Phase. The assay required 20 uL of saliva in addition to sufficient dead volume for aspiration and repeat analysis. The assay range is 0.07–7.84 ug/dL and the assay is standardized analytically and confirmed by gas chromatography mass spectroscopy.

Salivary cortisol measurements from the four collection time points (participants had to have all four completed) were used to estimate the total amount of cortisol exposure during waking hours, (i.e., AUC). AUC with respect to ground (Pruessner et al., 2003) was computed for each participant using the formula:

$$(((SalCort12 + SalCort8) * 4)/2) + (((SalCort4 + SalCort12) * 4)/ 2) + (((SalCort9 + SalCort4) * 4) / 2)$$

## Statistical Analyses

Participant characteristics were examined between the MDD and HC groups using analyses of variance (ANOVAs) for continuous variables and Chi-square analyses for categorical variables (See Table 1). Linear regression models were used to examine independent and interactive effects of age and depression on cortisol using AUC. Similar models were used to examine independent and interactive effects of age and depression on cognitive composites controlling for sex. To test the indirect effect of depression on cognitive composite variables via cortisol, the PROCESS macro for SPSS developed by Hayes (2017) was used with a bootstrap estimate (5,000 samples). All models controlled for sex. Significance was set at $p < .05$.

Analyses were conducted on SPSS (v 19.0) and SAS University Edition. Memory composite scores were derived using Bartlett's regression from confirmatory factor analysis of the

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following six scores from the CVLT-II: Total Learning Trials 1–5, Short Delay Free and Cued Recall, Long Delay Free and Cued Recall, and Recognition (Table 2). To obtain reliable data-driven composites of executive functioning and information processing, scores from the following variables were entered into a factor analysis using an oblimin rotation: WCST perseverative responses, WCST categories completed, TMT-A time to completion, TMT-B time to completion, PGNG levels 1–3 average response time, PGNG levels 2–3 mean inhibitory control accuracy, PGNG levels 1–3 average attention accuracy, and COWAT total raw score. Scores were inverted as needed so that greater values indicated superior performance. Missing values were mean imputed. The factor analysis resulted in four factors that accounted for 81.05% of the variance (Table 2). Weighted composites were created using the default regression setting in SPSS. Composite scores captured the following cognitive domains: auditory verbal learning and memory, processing, attention/fluency, inhibitory control, conceptual reasoning/set shifting.

## Results

### Depression and Age Associations with Cortisol

There was a significant effect of depression on estimated cortisol exposure throughout the day (AUC) regardless of age and sex, such that the MDD group exhibited greater estimated cortisol exposure across the day than the HC group [$ß = .24$, t(77) = 2.16, $p = .03$, $d = .50$]. There was no significant effect of age on AUC [$ß = -.08$, t(77) = −.61, $p = .54$, $d = .15$, *ns*] and no Depression x Age interaction on AUC [$ß = -.17$, t(76) = −1.20, $p = .23$, $d = .34$, *ns*]. See Figure 1 for cortisol plotted across the day in individuals with depression and healthy controls. ANCOVAs controlling for age and sex revealed that salivary cortisol was significantly greater in those with depression compared to controls at 12pm and 9pm collection points (See Figure 1).

### Depression and Age Associations with Cognition

Results of linear regression models testing independent and interactive effects of depression and age on cognitive composites are presented in Table 2. There was a significant main effect of depression on processing speed such that individuals with depression performed worse than controls [$ß = -.18$, t(84) = −2.19, $p = .03$, $d = .37$]. There was a significant negative association between age and memory, processing speed, attention/fluency, and conceptual reasoning/set shifting (see Table 2). Analyses exploring the interactive effects of age and depression were not significant for any of the cognitive composites (all $p$-values > .10).

### Mediation Models

Bootstrap estimated mediation models adjusting for sex examined the indirect effect of depression on processing speed via AUC (see Figure 2). The mediation analysis revealed a significant effect of depression on processing speed [*'c path'; b* = −.45, $p = .017$], a significant effect of depression on AUC [*'a path'; b* = 1.61, $p = .03$], and a significant effect of AUC on processing speed [*'b path';b* = .07, $p = .009$]. There was a significant indirect effect of depression on processing speed via AUC [*'c path'; b* = −.57, SE = .07, 95% CI: .01, .31].

