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## Digital clock drawing: Differentiating ‘*thinking*’ versus ‘*doing*’ in younger and older adults with depression

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### Abstract

**Objective**—Psychomotor slowing has been documented in depression. The digital Clock Drawing Test (dCDT) provides: i) a novel technique to assess both cognitive and motor aspects of psychomotor speed within the same task and ii) the potential to uncover subtleties of behavior not previously detected with non-digitized modes of data collection.

**Method**—Using digitized pen technology in 106 participants grouped by Age (younger/older) and Affect (euthymic/unmedicated depressed), we recorded cognitive and motor output by capturing *how* the clock is drawn rather than focusing on the final product. We divided time to completion (TTC) for Command and Copy conditions of the dCDT into metrics of percent of drawing (%*Ink*) versus non-drawing (%*Think*) time. We also obtained composite z-scores of cognition, including attention/ information processing (AIP), to explore associations of %*Ink* and %*Think* times to cognitive and motor performance.

**Results**—Despite equivalent TTC, %*Ink* and %*Think* Command times (Copy n.s.) were significant (AgeXAffect interaction: $p=.03$ )—younger depressed spent a smaller proportion of time drawing relative to thinking compared to the older depressed group. Command %*Think* time negatively correlated with AIP in the older depressed group ( $r=-.46$ ;  $p=.02$ ). Copy %*Think* time negatively correlated with AIP in the younger depressed ( $r=-.47$ ;  $p=.03$ ) and older euthymic groups ( $r=-.51$ ;  $p=.01$ ).

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**Conclusion**—The dCDT differentiated aspects of psychomotor slowing in depression regardless of age, while dCDT/cognitive associates for younger adults with depression mimicked patterns of older euthymics.

### Keywords

psychomotor slowing; clock drawing; digital technologies; age; major depressive disorder

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### Introduction

Approximately 70% of individuals suffering mild-moderate depression, particularly older adults, do not seek treatment (Pratt & Brody, 2008). If and when these individuals are seen medically, many are treatment refractory (Alexopoulos, 2011). Psychomotor speed, i.e., timed activity requiring ‘movement or action’ including perceptual processing, programming and execution (Schrijvers, Hulstijn, & Sabbe, 2008) has been used as a predictor of poorer treatment response in major depressive disorder (MDD) (Caligiuri et al., 2003). Furthermore, psychomotor slowing has been documented across tasks measuring cognitive and motor aspects of performance in MDD (Schrijvers et al., 2008); however, age has rarely been considered (Caligiuri et al., 2003; Pier, Hulstijn, & Sabbe, 2004a, 2004b; Tucha et al., 2002). Revisiting the role of psychomotor speed in unmedicated younger and older adults with MDD may help determine how age impacts slowing prior to the initiation of anti-depressant medication for more accurate predictive models of treatment response.

To date, MDD studies of psychomotor speed have outlined the negative impact of slowing on simple and complex motor tasks as well as the ‘upstream’ influences on higher-level cognitive processes. For example, studies using a simple handwriting task to assess time to drawing initiation (i.e., cognitive aspects of psychomotor speed including perceptual processing and programming) and total movement time (i.e., ‘execution’ or motor aspects of psychomotor speed) showed that medicated MDD patients were slower than controls across both aspects of performance (Pier, Hulstijn, & Sabbe, 2004c; Sabbe, Hulstijn, van Hoof, Tuyenman-Qua, & Zitman, 1999). Individuals with MDD were not only slower than non-depressed controls on simple handwriting tasks but also more complex drawing tasks (Lohr, May, & Caligiuri, 2012; Schrijvers et al., 2008; Sobin & Sackeim, 1997). Psychomotor slowing has also been shown to negatively impact performance on complex non-motor tasks including measures of executive functioning, learning and memory – particularly in older adults diagnosed with depression (Butters et al., 2004; Nebes et al., 2000; Pimontel, Culang-Reinlieb, Morimoto, & Sneed, 2012). Measures of slowing used in these studies were not derived from handwriting or figure drawing tasks per se, but from a variety of tasks incorporating perceptual processing, programming and motor speed (e.g., Trail Making Test Part A, Digit Symbol, Grooved Pegboard) (Butters et al., 2004; Nebes et al., 2000; Pimontel et al., 2012). Finding a way to disambiguate cognitive (i.e., perceptual processing and programming) from motor aspects of psychomotor slowing using one common and easily administered task that combines simple drawing with more complex functioning may allow for an expedited, more streamlined approach to identify individuals susceptible to negative outcomes in MDD (Schrijvers et al., 2008).

A recent study of specific cognitive constructs underlying speeded deficits in MDD may shed light on the task of choice for streamlining a psychomotor assessment in MDD. Using a finger tapping/button press task with internal versus external cuing for response initiation and selection, investigators revealed differential responses slowing in patients with MDD, but only when they were required to use internal rather than external cues for response selection (Hoffstaedter, Sarlon, Grefkes, & Eickhoff, 2012). Investigators concluded the cognitive resources required for responding to internal versus external cues differed and influenced speed of responding accordingly (Hoffstaedter et al., 2012). Thus, external cuing required fewer cognitive resources by providing a structure to facilitate motor performance in MDD. In contrast, internal cuing required more self-initiated cognitive processes like executive, attention and perceptual processing speed that took longer to mobilize in MDD and thus, slowed motor performance (Hoffstaedter et al., 2012). While this study employed one task, it did so in a young population and without a direct measure of cognitive speed to accompany their motor speed metric. Systematic experimentation of internal (high cognitive demand) versus external (low cognitive demand) cuing in combination with an assessment of the cognitive and motor aspects of psychomotor slowing may aid identification of individuals with depression at risk of poor outcomes.

The clock drawing test (CDT) has long provided a quick yet comprehensive snapshot into a patient's abilities (Cosentino, Jefferson, Chute, Kaplan, & Libon, 2004; Libon, Malamut, Swenson, Sands, & Cloud, 1996; Royall, Cordes, & Polk, 1998) and may also prove useful in distinguishing cognitive from motor aspects of slowing in depression across internal and external processing. To complete the CDT, participants draw the face of a clock with the hands set to a pre-designated time (typically '10 after 11') first to Command and then Copy where a model clock is provided. Given work using internal/external cueing (Hoffstaedter et al., 2012), we surmised the Command condition, when the participant initiates and completes the drawing unassisted, necessitates greater cognitive demands including executive, attention and perceptual processes than the Copy condition. In contrast, the Copy condition with its external cue (i.e., clock model) reduced the internal cognitive resources required (e.g., to transform the verbal commands of setting the hands of the clock into a graphomotor representation).

