Ethics Commentary

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Treatment of PTSD: Empirically Based and Ethical Clinical Decision Making

A physician has just completed an assessment of a female survivor of a rape that occurred 6 months earlier. She meets full criteria for chronic posttraumatic stress disorder (PTSD) and major depressive disorder of moderate severity. Although she does not meet criteria for alcohol dependence, she has a history of episodic binge drinking that has increased in frequency since the assault. Also since the assault, she has had intermittent bouts of suicidal ideation but denies any intent or specific plan and has no history of past suicide attempts or nonsuicidal self-injury. The patient indicates a clear preference for psychotherapy over medication as a starting point for treatment, but is willing to consider medication if psychotherapy is not a practical option or psychotherapy proves inadequate. The physician does not feel personally qualified to provide psychotherapy for PTSD and the patient asks the physician for a referral, with a plan for a follow-up visit in 3 months to reconsider the medication option. *What kind of referral should the physician provide and what ethical issues should be considered in making the referral?*

Although the preceding description is of a hypothetical patient, it illustrates a fairly typical case presentation. Our purpose is to use this case as a springboard to discuss ethical decision making with regard to treatment planning for PTSD. We build our discussion around the three ethical principles of autonomy, beneficence, and nonmalfeasance (1, 2) to illustrate the potential use of empirical evidence to guide clinical decision making.

Ethical principles

Autonomy

The principle of autonomy requires respect for the right of individuals to make informed decisions about matters that affect them. An important function of healthcare professionals in the protection of patient autonomy, then, is to provide patients with accurate information about their diagnosis, treatment options, and prognosis. Healthcare professionals involved in the diagnosis and treatment of PTSD should therefore be knowledgeable about the nature and prevalence of trauma; the nature and prevalence of posttraumatic stress reactions, including but not limited to PTSD, and common

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comorbidities; the natural course of posttraumatic stress reactions; and the efficacy of treatment options. An example of the kind of information that may be helpful to patients and their healthcare providers in making decisions about whether to pursue treatment in the immediate aftermath of a trauma or adopt a "watchful waiting" strategy is the phenomenon of natural recovery. Although symptoms of acute stress disorder are relatively common shortly after the event, the majority of individuals will experience substantial recovery from their symptoms within 1-3 months of the event without any formal intervention (3). At the same time, a significant minority of trauma survivors will go on to develop PTSD which, left untreated, can persist for years. A variety of factors related the nature of the traumatic event (e.g., sexual assault versus other kinds of assault), the survivor's personal history (e.g., history of prior mental illness), as well as current circumstances (e.g., presence or absence of social support) are known to influence the risk of developing chronic PTSD (4, 5). Information about such risk and resilience factors can help to inform patients and professionals in their decision making about whether or when to begin treatment.

A second way healthcare professionals can show respect for patient autonomy is take patient preferences into consideration when developing a treatment plan. This point may be of particular note in light of evidence indicating a strong preference in favor of therapy over medication in the treatment of PTSD (6, 7). In addition to respecting patient autonomy, there is accumulating evidence that matching treatments with patient preferences can enhance treatment compliance and outcome, consistent with the principle of beneficence, and decrease prematurely terminating treatment (i.e., dropout) (8), consistent with the principle of nonmaleficence.

BENEFICENCE

The principle of beneficence exhorts us to do good and to work for the benefit of our patients. One important way to accomplish this is to routinely provide treatments with the strongest evidence for efficacy, and an important tool for professionals is expert consensus guidelines. In addition to the role of the Food and Drug Administration in determining indicated usages for medications, with the SSRIs sertraline and paroxetine being the only two medications with such indications, several additional important institutions have undertaken to generate guidelines for the pharmacological and psychological treatment of PTSD including the American Psychiatric Association (9, 10), Division 12 of the American Psychological Association (the Society of Clinical Psychology) (11–13), International Society for Traumatic Stress Studies (ISTSS) (14), the United Kingdom's National Institute for Health and Care Excellence (NICE) (15), and the Institute of Medicine of the National Academies (IOM) (16), among others. Table 1 and Table 2 summarize the guidelines for pharmacotherapy and psychotherapy, respectively, of the institutions noted above.

