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Cognition and nondysphoric depression among adoptees at high risk for psychopathology

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Abstract

Background—Association between poor cognition and symptom clusters including depressive ideation (e.g., guilt) and vegetative symptoms in the absence of dysphoria (nondysphoric depression - NDD) has been suggested in the elderly. The current study examined associations between NDD and pre-morbid and concurrent cognitive functioning in younger adults at high risk for psychopathology. NDD and depressed subjects were expected to show poorer pre-morbid and current cognition than non-depressed participants.

Method—Subjects were adoptees enrolled in the Iowa Adoption Study [1]. NDD subjects were compared with non-depressed comparison subjects and with subjects with dysphoric depression (DD) on measures of pre-morbid cognition (estimated by standardized school achievement test scores) and concurrent cognition (intelligence, attention, memory, executive abilities).

Results—NDD and DD showed lower pre-morbid cognition and executive functioning, while DD showed lower verbal and performance IQ compared to non-depressed subjects. The size of the comparison between NDD and non-depressed subjects for pre-morbid cognition was double that between DD and non-depressed subjects. No significant differences in cognition were found between NDD and DD. These effects were no longer significant after controlling for pre-morbid cognition.

Conclusions—Poorer pre-morbid cognition and executive functions in NDD (and the absence of current cognitive differences compared with DD) suggest that NDD may be a condition of clinical interest. Because poor cognition is a known correlate of alexithymia, these results (including their magnitude) are consistent with the view that NDD may be a paradoxical presentation of depression in persons with limited ability to be aware and verbally report emotions.

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In the early 1900s, Kraepelin and other psychiatrists observed that some depressive conditions showed only mild affective or mood symptoms [2, 3]. In fact, as late as 1984, the official opinion of the American Psychiatric Association (APA) was that in major depression mood disturbances could be *prominent and relatively persistent, but not necessarily the most dominant symptom* [p. 213, 4]. This consensus changed in 1994 when emotional symptoms (e.g., sadness or loss of pleasure) became *essential* (and implicitly etiologically primary) to the diagnosis of depression [5]. As a result, research on depressive conditions without consistent endorsement of sadness slowed its pace [6, 7]. This occurred despite emphasis by multiple investigators that depressive ideation and vegetative symptoms may exist in the (paradoxical) absence of concurrent sadness or loss of pleasure (identified together as “dysphoria” by [8]) [8-15].

The aim of the present research report is to continue examining the extent to which cluster(s) constituted by depressive ideation and vegetative symptoms represent clinical conditions of psychiatric significance even in absence of dysphoria. It has been posited that this condition – or conditions - {referred to as nondysphoric depression (NDD) [6]} is an alternate phenomenological presentation of depression (not properly a different *type* of depression) resulting from limited capacity to endorse emotional symptoms. Multiple factors can limit the capacity of recognizing personal emotions and range from demographic and cultural [16] to biological [17]. All of these factors may (at least in theory) contribute to a nondysphoric presentation of the depressive illness or NDD. For instance, systematic research on individuals with brain injury has emphasized the critical role that damage to emotion-processing regions exerts in limiting the awareness of personal emotional changes [6, 18, 19] therefore leading to at best inconsistent reports of dysphoria but not reducing depressive ideation and vegetative symptoms [6, 18, 19].

A critical issue raised in the literature concerns the extent to which individuals identified as NDD are cognitively impaired and/or at risk of significant cognitive decline [8]. Among older adults presenting to primary care, nondysphoric depressive symptoms were associated with relatively mild cognitive weakness [20]. On the other hand, additional research has suggested that NDD constitutes risk for significant cognitive decline and even to frank dementia [8]. Inclusion of older individuals with impaired cognition at initial evaluation and use of limited cognitive screening tools [8] raises questions as to whether these findings can be generalized to non-cognitively impaired younger subjects. A closer examination of the association between NDD and cognition is warranted also because poor cognitive ability is a known correlate of alexithymia (a personality trait consisting of poor emotional awareness and poor ability to communicate emotions verbally) [21] and can be an antecedent (or risk factor) as well an outcome of NDD [8].