Administering the CDT using digital technology (i.e., the Digital Clock Drawing Test; dCDT) allows the examiner to measure distinct aspects or components of psychomotor slowing (Davis et al., 2010; Penney, Davis, et al., 2010). The precision with which data is collected also provides greater standardized administration and scoring for a test that has little consensus scoring to date (Cosentino et al., 2004; Libon et al., 1996; Royall et al., 1998). The digital technology of the current research measures pen position on coded paper 80 times per second enabling position detection and facilitating the distinctions between overlapping cognitive and motor components of psychomotor slowing in the CDT. Combining digital technology with standardized administration and computer-assisted scoring procedures (Davis et al., 2010; Penney, Davis, et al., 2010) allowed for the dissection of the total time to complete the dCDT into discrete segments such as time spent drawing on the paper versus time spent not drawing (i.e., pauses between pen strokes when the participant performed unobservable cognitive activity). We referred to these activity

distinctions as *Ink* time and *Think* time, respectively (Cunningham et al., 2012). Additionally, because the dCDT collected data across both Command and Copy conditions, exploration of the degree of resources required under each condition were possible.

Our study aim was to determine the utility of the dCDT to distinguish the cognitive and motor aspects of slowing in unmedicated depressed and non-depressed younger and older adults. We sought to determine the separate and interactive effects of Age and Affect on *Ink* time versus *Think* time for both Command and Copy dCDT conditions in a comprehensive 2×2 (AgeXAffect) study design. We investigated our variables of interest within the context of the resources previously assumed to be important in internally versus externally mediated performance in MDD (Hoffstaedter et al., 2012). For example, given the potential internal, i.e., self-initiated, nature of the Command condition, we hypothesized that speed would be affected by depression within this dCDT condition. Given internal cuing may require self-initiated cognitive processes including executive, attention and perceptual processing speed (Hoffstaedter et al., 2012), we further hypothesized that cognitive *Think* times would be lower relative to motor *Ink* times, and primarily in the older depressed group. We based our hypothesis regarding the older depressed group on studies showing deficits on tasks that incorporate aspects of psychomotor slowing, i.e., perceptual processing, programming and motor speed in a similarly aged depressed cohort (Butters et al., 2004; Nebes et al., 2000; Pimontel et al., 2012). We also explored associations between *Think* and *Ink* time variables to indices of cognitive functioning and hypothesized that only *Think* times would correlate with higher-level cognition in depressed and non-depressed groups.

## Methods

### Participants

Data was collected from a larger research program at the University of Illinois at Chicago (UIC) Department of Psychiatry including an observational study of Type 2 diabetes in depression. Informed consent was obtained according to the Institutional Review Board guidelines at UIC and in accordance with the Declaration of Helsinki.

Participants, 30 years old, were recruited through community outreach (e.g., advertisements, fliers). An initial telephone screen determined eligibility. Exclusion criteria at the time of the telephone screen included a diagnosis of any Axis I disorder except MDD, a history of head trauma or loss of consciousness, a history or presence of any neurological (e.g., dementia, stroke, seizure) disorders and a history or presence of any substance abuse or dependence. Depressed participants were free of antidepressant medication for at least 2 weeks to study MDD in an untreated state (no individual was taken off medication to participate). A portion of participants were medication naïve. A history of stable or remitted medical disorders was not an exclusionary factor.

Following the phone screen, participants were scheduled for an evaluation that included cognitive (Mini Mental State Examination; MMSE) (Folstein, Folstein, & McHugh, 1974) and affective (Structured Clinical Interview for the DSM-IV; SCID) (Spitzer, Williams, Gibbon, & First, 1992) screens, administered by a trained research assistant for final inclusion/exclusion criteria. A board certified (AK) or board eligible (OA) psychiatrist then

completed the 17-item Hamilton Rating Scale of Depression (HAM-D) (Hamilton, 1960) for final determination of the presence/absence of depression. Euthymic adults were defined by a HAM-D score  $\leq 8$  and an absence of depressive symptoms on the SCID. Adults with depression were defined by a presence of depressive symptoms on the SCID and a HAM-D score  $\geq 15$  (criteria for MDD per the DSM). All raters were blind to telephone screen information.

Of the 148 participants deemed eligible for inclusion based on the criteria above and the age bands below, 36 were excluded for: treatment non-compliance for thyroid dysfunction or sleep apnea-2; taking Gabapentin for nerve pain secondary to Type 2 diabetes-2; English as a second language-6. Ten were excluded to match groups on Type2 diabetes and/or education; 16 were excluded to match euthymic and depressed older adults on age. Diabetes matching was conducted using presence/absence counts by group; age/education matching was based on mean/standard deviation.

## Procedures

**Vascular Risk Assessment**—Given that depression in older adults may be associated with cardiovascular risk factors including diabetes (Alexopoulos et al., 1997), we calculated a Framingham Stroke Risk Profile score (FSRP) (Wolf, D'Agostino, Belanger, & Kannel, 1991) based on: age, systolic blood pressure, anti-hypertensive therapy, diabetes, current cigarette smoking, cardiovascular disease, atrial fibrillation, and left ventricular atrophy. Laboratory testing from non-fasting blood draws at the time of the study documented levels of health related variables including hemoglobin A1c (hA1c).

