Original Investigation

Transdiagnostic Factors and Mediation of the Relationship Between Perceived Racial Discrimination and Mental Disorders

Craig Rodriguez-Seijas, BSc; Malki Stohl, MS; Deborah S. Hasin, PhD; Nicholas R. Eaton, PhD

IMPORTANCE Multivariable comorbidity research indicates that many common mental disorders are manifestations of 2 latent transdiagnostic factors, internalizing and externalizing. Environmental stressors are known to increase the risk for experiencing particular mental disorders, but their relationships with transdiagnostic disorder constructs are unknown. The present study investigated one such stressor, perceived racial discrimination, which is robustly associated with a variety of mental disorders.

OBJECTIVE To examine the direct and indirect associations between perceived racial discrimination and common forms of psychopathology.

DESIGN, SETTING, AND PARTICIPANTS Quantitative analysis of 12 common diagnoses that were previously assessed in a nationally representative sample (N = 5191) of African American and Afro-Caribbean adults in the United States, taken from the National Survey of American Life, and used to test the possibility that transdiagnostic factors mediate the effects of discrimination on disorders. The data were obtained from February 2001 to March 2003. Latent variable measurement models, including factor analysis, and indirect effect models were used in the study.

MAIN OUTCOMES AND MEASURES Mental health diagnoses from reliable and valid structured interviews and perceived race-based discrimination.

RESULTS While perceived discrimination was positively associated with all examined forms of psychopathology and substance use disorders, latent variable indirect effects modeling revealed that almost all of these associations were significantly mediated by the transdiagnostic factors. For social anxiety disorder and attention-deficit/hyperactivity disorder, complete mediation was found.

CONCLUSIONS AND RELEVANCE The pathways linking perceived discrimination to psychiatric disorders were not direct but indirect (via transdiagnostic factors). Therefore, perceived discrimination may be associated with risk for myriad psychiatric disorders due to its association with transdiagnostic factors.

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Author Affiliations: Department of Psychology, Stony Brook University, Stony Brook, New York (Rodriguez-Seijas, Eaton); New York State Psychiatric Institute, New York (Stohl, Hasin); Department of Psychiatry, College of Physicians and Surgeons, Columbia University, New York, New York (Hasin); Department of Epidemiology, Mailman School of Public Health, Columbia University, New York, New York (Hasin).

Corresponding Author: Nicholas R. Eaton, PhD, Department of Psychology, Stony Brook University, Stony Brook, NY 11794-2500 (nicholas.eaton@stonybrook.edu).

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Although mental disorders are typically defined as discrete and independent in official nosologies, rates of comorbidity are significantly higher than would be expected by chance alone.[1] Multivariable modeling of this phenomenon has revealed that 2 core transdiagnostic factors (latent dimensions that cut across diagnostic boundaries) account for observed comorbidity patterns of common mental disorders and provide a better fit to the data than models reflecting current classification systems.[2-5] The internalizing (INT) transdiagnostic factor accounts for shared variance among the mood and anxiety disorders. The externalizing (EXT) transdiagnostic factor accounts for shared variance among the substance use disorders (SUDs) and disorders of impulsivity and antisociality (eg, attention-deficit/hyperactivity disorder and antisocial personality disorder). Therefore, these factors represent core constructs that saturate mental disorder, such that high levels of the factors manifest as multiple disorders. In this manner, they account for high rates of observed comorbidity.

