



Psilocybin-assisted psychotherapy for dying cancer patients – aiding the final trip

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Journal of Psychopharmacology

1–3

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DOI: 10.1177/0269881116675783

jop.sagepub.com



Why would you want to take a potentially "bad trip" just before your last journey? Why would you take a drug that can promote anxiety to face existential dread? Why would you want to lose mental control just before you lose physical control? Why imagine death before experiencing it? All of these questions make the idea that at the end of life, psychotherapy laced with psilocybin would seem an odd choice at best. Yet when we started our research in the 1970s on support groups for women with metastatic breast cancer we were warned that we would make them worse, that they would see one another die and be terrified and demoralized. That is not what happened. If anything they were remoralized, coming to value what was important in life, helping one another to face death. As one group member put it,

Being in the group is like looking into the Grand Canyon when you are afraid of heights. You know if would be a disaster if you fell, but you feel better about yourself because you're able to look. That is how I feel about death in the group. I can't say I feel serene, but I can look at it (Spiegel, 1994: 229).

Our experience is that facing the ultimate loss of control in a supportive psychotherapeutic setting actually enhances one's sense of control – it unifies rather than terrifies. One way we humans conceptualize death (to the extent that we can) is as the ultimate isolation. As the old spiritual says, "you gotta walk that lonesome valley by yourself." So feeling isolated while contemplating death makes one feel already dead – the process reinforces the content – while discussing dying and death with sympathetic people provides reassurance. The intensity of being with others in facing death creates a kind of life-affirming intimacy. The more one understands nonbeing, to the extent that one can, the more precious is the vitality of existence. We had been sufficiently concerned by warnings that patients in a group seeing one another get sicker and die would be demoralized that we conducted minute-to-minute analyses of group responses when there was bad news about members (Spiegel and Glafkides, 1983). We found that the content of discussions became more serious and focused on existential issues, but the emotional tone of the group, while appropriate to the content, did not descend into resignation or demoralization.

There is a growing body of work showing that psychotherapy in the face of cancer-related disease progression and death is helpful. In a series of randomized controlled trials, we demonstrated that supportive-expressive group therapy (SEGT) resulted

in reduced anxiety and depression (Classen et al., 2001; Spiegel and Yalom, 1978; Spiegel et al., 1981). Two other major clinical trials involving the use of SEGT in large samples of women with metastatic breast cancer have shown positive psychological outcomes. Kissane et al. (2007) randomized 485 women with advanced breast cancer to SEGT with three additional classes of relaxation therapy or relaxation therapy alone. SEGT prevented incidence of new depressive disorders ($p=0.002$), reduced hopeless-helplessness ($p=0.004$), decreased trauma symptoms ($p=0.04$), and improved social functioning ($p=0.03$). Goodwin et al. (2001) reported a seven-site randomized trial of SEGT among 235 women with metastatic breast cancer. The group psychotherapy resulted in a significant reduction in total mood disturbance and the depression, tension/anxiety, anger, and confusion subscales of the Profile of Mood States (McNair et al., 1981). Dignity therapy was more recently developed to help with psychosocial and existential distress among terminally ill cancer patients. In a randomized trial involving 326 patients in palliative care, there was significant improvement in quality of life (Chochinov et al., 2011). A randomized clinical trial of an early palliative care intervention that involved discussion of death and dying among 151 patients with advanced non-small-cell lung cancer resulted in significantly reduced depression, pain, and 2.5 months longer survival (Temel et al., 2010). More recently Breitbart and colleagues reported improvements in quality of life, depression, and hopelessness for advanced cancer patients randomized to meaning-centered group psychotherapy (Breitbart et al., 2015). A thorough Cochrane Database meta-analysis confirmed that psychotherapy in the setting of advanced cancer significantly reduces depression (Akechi et al., 2008). So there is no doubt that good psychotherapy that addresses existential concerns can effectively help dying patients.

From a cognitive-behavioral perspective, we know that avoidance fuels phobic anxiety, while exposure to feared situations and memories facilitates the process of desensitization, whether of flying in an airplane or reliving traumatic stressors (Institute of

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Medicine, 2007; Leiner et al., 2012). Engagement with even a feared or traumatic situation allows one to associate it with a growing sense of mastery, while avoidance reinforces existing negative associations.

One apparently conventional study of the treatment of major depression examined a serotonin–norepinephrine reuptake inhibitor antidepressant (nefazodone), cognitive-behavioral psychotherapy, or their combination (Nemeroff et al., 2003). The investigators were hardly surprised that the combination worked better than either treatment alone. But they decided to divide the population based upon the presence or absence of a history of childhood abuse. For those who had been abused, psychotherapy was better than antidepressant medication, and the combination added little to improvement, while for those without a trauma history, medication worked better. It is striking that the primary treatments for post-traumatic stress disorder are psychotherapeutic rather than pharmacological (Institute of Medicine, 2007). Existential threat, whether by history or in prospect, seems better ameliorated through psychotherapy, especially those treatments directed at addressing dying and death directly.

So what about the combination of an unconventional medication, the serotonin agonist psilocybin, with psychotherapy for terminally ill cancer patients? Two studies in this issue provide compelling evidence that the combination is effective. Both studies are well thought-out, rigorously conducted clinical trials that show impressively positive results on mood using standard measures. It must be said that they were conducted in a highly selected population. In the Griffiths et al. study (2016) only 10% of those initially screened made it into the study, and the reasons for exclusion were far more often not meeting inclusion criteria ($n=432$) rather than declining to participate ($n=78$). They had to be informed about the type of drug to be evaluated, so to begin with these were people inclined to believe that a psychedelic drug might help them at this time in their life. The authors attempted to deal with this using the low/high dose design, and it does support the effect of the pharmacology, albeit in conjunction with supportive psychotherapy. Nonetheless, the ultimate generalizability of the findings will be addressed more convincingly in future research.