NDD exists with varying frequencies among community-dwelling individuals [8, 13, 22]. Nonetheless, because by definition persons with NDD do not frequent mental health services (and only sparsely medical clinics – Paradiso unpublished data), large numbers of community-dwelling volunteers are to be screened in order to identify a large enough sample. Provided that the risk factors for poor emotional awareness are represented, a population with elevated risk to develop depression is presumed to be also at risk for NDD. Therefore, cohorts with elevated risk of depression (e.g., patients with injury to the brain) are a particularly well-suited to study NDD [6, 18, 19] because relatively fewer persons may be screened in order to identify suitable sample sizes. Due to their family history (i.e., one of the parents diagnosed with mood or substance misuse disorder) and elevated risk of depression, adoptees enrolled in the Iowa Adoption Study [23] represent a suitable population to identify individuals with depressive ideation and vegetative symptoms with and without dysphoric mood. Data from the Iowa Adoption Study also afford an unprecedented opportunity to examine the association between NDD, academic achievement

(a nationally standardized school achievement assessment was administered when the subjects were in elementary/junior high school) and neuropsychological functioning in a sample of young adults [24, 25].

Academic competence has been found to predict psychopathology (including depression) in childhood and adolescence [26, 27]. Therefore, because non-dysphoric and dysphoric depression are postulated to be differing phenomenological presentations of the same illness, the hypothesis was posited that younger subjects with NDD as well as subjects with dysphoric depression (DD) will show poorer childhood academic achievement compared to non-depressed comparison subjects. However, in light of the well-known inverse relationship between alexithymia and cognitive abilities [21] subjects with NDD were expected to show the worse academic achievement. Concurrent cognitive functioning differences were expected between NDD and non-depressed comparison subjects but less so between NDD and DD.

Methods

Subjects

The subjects in the present study were selected from a parent sample of 330 volunteer adoptees interviewed during years 2004-2008 in the context of a study examining the effects of substance use diagnoses on cognition [28-30]. At initial recruitment, half of the sample had birth parent(s) identified as having substance abuse problems and/or antisocial behaviors and neither of the birth parents had problems for the other half of the sample. During the current follow-up, one-third of the birth parent(s) had problems with alcohol and/or antisocial behaviors. Age of participants ranged between 31 and 64 years ($M = 44.3$, $SD = 7.2$) and 58% were women. Average household income was \$40,000 to \$49,999 per year. Subjects were predominantly White, non-Hispanic ($N = 304$, 94%) with the remainder of the participants African American, non-Hispanic ($N = 7$, 2%), African American, Hispanic ($N = 2$, ~1%), Caucasian, Hispanic ($N = 8$, 3%), or mixed race ($N = 2$, ~1%). All procedures were approved by the University of Iowa Internal Review Board.

The symptoms constituting the inclusion criteria were assessed using the Beck Depression Inventory – II [BDI-II, 31]. The inclusion criteria for the NDD group closely followed criteria of prior research [8] and were as follows: 1) presence of depressive ideation in the last two weeks (at least one BDI-II symptom among guilt, self-depreciation/self criticalness, worthlessness, pessimism and sense of failure assessed as 1), 2) presence of vegetative symptoms (2 or more BDI-II symptoms among change in appetite and sleep patterns, fatigue, agitation, and trouble concentrating assessed as 1), and 3) no endorsement of emotional symptoms (i.e., sadness, loss of pleasure, or low sex interest). History of prior major depression was an exclusionary criterion because subjects presenting with symptoms consistent with NDD can be partially remitted patients with a history of depression [32]. For this reason four subjects meeting criteria 1), 2) and 3), but reporting at least one prior major depression episode were not included in the NDD group.

