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Associations of DHEA(S) with negative and positive affect in people who smoke daily with elevated and low depression symptoms: A pilot laboratory study

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Abstract

Background: Individuals with depression symptoms have a harder time quitting smoking. High negative affect and low positive affect are core depression symptoms and arise following cigarette abstinence. Investigating associations of biological markers with negative and positive affect may provide valuable information about factors relevant to smoking cessation in individuals with elevated depression symptoms. Methods: Depression symptoms were measured at a baseline session. Participants then completed two counterbalanced experimental sessions (non-abstinent, abstinent) and completed measures of positive and negative affect, and provided saliva samples. Saliva samples were assayed at the Salimetrics' SalivaLab (Carlsbad, CA) using the Salimetrics Salivary Dehydroepiandrosterone (DHEA) Assay Kit (Cat. No. 1-1202) and Dehydroepiandrosterone-sulfate (DHEA-S) Assay Kit (Cat. No. 1-1252). Results: There were no main or interactive associations of DHEA with negative affect. However, there were significant DHEAS × experimental session and DHEAS × experimental session × depression symptom level interactions with negative affect. In the high depression symptom group, DHEAS positively associated with negative affect during the non-abstinent experimental session, but DHEAS negatively associated with negative affect during the abstinent experimental session. There were no associations of DHEA or DHEAS with positive affect. Conclusion: This study found that DHEAS negatively associated with negative affect during cigarette abstinence in individuals with elevated depression symptoms. This is important as high negative affect during cigarette abstinence may result in a return to smoking.

Keywords: people who smoke, depression symptoms, cigarette smoking, DHEA(S), positive affect, negative affect

1. [1]Introduction:

Tobacco smoking is the leading cause of preventable disease (Samet, 2013) and individuals with elevated depression symptoms are more likely to initiate smoking and have a harder time quitting smoking (Fluharty, Taylor, Grabski, & Munafò, 2017; Pang, Farrahi, Glazier, Sussman, & Leventhal, 2014). High negative affect and low positive affect are core symptoms of depression (Mathew, Hogarth, Leventhal, Cook, & Hitsman, 2017) and are prominent symptoms following cigarette abstinence (Klemperer, et al., 2021; Pang, Chai, et al., 2022). Investigating associations of biological markers with affect may provide valuable information about factors relevant to smoking cessation in individuals with elevated depression symptoms.

Naturally produced in the adrenal gland, dehydroepiandrosterone (DHEA) and dehydroepiandrosterone sulfate (DHEAS), which are often collectively referred to as DHEA(S), are precursors of sex hormones (Prough, Clark, & Klinge, 2016). DHEA(S) fulfills a central function as neurosteroids/neuroendocrine hormones and play important role as neural modulators (Maninger, Wolkowitz, Reus, Epel, & Mellon, 2009; Prough, et al., 2016). DHEA(S) may play a role in brain regions important for affect and affect regulation. fMRI studies have found that administration of DHEA (vs. placebo) reduces activity in brain regions associated with negative affect, increases activity in brain regions associated with affect regulatory processes, and modulates resting amygdala connectivity (Sripada, et al., 2013; Sripada, Welsh, Marx, & Liberzon, 2014). Another study found that higher endogenous DHEAS/DHEA ratio is associated with faster and smaller brain wave response to negative affective stimuli (do Vale, et al., 2015).

[1]DHEA – dehydroepiandrosterone
[2]DHEA(S) – dehydroepiandrosterone sulfate
[3]CO – carbon monoxide

Additionally, a handful of studies have investigated associations between DHEA(S) and affect in people who smoke. Studies in people who smoke have demonstrated an association of endogenous DHEA(S) with negative affect (Marx, et al., 2006; Van Voorhees, et al., 2013), but these prior studies did not investigate DHEA(S) and positive affect, which may be important to study in relation to cigarette smoking (Heffner, Mull, McClure, & Bricker, 2018; Hughes, Klemperer, & Peasley-Miklus, 2020; Klemperer, et al., 2021). Additionally, prior work has not investigated depression symptoms and abstinence as potential moderators of associations between DHEA(S) and negative affect.