The transdiagnostic factor literature grew from seminal research by Achenbach and Edelbrock,[6,7] who sought to characterize problem behaviors exhibited during childhood into fewer broad dimensions. More recently, factor analytic studies conducted by Krueger and colleagues[2,3] found that 2 higher-order factors better explained the high rates of comorbidity among common mood, anxiety, and SUDs than traditional *DSM*-type models of putatively distinct categorical disorders (for a more in-depth treatment of the analytic strategies behind this literature, see the study by Eaton and colleagues[8]). The existence of these factors has indeed been well replicated, with notable progress made in the characterization of these transdiagnostic factors.[9] Both INT and EXT have been shown to be dimensional in nature.[10-12] The 2 latent factors are stable over time,[5,13] serve as the primary pathways for continuity of common mental disorders over time,[10,14] and account for the associations between disorders and important outcomes (eg, suicide and alcohol dependence).[15,16] They account for comorbidity patterns in highly diverse cross-national samples[17] and are invariant across sex,[18,19] race/ethnicity,[15] age,[13] and sexual orientation.[20] In addition to their emergence in phenotypic self-report data, analyses of twin data indicate that these transdiagnostic factors are present at the level of genetic structural inquiry as well.[21,22] These factors are increasingly becoming a focus of treatment through transdiagnostic intervention approaches[23,24] based on the widespread nonspecific treatment effects of psychotherapeutic and psychopharmacological interventions.[25-29] Finally, less common disorders have also recently been incorporated into this latent transdiagnostic structure of psychopathology (see the study by Eaton et al[30] for a recent review), demonstrating that this approach can inform classification and comorbidity research beyond only mood, anxiety, and SUDs.

Previous studies have characterized the structure and statistical properties of transdiagnostic factors. Still, little is known about how they might serve as a link between environmental exposures and mental disorders. We are aware of only 3 studies[20,31,32] that have investigated how environmental exposures, transdiagnostic factors, and mental disorder diagnoses are related, but these studies did not formally test mediation. For instance, Keyes and colleagues[31] examined the relationships between childhood maltreatment and disorders, finding that the INT and EXT factors were significantly associated with retrospective maltreatment. Further investigation to determine whether modeling direct associations between diagnoses and maltreatment would improve model fit suggested that no residual associations between maltreatment and diagnoses should be incorporated. These findings indicated that when the relationship between childhood maltreatment and transdiagnostic psychopathology factors was fully accounted for, the associations between maltreatment and individual disorders were unnecessary to include.

Although the studies above are suggestive that transdiagnostic factors may have a mediating role in the associations between environmental stressors and observed disorders, no study to our knowledge has formally tested this mediation. Therefore, the relative importance of direct relationships (ie, the direct association between exposure and disorder) and indirect relationships (ie, the indirect association between exposure and disorder as mediated by transdiagnostic factors) is unknown. Formally investigating direct and indirect effects could lead to a better understanding of the importance of transdiagnostic factors in relation to environmental stressors and aid the understanding of pathways by which environmental stressors are linked to disorders. For example, is exposure to environmental stressors directly related to observed diagnoses, or is such exposure better considered associated at the higher transdiagnostic factor levels, which themselves manifest as multiple observed mental disorders? In recent years, sophisticated indirect effects modeling approaches have been developed to address such questions explicitly,[33-36] allowing for a close characterization of the degree to which transdiagnostic latent factors might mediate the associations between environmental exposures and observed mental disorders.

The present study sought to use an important environmental stressor, perceived racial discrimination, to examine how this stressor might relate with (1) specific diagnoses and (2) transdiagnostic factors, specifically testing the potential mediation of the former relationships by the latter. Previous research has indicated that racial discrimination experiences are robustly related to poorer mental health.[37-39] In a review of more than 47 studies, Williams and Mohammed[40] found consistent evidence that increased levels of perceived racial discrimination were associated with poorer mental health outcomes. The results of prospective studies also suggest that perceived discrimination temporally predicts subsequent mental disorder[41,42] but that the reverse is not true.[39] In terms of risk, perceived racial discrimination is associated with increased risk for any mental disorder.[39,43] Taken in conjunction with research demonstrating a temporal sequence of discrimination predicting later mental disorder symptoms, these findings suggest a potentially diffuse etiological pathway congruent with transdiagnostic factor mediation. That this environmental exposure is associated with multiple forms of psychopathology makes it a prime candidate for the proposed analytic strategy aimed at characterizing how environmental stressors relate to mental disorders by means of transdiagnostic factors.