The DD group was comprised of individuals endorsing 5 or more depressive symptoms (with dysphoria a necessary inclusion criterion) irrespective of reports of prior history of major depression. Inclusion criteria for the DD group were created with the intent to identify subjects that for the overall severity of their condition (i.e., number of symptoms and 2 weeks duration as assessed with the BDI-II) may meet DSM-IV criteria for diagnosis of major depressive episode. Given the aims of this study, subjects with subthreshold conditions (e.g., endorsing dysphoria but with a total of four symptoms or less) were not included in the analyses. The non-depressed comparison group consisted of subjects that did

not meet criteria for DD or NDD, had no prior history of major depression and did not endorse dysphoria on the BDI-II.

Measures

Demographic and clinical information

Demographic information, medical history, and Axis I diagnoses were collected using the Semi-Structured Assessment of the Genetics of Alcoholism [SSAGA-II, 33]. Lifetime occurrence of medical problems including diabetes, concussions, meningitis, thyroid disease, heart disease, high blood pressure, epilepsy, and cancer were assessed as present or absent using the SSAGA-II. Lifetime prevalence of Major Depressive Disorder (MDD) and substance abuse/dependence (i.e., alcohol, tobacco, marijuana, and other drugs) were also assessed using DSM-IV criteria on the SSAGA-II.

Pre-Morbid Cognition

Standardized school achievement test scores were collected from the centralized state records office (1999-2003). The Iowa Test of Basic Skills [ITBS, 34] is a standardized school achievement battery administered in Iowa classrooms by school districts from 3rd through 8th grade. Average ITBS has been shown to be an adequate proxy for pre-morbid cognition [24]. The average number of years of school data per subject was 4.82 (SD = 1.24; minimum = 2, maximum = 6) with 95% of the sample having 3 or more years of data. Achievement scores are reported as state-dependent percentile ranks for each year administered. The composite scores from each available year were averaged to create an overall summary score.

Cognitive Assessment

All study participants were administered a comprehensive neurocognitive battery assessing a broad range of cognitive domains including verbal and performance general intelligence, attention, memory, and executive functions. Due to the large number of measurements available, data reduction was attained via factor analysis of all measures (excluding the WAIS-III). Measures of global cognition [measured using the Wechsler Adult Intelligence Scales - III [WAIS-III, 35]], Verbal IQ (VIQ) and Performance IQ (PIQ) were examined as individual outcome measures. Memory was assessed using the Wechsler Memory Scales - III [WMS-III, 36]]. Index scores for Immediate Memory, General Memory, and Working Memory were included in the factor analysis. Executive function measures included: overall correct rates from Connor's Continuous Performance Test, 2nd Ed. [CPT-II, 37], letter (FAS) and category (animal) naming total scores from the Controlled Oral Word Association Test [COWAT, 38]], the interference score from the Stroop Color Word Test [SCWT, 39]], mean response times on Trails 1—3 and 4—5 from the Comprehensive Trail Making Test [CTMT, 40]], immediate and delayed response percent correct from the Rey Complex Figure task [RCFT, 41]], and percent conceptual levels reached from the computerized Wisconsin Card Sort Task [WCST, 42]].

The principal component analysis with varimax rotation identified three factors: 1) a general memory factor consisting of the RCFT immediate and delayed performance and General/Immediate Memory performance from the WMS-III [eigenvalue = 3.49, % variance = 34.93], 2) an attention factor comprised of the CPT-II and CTMT [eigenvalue = 1.36, % variance = 13.56], and 3) an executive function factor consisting of Working Memory from the WMS-III, the WCST, and the SCWT [eigenvalue = 1.19, % variance = 11.91].