Inspection of the tables indicates that there is both consensus and disagreement in recommendations across these different institutions. In brief summary, there is general consensus on the efficacy of the SSRIs, not limited to just those two medications with FDA indications, and serotonin-norepinephrine reuptake inhibitors (SNRIs). With respect to psychotherapy, there is unanimity of opinion about the demonstrated efficacy of exposure therapy. However, there is greater diversity of opinion as to the efficacy of various other interventions, such as cognitive therapy, stress inoculation training, EMDR, and present centered therapy. The differences in recommendations likely reflect differences in the methodologies adopted by the different institutions.

In addition to the ambiguity introduced by the inconsistency of recommendations across institutions, guidelines that identify multiple viable treatment options provide little help in selecting a specific treatment from among those alternatives. The evidence on the relative efficacy of the treatments listed in Tables 1 and 2 is limited in terms of the number of studies that have directly compared any two active treatments against one another (whether comparing two medications, two psychotherapies, or medication versus psychotherapy) and the results of such comparative studies generally show similar outcomes. Evidence for the relative efficacy of the combination of medication plus psychotherapy compared with medicine or psychotherapy alone is also quite limited, but the existing evidence tentatively suggests that combination treatment may be more efficacious than individual treatment for at least some individuals (17, 18).

Despite the strong support for exposure therapy, few therapists utilize this mode of treatment. One survey of therapists (19) identified three important barriers that limit patient's access to exposure therapy. First, very few therapists were trained in the use of exposure therapy. Second, many therapists expressed a preference for "individualized" treatment plans as opposed to manualized treatments. Third, many therapists expressed concern that repeatedly having patients intentionally and repeatedly recall the trauma memory in vivid detail as

Table 1. Representative Published Guidelines for Pharmacotherapy[a]

Organization	Recommendations
American Psychiatric Association	*2004 Guideline* (9) "SSRIs are recommended as first-line medication treatment for PTSD…Other antidepressants, including tricyclic antidepressants and…MAOIs… may also be beneficial in the treatment of PTSD." (p. 13) "Benzodiazepines may be useful in reducing anxiety and improving sleep…[a]lthough their efficacy in treating the core symptoms of PTSD has not been established..." (p. 13) "In addition to being indicated in patients with comorbid psychotic disorders, second-generation antipsychotic medications…may be helpful in individual patients with PTSD. Anticonvulsant medications…, Î±2-adrenergic agonists, and Î (2)-adrenergic blockers may also be helpful in treating specific symptom clusters in individual patients." (p. 13) *2009 Update* (10) "…[T]he SSRIs may no longer be recommended with the same level of confidence for veterans with combat-related PTSD as for patients with non-combat-related PTSD." (p. 3) "As described in the 2004 guideline, no significant differences among antidepressants, including the SSRIs, were found in the few head-to-head studies…Since that time, studies… have generally demonstrated the superiority of antidepressants to placebo but have done little to clarify the relative utility of these different antidepressants." (p. 4) "…[D]ata are encouraging for adjunctive treatment with a second-generation antipsychotic in patients who have partially responded to an SSRI or an SNRI, including for co-occurring psychotic symptoms." (p. 5) "Randomized controlled trials of anticonvulsant medications remain extremely limited in number and have shown mixed results…[Thus] limited evidence of efficacy precludes any recommendations for change in practice." (p. 5)
International Society of Traumatic Stress Studies	"The best evidence supports the use of SSRIs and SNRIs as first-line drugs for PTSD. There is also good evidence that augmentation with atypical antipsychotic agents is effective. Recent results with prazosin and mirtazapine are also promising. MAOIs are moderately effective and TCAs are mildly effective agents, although both may produce adverse side effects." (Foa et al. [14] p. 567)
National Institute for Health and Care Excellence	"Drug treatments for PTSD should not be used as a routine first-line treatment for adults (in general use or by specialist mental health professionals) in preference to a trauma-focused psychological therapy." (National Institute for Clinical Excellence [15], p. 5) "Drug treatments (paroxetine or mirtazapine for general use, and amitriptyline or phenelzine for initiation only by mental health specialists) should be considered for the treatment of PTSD in adults who express a preference not to engage in trauma-focused psychological treatment." (National Institute for Clinical Excellence [15], p. 5)
Institute of Medicine	"Based on its assessment of the medications for which randomized controlled trials were available…the committee found the evidence for all classes of drugs reviewed inadequate to determine efficacy for patients with PTSD. Important comments are appended to the conclusions for alpha-adrenergic blockers, novel antipsychotics, benzodiazepines, and SSRIs." (Institute of Medicine (16), p. 85)