We tested 2 hypotheses in a nationally representative probability sample of African American and Afro-Caribbean adults in the United States. First, we hypothesized that perceived racial discrimination would show positive zero-order associations with common mental disorders. Second, we hypothesized that the transdiagnostic latent factors would serve as strong mediators of the associations among discrimination and mental disorders. In other words, using an indirect effects modeling framework, we tested whether discrimination was directly associated with increased risk of observed mental disorders (direct effect) or whether discrimination was associated with higher transdiagnostic factor levels, which were then reflected as higher rates of mental disorders (indirect effect). A finding of full mediation would indicate that the only association between discrimination and mental disorder would be through the transdiagnostic factors (indirect effect), suggesting that transdiagnostic variance best explains the association between this environmental stressor, psychopathology, and SUDs.

Methods

Participants

We examined data from 5191 individuals who participated in the National Survey of American Life (NSAL), a national probability sample of noninstitutionalized African American adults in the United States (fielded from February 2001 to March 2003).[44] To date, the NSAL is the largest, most thorough investigation of mental health conducted on a national household sample of African Americans (n = 3570) and black individuals of Caribbean descent (Afro-Caribbeans) (n = 1621). The NSAL also included a smaller comparison sample of non-Hispanic white Americans (n = 891) with similar demographics to the African American sample. Our analyses were repeated with inclusion of this sample, and the pattern of results was unchanged. African American participants were oversampled, and design features of the study (eg, sampling weights) were used to correct for disproportionate sampling and to ensure representativeness of the sample for sociodemographic characteristics.

Institutional review board approval for the NSAL was provided by the University of Michigan, and the present study was approved by the institutional review board at Stony Brook University. Oral informed consent was obtained from all NSAL participants.

Assessment

Psychopathology

The *DSM-IV* diagnoses were made using the World Mental Health Composite International Diagnostic Interview,[45] which is a fully standardized, comprehensive diagnostic instrument for the assessment of psychopathology. The present study examined *DSM-IV* lifetime diagnoses of major depressive episodes (MDEs), dysthymic disorder, panic disorder, generalized anxiety disorder, social phobia, adult separation anxiety disorder, posttraumatic stress disorder, attention-deficit/hyperactivity disorder, oppositional defiant disorder, conduct disorder, and alcohol and drug SUDs (each coded as present if abuse or dependence criteria were met). The Composite International Diagnostic Interview demonstrates good test-retest (κ range, 0.69-0.78) and interrater (κ range, 0.67-0.98) reliability,[46] as well as convergent validity with interviews such as the Structured Clinical Interview for *DSM-IV*.[47]

Discrimination

Perceived race-based discrimination experiences were assessed across 9 situations, where participants reported the number of times in their lives they had experienced being (1) unfairly fired, (2) unfairly refused employment for a position, (3) denied a promotion, (4) discouraged from educational advancement, (5) prevented from moving into a neighborhood, (6) persecuted by neighbors, (7) denied a loan, (8) subjected to inferior service by a repairperson, and (9) abused by the police. Participants endorsing discrimination were asked to attribute a cause for each instance; the present study examined only those discrimination experiences attributed to ancestry, race, or shade of skin color, thereby focusing primarily on race-based discrimination. Participant-reported values for each type of discrimination experience that exceeded 5 instances were collapsed into a single category of more than 5 to correct for positive skew and outliers.

Analysis

Latent Variable Measurement Models

Analyses were conducted using statistical software (Mplus, version 7.11; http://www.statmodel.com/).[48] Latent factors were parameterized to have means of zero and variances of one. Model fit was evaluated using the Comparative Fit Index (CFI), Tucker-Lewis Index (TLI), and root-mean-square error of approximation (RMSEA). Hu and Bentler[49] reported interpretational benchmarks for good fit (CFI and TLI ≥0.95 and RMSEA ≤0.06). We began by testing the measurement models of the diagnostic and discrimination data separately (eResults in the Supplement). Given the frequent replications of the INT-EXT model with this set of diagnostic indicators, we parameterized a standard INT-EXT model using confirmatory factor analysis and a weighted least squares estimator (WLSMV [appropriate for categorical diagnoses]), where transdiagnostic factors were allowed to correlate. Next, guided by exploratory factor analyses, we examined the latent structure of the 9 discriminatory experience items using confirmatory factor analysis and a robust maximum likelihood (MLR) estimator. After characterization of the measurement models of the diagnostic and discrimination data, we added structural equations to conduct indirect effects modeling using the WLSMV estimator. All analyses took into account the complex survey design of the NSAL.