Data analysis

Chi-square analyses were used to examine associations between depression groups and nominal variables (e.g., health problems, substance diagnoses). Analysis of variance was used to examine continuous outcomes (e.g., demographics, neurocognition). Between-group differences were determined by contrasts on the adjusted means produced by the ANOVA and are only reported if the overall F-test for depression was significant. The p-value and 95% confidence interval (CI) around the differences are also reported. Prior analyses of the cognitive outcomes examined in this paper showed significant associations with subject sex and current age [28]; therefore, sex and current age were included as covariates in the ANOVAs. Following the initial analyses of the depression categories on adult cognition, we examined whether pre-morbid cognition influenced the significance of the association by covarying standardized ITBS test scores. Data are discussed in terms of statistical significance and also in reference to effect sizes because different sample sizes may have affected the *p* values in the between-group comparisons. Cohen's *d* was used to estimate effect sizes with .30 designated as a small effect, .50 as medium, and .80 as large [43].

Results

Sample description

Twenty subjects with NDD, 89 with DD, and 109 non-depressed comparisons were identified. Frequencies of DSM-IV depressive symptoms by group are shown in Table 1. The most common symptoms among subjects with NDD were worthlessness or guilt (95%), change in sleep patterns (80%), and fatigue (65%). Demographic variables are shown in Table 2. ANOVA analysis showed no significant differences between groups for current age [$F(2, N = 223) = 2.0, p = .138$] and years of education [$F(2, N = 223) = 2.0, p = .138$]. Chi-square analyses also showed no association between study groups and participant sex [$\chi^2(2, N = 227) = 2.69, p = .261$] and marital status [$\chi^2(2, N = 227) = 4.35, p = .113$]. Birth parent problems were significantly associated with depression category [$\chi^2(2, N = 227) = 6.49, p = .039$], signifying that problems with substance use or antisocial behaviors were more common among subjects with NDD and DD compared to nondepressed subjects.

Clinical conditions also are shown in Table 2. Depression status was not significantly associated with lifetime health problems [$\chi^2(df=2, 226) = 2.14, p = .11$] or substance abuse [$\chi^2(2, N = 227) = 4.31, p = .116$]. Lifetime substance dependence was significantly higher among subjects diagnosed with NDD [$\chi^2(2, N = 227) = 26.49, p < .001$]. Only the DD group showed an elevated rate of lifetime anxiety disorder diagnosis (formal statistical analyses were not done due to small cells).

Pre-morbid cognitive functioning

Pre-morbid cognition was significantly lower among subjects with depression compared to non-depressed subjects (Table 3, 4). The difference between non-depressed comparison and NDD groups [$\Delta_{\text{NDD-C}} = -15.7$ percentile points] was also significant [$p = .011$, 95% CI = -27.82, -3.60] and corresponded to a medium effect size (Table 3). Likewise subjects with DD showed lower performance with respect to comparison subjects ($p = .018$). This difference [$\Delta_{\text{DD-C}} = -8.25$ percentile point, 95% CI = -15.04, -1.46] corresponded to a small effect size (Table 3). The difference in pre-morbid cognition [$\Delta_{\text{NDD-DD}} = -7.46$, 95% CI = -19.67, 4.75] between the NDD and DD groups was not significant [$p = .230$], and corresponded to a small effect size.

Current cognitive functioning

The main effect of depression was significant for VIQ (Tables 3 and 4). VIQ was significantly lower in the DD group compared to non-depressed subjects [$\Delta_{DD-C} = -4.39$, $p = .020$, 95% CI = -8.09, -0.69], corresponding to a small effect (Tables 3 and 4). The comparison between the non-depressed and NDD subjects was not statistically significant despite the small-to-medium effect size [$\Delta_{NDD-C} = -5.43$, $p = .107$]. The difference in VIQ scores between the NDD and DD groups was not significant [$\Delta_{NDD-DD} = -1.05$, $p = .758$, 95% CI = -7.73, 5.63].

