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Temporal Stability of Cognitive Functioning and Functional Capacity in Women with Posttraumatic Stress Disorder

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Abstract

Objective: In addition to clinical symptoms, patients with posttraumatic stress disorder (PTSD) often experience considerable disability and may evidence minor impairments in performance on measures of cognition and functional capacity (FC). The objective of the present study was to determine if cognitive and functional skills manifest temporal stability as observed in other neuropsychiatric conditions in the presence of greater fluctuations in clinical symptoms.

Method: Assessments of cognition, FC, and clinical symptoms were conducted over two time points as part of a pre- and post-treatment assessment in a placebo-controlled clinical trial in 96 women with PTSD. The goal of these analyses was to examine the relative stability of scores and intercorrelations of measures of cognition, FC, and clinical symptoms.

Results: Cognitive and FC performance manifested considerably greater cross-temporal stability compared to clinical symptoms. FC performance did not change over time. Similar to previous findings in patients with schizophrenia and bipolar disorder measures of symptoms and self-reported disability did not correlate with measures of functional skills or cognitive performance.

Conclusions: Cognitive performance and functional capacity were temporally stable in women with PTSD. In contrast, clinical symptoms had much more cross-temporal fluctuation. Self-reported disability was correlated with current symptomatology but unrelated to objective measures of performance. Similar to other neuropsychiatric conditions, mood symptoms likely influence estimates of current level of functioning more than cognitive or functional skills.

Keywords: Posttraumatic stress disorder; Disability/handicaps; Everyday functioning

Introduction

Posttraumatic Stress Disorder (PTSD) is a disabling psychiatric disorder that develops following direct or indirect exposure to a traumatic event. PTSD is characterized by unwanted re-experiencing of the event, avoidance of reminders of the event, and increased arousal. The annual prevalence of PTSD is 3.5%, with a lifetime prevalence of 6–7% in the US. (Goldstein et al., 2016; DSM-IV). Patients with PTSD also experience declines in their daily functioning and frequently experience symptoms of mood disorders.

Alterations in cognitive functioning is a central feature of PTSD, in that subjective reports of challenges in recalling aspects of the trauma are part of the definition of the condition. Research on cognition in PTSD has focused on a broad range of

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processes including attention/working memory, processing speed, learning, and executive functioning (Bremner et al., 1993; Crowell Kieffer, Siders, & Vanderploeg, 2002; Gould, Bowie, & Harvey, 2011; Horner & Hamner, 2002; Samuelson et al., 2006; Stein, Kennedy, & Twamley, 2002; Twamley et al., 2009; Vasterling et al., 2002; Yehuda et al., 1995). Yet, it is also important to mention that while significant differences in performance across neurocognitive domains between PTSD patients and controls have been found, these differences do not necessarily represent clinically significant impairment on the part of patients with PTSD. This finding, combined with studies of premorbid functioning as a risk factor for PTSD, has led several authors to surmise there is no cognitive sequelae of PTSD alone after consideration of premorbid levels of cognitive functioning and various comorbidities (e.g. Wrocklage, Schweinsberg, & Krystal, 2016).

As PTSD leads to significant everyday disability, recent studies have also examined the correlations between cognitive performance and the ability to perform everyday tasks, referred to as functional capacity (FC) (Kaye et al., 2014) as well as correlations with impairments in everyday functioning. Among patients with mood disorders including bipolar disorder and schizophrenia (Bowie et al., 2010), as well major depression (Harvey et al., 2017a), FC performance is among the most potent predictors of real world functioning, with functional capacity deficits sometimes found to fully mediate the effects of cognitive deficits on everyday disability (Strassnig et al., 2015).

Studies on the cross-sectional and longitudinal relationships between clinical symptoms, neurocognitive abilities, and FC have been conducted with patients with schizophrenia, major depression, and bipolar disorder, with a focus on stability and course of both clinical symptoms and cognition and FC. In those conditions, the definitional symptoms are typically minimally related to performance on neurocognitive and FC measures on a cross sectional basis (Depp et al., 2009; Keefe et al., 2006, 2015; Neu et al., 2005; Nuechterlein, Edell, Norris, & Dawson, 1986), and cognitive performance and impairments in FC are relatively stable over time, including persisting into states of remission or euthymia (Gould et al., 2015; Harvey, Docherty, Serper, & Rasmussen, 1990; Harvey, Wingo, Burdick, & Baldessarini, 2010; Jaeger, Berns, Uzelac, & Davis-Conway, 2006; Kalin et al., 2015). These findings have led to the suggestions that cognition and FC impairments are stable traits (Leifker, Patterson, Bowie, Mausbach, & Harvey, 2010) that may be determined by a wholly different set of risk factors compared to symptoms, including the suggestions that functional capacity and cognitive performance may have similar genomic origins across neuropsychiatric conditions that have different susceptibility genes for definitional illness symptoms (Harvey et al., 2012).