Indirect Effects Modeling

After identifying the 2 measurement models of (1) discrimination and (2) psychopathology and SUD latent structures, indirect effects structural equation modeling was used to determine the direct or indirect pathways by which the discrimination latent variable was associated with diagnoses. Direct effects of discrimination represent the direct associations between the discrimination factor and diagnoses, and indirect effects represent the pathways from discrimination (to a

mediating INT or EXT transdiagnostic factor) to the diagnoses. We applied a counterfactual framework in our analyses.[34,50-53] The indirect effect of discrimination (its effect that acts through the transdiagnostic INT-EXT factors) is defined as the probability of experiencing a disorder predicted if one changed the level of INT or EXT to the level that would reflect a 1-U (ie, 1 SD) increase in the discrimination factor, while actually holding the discrimination factor constant. If the probability of experiencing a disorder given (1) the change in INT or EXT reflecting a unit increase in discrimination (while simultaneously holding the actual discrimination level constant) was not significantly different from (2) the probability of disorder given a unit increase in discrimination itself, then it would indicate that the association between discrimination and disorder was fully mediated by transdiagnostic factors.

Using regression analyses (**Figure 1** and **Figure 2**), we compared the associations among discrimination, the transdiagnostic factors, and the diagnoses. Probit regressions predicted each diagnostic variable from the discrimination factor (τ) (Figure 1). Via linear regression, we then simultaneously regressed the transdiagnostic factors on the discrimination factor (α), the diagnoses on the transdiagnostic factors using probit regression (β), and the diagnoses on the discrimination factor (τ′) (Figure 2). This multiple mediator model allowed us to compare the results of the regression of the diagnoses on the discrimination factor from models in which INT and EXT were included and excluded. In other words, the indirect model compared the association of discrimination with transdiagnostic variance vs the association of discrimination with observed disorders when the relationship with transdiagnostic factors was held constant.

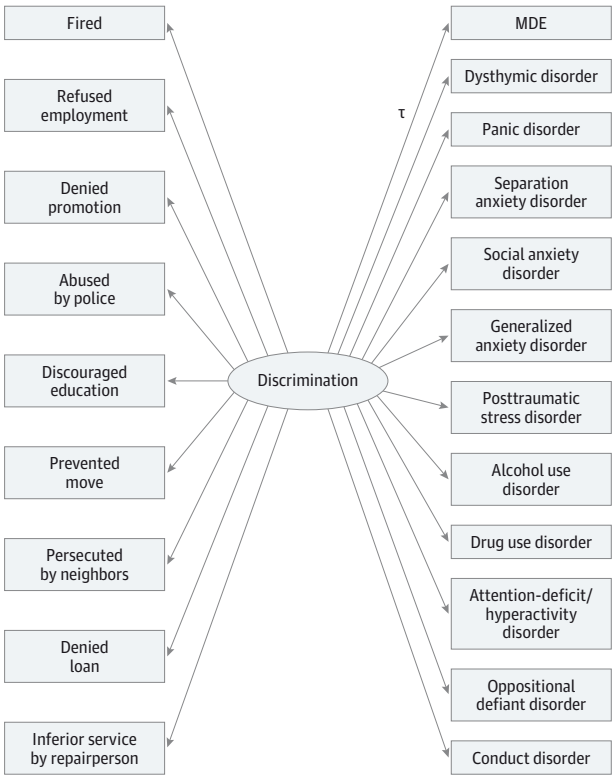
Following J. C. Elliott and colleagues (and coauthors M.S., D.S.H., and N.R.E., unpublished data, 2001-2005), we back-transformed the resulting probit regression indirect effects estimates to probabilities. Indirect effects represented the difference between τ and τ′ (ie, τ minus τ′). We used the delta method to then test whether this difference equaled zero. Each indirect effect was divided by the total effect to determine the percentage of the change in the probability of each diagnosis that reflected the above-described indirect association with discrimination. These estimates differ across levels of discrimination due to nonlinearity of the probit function, so results are presented as changes to the base probability reference values for each diagnosis when discrimination was at its mean (zero). Following recommendations by Preacher and Hayes,[54] we bootstrapped all analyses 5000 times to obtain appropriate (and potentially nonsymmetric) CIs around estimates.