A significant main effect of depression was also found for PIQ (Table 4). Between-group contrasts showed significantly lower PIQ scores among DD compared to non-depressed subjects [$\Delta_{DD-C} = -5.03$, $p = .005$, 95% CI = -8.56, -1.50]. The difference between NDD and non-depressed subjects failed to reach significance [$\Delta_{NDD-C} = -5.86$, $p = .069$, 95% CI = -12.19, 0.47]. The difference between the NDD and DD groups on PIQ scores was also not statistically significant [$\Delta_{NDD-DD} = -0.83$, $p = .80$, 95% CI = -7.21, 5.55]. Executive functions showed a significant main effect of depression (Table 4). Significantly lower z-transformed scores were found in the NDD and DD groups compared to non-depressed subjects [$\Delta_{NDD-C} = -0.34$, $p = .041$, 95% CI = -0.66, -.01 and $\Delta_{DD-C} = -0.22$, $p = .018$, 95% CI = -0.40, -0.04, respectively] corresponding to small to medium effect sizes (Table 3). The difference between the depressed groups on executive functions was not significant [$\Delta_{NDD-DD} = -0.12$, $p = .477$, 95% CI = -0.45, 0.21]. Finally, overall group differences were not statistically significant for general memory and attention (Table 4).

Because pre-morbid cognition was significantly lower among subjects with NDD and DD, and this measure has been shown to be highly correlated with adult cognitive performance, [24] the associations between VIQ, PIQ, and executive functions and depression categories were reexamined after controlling for pre-morbid cognition (Table 4). After covarying, the overall main effect of depression category was no longer statistically significant for VIQ [Adjusted means and standard errors: C ($M_{adj} = 105.17$, $SE = 0.90$), NDD ($M_{adj} = 105.77$, $SE = 2.15$), DD ($M_{adj} = 104.14$, $SE = 0.96$)], PIQ [Adjusted means and standard errors: C ($M_{adj} = 108.45$, $SE = 1.45$), NDD ($M_{adj} = 105.66$, $SE = 2.76$), DD ($M_{adj} = 105.25$, $SE = 1.23$)], and executive functions [Adjusted means and standard errors: C ($M_{adj} = 0.05$, $SE = 0.06$), NDD ($M_{adj} = -0.14$, $SE = 0.14$), DD ($M_{adj} = -0.09$, $SE = 0.06$)].

Discussion

The present study examined the relationship between dysphoric (DD) and non-dysphoric depression (NDD) with pre-morbid and concurrent cognitive abilities in a sample of adult adoptees from the Iowa Adoption Study [1]. NDD is a subsyndromal (i.e., not meeting DSM criteria for major depression or other unipolar conditions) depressive condition [13, 22] that has been posited to be a phenomenological variant of depression in individuals with limited capacity to perceive and express despondent mood and loss of pleasure (poor emotional self-awareness) despite the presence of other depressive symptoms [6].

Recognizing and treating subsyndromal depressive conditions is critical due to their high risk of disability, morbidity and mortality [12, 44-51], however because NDD has been often included with other subsyndromal depressions (e.g., with dysphoria as part of the symptom clustering), its empirical understanding has been neglected [52].

Epidemiological studies suggest that the rates of NDD in the community are sizeable. One-year prevalence rates for all subsyndromal depressions in community-dwelling individuals are as high as 11.8% in the USA [13] and 15.3% in Germany [22]. Of the subsyndromal depressions, NDD may be the most predominant manifestation since up to 2/3 of individuals

with subsyndromal depression show limited capacity to endorse sad mood [13]. This is consistent with the findings of Gallo and colleagues who reported a prevalence of about 5% in persons age 50 and over [8]. This study suggested that NDD may be a risk factor to dementia in older community dwelling individuals [8]. While other research is consistent with poorer cognition in older adults with nondysphoric conditions [20], an issue is raised as to what extent poor cognition is pre-morbid to NDD, a finding of potential interest given the established association between poorer cognition and alexithymia [21].