Previous studies have revealed lower endogenous DHEA(S) levels in individuals with elevated depression symptoms (Barrett-Connor, von Mühlen, Laughlin, & Kripke, 1999; Michael, Jenaway, Paykel, & Herbert, 2000; Walther, et al., 2019). Furthermore, individuals with depressive disorders have been found to have an attenuated salivary DHEA(S) response to a psychosocial stressor (Jiang, et al., 2017). DHEA supplementation has been shown to improve depression symptoms in individuals with disorders characterized by elevated depression symptoms (Peixoto, et al., 2018). Taken together, these studies suggest that DHEA(S) may be dysregulated in individuals with elevated depression symptoms, especially in response to stress, and that increasing DHEA(S) may improve affect symptoms in individuals with elevated depression symptoms.

Cigarette abstinence effects include low positive affect and high negative affect (Hughes, et al., 2020; Klemperer, et al., 2021; Pang, Chai, et al., 2022). Studies have also shown that cigarette abstinence decreases DHEA(S) (Beckham, Calhoun, Dennis, Wilson, & Dedert, 2013). Furthermore, one study found that decreases in plasma DHEA/cortisol ratio during eight days of cigarette abstinence during a quit attempt were associated with cigarette relapse (Rasmusson,

Wu, Paliwal, Anderson, & Krishnan-Sarin, 2006). Thus, it is important to investigate whether both depression symptoms and cigarette abstinence may moderate associations between DHEA(S) and affect because this could provide suggestive evidence concerning whether DHEA supplementation may be helpful during cigarette abstinence particularly in individuals with elevated depression symptoms.

The current laboratory study included experimental manipulation of acute cigarette abstinence in individuals with low and elevated depression symptoms not attempting to quit smoking. The first aim is to characterize the effects of DHEA(S) on negative and positive affect. We hypothesize that DHEA(S) will negatively associate with negative affect. As prior studies have not investigated DHEA(S) associations with positive affect, we do not propose a specific hypothesis for DHEA(S) with positive affect. The second aim is to investigate whether depression symptom level and acute cigarette abstinence moderate associations of DHEA(S) with affect. We hypothesize that the association of DHEA(S) with negative and positive affect will be greater for individuals with elevated depression symptoms and during abstinent sessions. We will also explore the three-way interaction between DHEA(S), abstinence, and depression symptom level on negative and positive affect, but we do not propose any specific hypotheses.

2. Material and Method

2.1: Participants

Non-treatment seeking people who smoke cigarettes were recruited from the Los Angeles, California (US) metropolitan area. To be eligible for the study, participants had to (1) be ≥21 years of age; (2) report regular cigarette smoking for at least the past year; (3) currently smoke 5+ cigarettes/ day; and (4) be fluent in English. Participants were excluded for (1) meeting diagnostic criteria for lifetime bipolar disorder, current posttraumatic stress disorder, or

a current substance use disorder for substances other than nicotine assessed via a structured clinical interview—the Mini International Neuropsychiatric Interview (M.I.N.I.; Sheehan et al., 1998) by a research assistant; (2) an expired breath carbon monoxide (CO) level < 8 ppm at the baseline screening session; (3) current use of nicotine replacement or other medications implicated in smoking cessation (e.g., Chantix [varenicline], Wellbutrin/Zyban [bupropion]); (4) daily use of non-cigarette tobacco and nicotine products (e.g., e-cigarettes/vaping devices, cigars); (5) current pregnancy or intent to get pregnant; and (6) current detailed plans to cut down or quit smoking.