Results

Transdiagnostic Factor Structure

We parameterized a confirmatory factor analysis model with the mood and anxiety disorders loading on the INT factor and the SUDs and behavioral disorders loading on the EXT factor. This model provided an overall good fit (CFI of 0.95, TLI of 0.94, and RMSEA of 0.02). Examination of the discrepancy between observed and model-implied correlations suggested inclusion of correlated residuals between (1) MDEs and dysthymia and (2) alcohol and drug SUDs. Our final INT-EXT measurement model demonstrated excellent fit (CFI of 0.99, TLI of 0.98, and RMSEA of 0.01) (eFigure 1 in the Supplement).

Figure 1. Simplified Model Showing the Direct Effect of Discrimination on Psychopathology Variables, Without Mediating Transdiagnostic Factors



The model highlights major depressive episode (MDE) as an example. See the main text (Indirect Effects Modeling under the Analysis subheading in the Methods section) for description of discrimination indicators and τ parameter. Residuals are not depicted for simplicity of presentation.

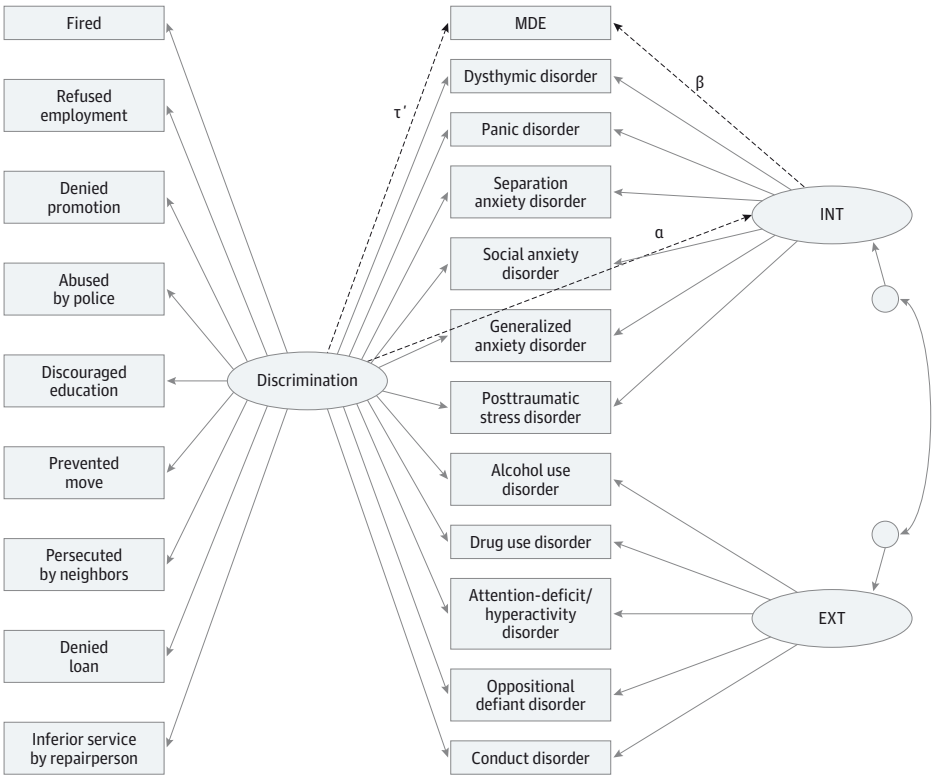
Discrimination Factor Structure

Guided by exploratory factor analysis results (details on exploratory factor analysis parameters are available in the eResults and eTable in the Supplement), we parameterized a one-factor discrimination model, which provided good fit to the data (CFI of 0.95, TLI of 0.93, and RMSEA of 0.02). Examination of the discrepancy between observed and model-implied correlations suggested inclusion of correlated residuals between the 2 neighborhood-related items (ie, persecuted by neighbors and prevented from moving into a neighborhood). Our final discrimination measurement model fit well (CFI of 0.96, TLI of 0.95, and RMSEA of 0.01) (eFigure 2 in the Supplement).