The present study is essentially a proof of concept. The use of a convenience sample [for description of original study purpose see 1] comprised of “high risk” subjects due to familial psychopathology among a portion of the sample allowed the unprecedented opportunity to examine pre-morbid cognitive functioning and a broad spectrum of cognitive domains in subjects with concurrent NDD and no prior history of dysphoric depression. The main hypotheses of the study were generally substantiated. Subjects with NDD and DD showed lower pre-morbid cognition and relatively weaker executive functioning compared with non-depressed subjects. Whereas DD showed lower general intelligence measured concurrently with depression symptoms (albeit not grossly impaired) the difference between NDD and non-depressed individuals did not reach statistical significance. No difference in overall cognitive performance was found between NDD and DD. When analyses used pre-morbid cognition (i.e., ITBS school achievement scores) as a covariate, the main depression group effects for adult cognition were no longer significant.

Before discussing the findings of this study the special nature of this sample needs to be remarked [1]. *First of all, this study should be considered a preliminary study in a selective sample of patients.* The nature of the sample is reflected in the total lifetime prevalence for major depression (30.1%) (64.9% of which were primary, 28.7% substance induced, and 6.4 % associated with bereavement) and substance abuse and dependence but its nature was the very reason to interrogate the data to study NDD. While more subjects in the depression categories reported substance dependence, we did not control for this variable because the observed differences between the depression groups and nondepressed comparisons were no longer significant after controlling for pre-morbid cognitive functioning. A group representing individuals endorsing dysphoria was included in the analyses. This dysphoric group (DD, 98/330 or 27%) was selected based on endorsing 5 or greater depressive symptoms. Whereas 44.2% of subjects with DD reported a lifetime history of major depression, this group should not be considered as having exclusively major depression episode at the time of assessment because symptoms were self-report and assessed in a nonclinical setting. This method of assessment as well as the nature of the sample may have inflated the rates of current (dysphoric) depression. Although consistent with the literature, [8, 13] the point-prevalence for NDD (20/330 or 6%) in the present study should also be viewed with this caveat in mind. In addition, while subjects were included in the NDD category if they reported no past history of depression, some recollection bias is possible and consistent with any such study. Also, no measures of emotional awareness were available limiting inferences on the potential underlying mechanisms of NDD. The results of the present study may help to plan for future studies on *larger* and random samples which should include measures of emotional awareness and/or alexithymia. Finally, the scope of this report is limited due to secondary analyses of data not designed to assess NDD. As a result, the *power was low for comparisons including the NDD*. Effect sizes were included to allow comparisons beyond p-values.

Cognitive competence and academic achievement

To our knowledge, this is the first study to comprehensively assess current and past (estimated using standardized school achievement test scores) cognitive functioning in subjects with NDD without history of depression. This consideration is key in light of the

fact that symptom clusters consistent with NDD may represent partially treated depression and that poor cognition may be a consequence of past depression [53, 54]. Based on the sizeable academic achievement effect, it is parsimonious to interpret that the cognitive functioning deficits of the NDD subjects may be in part construed as pre-morbid. Notably the size of the effect in academic achievement in NDD was nearly double that for DD (also statistically significant). This finding is consistent with the possibility that poorer educational achievement may play a role shaping (poor) emotional awareness [21] or represent a susceptibility to later psychiatric disorders [25] rather than solely be ascribed to the neurobiological/ neurocognitive effects of past episodes of typical depression [55].

An earlier study showed that clusters of ideational and vegetative depressive symptoms may increase the long term risk of cognitive decline [8]. In this study subjects were age 50 or older and there was low cognitive threshold for inclusion (e.g., initial assessment MMSE scores of 18/30 or lower) [8]. These results are consistent with another study showing poorer cognition (albeit on average no gross impairment) among older subjects (average age=73) presenting exclusively with vegetative symptoms of depression (the nondysphoric condition) and subjects presenting with vegetative symptoms and dysphoria (the dysphoric condition) [20]. In the present study examining a sample of younger subjects of average general intelligence, an extensive neuropsychological battery found only executive difficulty among subjects with NDD. The findings of lower general intelligence and executive function scores among DD subjects are in line with the widely established association of sad mood and poor cognitive performance [56, 57].