**Neuropsychological Assessment**—Participants completed a comprehensive neuropsychological protocol that included the dCDT. In addition to the four cognitive domains below, it included a subjective measure of depressive symptomatology (Center for Epidemiological Study of Depression scale, CESD) (Radloff, 1977; Radloff & Teri, 1986) and a measure of gross motor speed (Motor Trail Making Task, TMT-M) modeled after the Delis-Kaplan Executive Function System (D-KEFS) (Delis, Kaplan, & Kramer, 2001), but confined to one-page to mimic the traditional Trail Making Test (TMT) employed in this study. Cognitive domains were based on the following: executive functioning (EF) included D-KEFS Verbal Fluency Category Switching total switching accuracy raw score (Delis et al., 2001), TMT-B time to completion, Stroop Interference Score (Golden, 1978), Wechsler Adult Intelligence Scale 3<sup>rd</sup> Edition (WAIS-III) (Wechsler, 1997a) Digit Span-Backward subtest raw score, and Self-Ordered Pointing Task total errors (Petrides, Alivisatos, & Frey, 2002); attention and information processing (AIP) included raw scores from the Stroop Color Naming and Word Reading trials (Golden, 1978), TMT-A time to completion, and WAIS-III Digit-Symbol Coding raw score (Wechsler, 1997a); learning, memory, and recognition (LMR) included California Verbal Learning Test – 2<sup>nd</sup> Edition (CVLT) (Delis & Kramer, 2000) Short and Long Delay Free Recall totals and Recognition Discriminability Index calculated by  $[1 - (\text{false positive} + \text{misses} / \# \text{ possible correct})] * 100$ , Wechsler Memory Scale – 3<sup>rd</sup> Edition (WMS-III) (Wechsler, 1997b) Logical Memory I and II and Recognition raw scores, as well as Visual Reproduction I and II and Recognition raw scores; and semantic language (SEM) included Animal fluency measures of total correct, percent in



cluster, and the Association Index (Carew, Lamar, Cloud, Grossman, & Libon, 1997). Participants also completed the Wechsler Test of Adult Reading (WTAR) (Wechsler, 2001) to obtain a predicted verbal IQ (pVIQ).

Cognitive scores were standardized using the non-depressed control sample means and standard deviations by age group, with scores reversed where appropriate so that high scores reflected better performance. Composite Z scores were then calculated for EF, AIP, LMR, and SEM. Cronbach's alpha was computed for each cognitive domain to evaluate how well the variables measured each latent construct across the entire sample; resulting values suggested each composite score measured a unidimensional latent construct (EF,  $\alpha=.82$ ; AIP,  $\alpha=.78$ ; LMR,  $\alpha=.90$ ; SEM,  $\alpha=.71$ ).

**The Digital Clock Drawing Test (dCDT) (Davis et al., 2010; Penney, Davis, et al., 2010)**—The dCDT was developed by Lahey Clinic and MIT in collaboration with the ClockSketch Consortium to provide a degree of detail and accuracy in the CDT impossible to achieve with ordinary pen and paper; potentially enabling a new degree of diagnostic information not hitherto detected. The dCDT uses digital pen technology developed by Anoto, Inc. The pen works as an ordinary ballpoint pen while capturing pen position 80 times/second  $\pm .002$ . The Lahey/MIT software classifies each pen stroke (e.g., determines whether a stroke is the clock face, a hand, a digit, etc.) with up to 84% accuracy in healthy controls (Penney, Libon, et al., 2010). The data reported by the pen is time-stamped, allowing the pen to capture both the final product (i.e., the clock drawing) and the behavior that produced it. This allows for more accurate classification of pen strokes.

As with the traditional CDT, the dCDT utilizes two conditions: Command and Copy. In the Command condition, participants are asked to “draw the face of a clock with all of the numbers and set the hands to 10 after 11.” Copy condition asks participants to copy a model of a clock with the hands set for ‘10 after 11’. The Copy condition is presented only after the Command condition is complete. Below are the dCDT parameters for the current research.

#### **dCDT variables**

- *Total Time To Completion (TTC)* – The time taken for the dCDT to be completed for Command and Copy separately measured from when the participant begins drawing the clock to the end of the clock's final element, but excludes the time taken to draw the clock circle. Clock circle drawing time was excluded because, unlike other clock elements, it is a single conceptual unit involving a large amount of ink placed quickly.
- *Percent Ink Time (%Ink)* – The total time the pen is in contact with the paper for each (Command and Copy) clock, excluding the time taken to draw the clock circle. *%Ink* is computed as  $(\text{total ink time} / \text{TTC}) * 100$ . It indicates what percent of the TTC was spent drawing, and may serve as a way to assess motor execution or ‘doing’ while taking into account individual differences in total drawing time.
- *Percent Think Time (%Think)* – The total time the pen is *not* in contact with the paper, measured from the completion of the first pen stroke to the beginning of the last pen stroke made during each clock. The intervening period of time between

verbal instruction and drawing start time is not included in *%Think*. This is because the Command condition calculations for time begins at the first Command pen stroke and ends at the completion of the last Command stroke – determined using the computerized scoring program. Timing for the Copy condition was conducted in the same fashion. *%Think* may provide a way to assess unobservable cognitive activity during the dCDT, e.g., ‘thinking’ activity including perceptual processing and programming, and is calculated as: (total think time / TTC)\*100 for each clock separately. (It is also 1 - *%Ink*.)

- *Total Number of Strokes* – This is a measure of the total number of distinct graphomotor marks completed with the pen during clock drawing to Command and Copy test conditions separately excluding strokes made in drawing the clock circle.

### Statistical analyses

Participants were divided into four groups based on age and affect: younger (30–50 years) euthymic and depressed groups, older (60+ years) euthymic and depressed groups. We constructed these groups with the expectation that providing a gap between young and old would better discriminate effects of cognitive and motor speed in aging and depression.

Group differences for demographic variables were measured using IBM SPSS Statistics 20 analysis of variance (ANOVA) for continuous variables and chi-square tests for categorical variables. Where indicated, significant demographic differences were then entered as covariates in all subsequent analyses. For our dCDT variables of interest, individual 2×2 ANCOVAs were performed for Command and Copy conditions separately. Follow-up comparisons of estimated marginal means using least squares difference (LSD) was performed as needed. A series of Pearson Product Moment Correlations (2-tailed) explored the relationship between *%Ink* and *%Think* times and cognitive domains (EF, AIP, LMR, SEM). Given the exploratory nature of these correlations, significance was set at  $p=.05$ . While *%Think* and *%Ink* sum to 100% and thus results for each will mirror the other, it is still important to consider the data from both perspectives, given that increased ink time could be due to drawing more rather than drawing slower, and vice versa.

### Results

Of the 112 eligible participants, 106 (54 men, 52 women) had complete neuropsychological test data including the dCDT. Younger adults averaged 41 years of age ( $40.98\pm 5.27$ ) while older adults averaged 65 years of age ( $65.41\pm 4.92$ ). Both the depressed and euthymic groups averaged ~54 years of age (depressed= $53.74\pm 12.62$ ; euthymic= $54.04\pm 14.01$ ). All subjects were native English speakers (39 Caucasian, 51 African American, 16 Hispanic/Asian/Other) with ~15 years of education ( $14.78\pm 2.40$ ) and all had MMSE scores = 26 (Table 1).