In contrast to the large literature on stability and course of cognition, functional capacity, and disability in severe mental illness, there has been a striking lack of similar research in PTSD. A Medline search for "Cognition, PTSD, and remission" yields no longitudinal studies of cognitive performance and searches for the course of cognitive performance in PTSD also yield no findings. As a result, there is information on the separation of the course of cognition and FC versus symptoms. The present study uses the results of a clinical trial to perform those analyses.

Another critical topic in the area of mood and anxiety symptoms, cognition and functioning has been self-assessment. A series of studies have shown in people with major depression (Harvey et al., 2017a), bipolar disorder (Harvey, Paschall, & Depp, 2015; Strassnig et al., 2018), and schizophrenia (Harvey et al., 2017b; Strassnig et al., 2018) have shown that self-reports of everyday functioning manifest a substantial correlation current mood symptoms, but remarkably little correlation with objective performance data in the domains of cognition or functional capacity. There is one study in the literature on the correlation of self-reports of clinical symptoms and disability and their correlation with performance-based measures of cognition and functional capacity. That study, Kaye and colleagues (2014), examined cognitive performance and FC at the baseline time point of a clinical trial which aimed to treat the PTSD patients in this report. They found that self-report and clinician measures of the severity of PTSD, depression, and disability in PTSD patients were unrelated to performance-based assessments of cognition and FC. Thus, similar to studies of mood and psychotic disorders, clinical symptoms were not correlated with indices of cognition, FC, and everyday disability.

The current study represents a follow-up of that sample previously reported on by Kaye and colleagues (2014). Herein we use the complete baseline sample and a second assessment time point to examine performance over time, self-reported symptoms and their correlation with objective performance measures, and the differential stability of clinical symptoms and measures of cognition and FC. The PTSD participants were in a clinical trial of an investigational corticotropin releasing hormone (CRH) type 1 receptor antagonist which failed to improve PTSD symptom severity beyond that of placebo (Dunlop et al., 2017). We hypothesized that, similar to other neuropsychiatric conditions, cognitive and functional capacity performance would manifest temporal stability, more so than clinical symptoms, and that the low correlations present at baseline between clinical symptoms and these other two domains would be stable over time.

Methods

Study Overview

Women diagnosed with chronic PTSD of moderate or greater severity were enrolled in a double-blind, placebo-controlled, parallel-group, randomized clinical trial examining the clinical effects of a CRH type 1 receptor antagonist. The complete study protocol and study results are published elsewhere (Dunlop et al., 2014, 2017). Study visits included screening, pre-baseline neuropsychological assessment, baseline, and then post-randomization visits at Weeks 1, 2, 4, and 6. As part of the clinical investigation, participants completed a standardized battery of cognitive tests and an assessment of FC both at a baseline pre-randomization visit and again after 5 weeks on treatment. The study was conducted at four academic sites in the United States: Emory University School of Medicine, Mount Sinai School of Medicine (MSSM), Baylor College of Medicine (BCM), and the University of California, San Francisco (UCSF). The Institutional Review Boards of the four sites approved the study design, procedures, and recruitment strategies. Emory University served as the lead site.

Participants

Women between the ages of 18 and 65 years who met DSM-IV criteria for current PTSD of at least 3 months' duration were eligible. Men were not eligible because pre-clinical safety data with the investigational compound suggested a sex-specific risk for adverse events (Dunlop et al., 2014). For inclusion, patients also had to have total Clinician-Administered PTSD Scale for DSM-IV (CAPS) (Blake et al., 1995) past week and past month scores ≥50 at both the screening and baseline (randomization) visits. Key exclusion criteria included unstable medical conditions, substance abuse in the 3 months prior to baseline, current pregnancy or lactation, and concurrent treatment with another psychotropic agent or participation in an evidence-based psychotherapy for PTSD. No one was recruited into this study if they had an active court case. Participants were informed that their data were for research only and that the study team would be unable to provide any clinical information to them as a result of their participation.