2.2: Procedure

Participants were screened for eligibility and completed baseline measures. Eligible participants completed two counterbalanced experimental sessions (16 hours abstinent and 16 hours non-abstinent). We chose 16 hours of abstinence based on previous studies that suggest this acute abstinence period generates reliable affect related to cigarette withdrawal (Pang & Leventhal, 2013; Smith, et al., 2008) and affect related withdrawal following acute cigarette abstinence in the laboratory is predictive of affect related withdrawal during a cigarette quit attempt (Strong, et al., 2011). Sessions began between 11am and 1pm to control for the abstinence period and diurnal variation in DHEA(S) (Prough, et al., 2016; Whetzel & Klein, 2010). At each experimental session, participants completed breath tests to confirm alcohol abstinence and carbon monoxide (CO) levels (Vitalograph breath CO monitor) and asked to rinse their mouth if they had recently had food or drink (other than water) in the last hour. Five saliva samples were collected at repeated intervals for each session, and participants completed self-report questionnaires prior to and following smoking one of their own cigarettes (non-abstinent session) or a 5-minute break (abstinent session). Sample 1 was collected immediately following

beath tests. The following samples were timed at +5, +20, +35 and +50 mins after the end of the cigarette break or rest period. Participants completed the Profile of Mood States (POMS) following the end of saliva sample 3 collection. The authors declare no conflict of interest.

2.3: Measures

REDCap electronic data capture tools hosted at the University of Southern California (Harris et al., 2009) was used to administer measures.

2.3.1: Baseline Measures

Demographics, smoking history, and Fagerström Test for Cigarette Dependence (FTCD). Demographics (e.g., age, race/ethnicity) and cigarette history (e.g., cigarettes per day, age started smoking) were assessed using an author-constructed questionnaire. The FTCD is a widely used 6-item self-report measure of cigarette dependence (Fagerström, 2003, 2012).

The Center for Epidemiologic Studies Depression Scale (CES-D). The CES-D is a 20-item self-report scale that measured the frequency of past week depression symptoms (Radloff, 1977). Participants rate responses from 0 (*Rarely or none of the time, 0-1 days*) to 3 (*Most or all of the time, 5-7 days*) on a 4-point Likert scale. Items are summed to determine a total score ranging from 0 to 60. As in our prior work (Pang, Tucker, D'Orazio, Weinberger, & Guillot, 2022; Tucker, et al., 2022), a binary CESD score was created for elevated depression symptoms (≥20) and low depression symptoms (<20). A meta-analysis in general populations and primary care settings found a cutoff of 20 showed better sensitivity to specificity trade-off than the generally recommended cutoff of 16 (Vilagut, Forero, Barbaglia, & Alonso, 2016).

2.3.2: Experimental Measures

Profile of Mood States (POMS). The POMS was used to assess positive and negative affect (Grove & Prapavessis, 1992). The 40-item scale is used to assess short-term

mood states including tension, depression, fatigue, vigor, confusion, anger, and esteem-related affect with responses ranging from 0 (*Not at all)* to 4 (*Extremely*) on a 5-point Likert scale. We computed a mean score for positive and negative affect. Mean negative affect did not include negative affect fatigue items based on prior study that did not find fatigue to associate with other negative affect subscales (Grove & Prapavessis, 1992). This scoring was also used in our prior publication (Pang, Tucker, et al., 2022)

DHEA(S). Saliva samples were collected using the passive drool method in 2 ml tubes. Following the fifth sample collection, saliva samples were carried in a water-resistant laminated cryostorage box to a Thermo Scientific high-performance freezer and stored at -20C. For shipping, saliva samples were packed using dry ice and insulation materials in a Styrofoam insulated cooler designed by Salimetrics to maintain the cold-chain and protect sample integrity in transportation. Samples were shipped overnight (from Los Angeles, CA to Salimetrics SalivaLab in Carlsbad, CA).

Samples were assayed at the Salimetrics' SalivaLab (Carlsbad, CA) using the Salimetrics Salivary DHEA Assay Kit (Cat. No. 1-1202) and DHEA-S Assay Kit (Cat. No. 1-1252), without modifications to the manufacturers' protocol. Samples were thawed to room temperature, vortexed, and then centrifuged for 15 minutes at approximately 3,000 RPM (1,500 × g) immediately before performing the assay. Salivary DHEA sample test volume was 50 µl of saliva per determination. The DHEA assay has a lower limit of sensitivity of 5 pg/mL, a standard curve range from 10.2-1000 pg/mL, and an average intra-assay coefficient of variation of 5.55%, and an average inter-assay coefficient of variation 8.20%. Salivary DHEAS sample test volume was 100 µl of saliva per determination. The DHEAS assay has a lower limit of sensitivity of 43 pg/mL, a standard curve range from 189-15,300 pg/mL, and an average intra-assay coefficient of

variation of 7.25%, and an average inter-assay coefficient of variation 7.55%. These values meet the manufacturers' criteria for accuracy and repeatability in Salivary Bioscience and exceeds the applicable NIH guidelines for Enhancing Reproducibility through Rigor and Transparency. For ease of interpretation of estimates, DHEA and DHEAS were converted to ng/mL.