All participants produced ‘normal’ clock performance. Clocks were deemed normal (Table 1) based on a comparison to previously published work in healthy controls using a well-known scoring system that quantifies the size, shape and position of the clock face, numbers, and hands on a 0–10 scale (Libon et al., 1996; Libon, Swenson, Barnoski, & Sands, 1993). Participants showed nearly identical means and standard deviations to Libon healthy



controls across command (our sample=8.73±0.96; Libon sample=8.7±1.1) and copy (our sample=9.18±0.71; Libon sample=9.2±0.8) conditions (Libon et al., 1996; Libon et al., 1993).

### Demographics and Vascular Risk

Individual 2 (Age) X 2 (Affect) ANOVAs were not significant for MMSE or years of education. Chi-square analyses revealed an equal distribution of sex (51.1% male, 48.9% female) and race across groups. As expected given group divisions, there was a significant difference between groups on age [F(1, 102)= 611.35; p<.001,  $\eta_p^2$ =.85], and affect [CESD: F(1, 102)= 342.21; p<.001,  $\eta_p^2$ =.77]. There was a main effect of Age for pVIQ with older adults scoring higher than younger adults [F(1, 102)= 7.24; p<.01,  $\eta_p^2$ =.06].

There was a main effect of Age for FSRP scores with older adults showing higher risk of stroke than their younger counterparts [F(1, 98)=46.00; p<.001,  $\eta_p^2$ =.32] although there was no significant difference in duration of diabetes. More specific assessment of Type 2 diabetes (37 of our 106 participants had Type 2 diabetes), revealed equal numbers of diabetics across our 4 groups: each group included 8–10 diabetics equally distributing the impact of this variable across Age and Affect. This was confirmed by a separate series of (non-significant) analyses investigating Type 2 diabetes within each group (i.e., younger depressed, younger euthymic, older depressed and older euthymic) for affect, dCDT and neuropsychological domain variables of interest. Only after controlling for FSRP and verbal IQ was there a significant difference in hA1c levels (Table 1). Thus, covariates in all dCDT analyses included FSRP and pVIQ and we re-ran all analyses controlling for the additional covariate of hA1c.

### dCDT

There were no main effects or significant interactions for TTC and total strokes in either the Command or Copy condition. In contrast, analyses of %*Ink* and %*Think* revealed a significant interaction of Age and Affect for the Command condition only [%*Ink*: F(1, 96)=4.55, p=.03,  $\eta_p^2$ =.05; %*Think*: F(1, 96)=4.55, p=.03,  $\eta_p^2$ =.05] (Figure 1). Results did not change if we included the clock circle in the %*Ink* time variable. Follow-up LSD comparisons revealed younger depressed participants tended to spend a relatively larger percentage of their time thinking compared to the younger euthymic (p=.06) or older depressed participants (p=.08) with the younger/older depressed comparison reaching significance (p=.03) when the clock circle was included in %*Ink* time calculation. As expected, this pattern of results was reversed for %*Think* during the Command condition such that younger depressed participants tended to spend a smaller percentage of their time drawing compared to the younger euthymic (p=.06) or older depressed (p=.08/p=.03 without/with clock circle) groups. Results did not change if we added the additional covariate of hA1c.

### Neuropsychological Assessment

Individual 2 (Age) X 2 (Affect) ANCOVAs controlling for FSRP and pVIQ revealed significant main effects for Age (p-values <.001,  $\eta_p^2$  .13) and Affect (p-values <.05,  $\eta_p^2$  .04) within the cognitive domains of EF and AIP (Table 2). There were no significant

interactions for either composite score. Across both EF and AIP, however, younger groups performed significantly better than older groups and euthymic groups performed significantly better than depressed groups. Neither the interactions nor main effects of the 2 × 2 ANCOVAs for LMR, SEM or gross motor speed measured by TMT-M (Table 1) were significant. Results did not change with the additional covariate of hA1c.

### Neuropsychological Associates to dCDT Performance

Partial correlations controlling for FSRP and pVIQ examined the relationship between %*Ink* and %*Think* times across Command and Copy for EF and AIP given the group differences reported above. Within the younger groups, only individuals with depression showed a significant negative correlation between AIP and %*Think* during the Copy condition  $r(19) = -.47, p = .03, 95\% \text{ confidence interval (CI)} [-.74, -.07]$ . Similarly, the older euthymic group had a significant negative correlation between AIP and %*Think* during the Copy condition,  $r(21) = -.51, p = .01, 95\% \text{ CI} [-.75, -.14]$ . In contrast, the older depressed group had a significant negative association between AIP and %*Think* during the Command condition only,  $r(22) = -.46, p = .02, 95\% \text{ CI} [-.72, -.09]$  (see Table 3 for details). For completeness, we ran a similar set of correlations for SEM, LMR and TMT-M; none of the results for SEM and LMR were significant. Results did not change if we added hA1c as an additional covariate. TMT-M associated with Copy condition %*Ink* only and only for young depressed,  $r(20) = -.52, p = .01, 95\% \text{ CI} [-.76, -.15]$ ; however, this did not remain significant once hA1c was added as an additional covariate.

### Discussion

This study dissociated aspects of psychomotor slowing in depression using an innovative digital CDT in younger and older adults. Unlike previous studies (Caligiuri et al., 2003; Pier et al., 2004b, 2004c; Sabbe et al., 1999; Tucha et al., 2002), we investigated performance across distinct age bands of unmedicated individuals to examine speed in MDD without the confounding effects of medication-related slowing. Furthermore, we assessed different aspects of psychomotor speed within the same task and capitalized on increasing levels of difficulty inherent in the task (i.e., internal/Command versus external/Copy conditions), eliminating confounds due to different test measures. Thus, by applying novel technology to the widely-used CDT, the dCDT provided precise and standardized measurement of the duration of drawing (%*Ink*) and non-drawing (%*Think*) activities to differentiate between motor and cognitive aspects of psychomotor slowing in aging and depression.