Relationships Between Discrimination and Disorders

Zero-order tetrachoric correlations between the discrimination factor and each diagnosis were significant and positive (**Table 1**). Discrimination increases were also associated with significantly increased probability of diagnosis in a regression context (τ), with the exception of attention-deficit/

Figure 2. Simplified Model Showing the Indirect Effect of Discrimination on Psychopathology Variables, With Mediating Transdiagnostic Factors



The model highlights major depressive episode (MDE) as an example. See the main text (Indirect Effects Modeling under the Analysis subheading in the Methods section) for description of discrimination indicators α, β, and τ′ parameters. Residuals are not depicted for simplicity of presentation. Circles and arrows connecting INT and EXT represent correlated residuals of the transdiagnostic factors in the full model, where EXT was also regressed on discrimination (not pictured for simplicity). INT indicates internalizing; EXT, externalizing.

hyperactivity disorder (**Table 2**). For example, a unit increase in discrimination predicted an increase of 3.6 percentage points ($P < .001$) in the probability of MDEs over and above the base probability of 12.1%.

When the transdiagnostic factors were included as predictors of diagnoses, the direct effect of discrimination (τ′ in Table 2) was reduced in magnitude in all cases and remained significant only for separation anxiety and the 2 SUDs. In contrast, the indirect effect (τ minus τ′) through INT and EXT was significant ($P < .001$) for all diagnoses. For example, when the effect of discrimination on MDEs via INT was included, a 1-U increase in discrimination was directly associated with a 0.6-percentage point direct effect increase in the probability of MDEs over the base value (compared with a 3.6-percentage point increase when transdiagnostic factors were not modeled). However, the indirect effect of discrimination through INT indicated that a 1-U increase in discrimination was associated with an increase of 2.9 percentage points. This revealed that 83.3% (τ minus τ′, divided by τ) of the association between discrimination and the probability of MDEs occurred indirectly through both variables' association with INT. Overall, the indirect effects accounted for the majority of the total association (direct plus indirect) between discrimination and all diagnoses, with the exceptions of alcohol (42.9%) and drug (45.7%) use disorders. Indeed, 100% of the total association with discrimination was indirect (through the transdiagnostic factors) for social anxiety disorder and attention-deficit/hyperactivity disorder. Due to negative direct effects from the discrimination factor, some percentages exceed 100. For clarity, we refer to these values as 100%.

Discussion

To our knowledge, this is the first study to formally examine the mediating role of transdiagnostic factors in the relationship between an environmental exposure and mental health outcomes. Using an indirect effects modeling framework, we found that the associations between racial discrimination and disorders were largely (and sometimes completely) mediated through the transdiagnostic INT and EXT latent factors. For all non-SUD disorders, the indirect effects through INT and EXT accounted for the majority of the total association between discrimination and disorders (54.8%-100%). Even for SUDs, a sizable proportion of discrimination's total association was mediated (42.9% for alcohol and 45.7% for drug use disorders). In most cases, the direct association with discrimination became nonsignificant (and sometimes negative) when indirect effects were modeled, even with our large and statistically powerful sample size. To a large degree, the link between perceived discrimination and elevated rates of mental disorder generally reflects the associations with transdiagnostic factors. That is, while increased levels of perceived discrimination are indeed associated with higher rates of mental disorders, this phenomenon can be explained by the higher transdiagnostic factor levels related to higher perceived levels of discrimination.

These elevated transdiagnostic factor levels are associated with higher rates of multiple forms of mental disorder. When discrimination's relationship with transdiagnostic factors is modeled, our results further reveal that discrimination's associations with specific disorders becomes trivial, with few exceptions to this rule.