Implications for psychiatric nosology

Prominence assigned to emotional symptoms (i.e., sad mood and/or loss of ability to experience pleasure) in diagnosing depression has contributed to a relative dearth of research concerning the significance and the mechanism of symptom clusters including depressive ideation and vegetative symptoms not always accompanied by dysphoric mood [6, 8, 13, 58]. NDD may be a phenomenological variant of depression (*not* necessarily a pathophysiologically different illness) occurring among persons who inconsistently express emotional symptoms in the presence of other depressive symptoms [6]. This view is consistent with the observation that DD and NDD showed similar phenomenology of non-emotional symptoms (Table 2) with worthlessness and guilt, sleep changes, and fatigue being among the most common; and had also significantly greater rates of psychopathology in the birth parents compared to non-depressed subjects. The widely-accepted diagnostic system of the American Psychiatric Association (APA, 2000) considers sadness or loss of pleasure as essential symptoms to diagnose depression. This essentialist position with reference to nosologic approaches in multiple disciplines has been eloquently criticized on philosophical grounds: "... the essentialist error (is) thinking that there are such things as essential characteristics" [59]. The DSM-IV (APA, 2000) view of dysphoria implies (albeit implicitly) that all depression symptoms stem from an emotional disturbance that is perceived and reported by the patient or assessed by the clinician during the mental state examination. Recent acquisitions in psychoimmunology challenge the view that depressed mood is always essential and a primary precursor to the depressive syndrome. On the contrary, depressed mood may in fact be primed by a cascade of somatic events [60]. The requirement of dysphoria for diagnosing depressive disorder also ignores the possibility that individual differences in perception and expression of personal emotions may influence reporting of emotional symptoms [61]. Low reported inner (i.e., subjective) agitation in NDD in the present study, for instance, is consistent with limited endorsement of emotional symptoms. Such individual differences may result in under-recognition of subsyndromal depressive disorders (e.g., NDD) especially in certain clinical settings where self-report screening instruments are used and items on change in emotional state are critical triage

questions [62]. Specifically, patients with ideational and vegetative symptoms alone may not be identified and go untreated.

Summary and future directions

The present study found that subjects endorsing depressive ideation and vegetative symptoms, but not current or prior dysphoria (nondysphoric depression, or NDD), show poorer cognitive functioning during school years that may carry over into poorer executive functioning in adult years. These findings suggest that NDD may be relevant as a psychiatric condition. History of poor pre-morbid cognitive functioning (especially because two-fold greater compared with dysphoric depression) is consistent with a deficit in the domain of personal emotions processing and awareness posited as the underpinning of this atypical presentation of depression [21]. Research on atypical expressions of depression has been advocated and has shown that subthreshold depressive conditions carry significant risk of morbidity, [63] and may respond to treatment [64-66]. Further studies are needed to *confirm these findings in other populations* and to determine the most appropriate treatment for nondysphoric depressive conditions.

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Table 1

Frequency of DSM-IV major depression symptoms

Major Depression Symptoms	Comparisons (n = 109)		NDD (n = 20)		DD (n = 98)	
	n	%	n	%	n	%
1. Sadness	0	0%	0	0%	43	44%
2. Loss of pleasure	0	0%	0	0%	96	98%
3. Suicidal Plans	0	0%	1	5%	29	30%
4. Worthlessness or guilt	19	17%	19	95%	86	88%
5. Change in appetite	5	5%	8	40%	55	56%
6. Change in sleep patterns	18	17%	16	80%	79	81%
7. Fatigue	35	32%	13	65%	92	94%
8. Agitation	5	5%	4	20%	58	59%
9. Trouble concentrating	8	7%	9	45%	75	77%

NDD = Nondysphoric Depression. DD = Dysphoric Depression. Symptoms assessed using BDI – II.