Our results suggested *Ink/Think* alterations within the context of equivalent overall performance by age and depression. There were no differences in dCDT TTC or total number of strokes between groups; nor were there differences in gross motor speed (TMT-M). Despite these non-significant results, the younger depressed group spent a greater proportion of time thinking (hence a smaller proportion of time drawing) than the younger euthymic or older depressed groups. Furthermore, this significant interaction was seen only during the Command condition when internal cuing was high. We suggest that the Command condition required greater cognitive resources due to a reliance on internal cues for response selection (Cosentino et al., 2004; Hoffstaedter et al., 2012). The higher demand

for cognitive resources appeared to have slowed %Think only in younger adults with depression. In contrast, no significant differences were seen during the Copy condition when internal cuing was low and fewer cognitive resources were required given the presences of an external cue. This is consistent with other studies that showed external cuing facilitated performance in depressed individuals who were relatively younger in age (Hoffstaedter et al., 2012).

Between-group analyses supported the increased cognitive demands of internal cuing in the younger depressed group. Additionally, correlation analysis suggested that %Think may be associated with cognitive demands that differ based on age and affect. Among older adults with depression, as AIP scores increased (suggesting greater availability of cognitive resources in this domain), the proportion of time spent thinking during the internal/Command condition decreased. In contrast, younger adults with depression and older euthymics showed increased AIP with decreased proportion of time spent thinking only in the external/Copy condition. While the increased focus on the model during Copy may have eliminated between-group differences in %Think time seen during the Command condition in younger adults with depression, it revealed a pattern of increased AIP associated with decreased %Think that was comparable to older adults without depression. Perhaps the presence of the model subtly stressed the importance of accuracy for these groups and led to heightened use of AIP resources for completion under an otherwise less demanding 'externally mediated' Copy condition. Another possibility, at least for the younger depressed group, may be related to the impact of excessive rumination – often seen in depression and linked to attentional dysfunction (Koster, De Lissnyder, Derakshan, & De Raedt, 2011); perhaps increased attention to the model decreased rumination in this group and hence decreased %Think as well. More directed studies are needed to explore these possibilities.

Although we hypothesized that deficits would be greatest in the older depressed cohort, this was not the case. Similarities in cognitive correlates existed across younger depressed and older euthymic groups, while only the older depressed group showed a pattern of association between Command condition %Think and AIP. This may be due in part to differences in the manifestation of depressive symptomatology known to exist at different ages (Charlton, Lamar, Ajilore, & Kumar, 2013; Gallo & Rabins, 1999). Depression in younger adults lends itself to the stereotypic symptoms of sadness and slowed initiation of activities, the latter of which may also occur during normal aging. In contrast, depression in older adults, particularly in our sample cohort, is more reflective of physical symptoms (Charlton et al., 2013), which may lead to widespread slowing across cognitive *and* motor aspects. In fact, older adults with depression spent almost equivalent time thinking and drawing in contrast to other groups. The need for greater AIP during %Think under the Command condition may reflect internal cuing in depression that may be more specific to older adults than that seen in previous studies of younger medicated inpatients with depression (Hoffstaedter et al., 2012).

Between-group comparisons of cognitive performance are in keeping with the literature (Butters et al., 2004; Grant, Thase, & Sweeney, 2001; Jungwirth et al., 2011; Nebes et al., 2000; Pimontel et al., 2012; Stordal et al., 2004) and show age negatively impacts cognition, as does depression. Both older groups, regardless of depression, performed worse than their

younger counterparts on EF and AIP. Similarly, there was a main effect of depression on these scores that favored the euthymics over the depressed groups. There was not, however, a significant interaction, which suggests that older and younger euthymics were not different on cognitive measures per se, nor were depressed older adults overly burdened by possible vascular dementia (VaD) when compared to their older euthymic counterparts. Thus, while the possibility of vascular cognitive impairment (VCI) or even VaD cannot be completely ruled out, the fact that older adults with depression were not disproportionately “slowed” in *%Ink* versus *%Think* by increasing cognitive demands (internal cuing) provides evidence against VaD/VCI claims and for widespread slowing secondary to MDD as noted above. Additionally, our results suggested similarities between cognition and dCDT performance in younger depressed and older euthymic groups; further evidence against VCI/VaD in our older adults.

Study results should be considered within the context of our sample: community-dwelling participants responding to advertisements about untreated depression. It could be suggested that their depressive symptoms were not severe enough to seek treatment; however, participants met DSM criteria for MDD. Further, HAM-D scores suggested a mild-moderate form of depression; however, this still resulted in relatively intact overall clock performance. We would argue that this makes detecting differences in the subtle metrics of *%Think* and *%Ink* even more important, given that this potentially milder form of depression may be more representative of the larger community (Little et al., 1998; Pratt & Brody, 2008). Thus, the dCDT may be clinically useful in identifying individuals in this vulnerable population, given that it capitalizes on both internal and external resource allocation to disambiguate aspects of psychomotor slowing. Furthermore, while there are other ways to distinguish depression via clock drawing error analyses (Bodner et al., 2004; Royall et al., 1998), these methods are labor intensive with scoring procedures that are potentially subjective compared to our digitized, semi-automated technique sensitive to reaction times. Thus, the dCDT provides an efficient and standardized way to differentiate the impact of depression on aspects of psychomotor speed in an otherwise highly functioning cohort.

While we attempted to disentangle behavior by dividing TTC into time spent drawing (*%Ink*) and time spent not drawing (*%Think*), our metrics are still not ‘pure’ measures of one construct versus the other – some ‘thinking’ undoubtedly occurred during ‘inking’. The pattern of *%Think* and *%Ink* results did, however, differentiate performance in depression at different age ranges and associated with distinct aspects of cognition. This study, and the directions suggested for future research, answered calls in the literature for a simple way to measure and understand the psychomotor aspects of depression (Buyukdura, McClintock, & Croarkin, 2011). As such, continued research is needed exploring dCDT variables with distinct metrics of gross (e.g., finger tapping) and fine (e.g., grooved pegboard) motor functioning, as well as more detailed analysis of cognitive (e.g., impulsivity and planning) and depressive symptoms. Incorporating the dCDT in this work may allow for new constructs like *%Ink* and *%Think* to emerge and inform our conceptualizations of a variety of normal and pathological processes in addition to aging and depression.