Table 1. Zero-Order Correlations Between Discrimination and Diagnoses

Variable	Discrimination
MDE	0.17[a]
Dysthymic disorder	0.16[a]
Generalized anxiety disorder	0.15[a]
Panic disorder	0.16[b]
Social anxiety disorder	0.09[c]
Separation anxiety disorder	0.20[a]
Posttraumatic stress disorder	0.17[a]
Alcohol use disorder	0.23[a]
Drug use disorder	0.22[a]
Attention-deficit/hyperactivity disorder	0.13[c]
Oppositional defiant disorder	0.16[a]
Conduct disorder	0.22[a]

Abbreviation: MDE, major depressive episode.

[a] $P < .001$.

[b] $P < .01$.

[c] $P < .05$.

Implications

Importance of Transdiagnostic Variance

Our results add to a growing body of literature demonstrating the critical importance of understanding transdiagnostic variance as a more parsimonious and conceptual way to understand the comorbidity of mental disorders than multiple pairwise associations. In contrast to current classification systems that include categorical putatively distinct disorders, these results highlight that in most cases the shared transdiagnostic variance is related to minority stress in the form of perceived racial discrimination rather than the unique disorder-specific variance. This transdiagnostic variance has many important properties (eg, cross-group invariance, stability over time, and closeness to genetic substrates) and accounts for continuity and development of onset and comorbidity over time, as well as prediction of important outcomes, potentially serving as a treatment focus.[5,10,13-24] Most important, the present study demonstrates for the first time to date that transdiagnostic factors account for the majority of the association between disorders and at least 1 important environmental

Table 2. Experiences of Discrimination, Transdiagnostic Factors, and Diagnoses[a]

Outcome	Discrimination, Without INT-EXT	Discrimination: Direct Effects on Mental Disorders and Mediated Effects Through INT-EXT				
	Total Effect on Diagnosis (τ),[b] % Point Change[c]	Direct Effect of Discrimination on Diagnosis (τ′),[b] % Point Change[d]	Direct Effect of Discrimination on INT-EXT (α),[e] Change in INT-EXT[c]	Direct Effect of INT-EXT on Diagnosis (β),[b] % Point Change[f]	Indirect Effect via INT-EXT (τ − τ′), % Point Change[g]	Total Effect Explained by INT-EXT (τ − τ′) / τ, %
INT	NA	NA	0.19	NA	NA	NA
EXT	NA	NA	0.22	NA	NA	NA
MDE	3.6[h]	0.6	NA	21.0[h]	2.9[h]	83.3
Dysthymic disorder	1.4[i]	0.2	NA	10.4[h]	1.2[h]	84.7
Panic disorder	1.2[j]	0.3	NA	7.3[h]	0.9[h]	75.0
Separation anxiety disorder	3.1[h]	1.1[i]	NA	13.3[h]	1.7[h]	54.8
Social anxiety disorder	1.3[j]	−0.3	NA	11.7[h]	1.6[h]	100
Generalized anxiety disorder	1.6[i]	0.2	NA	11.3[h]	1.3[h]	81.3
Posttraumatic stress disorder	3.1[h]	0.9	NA	15.6[h]	2.1[h]	67.7
Alcohol use disorder	4.9[h]	2.4[h]	NA	12.0[h]	2.1[h]	42.9
Drug use disorder	3.5[h]	1.6[j]	NA	9.8[h]	1.6[h]	45.7
Attention-deficit/hyperactivity disorder	1.4	−0.5	NA	13.9[h]	2.0[h]	100
Oppositional defiant disorder	2.7[i]	0.2	NA	15.1[h]	2.5[h]	92.6
Conduct disorder	4.6[h]	1.0	NA	19.9[h]	3.4[h]	73.9

Abbreviations: EXT, externalizing; INT, internalizing; MDE, major depressive episode; NA, not applicable.

[a] Values representing the percentage change in probability use baseline reference values for risk in the sample of 12.1% (MDE), 3.5% (dysthymic disorder), 3.4% (panic disorder), 6.3% (separation anxiety disorder), 7.5% (social anxiety disorder), 5.7% (generalized anxiety disorder), 9.0% (posttraumatic stress disorder), 11.8% (alcohol use disorder), 6.3% (drug use disorder), 7.3% (attention-deficit/hyperactivity disorder), 8.6% (oppositional defiant disorder), and 12.9% (conduct disorder). Percentage change is computed by calculating the inverse probit of the regression coefficient from the probit model and subtracting the inverse probit from the baseline value.