2.4: Data analysis

Preliminary analyses included running descriptives and checking for DHEA(S) outliers (i.e., values that were more than 3 standard deviations from the mean). Primary analyses were run excluding DHEA (n=2) or DHEAS (n=2) outliers and used multilevel linear models to investigate the associations of DHEA(S) with negative and positive affect. DHEA and DHEAS were run in separate models. First, models were run with hormone (DHEA or DHEAS), experimental session (abstinent vs non-abstinent), depression symptom levels, and covariates on positive and negative affect. We then ran models with two-way interactions between hormone (DHEA or DHEAS) × experimental session, hormone (DHEA or DHEAS) × depression symptom level, and depression symptom level × experimental session. Last, exploratory models were run looking at the three-way interaction of hormone (DHEA or DHEAS) × experimental session × depression symptom level. Significant interactions were followed up by stratified models. Effect sizes for significant findings were calculated using Xu (2003) operationalization of R^2 as the residual variance of the model compared to the residual variance of the intercept-only model.

3. Results

3.1: Preliminary results

Eighty-eight participants were found eligible at a baseline study and enrolled in the study. Of the 88 enrolled in the study, 8 did not complete any experimental sessions (unable to

complete study tasks n=2; no longer interested/lost to follow-up n=6). This left 80 participants that completed at least one experimental session including saliva collection for DHEA(S) analyses. Those completing an experimental session (n=80) did not differ from those not completing an experimental session (n=8) in age, sex, depression symptoms (continuous CESD) or depression symptom level (binary CESD), cigarette dependence, and baseline cigarettes per day (ps>.05).

In the analytic sample (n=80, 40% female), participants were on average 41.2 (SD=13.3) years old, and had an average FTCD of 4.9 (SD=1.85) indicating a low to moderate level of cigarette dependence (Fagerstrom, Heatherton, & Kozlowski, 1990). The low depression symptom group (n=51, 63.7%) had an average CESD score of 8.27 (SD=6.13), and the elevated depression symptom group (n=29, 36.3%) had an average CESD score of 32.17 (SD=9.18). The low and elevated depression symptom groups did not significantly differ by sex, cigarette dependence, or baseline cigarettes per day (ps>.05). The elevated depression symptom group was significantly younger and had significantly higher depression symptoms (ps<.001).

A total of 780 samples from 156 experimental sessions (5 samples/session) were sent to Salimetrics for DHEA(S) analysis. Seventeen (2.18%) samples were unable to calculate a DHEA mean value due to one or both of the repeats not having enough saliva to run the test (n=4) or DHEA not being detected or below the assay sensitivity threshold (n=13). Twelve samples were unable to calculate a DHEAS mean value due to one or both of the repeats not having enough saliva to run the test (n=10) or DHEAS not being detected or below the assay sensitivity threshold (n=2). Our primary predictor was the average of the first 3 saliva collection time points, which were collected prior to the completion of our primary outcome questionnaires. A total of 154 values from 79 individuals were calculated for DHEA. One person did not have any

valid DHEA values from any session (i.e., all DHEA samples were not detected or below the sensitivity threshold). A total of 156 values from 80 individuals were calculated for DHEAS. Outliers were calculated as 3 standard deviations above the mean and removed from models (DHEA outliers n=2; DHEAS outliers n=2). This left a final sample of 152 DHEA and 154 DHEAS averages for the primary analyses. Excluding outliers, on average DHEA was 0.13 (SD=0.10) and DHEAS was 3.76 (SD=3.51).