Screening and Treatment Assessments

After signing the study informed consent document at the screening visit, patients underwent evaluation with the Structured Clinical Interview for DSM-IV (SCID) (First, Spitzer, Gibbon, & Williams, 1995) to diagnose PTSD and comorbid disorders, which were confirmed through an interview with a study psychiatrist. The CAPS assesses each of the 17 DSM-IV PTSD symptom diagnostic criteria. At screening and baseline, the CAPS was scored separately for the period of the past week and the past month. After baseline, the CAPS was assessed only for the past week.

The severity of depressive symptoms in the previous week was assessed using the Montgomery–Asberg Depression Rating Scale (MADRS) (Montgomery & Asberg, 1979; Williams & Kobak, 2008), a 10-item instrument with item scores ranging from 0 to 6, for a total score range of 0–60. In addition to ratings on the CAPS, self-reported symptoms of PTSD were evaluated using the PTSD Symptom Scale, Self-Report (PSS-SR) (Foa et al., 1993; Foa et al., 1997). The PSS-SR indicates the frequency of the 17 DSM-IV symptom criteria items over the past week, each rated on a 0–3 scale. The Symptom Validity Index is a six-item measure designed to assess the validity and over-reporting of subject responses that was embedded in the version of the PSS-SR used in the trial (Margolies, Rybarczyk, Vrana, Leszczyszyn, & Lynch, 2013). Each item of the index is unrelated to PTSD symptoms as defined by the DSM-IV. The six items are rated on the same 0–3 scale as the PSS-SR. As a measure of everyday disability, patients completed the Sheehan Disability Scale (SDS; Sheehan, 1983).

Neuropsychological Assessments

The MATRICS Consensus Cognitive Battery (MCCB) was used to evaluate cognitive impairment (Kern et al., 2008). This assessment was administered to detect improvements or unanticipated deterioration in neuropsychological test performance. The MATRICS Battery includes nine different standard cognitive tests selected for broad coverage of functionally relevant domains of cognitive performance: Category Fluency; Brief Assessment of Cognition in Schizophrenia Symbol Coding; Trail-Making Test, Part A; Continuous Performance Test, Identical Pairs Version; University of Maryland Letter-Number Span; Wechsler Memory Scale-III Spatial Span; Hopkins Verbal Learning Test-R; Brief Visual Memory Test–Revised; and Neuropsychological Assessment Battery Mazes. Tests were scored with the normative computer program developed for the MCCB; these norms are based on a large sample of healthy controls who ranged in age from 18 to 80. The composite score

was derived from the MCCB subtest performances and was used as global or composite measure of cognitive functioning and detailed methods on its calculation have been published by our group previously (Hodgins et al., 2018).

Performance-Based Measures of Functional Capacity

Assessment of FC used the UCSD performance-based skills assessment, brief version (UPSA-B; Mausbach, Harvey, Goldman, Jeste, & Patterson, 2007). The UPSA-B's two domains (Communication and Finance) result in a summary score ranging from 0 to 100. Average performance of healthy controls on the UPSA-B (Vella et al., 2017) was 83.7 with a standard deviation of 10.2.

Statistical Analyses

In these analyses, we first performed a repeated-measures analysis of variance (ANOVA), wherein we examined the effects of treatment group (Active, Placebo) × time (Baseline, Endpoint) for each of the variables. We then examined the change scores with paired *t*-tests, in order to determine the effect sizes for time-related changes across clinical symptom and performance-based measures. Pearson-product moment correlations were computed between the variables at baseline and end of treatment as well as correlations of change scores in order to determine if change scores within the same assessment modality were more highly intercorrelated than those correlations that crossed assessment modalities.

Results

Two-hundred sixty-six patients were enrolled in the trial (see Supplemental figure for the CONSIST diagram), of whom 128 (48%) completed the baseline neuropsychological assessments. Of these, 96 (75%) completed the repeat testing at

Table 1. Demographic information on participants at baseline

Variable	Placebo $n = 65$ n (%)	GSK561679 $n = 63$ n (%)
Race		
White/Caucasian	32 (49)	40 (64)
African American	28 (43)	18 (29)
Other	5 (8)	5 (8)
Hispanic	5 (8)	8 (13)
Current Major Depression	43 (66)	41 (65)
Education ($n = 125$)		
<High School	4 (6)	7 (11)
High School degree/Some college	29 (45)	24 (38)
College degree	15 (23)	19 (30)
Graduate degree	16 (25)	11 (18)
Current Smoker	17 (26)	12 (19)
Time since primary trauma ($n = 125$)		
≤6 months	5 (8)	6 (10)
6 months – 3 years	15 (24)	11 (18)
3–5 years	11 (18)	5 (8)
≥5 years	32 (51)	39 (64)
	Mean (SD)	Mean (SD)
Age (yrs)	40.4 (12.3)	40.6 (11.8)
Traumatic events, lifetime	3.7 (2.2)	3.5 (1.6)
CAPS Past Month Total	79.8 (15.6)	82.0 (12.5)
CAPS Past Week Total	74.8 (17.6)	77.5 (14.3)
PSS-SR Total	30.0 (9.3)	31.1 (7.1)
MADRS	25.1 (8.3)	26.5 (7.0)
SDS	16.3 (7.1)	15.5 (7.1)
CGI-S	4.7 (0.7)	4.7 (0.7)