Table 2
Demographic and lifetime medical conditions, substance misuse, and anxiety disorder

	Comparisons (<i>n</i> = 109)		NDD (<i>n</i> = 20)		DD (<i>n</i> = 98)	
Birth parent problems present (<i>n</i> , %)	32	29%	11	55%	41	42%
Age (<i>M</i> , <i>SD</i>)	44.72	7.01	41.21	6.43	44.57	7.52
Sex (# female, %)	58	53%	11	55%	63	64%
Education (years: <i>M</i> , <i>SD</i>)	14.17	1.78	13.60	1.57	13.82	2.10
Married (<i>n</i> , %)	79	72%	12	60%	58	59%
Any Health Problem (<i>n</i> , %)	63	58%	11	58%	66	67%
Any Substance Abuse (<i>n</i> , %)	39	39%	9	45%	49	50%
Any Substance Dependence (<i>n</i> , %)	15	14%	8	40%	45	46%
Any Anxiety Diagnosis (<i>n</i> , %)	1	<1%	2	10%	12	12%

NDD = Nondysphoric Depression. DD = Dysphoric Depression.

Table 3

Academic achievement and cognitive functioning

	Comparisons (n=109)				DD (n=98)				Cohen's d			
	M	SD	M	SD	M	SD	M	SD	C vs NDD	C vs DD	NDD vs DD	
<i>Pre-Morbid Cognition (ITBS)</i>	65.07	25.83	49.32	25.93	57.44	23.37			.61	.31	.33	
<i>Cognitive Functioning</i>												
WAIS-III VIQ	106.72	14.30	100.90	13.63	102.05	12.33			.42	.35	.09	
WAIS-III PIQ	109.30	13.38	105.20	13.56	104.72	12.52			.30	.35	.04	
General Memory	0.07	0.74	-0.08	0.72	-0.11	0.80			.21	.24	.04	
Attention	0.03	1.02	-0.04	0.77	0.00	0.91			.08	.03	.05	
Executive Functions	0.09	0.65	-0.16	0.59	-0.12	0.69			.40	.31	.06	

Means (*M*) and standard deviations (*SD*) are presented. Effect sizes are presented for each pair-wise comparison (i.e., non-depressed comparisons versus NDD, comparisons versus DD). *C* = non-depressed comparisons. NDD = nondysphoric depression. DD = dysphoric depression. ITBS = Iowa Test of Basic Skills. General Memory = RCFT immediate and delayed performance, WMS-III General and Immediate Memory. Attention = CPT-II and CTMT. Executive function = WMS-III working memory, WCST, and SCWT.

Table 4
Analysis of Variance and Cognitive Outcomes

Cognitive Outcomes	Initial Models ^a			Adjusted Models ^b		
	df	F	p	df	F	p
Pre-Morbid Cognition (ITBS) Percentile Points	2, 218	4.85	.009	na	na	na
WAIS-III Index Scores						
VIQ	2, 221	3.27	.040	2, 217	0.44	.647
PIQ	2, 221	4.56	.011	2, 217	1.88	.155
Z-transformed Factor Scores						
General memory	2, 221	1.90	.153	-	-	-
Attention	2, 220	0.22	.807	-	-	-
Executive Functions	2, 221	3.93	.021	2, 217	1.52	.220

ITBS = Iowa Test of Basic Skills. General Memory = RCFT immediate and delayed performance, WMS-III General and Immediate Memory. Attention = CPT-II and CTMT. Executive function = WMS-III working memory, WCST, and SCWT. Na = ITBS school achievement scores included as covariate in adjusted models. Dash means analyses not conducted because initial models were not significant.

^aInitial ANOVA models adjusted for sex and current age.

^bAdjusted models added ITBS school achievement scores as covariate.