3.2: Primary results

There were no significant main, two-way, or three-way interactive effects of DHEA with negative affect (Table 1). There was a significant two-way DHEAS × experimental session interaction with negative affect (DHEAS model 2 R^2=0.23). DHEAS positively associated with negative affect during the non-abstinent experimental session, but DHEAS negatively associated with negative affect during the abstinent experimental session (Table 1). There was also a significant three-way interaction of DHEAS × experimental session × depression symptom level (Figure 1, DHEAS model 3 R^2=0.21). Models stratified by depression symptom level demonstrated a significant DHEAS × experimental session interaction with negative affect in individuals with elevated depression symptoms (Table 1). There was not a significant DHEAS × abstinence interaction with negative affect in individuals with low depression symptom levels (Table 1). There were no significant main, two-way, or three-way interactive effects of DHEA or DHEAS with positive affect (Table 1).

4. Discussion

In this study, we investigated main and interactive associations of DHEA(S) associations with positive and negative affect. We did not find any main or interactive effects of DHEA with negative affect. This was somewhat surprising, given findings demonstrating that

endogenous DHEA is associated with negative affect and depression symptoms (Sonnenblick, Taler, Bachner, & Strous, 2018; Walther, et al., 2019), and that DHEA supplementation improves negative affect and depression symptoms (Ohana, et al., 2016; Peixoto, et al., 2018; Sripada, et al., 2013; Sripada, et al., 2014). This finding is consistent with other work that has not found an association of DHEA with affect and depression symptoms (Dos Santos, et al., 2019; Rasmusson, et al., 2006). However, this finding is inconsistent with a prior study showing an association of DHEA with negative affect in people who smoke (Van Voorhees, et al., 2013).

We did not find a main effect of DHEAS or a DHEAS by depression interaction with negative affect. We did find a significant DHEAS by abstinence interaction with negative affect. We also found a significant three-way interaction between DHEAS, abstinence, and depression symptom level with negative affect. We found that associations of DHEAS by abstinence interaction with negative affect was significant in individuals with elevated depression symptoms, but was not significant in individuals with low depression symptoms. Specifically, in the elevated depression symptom group we found a positive association between DHEAS with negative affect during non-abstinent sessions and a negative association between DHEAS with negative affect during abstinent sessions. This is consistent with two prior studies in samples of people who smoke found DHEAS was inversely associated with negative affect (Marx, et al., 2006; Van Voorhees, et al., 2013). However, it is inconsistent with one prior study, which found that DHEAS did not associate with changes in affect symptoms (measured by the CESD) during a cigarette quit attempt (Rasmusson, et al., 2006). The current study expands prior research in a few ways. First, this study investigated DHEAS and negative affect associations during both cigarette abstinence and non-abstinence and focused on depression symptom levels. Specifically, this finding is consistent with our hypothesis that DHEAS associations with negative affect

would be greater in those with elevated depression symptoms. This hypothesis was based on prior work showing that individuals with elevated depression symptoms have an attenuated salivary DHEA(S) response to stress (Jiang, et al., 2017), improved affect symptoms with DHEA supplementation (Peixoto, et al., 2018), and greater negative affect withdrawal during cigarette abstinence (Copeland, Kulesza, & Hecht, 2009; Gilbert, Rabinovich, Gilbert-Matuskowitz, Klein, & Pergadia, 2019). While we hypothesized that both DHEA and DHEAS would associate with negative affect, there are a few reasons why we might have found a significant effect for DHEAS, but not DHEA. A prior study reported that DHEA may be less robustly associated with negative affect symptoms compared to DHEAS (Van Voorhees, et al., 2013), which is consistent with the findings from the current study. It is also possible that the difference in associations is related to DHEAS levels being significantly higher than DHEA levels (Kroboth, Salek, Pittenger, Fabian, & Frye, 1999), which may make it more sensitive to measuring changes in negative affect. It is also possible that the differences are related to specific functions of DHEA compared to DHEAS. While there is some debate about the specific functions of DHEA compared to DHEAS, research supports DHEA primarily serving as a precursor hormone with a fundamental role in steroid metabolism (Labrie, et al., 2005) and DHEAS mainly functioning as a neurosteroid (Svob Štrac, Jazvinšćak Jembrek, Erhardt, Mirković Kos, & Peričić, 2012). Given the pilot nature of this study, it will be important for future studies to determine whether DHEAS is more robustly related to negative affect in individuals with elevated depression symptoms compared to DHEA.