Note: CAPS = Clinician-Administered PTSD Scale, CGI-S = Clinician Global Impression-Severity, CTQ = Childhood Trauma Questionnaire, MADRS = Montgomery Asberg Depression Rating Scale, PSS-SR = PTSD Symptom Scale – Self-report, SDS = Sheehan Disability Scale.

endpoint. Information regarding the demographic features of the sample at baseline are presented in Table 1. Mean performance on measures of cognition, functional capacity, and symptoms of PTSD or depression at baseline and endpoint are presented in Table 2, along with paired *t*-tests analyzing performance over time and Pearson correlations on these measures.

For 6 of the 7 variables presented in Table 2 the effect of time was statistically significant, all $F(1,92) > 53.02$, all $p < .001$. The only variable without a significant time effect was the UPSA-B, $F(1,92) = 0.67$, $p = .42$. However, the interaction of group × time was non-significant for all of the variables, all $F(1,92) < .71$, all $p > .40$. The effect sizes for changes in the placebo group were quite substantial, ranging from .63 to 1.70. Similarly large effect sizes were seen in the GSK561679 treatment group, ranging from .26 to 2.62. As shown in Table 2, the changes from baseline to endpoint were significant using paired *t*-tests for all variables in the combined group, other than for the UPSA-B.

Pearson correlations revealed significant intercorrelations between baseline and endpoint assessments on all measures of cognition, functional capacity, and symptoms. When the test–retest correlation for the most stable clinical measure, the SDS, was compared to the test–retest correlation for the cognitive composite score, the cognition composite score was significantly more stable over time, $z = 4.91$, $p < .001$. Paired *t*-tests revealed relative stability of performance on measures of functional capacity; differences between baseline and endpoint performance were not statistically significant ($p > .05$). However, in the present sample, significant changes from baseline to endpoint were observed across all symptom and cognitive measures ($p < .001$). In order to ensure that there were no differences in the stability of cognition and functional capacity as a function of treatment, these correlations were completed separately in the two treatment samples. The test–retest reliability of cognition in the placebo group was $r = .78$ and the stability in the active treatment group was $r = .92$. For the UPSA-B, the test–retest correlations were $r = .64$ in the placebo group and $r = .45$ in the active treatment group. Thus, the overall patterns for correlation for all patients were similar to those seen in the active treatment group alone.

Table 3 presents the intercorrelations between symptom, cognitive, and functional capacity measures at both baseline and endpoint/follow-up assessments. A significant correlation was observed between cognition and functional capacity at both baseline ($p < .001$) and end point ($p < .001$). Self-report (PSS-SR) and clinician rated measures (CAPS) of PTSD were intercorrelated at both baseline ($p < .001$) and endpoint ($p < .001$) providing evidence of convergent validity. Self-reported disability (SDS) and clinician rated depression (MADRS) were correlated at both baseline ($p < .001$) and follow-up ($p < .001$).

Table 2. Performance on cognitive, functional and symptom measures at baseline and endpoint in the combined group

	Baseline ($n = 128$)		Endpoint ($n = 96$)		*t*	*P*	*r*	*p*
	Mean	SD	Mean	SD				
COG	45.22	7.18	47.95	7.21	−6.53	.001	.846	>.001
UPSA	79.27	17.20	81.04	17.83	−.836	.405	.509	>.001
CAPS	75.98	16.60	55.46	22.44	9.96	.001	.479	>.001
PSSSR	31.62	8.79	20.30	10.23	9.79	.001	.414	>.001
MADRS	26.59	7.97	20.57	9.70	6.54	.001	.420	>.001
SDS	15.91	7.10	10.02	8.20	7.25	.001	.488	>.001

Note: COG = Composite Cognition Score, UPSA-B = UCSD Performance-Based Skills Assessment, Brief version, CAPS = Clinician-Administered PTSD Scale, PSSSR = Posttraumatic Symptoms Scale Self Report, MADRS = Montgomery–Asberg Depression Rating Scale, SDS = Sheehan Disability Scale. Composite cognition scores are *t*-scores (mean=50, SD = 10). UPSA scores range from 0 to 100.