[a] Key to abbreviations: SSRIs=selective serotonin reuptake inhibitors; SNRIs=serotonin–norepinephrine reuptake inhibitors; MAOIs=monoamine oxidase inhibitors; TCAs=tricyclic antidepressants.

happens in imaginal exposure therapy might cause patients to decompensate. In addition, we note that lack of specialized training and negative attitudes toward the use of treatment manuals are likely to limited patient's access to most of the other specific forms of psychotherapy in Table 2, with the possible exception of present centered therapy. Due to this combination of factors, sadly, the best established psychological treatments are the least available.

NONMALFEASANCE

Whereas beneficence is the exhortation to do good, nonmalfeasance is the exhortation to refrain from doing harm. All medications have the potential for negative side effects and, as briefly alluded to above, many therapists have expressed concern about the safety of exposure therapy in the treatment of PTSD. Although examples of higher rates of dropouts (20) and symptom worsening from pre- to posttreatment (21) in exposure therapy compared with other active treatments exist among certain populations, such reports are the exception rather than the rule (22, 23). Moreover, researchers have found training in affect regulation skills, such as in dialectical behavior therapy, prior to beginning exposure therapy can mitigate these concerns in vulnerable populations with PTSD, such as adult survivors of childhood

Table 2. Representative Published Guidelines for Psychotherapy[a]

Organization	Recommendations
American Psychological Association Division 12 (13)	Strong research support for prolonged exposure, cognitive processing therapy, EMDR, present-centered therapy, seeking safety (for PTSD with comorbid substance use disorder). Modest research support for stress inoculation training.
International Society of Traumatic Stress Studies	CBT that comprises exposure therapy (imaginal and in vivo exposure), CT, SIT or one of the many combination programs that incorporate some form exposure with CT (e.g. CPT) or SIT is recommended as a first line treatment for chronic PTSD." (Foa et al. [14], p. 556) "EMDR is widely applicable to civilian PTSD cases and also has some efficacy with combat-related PTSD." (Foa et al. [14], p. 574)
National Institute for Health and Care Excellence	"All people with PTSD should be offered a course of trauma-focused psychological treatment (trauma-focused cognitive behavioural therapy [CBT] or eye movement desensitisation and reprocessing [EMDR]). These treatments should normally be provided on an individual outpatient basis." (National Institute for Clinical Excellence [15], p. 4)
Institute of Medicine	"Based on its assessment of the psychotherapy approaches for which randomized controlled trials were available…the committee found the evidence for all but one psychotherapeutic approach inadequate to reach a conclusion regarding efficacy. The evidence was sufficient to conclude the efficacy of exposure therapies in treating patients with PTSD." (Institute of Medicine [16], p. 85) *Note:* CPT (27) was included as an exposure therapy. Resick and colleagues (28) have since published a dismantling study that indicates removing the exposure components from the protocol did not decrease the efficacy of the treatment, suggesting this treatment is perhaps better thought of as primarily a variant of cognitive therapy than a form of exposure therapy.

[a] Key to abbreviations: CBT=cognitive behavior therapy; CT=cognitive therapy; SIT=stress inoculation training; CPT=cognitive processing therapy; EMDR=eye movement desensitization and reprocessing.

abuse (24) and those with borderline personality disorder (25).

We may further differentiate between some forms of harm that are relatively direct results of an intervention, such as an adverse reaction to a medication or specific psychotherapy, from less direct forms of harm that come about through the unnecessary loss of resources (26). For example, time, money, and energy invested in ineffective treatments for a given condition are resources that cannot be invested in other valued goals, including obtaining effective treatments for that same condition. Thus, suboptimal treatments that are otherwise benign can also cause indirect harm through loss of resources.

Discussion

Based on the principles of autonomy, beneficence, and nonmaleficence, and considering empirical evidence on the efficacy and safety of various treatment options for PTSD, we now return to our hypothetical case study and consider several possible treatment plans, from our perspective, in roughly descending order of justifiability.