We did not find any associations of DHEA(S) with positive affect. Low positive affect is an important symptom of depression (Mathew, et al., 2017) and cigarette withdrawal (Klemperer, et al., 2021). Prior work in people who smoke has focused on DHEA(S) associations

with negative affect and these preliminary results suggest that DHEA(S) may be more relevant to negative affect compared to positive affect.

The results of the current study should be interpreted in the context of study limitations. We utilized a binary cutoff score of CESD for this study and not a clinical diagnosis of depression. It will be important for future studies to determine whether a clinical diagnosis differs from self-reported scores on the CESD. We focused on DHEA(S) values and not ratios with cortisol, which may be important for smoking cessation (Rasmusson, et al., 2006). We did not measure cortisol in most participants and are unable to run the ratios and it will be important for future studies to investigate DHEA(S)/cortisol ratios with the outcomes. Importantly, this study was conducted in a sample of individuals who smoke who were not currently attempting to quit, and thus cigarette abstinence was experimentally induced. It will be informative for future studies to investigate these relations during a cigarette quit attempt. This study also used self-report measures of affect, and findings may be most applicable to self-reported symptoms and states related to depression symptoms. To be eligible for participation in the study, individuals were required to smoke five or more cigarettes per day, and the overall level of dependence within the sample might impact the outcomes. Lastly, due to the pilot nature of the study, small subsamples may have impacted insignificant findings.

5. Conclusions

The current study found that during abstinence higher DHEAS significantly associated with lower negative affect in individuals with elevated depression symptoms. Negative affect is an important cigarette withdrawal symptom and associates with poor cessation outcomes (Baker, Piper, McCarthy, Majeskie, & Fiore, 2004; Conti, Tolomeo, Steele, & Baldacchino, 2020; Pang, Chai, et al., 2022; Pang & Leventhal, 2013; Shiffman & Waters, 2004). Current findings suggest

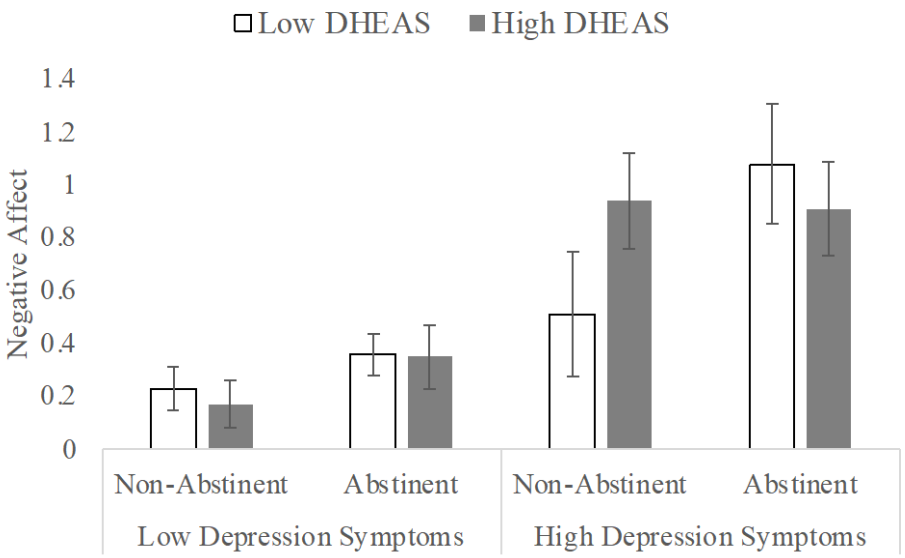
that future studies should investigate whether DHEA supplementation may be helpful for mitigating negative affect during cigarette abstinence in individuals with elevated depression symptoms. We did not find any main or interactive associations of DHEA or DHEAS with positive affect.