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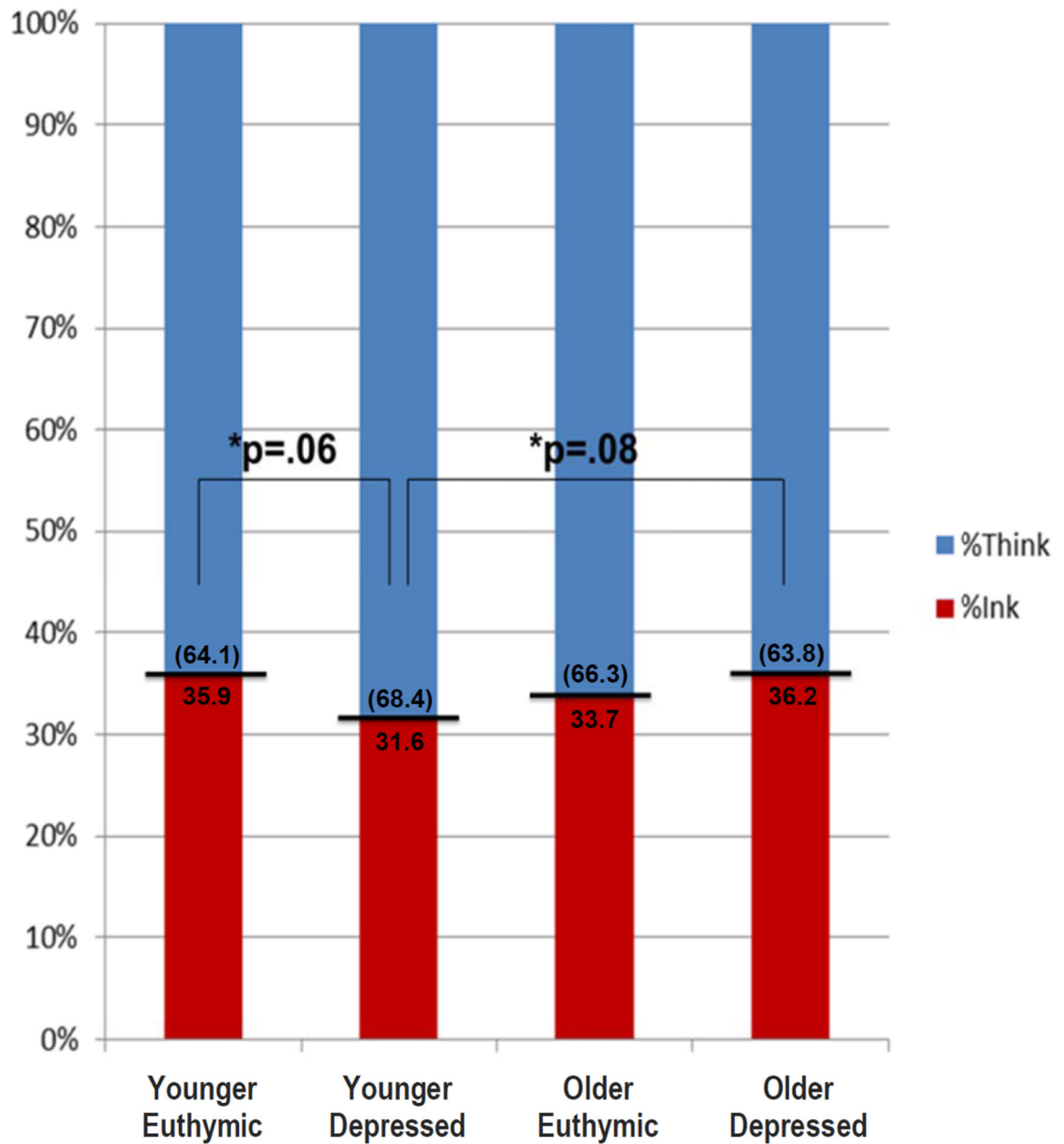
## References

- Alexopoulos GS. Pharmacotherapy for late-life depression. *J Clin Psychiatry*. 2011; 72(1):e04. [PubMed: 21272511]
- Alexopoulos GS, Meyers BS, Young RC, Campbell S, Silbersweig D, Charlson M. 'Vascular Depression' Hypothesis. *Archives of General Psychiatry*. 1997; 54(10):915–922. [PubMed: 9337771]
- Bodner T, Delazer M, Kemmler G, Gurka P, Marksteiner J, Fleischhacker WW. Clock drawing, clock reading, clock setting, and judgment of clock faces in elderly people with dementia and depression. *Journal of the American Geriatrics Society*. 2004; 52(7):1146–1150. [PubMed: 15209653]
- Butters MA, Whyte EM, Nebes RD, Begley AE, Dew MA, Mulsant BH, Becker JT. The nature and determinants of neuropsychological functioning in late-life depression. *Archives of General Psychiatry*. 2004; 61(6):587. [PubMed: 15184238]
- Buyukdura JS, McClintock SM, Croarkin PE. Psychomotor retardation in depression: biological underpinnings, measurement, and treatment. *Progress in Neuro-Psychopharmacology and Biological Psychiatry*. 2011; 35(2):395–409. [PubMed: 21044654]
- Caligiuri MP, Gentili V, Ebersson S, Kelsoe J, Rapaport M, Gillin JC. A quantitative neuromotor predictor of antidepressant non-response in patients with major depression. *J Affect Disord*. 2003; 77(2):135–141. [PubMed: 14607390]
- Carew TG, Lamar M, Cloud BS, Grossman M, Libon DJ. Impairment in category fluency in ischemic vascular dementia. *Neuropsychology*. 1997; 11(3):400. [PubMed: 9223144]
- Charlton RA, Lamar M, Ajilore O, Kumar A. Preliminary analysis of age of illness onset effects on symptom profiles in major depressive disorder. *International Journal of Geriatric Psychiatry*. 2013
- Cosentino S, Jefferson A, Chute DL, Kaplan E, Libon DJ. Clock drawing errors in dementia: neuropsychological and neuroanatomical considerations. *Cogn Behav Neurol*. 2004; 17(2):74–84. [PubMed: 15453515]
- Cunningham, H.; Penney, D.; Davis, R.; Tanner, JJ.; Nguyen, PT.; Schwab, N.; Price, CC. Clock Drawing in PD: What makes the clock drawing test tick?; Montreal, Canada. Paper presented at the The International Neuropsychological Society; 2012.
- Davis, R.; Penney, DL.; Pittman, D.; Libon, DJ.; Swenson, R.; Kaplan, E. The Digital Clock Drawing Test (dCDT) I: Development of a new computerized quantitative system; Montreal, Canada. Paper presented at the The International Neuropsychological Society; 2010.
- Delis DC, Kaplan E, Kramer JH. Delis-Kaplan executive function system (D-KEFS). Psychological Corporation. 2001
- Delis DC, Kramer JH. California Verbal Learning Test: CvLT-II; Adult Version. Psychological Corporation. 2000
- Folstein MR, Folstein SE, McHugh PR. Mini-mental state: A practical method for grading the cognitive state of patients for the clinician. *Journal of Psychiatric Research*. 1974; 12:189–198. [PubMed: 1202204]
- Gallo JJ, Rabins PV. Depression without sadness: Alternative presentations of depression in late life. *American Family Physician*. 1999; 60(3):820–826. [PubMed: 10498109]
- Golden C. Stroop colour and word test. 1978
- Grant MM, Thase ME, Sweeney JA. Cognitive disturbance in outpatient depressed younger adults: evidence of modest impairment. *Biological Psychiatry*. 2001; 50(1):35–43. [PubMed: 11457422]
- Hamilton MA. A rating scale for depression. *Journal of Neurology, Neurosurgery, and Psychiatry*. 1960; 23:56–62.