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## Discussion

The current study used mediation models to examine indirect effects of depression on cognition in multiple domains as a function of HPA-axis functioning in a sample of adults across the lifespan. In contrast to previous investigations of diurnal cortisol and cognition in depression, we excluded for late onset depression, which may have a distinct etiology and neuropsychological profile that is not tied to early alterations in the HPA-axis (Naismith et al., 2012). Consistent with the literature, across participants with and without depression, increasing AUC measurements were associated with slower processing speed. However, while previous work infers (but does not directly test) that cortisol production mediates differences between individuals with depression and without depression on cognition, our mediational model does not support this conclusion. In fact, our results suggest that variation in exposure to cortisol across the day as measured by AUC has a suppression effect on the relationship between depression and processing speed. This work highlights the importance of testing underlying mechanisms of cortisol in the role of the effect of depression on cognition directly using mediation models.

Extensive work in animal models and humans has led to the hypothesis that cognitive and brain structural alterations often present in depression may be due in part to a resistant HPA-axis. Specifically, there is work to suggest that chronic, repeated and elevated exposure to glucocorticoids can lead to retraction of dendritic spines or stunted neurogenesis in brain regions with glucocorticoid receptors (e.g., CA3 region of the hippocampus; McEwen, 1999). On the basis of this literature, we hypothesized that AUC would mediate, i.e., significantly reduce the strength of the relationship, between depression status and cognition, particularly memory. However, our mediation models examining the indirect effect of depression on cognition via AUC showed no mediating effect of auditory verbal learning and memory, and a suppression effect of speeded processing. One potential interpretation of this suppression effect is that some individuals with depression exhibiting a particular pattern of hypercortisolemia may be less prone to slowed processing to the same extent as others with depression. In addition to this interpretation of these findings, depression may be concurrently driving changes in cortisol and processing speed (den Hartog et al., 2003). Per the bootstrapped mediation models and consistent with the literature, AUC was negatively associated with both processing speed and auditory learning and memory. Of note, previous work with similar results has interpreted the direct association between HPA-axis functioning and cognition to support the aforementioned glucocorticoid hypothesis. However, it is conceivable that the relationship between altered HPA-axis functioning and cognition is not ubiquitous in or exclusive to depression, and therefore controlling for variability in AUC (in individuals with depression or healthy controls) strengthened the existing relationship between depression and processing speed.

The lack of mediation effects in relation to auditory learning and memory was surprising, particularly given meta-analytic work to suggest that evening cortisol is negatively associated with hippocampal volume in older adults with depression (Geerlings & Gerritsen, 2017). Further, afternoon administration of fludrocortisone elicits beneficial effects on memory retrieval in younger adults with depression (Otte et al., 2015a), but detrimental effects on memory retrieval in older adults with depression (Otte et al., 2015b). Possibly due

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to lack of power, the current study may not have observed an effect of cortisol on memory, but future work with larger sample sizes could ascertain whether moderated (age) mediation (HPA-axis functioning) is present. Further, longitudinal evidence indicates that persistent elevated daily cortisol exposure is a better predictor of memory in healthy older adults than single measurements alone (Segerstrom et al., 2016). Antidepressant use in a portion of our sample ($n$ = 22; ~58%) may also contribute to these null results, a notable limitation of the design as it related to the current investigation.

In the context of aging, it has been further hypothesized that a resistant HPA-axis may confer increased risk for cognitive decline and the development of dementia in late life depression (Butters et al., 2008). Given the lack of depression-by-age interactive effects and our limited sample size, we did not examine mediation models related to this hypothesis. However, it is important to note that previous work including samples of adults with depression may be confounded by inclusion of late onset depression. In addition, previous work has identified the presence of both hypo- and hypercortisolemia in late life depression (Bremmer et al., 2007; Penninx et al., 2007). While, our data did not descriptively suggest this AUC pattern in our older adults, the presence of relative hypocortisolemia may nevertheless contribute to null findings. As there are no known normative ranges for salivary diurnal cortisol, this could not be examined more directly.