Table 1. Models of DHEA and DHEAS with positive and negative affect.

	Model 1			Model 2			Model 3		
Parameter	Estimate	(SE)	p	Estimate	(SE)	p	Estimate	(SE)	p
POMS NA DHEA									
Abstinence	-0.17	(0.06)	**.005**	-0.37	(0.15)	**.02**	-0.49	(0.18)	**.01**
Depression	-0.56	(0.13)	**.000**	-0.50	(0.20)	**.01**	-0.64	(0.23)	**.01**
DHEA	0.55	(0.54)	.31	0.00	(0.86)	1.00	-0.53	(0.96)	.58
Depression x abstinence				0.07	(0.13)	.58	0.29	(0.22)	.19
Depression and DHEA				-0.81	(1.02)	.43	0.41	(1.43)	.77
Abstinence and DHEA				1.27	(0.71)	.08	2.00	(0.93)	**.03**
Abstinence by Depression by DHEA							-1.75	(1.43)	.23
POMS PA DHEA									
Abstinence	0.22	(0.08)	**.01**	0.31	(0.21)	.15	0.33	(0.25)	.20
Depression	0.51	(0.17)	**.004**	0.42	(0.26)	.12	0.44	(0.31)	.16
DHEA	0.32	(0.71)	.66	0.89	(1.15)	.44	0.96	(1.30)	.46
Depression x abstinence				0.08	(0.18)	.65	0.05	(0.31)	.88
Depression and DHEA				0.44	(1.36)	.75	0.26	(1.92)	.89
Abstinence and DHEA				-1.10	(0.97)	.26	-1.22	(1.29)	.35
Abstinence by Depression by DHEA							0.28	(1.98)	.89
POMS-NA DHEAS									
Abstinence	-0.16	(0.06)	**.01**	-0.34	(0.13)	**.01**	-0.58	(0.16)	**<.001**
Depression	-0.57	(0.14)	**<.001**	-0.44	(0.20)	**.03**	-0.63	(0.22)	**.004**
DHEAS	0.00	(0.02)	.85	0.00	(0.03)	.91	-0.02	(0.03)	.54
Depression x abstinence				0.09	(0.12)	.49	0.44	(0.18)	**.02**
Depression and DHEAS				-0.04	(0.03)	.19	0.01	(0.04)	.78
Abstinence and DHEAS				0.04	(0.02)	**.04**	0.08	(0.03)	**.001**
Abstinence by Depression by DHEAS							-0.09	(0.03)	**.01**
POMS-PA DHEAS									
Abstinence	0.24	(0.08)	**.004**	0.17	(0.18)	.35	0.36	(0.23)	.12
Depression	0.47	(0.17)	**.01**	0.38	(0.26)	.14	0.53	(0.28)	.06
DHEAS	-0.02	(0.02)	.48	-0.01	(0.03)	.75	0.00	(0.04)	.91
Depression x abstinence				0.16	(0.17)	.36	-0.12	(0.27)	.65
Depression and DHEAS				0.00	(0.04)	.96	-0.04	(0.05)	.44
Abstinence and DHEAS				-0.01	(0.03)	.72	-0.05	(0.04)	.21
Abstinence by Depression by DHEAS							0.07	(0.05)	.17
POMS-NA DHEAS: Low Depression									
Abstinence				-0.14	(0.08)	.12			
DHEAS				0.00	(0.02)	.94			
Abstinence and DHEAS				-0.01	(0.02)	.77			
POMS-NA DHEAS: Elevated Depression									
Abstinence				-0.59	(0.18)	**.004**			
DHEAS				-0.02	(0.04)	.53			
Abstinence and DHEAS				0.09	(0.03)	**.008**			

Notes. All models controlled for cigarette dependence, age, and gender identity. P-values <.05 are bolded.

Figure 1. Abstinence × Depression × DHEAS interaction on negative affect



Note. Data from models stratified by depression symptoms. Estimated marginal mean values ± standard error of negative affect at 1 standard deviation below the mean (i.e., low DHEAS) and 1 standard deviation above the mean (i.e., high DHEAS).

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