Table 3. Correlations between cognitive, functional, and clinical variables at both assessments

	Cognition	UPSA	CAPS	PSSSR	MADRS	SDS
Cognition	1	.36***	−.11	−.12	−.11	.01
UPSA	.55***	1	−.08	−.15	.01	.06
CAPS	−.13	−.11	1	.33**	.33**	.38***
PSSSR	−.11	−.02	.79***	1	.22	.37***
MADRS	−.14	.03	.71***	.63***	1	.40***
SDS	−.01	−.07	.55***	.44***	.56***	1

Note: Correlations for first assessment are above the diagonal. Correlations for the second assessment are below. UPSA-B = UCSD Performance-Based Skills Assessment, Brief version, CAPS = Clinician-Administered PTSD Scale, PSSSR = Posttraumatic Symptoms Scale Self Report, MADRS = Montgomery–Asberg Depression Rating Scale, SDS = Sheehan Disability Scale.

***p<.001.

**<p<.01.

Those relationships remained constant at follow-up when depression symptoms were again significantly correlated with both clinician ($p < .001$) and self-reported PTSD symptoms ($p < .001$) at follow-up. Validity scores were not correlated with the performance-based measures or symptoms measures

In contrast to these findings, the correlations between cognition and functional capacity and the clinical symptoms scores were non-significant at both assessments. The largest of these correlations accounted for 2% shared variance. Self-reported disability measured by the SDS shared less than 0.5% of the variance with performance-based measures of cognition and FC at both assessments.

Discussion

The results of the present study of cognition, functional capacity, and clinical symptoms, assessed in a sample of women with moderate to severe PTSD, provided support for our hypotheses. Specifically, cognitive functioning and functional capacity performances seemed to manifest temporal stability, and did so to a greater extent than clinical symptoms within the context of a clinical trial. Support was also obtained for our additional hypothesis that the lack of correlation between clinical symptoms and cognition and FC, reported at baseline, would be stable over time as well. However, in the present sample, only FC performance did not change over time, with MCCB scores showing a statistically significant practice effect in the context of very high correlations across the two assessments (Dunlop et al., 2017; Hodgins et al., 2018). The level of cognitive performance of our sample was approximately 0.5 *SD* on average less than a national normative sample used in the creation of the MCCB norms and performance on the functional capacity measure was 0.43 *SD* worse than the data published in a previous normative study of the UPSA (Vella et al., 2017).

Otherwise the results in these patients with PTSD were similar to those in patients with schizophrenia and bipolar disorder, which have typically found measures of clinical rated symptoms and self-reported disability to be weakly associated with objective indices of real world functioning or cognitive performance (Harvey et al., 2014). In fact, across all of these studies and many others, in schizophrenia, bipolar disorder, and major depression, self-reported cognitive impairments and everyday functioning have proven to be essentially unrelated to cognitive impairments.

Limitations of the present study include the use of an exclusively female sample and moderate sample size. However, despite the moderate sample size, all change scores other than the UPSA were statistically significant and all Pearson correlations reflecting temporal stability were statistically significant as well. For the UPSA change score to be significant over time (ES = 0.1 *SD*), a sample of 787 subjects would be required for significance. Additionally, measures of real world functioning, milestones, and social functioning were not obtained from informant sources. Future studies should include male subjects and use objective, clinician rated measures of real world and social function to determine the ideal treatment targets for reducing the impact and disability resulting from PTSD. Finally, the patients in this study showed a variable degree of placebo response across all of their clinician rated and self-reported clinical symptom variables, although overall, a 20-point decrease in the CAPS is considered clinically meaningful. Although the magnitude of change in cognitive performance was much smaller and is in the realm of previously reported practice effects, the results could have been different in a sample who showed less of a placebo effect (Hodgins et al., 2018). It should be noted, however, that the lack of correlation between cognition and functional capacity and the clinical measures was present prior to the initiation of treatment and is simply replicated after treatment.

Thus, clinically, based on the present data, we can surmise that when conducting serial cognitive assessments with PTSD patients, some practice effects are equally likely to be observed. Both FC and cognitive performance were slightly lower than population mean values but not in the range that would suggest impairment or similarity in performance to patients with severe mental illness.