Our results support previous work identifying separate positive associations of both depression and age on cortisol across the day (Halbreich et al., 1984; Deuschle et al., 1997; Stetler & Miller, 2011). In our MDD group specifically, salivary cortisol measurements were significantly greater at the 12pm and 9pm time points, and marginally greater at 4pm. While data was not available regarding post-awakening cortisol levels, our findings suggest moderate-sized effects of depression on HPA-axis functioning across the day. Associations between decreased performance and increased age were present for nearly all cognitive composites including auditory learning and memory, processing speed, attention/fluency, and conceptual reasoning/set shifting.

While depression was also associated with processing speed and auditory learning and memory, no hypothesized interactive effects of depression and age were present on any of the cognitive composites. This may be due to our limited sample size, or idiosyncratic characteristics of our sample. Specifically, given that our sample is highly educated and has above average intelligence on average, cognitive reserve may buffer the combined effects of aging and depression on cognition. Further, our lack of interactive effects may be due in part to the lack of age effects on AUC.

In conclusion, our findings suggest that while HPA-axis functioning is associated with processing speed and memory, the role it plays in the cognitive sequelae observed in depression may be more complex than what is currently hypothesized. Future work can address this complex issue by obtaining multiple measures of HPA-axis dysfunction in a longitudinal design to 1) reliably identify individuals experiencing chronic exposure to excess glucocorticoids and 2) examine mediation models that can infer directionality and causation. Understanding the interplay of biomarkers such as diurnal cortisol and cognitive performance that predict treatment outcomes is important for providing appropriate

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interventions. Increasing evidence suggests that altered patterns of HPA-axis functioning is can be attributed to depression subtypes (e.g., hypoactivity in atypical depression), genetic predisposition (e.g., 5-HTTLPR or NR3C2 genes; Smart et al., 2015; Ancelin et al., 2017; Keller et al., 2017) and early development experiences (e.g., trauma; Heim et al., 2010). However, the extent to which the cognitive sequelae associated with depression is a result of altered HPA-axis functioning is yet to be determined.

## Limitations

Limitations exist that may influence the interpretation of these results. First, the individuals in this study are representative of highly educated non-minority individuals likely from higher socioeconomic strata, and thus limit generalizability to other populations. In addition, the sample size may have limited our power to detect significant relationships, though our sample was larger than the majority of other studies examining diurnal cortisol and cognition in depression. Third, as the study design is cross-sectional, we cannot infer causation. Particularly in relation to older adults, it is conceivable that functional and structural brain changes associated with depression and common comorbidities (e.g., vascular diseases) may precede alterations in HPA-axis functioning, further maintaining depressive symptoms including cognitive complaints. Fourth, limitations related to our statistical approach include lack of control for multiple comparisons and the mean imputation of missing values. Fifth, we did not distinguish between typical versus atypical depression, which may be associated with distinct HPA-axis profiles. Finally, the times at which cortisol collections were made were the same for all participants, and not dependent upon usual awakening and bed times. In this vain, our findings may be influenced by individual differences in circadian rhythms (i.e., as cortisol was collected at the same time of day and not in intervals upon waking). Thus, findings may have been different had an alternative time sequence for cortisol collections been used.