In the other study, Ross and colleagues (2016) used a similar crossover design, but with niacin rather than low-dose psilocybin as the control. They found similar reductions in anxiety and depression, associated with personally meaningful and mystical experiences. The factors of those experiences were mystical, positive mood, transcendence of time and space, and ineffability. The psychotherapy was composed of various existential and meaning-based psychotherapies. It is interesting to note that Beck Depression Inventory and Hamilton Anxiety and Depression Scale scores after session two favored those patients who had received psilocybin first rather than second (Ross et al., 2016; Figure 5), suggesting that there was a positive effect if the initial treatment met expectations of a pharmacologically transformative experience right away, and that there could even have been some disappointment if the niacin was given first.

What is it about the combination of this mind-altering substance and psychotherapy in the face of death that seems to have such positive and relatively lasting effect? These papers contribute to a new model of psychopharmacology, along with work on the use of MDMA for PTSD and ketamine for depression (Abdallah et al., 2016; Amoroso and Workman, 2016; Duman

et al., 2016; Feder et al., 2014; Mithoefer et al., 2016; Sessa, 2016). Instead of continuously occupying serotonin, norepinephrine, or dopamine receptors to reduce depression or anxiety, these drugs seem to “reboot” the brain, leaving it changed long after the drug is gone. The effect of psilocybin seems to last much longer than that of ketamine, though both alter mental state acutely.

A careful phenomenological analysis (Belser et al., in press) of the experiences of 13 subjects from the Ross et al. study (2016) describes profound and generally very positive affective experiences:

Exalted feelings of joy, bliss, and love; embodiment; ineffability; alterations to identity; a movement from feelings of separateness to interconnectedness; experiences of transient psychological distress; the appearance of loved ones as guiding spirits; and sharing the experience with loved ones post-treatment (Belser et al., in press, p.2).

Intense perceptual experiences were generally experienced as enlightening rather than frightening. Subjects reported coming to a new understanding of important people in their lives, being able to accept and forgive disappointments and hurts, ranging from estrangement from parents to infidelity. Some reported a shift from doing to being, coming to value everyday experience more than accomplishments, often reported by people engaging in mindfulness training (Paulson, et al., 2013). Many described a letting go of a fixed identity, experiencing themselves in different ways: “my consciousness, or my soul, or whatever, was flying out of my body.” (p. 20) There was, in some descriptions, access to and deep experience of long-suppressed emotions, including sadness, grief, and traumatic pain. Oddly enough for a group of cancer patients, the experience was more life-affirming than death-defying. In this report there was comparatively little discussion of death and dying. Other than that and the discussion of synesthesias and other perceptual alterations, the themes are remarkably similar to those we observed in groups of women with metastatic breast cancer undergoing weekly supportive-expressive group therapy (Spiegel and Classen, 2000). The seven key themes of this intervention are: creating social bonds, expression emotion, detoxifying dying, reordering life priorities, improving interaction with family and friends, enhancing communication with physicians, and learning to control symptoms such as pain and anxiety. Like the psilocybin-supplemented psychotherapy, this group experience involved engaging with rather than avoiding anxiety-provoking experiences, and they both provided an enhanced sense of confidence in facing life challenges and deeply strengthened personal relationships. They both involved intensifying connection with life rather than despair over impending death.

Good psychotherapy involves learning to restructure one’s perspective on one’s problems in life. Cognitive-behavioral therapy deliberately trains people to challenge routine assumptions and think about problems in new ways. Interpersonal psychotherapy invites people to reflect on patterns of relating and assumptions about how other people think about you. Psychodynamic psychotherapy asks people to introspect about how their earlier life influences who they are, how they transfer experiences of key figures in their life to others and consequently distort their perceptions of them. Techniques like hypnosis and mindfulness take a more experiential approach, asking people to engage in highly focused attention coupled with dissociation or

nonjudgmental awareness. The idea here is that one can use such state alteration (Jiang et al., 2016) to see a problem from a new point of view (cognitive restructuring with hypnosis) (Spiegel, 2013; Spiegel and Spiegel, 1987) or cease struggling against adverse events and negative feelings, watching them flow by like a passing storm (mindfulness) (Paulson et al., 2013). There may be something about the change of mental state itself that conveys cognitive flexibility – there is more than one way to experience things, including oneself, and potentially one's mortality. Kierkegaard called fear the “sickness unto death,” (Kierkegaard, 1941: 9) a limiting state of mind that restricts people from living fully and authentically. A dull, drab or empty life, one barely worth living, this is a high price to pay for, in imagination, trying to reduce existential dread eliminating the pain of dying by decreasing reducing the contrast between its contrast from life and death. Altered mental states, whether via psychedelic drugs or hypnosis and mindfulness, convey an enriched experience of being by their very contrast with everydayness. One answer to death anxiety is enriching life, savoring it. The effect of such an experience seems to be powerful and lasting, and cannot be fully explained by simple neuropharmacology. Intensification of subjective experience is invigorating. Even depressed patients have told me, “I wish I could just have a good cry.” They feel numb as well as sad. So, increasing the power of experience may help people acquire a new perspective on themselves and their lives, even as they near the end of them, helping people go out with a bang, not a whimper.

Declaration of conflicting interests

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The authors received no financial support for the research, authorship, and/or publication of this article.

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