Option 1

The physician could refer the patient to a therapist trained in the treatment of PTSD with exposure therapy, EMDR, cognitive therapy, or stress inoculation training. This plan is consistent with the patient's preference, thereby respecting her autonomy, and is consistent with the principle of benevolence by offering treatments with the strongest evidence of efficacy. The major limitation of this plan has to do with the general limited availability of therapists with training in these specific treatments. A second limitation is that the referring professional may have reservations about the safety of exposure therapy for the patient (e.g., concerns about the patient dropping out from treatment or experiencing a worsening of symptoms). In cases where the patient may have inadequate affect regulation skills (e.g., cases of borderline personality disorder), skills training or formal dialectical behavior therapy prior to beginning trauma-focused therapy may help to mitigate these risks while permitting such patients to benefit from targeted treatments for their PTSD.

Option 2

The physician could recommend initiating treatment with paroxetine, sertraline, or another selective serotonin or a serotonin-norepinephrine reuptake inhibitor. In cases where the patient has a preference to *not* engage in trauma-focused therapy, this plan would be consistent with both the principles of beneficence and respect for autonomy. However, a conflict between the principles of beneficence and

autonomy potentially arises in cases where the patient has a preference for psychotherapy but a therapist properly trained in best practice treatments for PTSD is not available. Here, the principle of beneficence may be best served by the physician attempting to persuade the patient to accept pharmacotherapy, but doing so may be at the risk of not respecting the patient's autonomy. Moreover, failure to respect a patient's preference may result in noncompliance and thereby reduce the effectiveness of the treatment.

OPTION 3

The physician could refer the patient for present centered therapy or provide a general psychotherapy referral, which is likely to have many features of present centered therapy. Such a referral would be respectful of the patient's preference, and thereby would be consistent with the principle of autonomy. However, such treatment will likely be significantly less effective than beginning medication or beginning more specialized psychotherapy for PTSD, thereby limiting beneficence. This plan is least objectionable in cases where there is no access to a therapist qualified to provide specialized treatments for PTSD. A referral for present centered therapy or a general psychotherapy is objectionable when there is access to a therapist with training in specialized treatment for PTSD. In this latter case, not only are the benefits of therapy potentially limited, but the person may incur costs due to less than optimal treatment.

OPTION 4

A fourth option would be for the physician to both provide the requested referral and persuade the patient to begin a course of pharmacotherapy. In some respects this may be viewed as an ideal solution. Such a "best of both worlds" approach, however, also has the potential for the "worst of both worlds." Both approaches to treatment have their own attendant risks for discomfort, side effects, stigmatization, and financial costs. Moreover, the evidence for the superiority of combined treatments is quite limited and the results suggest the benefits may be limited to only a subset of patients. Thus, the patient and her physician in this case would need to consider whether the increased financial costs and risk of side effects from the medication are outweighed by the incremental benefit that might occur from combined treatment. In addition, there can be a fine line between attempts to "persuade" patients to begin a less preferred treatment and coercing them. In our view, the combined treatment approach might have greater merit in cases where the psychotherapy referral is for general counseling as compared with when a referral can be made to a therapist with training in more specialized treatments for PTSD.

CLOSING COMMENTS

Despite significant advances in the development of efficacious treatments for PTSD, there still remain significant empirical challenges to overcome and gaps in our knowledge to fill. Even with the best available treatments, a substantial proportion of patients do not show adequate resolution of symptoms and, in general, we lack empirical evidence on the best "next step" treatments when an initial treatment is inadequate. In addition, we have not yet identified a robust set of predictor variables to help clinicians identify which individuals will most benefit from what treatments. Perhaps the most promising approach at this point is matching patients to their preferred modality when this is possible. However, the research into this strategy is still in its infancy and the best supported psychological treatments are not yet widely available.

Finally, we note that the topic of this special issue, traumatic brain injury, further complicates the ethical issues in the selection and delivery of treatment for PTSD. Depending on its nature and extent, brain injury may compromise patients' ability to understand information provided by their health care professionals and effectively use it to make informed choices in their own best interests. This is not unique to PTSD, but would be applicable to the treatment of any medical or psychiatric condition among people with significant cognitive impairments. Perhaps more importantly, there is a significant gap in the research on the efficacy of treatments for PTSD among individuals with significant brain injuries. All treatments, whether psychological or pharmacological, ultimately achieve their effects through the nervous system. Therefore it is likely that significant brain injury will impair the effectiveness of treatments and it may be that alternative treatments need to be developed specifically for those with significant brain injuries.

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