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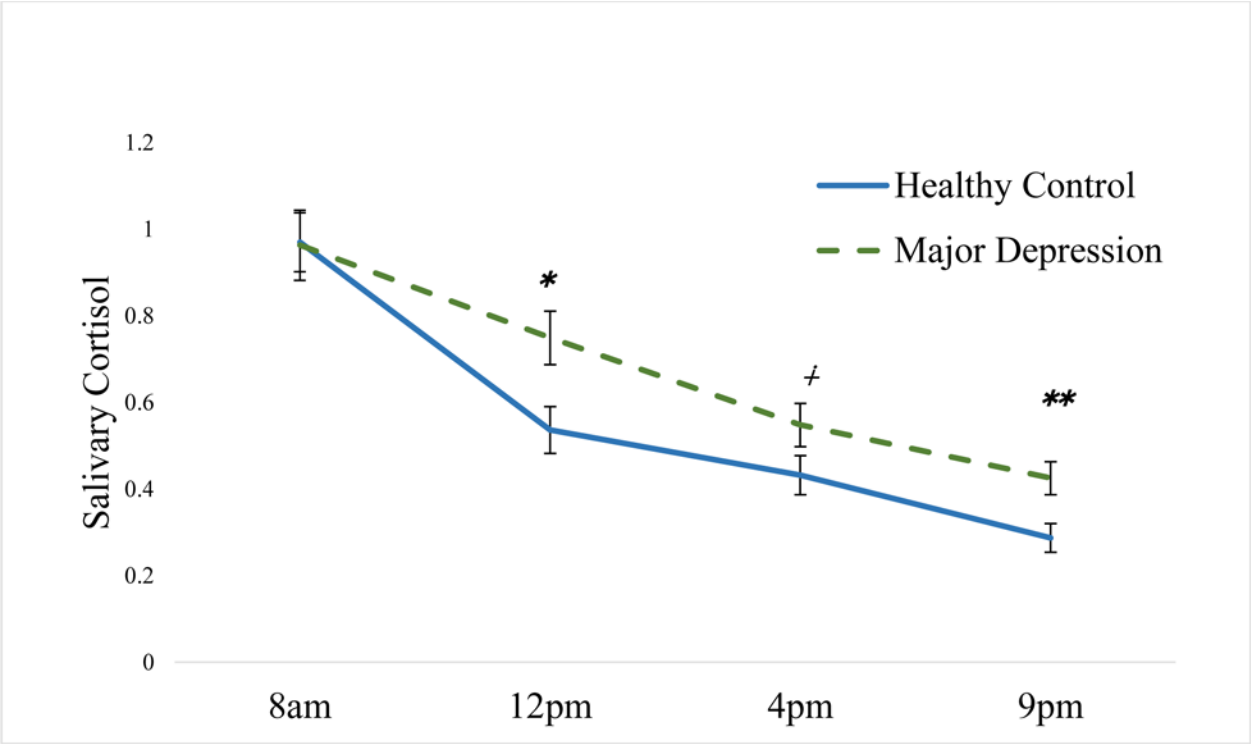


**Figure 1.**
Estimated group mean and standard error of the mean salivary diurnal cortisol measurements.
+$p$<.10, * $p$ < .05, **$p$ < .01

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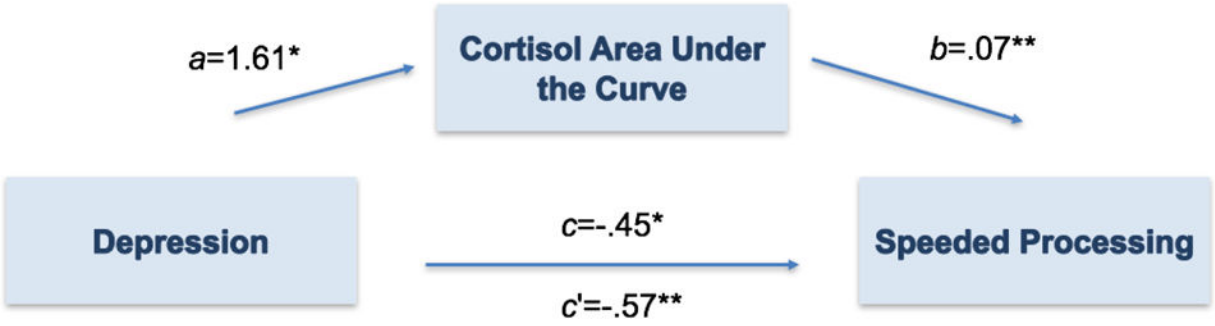


**Figure 2.**

Mediation model test the indirect effect of depression on speeded processing via area under the curve.