- Hoffstaedter F, Sarlon J, Grefkes C, Eickhoff SB. Internally vs. externally triggered movements in patients with major depression. *Behavioural Brain Research*. 2012; 228(1):125–132. [PubMed: 22142951]
- Jungwirth S, Zehetmayer S, Hinterberger M, Kudrnovsky-Moser S, Weissgram S, Tragl KH, Fischer P. The influence of depression on processing speed and executive function in nondemented subjects aged 75. *Journal of the International Neuropsychological Society*. 2011; 17(5):822–831. [PubMed: 21880169]
- Koster EH, De Lissnyder E, Derakshan N, De Raedt R. Understanding depressive rumination from a cognitive science perspective: the impaired disengagement hypothesis. *Clin Psychol Rev*. 2011; 31(1):138–145. [PubMed: 20817334]
- Libon DJ, Malamut BL, Swenson R, Sands LP, Cloud BS. Further analyses of clock drawings among demented and nondemented older subjects. *Archives of Clinical Neuropsychology*. 1996; 11(3):193–205. [PubMed: 14588923]
- Libon DJ, Swenson RA, Barnoski EJ, Sands LP. Clock drawing as an assessment tool for dementia. *Archives of Clinical Neuropsychology*. 1993; 8(5):405–415. [PubMed: 14589710]
- Little JT, Reynolds CF, Dew MA 3rd, Frank E, Begley AE, Miller MD, Kupfer DJ. How common is resistance to treatment in recurrent, nonpsychotic geriatric depression? *Am J Psychiatry*. 1998; 155(8):1035–1038. [PubMed: 9699690]
- Lohr JB, May T, Caligiuri MP. Quantitative assessment of motor abnormalities in untreated patients with major depressive disorder. *Journal of Affective Disorders*. 2012; 146(1):84–90. [PubMed: 22985485]
- Nebes RD, Butters MA, Mulsant BH, Pollock BG, Zmuda MD, Houck PR, Reynolds CF. Decreased working memory and processing speed mediate cognitive impairment in geriatric depression. *Psychological Medicine*. 2000; 30(3):679–691. [PubMed: 10883722]
- Penney, DL.; Davis, R.; Libon, DJ.; Lamar, M.; Price, CC.; Swenson, R.; Kaplan, E. The Digital Clock Drawing Test (dCDT) - II: A new computerized quantitative system; Montreal, Canada. Paper presented at the The International Neuropsychological Society; 2010.
- Penney, DL.; Libon, DJ.; Lamar, M.; Swenson, R.; Price, CC.; Weninger, C.; Davis, R. The Digital Clock Drawing Test (dCDT) - III: Clinician reliability for a new quantitative system; Montreal, Canada. Paper presented at the The International Neuropsychological Society; 2010.
- Petrides M, Alivisatos B, Frey S. Differential activation of the human orbital, mid-ventrolateral, and mid-dorsolateral prefrontal cortex during the processing of visual stimuli. *Proceedings of the National Academy of Sciences of the USA*. 2002; 99(8):5649–5654. [PubMed: 11960018]
- Pier MP, Hulstijn W, Sabbe BG. Differential patterns of psychomotor functioning in unmedicated melancholic and nonmelancholic depressed patients. *J Psychiatr Res*. 2004a; 38(4):425–435. [PubMed: 15203295]
- Pier MP, Hulstijn W, Sabbe BG. No psychomotor slowing in fine motor tasks in dysthymia. *J Affect Disord*. 2004b; 83(2–3):109–120. [PubMed: 15555703]
- Pier MP, Hulstijn W, Sabbe BG. Psychomotor retardation in elderly depressed patients. *J Affect Disord*. 2004c; 81(1):73–77. [PubMed: 15183603]
- Pimontel MA, Culang-Reinlieb ME, Morimoto SS, Sneed JR. Executive dysfunction and treatment response in late-life depression. *International Journal of Geriatric Psychiatry*. 2012; 27(9):893–899. [PubMed: 22009869]
- Pratt LA, Brody DJ. Depression in the United States household population, 2005–2006. *NCHS Data Brief*. 2008; (7):1–8. [PubMed: 19389321]
- Radloff LS. The CES-D Scale: a self-report depression scale for research in the general population. *Applied Psychological Measures*. 1977; 1:385–401.
- Radloff LS, Teri L. Use of the Center for Epidemiological Studies Depression Scale with older adults. *Clinical Gerontology*. 1986; 5:119–136.
- Royall DR, Cordes JA, Polk M. CLOX: an executive clock drawing task. *Journal of Neurology, Neurosurgery, and Psychiatry*. 1998; 64(5):588–594.
- Sabbe B, Hulstijn W, van Hoof J, Tuynman-Qua HG, Zitman F. Retardation in depression: assessment by means of simple motor tasks. *Journal of Affective Disorders*. 1999; 55(1):39–44. [PubMed: 10512604]