Given the stability and informative nature of functional capacity measures they may be valuable tools for clinicians making "return to work" decisions. However, it is clear that many of the participants in the present study believed that they had significant symptoms. Despite the relatively reduced stability of symptoms in the current sample these symptoms still warrant consideration for return to work decisions. Thus, an algorithm that considers both subjective symptoms (and hence motivation) and actual ability is recommended for clinical use.

PTSD symptoms can be highly distracting, inhibiting, and devastating, yet much like positive symptom severity in schizophrenia, they appear in this sample to be unrelated to cognitive impairment (Addington, Addington, & Maticka-Tyndale, 1991; Davidson et al., 1995; Keefe et al., 2006). These results offer little support for the idea that cognitive performance is in some way a result of or reaction to the occurrence of PTSD symptoms. This lack of association is also seen in patients with bipolar disorder, whose performance is considerably more impaired on average than the PTSD sample reported here, but performance-based assessments of cognition are also minimally related to concurrent symptom severity within that population

(Bowie et al., 2006; Bowie et al., 2010; Depp et al., 2009; Gildengers et al., 2007; Harvey et al., 2015; Strassnig et al., 2018). Additionally, patients with schizophrenia who were tested during psychosis and again during remission (Harvey et al., 1990; Nuechterlein et al., 1986) displayed the same consistent impairments in cognitive functioning, similar to results reported in patients with major depression (Neu et al., 2005) and bipolar disorder (Bora, Yucel, & Pantelis, 2009). Similar to previous reports in patients with bipolar disorder (Harvey et al., 2015; Strassnig et al., 2018) and major depression (Baer et al., 2014), patients reported disability that was consistent with their current illness symptomatology, but unrelated to objective measures of performance. Thus, it is common for individuals experiencing distress, in the form of mood symptoms, to gauge their current level of functioning on the basis of their emotional symptoms. The convergence of data amongst bipolar disorder, schizophrenia, and PTSD in the realm of cognitive stability draws attention to the need for further research into treatments that target cognition and improve real world functioning, rather than simply symptom reduction.

Supplementary Material

Supplementary material is available at *Archives of Clinical Neuropsychology* online.

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Conflict of interest

Dr. Gould has received honorarium from Clintara Inc. Dr. Dunlop reports research funds from Assurex, Axsome, Bristol-Myers Squibb, GlaxoSmithKline, Janssen, National Institute of Mental Health (R01MH108348 and U19MH69056), Otsuka, Pfizer, and Takeda. Dr. Dunlop has served as a paid consultant to Pfizer and Medavante. Ms. Rosenthal declares that she has no conflict of interest. In the past five years, Dr. Iosifescu has consulted for Avanir, Axome, CNS Response, INSYS Therapeutics, Lundbeck, Otsuka, Servier, and Sunovion and he has received grant/research support through the Icahn School of Medicine at Mount Sinai from Alkermes, Astra Zeneca, Brainsway, Euthymics, Neosync, Roche, Shire. Dr. Mathew has received research funding from the NIH, Department of Veterans Affairs, Johnson Family Chair, and Janssen Research & Development.He has served as a consultant to Acadia, Alkermes, Cerecor, Otsuka, and Valeant, and serves on an Advisory Board for VistaGen Therapeutics. Dr. Neylan has received research support from the NIMH, Department of Defense, and Department of Veterans Affairs. In the past three years he has served as a consultant to Resilience Therapeutics and Insys Therapeutics. Dr. Rothbaum receives funding from Wounded Warrior Project, Department of Defense, the National Institute of Mental Health Grant, the Brain and Behavior Research Foundation, and McCormick Foundation. Dr. Rothbaum receives royalties from Oxford University Press, Guilford, APPI, and Emory University and has received one advisory board payment from Genentech. Dr. Nemeroff has received grant support from National Institute of Mental Health and has received honoraria for consulting from Xhale, Takeda, Mitsubishi Tanabe Pharma Development America, Taisho Pharmaceutical Inc., Lundbeck, Prismic Pharmaceuticals, Bracket (Clintara), Total Pain Solutions (TPS), Gerson Lehrman Group (GLG) Healthcare & Biomedical Council, Fortress Biotech, Sunovion Pharmaceuticals Inc., & Sumitomo Dainippon Pharma. Dr. Harvey has received grant support from National Institute of Mental Health and has received honoraria for consulting from Akili, Allergan, Boeheringer Ingelheim, Brackett, Lundbeck, Otsuka Digital Health, Roche, Sanofi, Sunovion, and Takeda.

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