* $p < .05$, ** $p < .01$

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**Table 1.**

Participant Characteristics

| | MDD (38) | HC (50) |
|---|---|---|
| Age, M(SD) | 43.0 (19.5) | 45.9 (22.3) |
| Education, M(SD) | 15.5 (2.4) | 16.0 (2.2) |
| Female, % | 25, 65.8% | 26, 52.0% |
| MMSE, M(SD) | 28.4 (1.5) | 28.2 (1.8) |
| Shipley Estimated IQ, M(SD) | 111.1 (9.7) | 112.5 (9.0) |
| Age at first episode, M(SD) | 20.3 (11.7) | — |
| HDRS, M(SD) ** | 18.6 (5.9) | 0.9 (1.5) |
| BDI, M(SD) ** | 29.5 (10.1) | 1.5 (2.5) |
| BAI, M(SD) ** | 15.6 (11.6) | 1.3 (2.2) |

Note: BAI: Beck Anxiety Inventory; BDI: Beck Depression Inventory II; HDRS: Hamilton Depression Rating Scale

** $p<.001$

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**Table 2.**

Factor loadings for cognitive scores with oblimin rotation and linear multivariable regression results.

| Factor | Test | Loading | Depression | Age | DepressionXAge |
|---|---|---|---|---|---|
| Auditory Verbal Learning & Memory | | | ß = −.16, *t*(84) = −1.85, *p* = .07, *d* = .33 † | ß = −.03, *t*(84) = −6.83, *p*<.001, *d* = 1.47 ** | ß = −.09, *t*(83) = −.86, *p* = .39, *d* = .18 |
| | California Verbal Learning Test-II | | | | |
| | Trials 1–5 | .89 | | | |
| | Short Delay Free Recall | .95 | | | |
| | Short Delay Cued Recall | .93 | | | |
| | Long Delay Free Recall | .97 | | | |
| | Long Delay Cued Recall | .96 | | | |
| | Recognition hits | .70 | | | |
| Processing Speed | | | ß = −.18, *t*(84) = −2.19, *p* = .03, *d* = .37 * | ß = −.63, *t*(84) = −7.56, *p* < .001, *d* = .1.65 ** | ß = .05, *t*(83) = .48, *p* = .63, *d* = .10 |
| | Trail Making Test Form A | .85 | | | |
| | Trail Making Test Form B | .88 | | | |
| | Parametric Go/No-Go Test Mean Target Response Time | .76 | | | |
| | Wisconsin Card Sorting Test Correct | .49 | | | |
| | Wisconsin Card Sorting Test Perseverative Responses | .52 | | | |
| Attention/Fluency | | | ß = −.03, *t*(84) = −.25, *p* = .80, *d* = .05 | ß = −.26, *t*(84) = −2.44, *p* = .02, *d* = .54 * | ß = .004, *t*(83) = .03, *p* = .98, *d* = .01 |
| | Controlled Oral Word Association Test Total | .90 | | | |
| | Parametric Go/No-Go Mean Target Trials Accuracy | .61 | | | |
| | Parametric Go/No-Go Mean Target Response Time | .40 | | | |
| Inhibitory Control | | | ß = −.06, *t*(84) = −.55, *p* = .58, *d* = .12 | ß = −.02, *t*(84) = −.15, *p* = .88, *d* = .12 | ß = −.23, *t*(83) = −1.68, *p* = .10, *d* = .48 |
| | Parametric Go/No-Go Mean Inhibitory Trials Accuracy | .97 | | | |
| Conceptual Reasoning and Set-Shifting | | | ß = .01, *t*(84) = .15, *p* = .88, 1.025, *d* = .03 | ß = −.02, *t*(84) = −5.12, *p* < .001, *d* = 1.11 ** | ß = −.03, *t*(84) = −.28, *p* = .78, *d* = .07 |
| | Wisconsin Card Sorting Test Correct | .92 | | | |
| | Wisconsin Card Sorting Test Perseverative Responses | .93 | | | |
| | Parametric Go/No-Go Mean Target Trials Accuracy | .65 | | | |

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| Factor | Test | Loading | Depression | Age | DepressionXAge |
|---|---|---|---|---|---|
| | Trail Making Test Form A | .47 | | | |
| | Trail Making Test Form B | .48 | | | |

*Note*: All regression analyses controlled for sex.

$^{**}p < .01$

$^{*}p < .05$

$^{\dagger}p < .10$