- Schrijvers D, Hulstijn W, Sabbe BG. Psychomotor symptoms in depression: a diagnostic, pathophysiological and therapeutic tool. *Journal of Affective Disorders*. 2008; 109(1):1–20. [PubMed: 18082896]
- Sobin C, Sackeim HA. Psychomotor symptoms of depression. *American Journal of Psychiatry*. 1997; 154(1):4–17. [PubMed: 8988952]
- Spitzer RL, Williams JBW, Gibbon M, First MB. The Structured Clinical Interview for DSM-III-R (SCID) I: History, Rationale, and Description. *Archives of General Psychiatry*. 1992; 49(8):624–629. [PubMed: 1637252]
- Stordal KI, Lundervold AJ, Egeland J, Mykletun A, Asbjørnsen A, Landrø NI, Lund A. Impairment across executive functions in recurrent major depression. *Nordic Journal of Psychiatry*. 2004; 58(1):41–47. [PubMed: 14985153]
- Tucha O, Aschenbrenner S, Eichhammer P, Putzhammer A, Sartor H, Klein HE, Lange KW. The impact of tricyclic antidepressants and selective serotonin re-uptake inhibitors on handwriting movements of patients with depression. *Psychopharmacology (Berl)*. 2002; 159(2):211–215. [PubMed: 11862351]
- Wechsler D. Wechsler Adult Intelligence Scale (WAIS-III). Psychological Corporation. 1997a
- Wechsler D. Wechsler memory scale (WMS-III). Psychological Corporation. 1997b
- Wechsler D. Wechsler Test of Adult Reading: WTAR. Psychological Corporation. 2001
- Wolf PA, D'Agostino RB, Belanger AJ, Kannel WB. Probability of stroke: a risk profile from the Framingham Study. *Stroke*. 1991; 22(3):312–318. [PubMed: 2003301]



Interaction between Age and Affect:  $p=.03$

Figure 1. Percent of *Ink* and *Think* times across all groups with individual percentages for each variable outlined by group

**Table 1**

Demographics and gross motor function across all groups.

	Younger euthymic	Younger depressed	Older euthymic	Older depressed
<b>n</b>	24	26	28	28
<b>DEMOGRAPHICS</b>				
Age <sup>ME-A</sup>	40.04±6.00	41.85±4.45	66.04±4.10	64.76±5.65
Sex (M:F)	14:10	12:14	14:14	14:14
Education (yrs)	15.15±2.76	13.89±1.97	15.07±2.37	15.04±2.36
MMSE	29.04±1.16	28.96±1.25	28.93±1.09	29.00±1.02
HAM-D <sup>ME-D</sup>	0.67±1.17	18.92±3.12	1.39±1.73	18.57±3.24
FSRP <sup>ME-A</sup>	4.79±4.38	5.21±4.44	10.41±3.62	10.56±3.88
pVIQ <sup>ME-A</sup>	100.25±11.88	97.27±11.75	103.61±14.39	106.86±11.04
CESD <sup>ME-D</sup>	4.42±4.37	33.81±10.09	6.21±5.77	30.86±8.29
hA1c <sup>ME-A</sup>	6.16±1.45	6.44±1.57	6.29±1.22	6.16±0.90
<b>MOTOR FUNCTION</b>				
TMT-M	22.37±14.87	24.81±12.30	28.79±12.46	26.46±9.81
COMM Drawing Time	39.26±16.91	41.11±23.04	35.91±12.70	43.22±16.75
COPY Drawing Time	33.10±13.48	31.83±10.93	31.58±11.18	40.48±22.88
COMM # of Strokes	24.38±3.81	23.31±3.82	23.61±6.53	23.12±3.15
COPY # of Strokes	22.54±2.77	22.23±2.39	23.57±3.46	20.07±17.46
<b>GENERAL CLOCK PERFORMANCE</b>				
Libon Clock Score (Comm)	8.98±0.77	8.67±0.89	8.48±1.30	8.82±0.71
Libon Clock Score (Copy)	9.40±0.59	9.29±0.70	8.98±0.74	9.13±0.77

NOTE: ME-A=main effect across age; ME-D=main effect across depression (see p-values below); M:F=male:female; yrs=years; pVIQ=predicted verbal intelligence quotient; MMSE=Mini-Mental State Examination; HAM-D=Hamilton

Depression Rating Scale; CESD=Center for Epidemiological Study of Depression; FSRP=Framingham Stroke Risk Profile; TMT-M=Trails part Motor

ME-A: age ( $Y < O$ ,  $p < .001$ ); pVIQ ( $Y < O$ ,  $p = .008$ ); FSRP ( $Y < O$ ,  $p < .001$ ); hA1c ( $Y > O$ ,  $p = .008$ ) but only after controlling for FSRP and verbal IQ, please note hA1c data shown in table is unadjusted.

ME-D: HAM-D ( $E < D$ ,  $p < .001$ ), CESD ( $E < D$ ,  $p < .001$ )

**Table 2**

Cognitive performance by Age or Affect.

	Main Effect of Age		Main Effect of Depression	
	Younger	Older	Euthymic	Depressed
<b>zAIP</b>	$0.10 \pm 0.82^{**}$	$-0.28 \pm 0.79^{**}$	$0.04 \pm 0.76$	$-0.24 \pm 0.86$
<b>zEF</b>	$0.17 \pm 0.64^{**}$	$-0.32 \pm 0.66^{**}$	$0.03 \pm 0.75^*$	$-0.20 \pm 0.63^*$

\*\*  
p<.

\* 001p<.05;

NOTE: zAIP=z-score for Attention and Information Processing; zEF=z-score for Executive Functioning

**Table 3**

Correlations between %Think under Command and Copy conditions and cognitive performance.

Affect x Age		COMM Percent Think Time	COPY Percent Think Time
Younger Euthymic df=18	zEF	r= -.21, p=.39	r=.09, p=.69
	zAIP	r= -.36, p=.12	r=.22, p=.36
Younger Depressed df=19	zEF	r= -.41, p=.07	r= -.41, p=.07
	zAIP	r= .07, p=.78	<b>r= -.47, p=.03</b>
Older Euthymic df=21	zEF	r= .06, p=.78	r= -.28, p=.20
	zAIP	r= -.29, p=.18	<b>r= -.51, p=.01</b>
Older Depressed df=22	zEF	r= -.35, p=.09	r= .04, p=.87
	zAIP	<b>r= -.46, p=.02</b>	r= -.19, p=.37

NOTE: COMM=Command condition; COPY=Copy Condition; df=degrees of freedom; zEF=composite z-score for Executive Functioning; zAIP=composite z-score for Attention and Information Processing;