[b] Regression parameters are probit.

[c] Change in outcome for a unit-increase in discrimination.

[d] Change in outcome for a unit-increase in discrimination, holding INT-EXT constant.

[e] Regression parameters are linear.

[f] Change in outcome for a unit-increase in INT-EXT factors, holding discrimination constant.

[g] Indirect effect may not exactly equal the difference between total and direct effects due to rounding.

[h] $P < .001$.

[i] $P < .01$.

[j] $P < .05$.

stressor. Given its importance to understanding disorders, further research on (and perhaps reclassification to capture) transdiagnostic variance is critical. In terms of implications for discrimination research, our results suggest that observed, diffuse impacts of discrimination on multiple disorders as seen in previous literature may reflect the impact of discrimination on transdiagnostic factors, highlighting the necessity of studying transdiagnostic variance explicitly in discrimination research.

Clinical Implications

From a public health perspective, our findings suggest that transdiagnostic factors may be a key level of focus for intervention, assessment, and prevention efforts. Taken together with previous evidence, transdiagnostic variance predicts outcomes of clinical interest (eg, suicide and substance dependence).[15,16] Furthermore, transdiagnostic variance mediates the stressor-disorder link, suggesting that targeting it clinically could potentially (1) reduce negative outcomes, (2) buffer against environmental stressors, and (3) have diffuse efficient impacts on multiple disorders. Given the recent interest in (and emergence of) transdiagnostic treatment approaches,[55] transdiagnostic factor levels may potentially be decreased through behavioral[23,24] and psychopharmacological[26,56] means. Therefore, interventions that treat disorders at the transdiagnostic level appear to be a worthwhile pursuit.

Limitations

We note several study limitations. First, we examined retrospective lifetime data, which can be subject to memory biases. However, research suggests that retrospective reports of mental disorder, when biased, are typically underestimates rather than overestimates,[57] ameliorating somewhat the concerns about potential overreporting of lifetime disorders. In addition, evidence suggests that the retrospective reports of early experiences by individuals with mental disorder are no less reliable or valid than healthy individuals' reports, nor are they exaggerated by comparison.[58] Similarly, research substantiates the reliability of retrospective recall of discrimination-like experience such as bullying.[59] Second, given the cross-sectional nature of our data, no causality inferences can be drawn. Indeed, it is possible that some mental disorders preceded some discriminatory experiences. Prospective data will be required to understand temporal sequencing and strengthen causal inference and will be a key area for further research. This being said, previous research has found that perceived discrimination often precedes mental disorder symptom increases,[41,42] but that mental disorder does not temporally predict perceived discrimination reports.[39] This suggests that a similar sequencing may be at play with transdiagnostic factors as well. In addition, there is accumulating evidence for transdiagnostic factors in addition to INT and EXT (eg, psychosis),[12,30,60,61] which we could not model in the present study due to necessary diagnoses not being assessed in the NSAL. Studies methodologically similar to this report using other transdiagnostic factors will be an important future direction. Third, diagnostic information was collected by extensively trained lay interviewers rather than clinicians. However, the diagnostic instrument was fully structured, with good diagnostic reliability.

Conclusions

We demonstrated that transdiagnostic factors mediate the relationship between perceived racial discrimination and mental disorders. More generally, transdiagnostic factors may mediate environmental stressors' associations with disorders, which is a question for further study. These findings support the key importance of transdiagnostic factors in characterizing mental disorder. Transdiagnostic factors appear to be critical in further understanding the etiology, onset, and persistence of psychopathology and SUDs.

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Study concept and design: Rodriguez-Seijas, Hasin, Eaton.
Acquisition, analysis, or interpretation of data: All authors.
Drafting of the manuscript: Rodriguez-Seijas, Stohl, Eaton.
Critical revision of the manuscript for important intellectual content: Rodriguez-Seijas, Hasin, Eaton.
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