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Hypnosis for Treatment of HIV Neuropathic Pain: A Preliminary Report

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Abstract

Objective. Painful HIV distal sensory polyneuropathy (HIV-DSP) is the most common nervous system disorder in HIV patients. The symptoms adversely affect patients' quality of life and often diminish their capacity for independent self-care. No interventions have been shown to be consistently effective in treating the disorder. The purpose of the present study was to determine whether hypnosis could be a useful intervention in the management of painful HIV-DSP.

Method. Participants were 36 volunteers with HIV-DSP who received three weekly training sessions in self-hypnosis. Participants were followed for pain and its sequelae for 7 weeks prior to the intervention, and for 7 weeks postintervention. Participants remained on the same standard-of-care pain regimen for the entire 17 weeks of the protocol. The primary outcome measure was the Short Form McGill Pain Questionnaire cale (SFMPQ) total pain score. Other outcome measures assessed changes in affective state and quality of life.

Results. Mean SFMPQ total pain scores were reduced from 17.8 to 13.2 ($F[1, 35] = 16.06$, $P < 0.001$). The reductions were stable throughout the 7-week postintervention period. At exit, 26 out of 36 (72%) had improved pain scores. Of the 26 who improved, mean pain reduction was 44%. Improvement was found irrespective of whether or not participants were taking pain medications. There was also evidence for positive changes in measures of affect and quality of life.

Conclusion. Brief hypnosis interventions have promise as a useful and well-tolerated tool for managing painful HIV-DSP meriting further investigation.

Key Words. Pain; Neuropathy; HIV; Hypnosis

Distal sensory polyneuropathy (DSP) is the most common nervous system complication of HIV disease. It affects at least 29% of HIV patients, with some estimates as high as 62% [1–3]. The disorder is caused by the virus itself through a not yet understood mechanism, as well as by the neurotoxicity of certain drugs used in the treatment of HIV patients [4–7]. The symptoms such as burning pain, tingling, and numbness adversely affect patients' quality of life and are often severe enough to impact their capacity for independent self-care [8,9]. The presence of this disorder can also complicate the medical management of HIV infection because as noted earlier, several widely used HIV medications are neurotoxic.

Pharmacological analgesia is still the standard tool for managing neuropathic pain [10]. Yet there is no clear evidence that the typical first-line agents for neuropathic pain are effective for the management of HIV neuropathy. Indeed, a recent meta-analysis of randomized placebo-controlled trials found no evidence that any routinely available pharmacological agents are any better than placebo [11]. In this context, developing additional methods for managing HIV neuropathy is an urgent need [4].

The search for additional clinical tools need not be confined to pharmacological agents, but should extend to other methods that have proven effective in pain management. Hypnosis is one of these methods. Hypnosis has five characteristics which make it particularly attractive as a possible treatment for painful DSP in HIV patients. First, an extensive literature supports its usefulness across a variety of pain syndromes [12,13]. Second, quite brief treatments (1–3 sessions) can have long-term effectiveness [14]. Third, self-hypnosis can be taught, even with brief interventions [15]. That is, patients can be taught to use hypnosis whenever necessary for pain control. Thus, patients could be given a tool to help control their pain independently of medication or the availability of a provider. Fourth, pharmacoeconomic studies have shown that hypnosis is a cost-effective intervention in medical populations [16,17]. Fifth, in common with other behavioral interventions, hypnosis has the major advantage over pharmacologic analgesia of having no risk of systemic adverse effects and drug–drug interactions.

While hypnosis is a proven pain management modality for acute pain, its effectiveness in treating nonmalignant chronic pain is not well documented. For example, Montgomery and colleagues [12] reported a meta-analysis of 18 controlled studies. Only four of these studies addressed nonmalignant chronic pain. Of these four studies, three investigated headache patients, and one, patients of mixed etiologies [18]. The literature addressing the treatment of neuropathic pain is particularly sparse. Several recent extensive reviews of the literature concerning the effectiveness of hypnosis in treating chronic pain [13,19,20] reported only one controlled study in which the patients had neuropathic pain [21]. The neuropathic disorder in this case was fibromyalgia. We have been unable to find any other controlled studies investigating the use of hypnosis to treat neuropathic pain.

In the current study, we furnish preliminary evidence that training in self-hypnosis is a plausible and potentially effective tool for the management of painful HIV-DSP, and by extension other chronic neuropathic pain syndromes arising from identifiable medical conditions, such as diabetes mellitus. We further show that these benefits are independent of whether or not patients are taking medications typically prescribed for managing chronic pain.

Method

Participants

Participants were outpatients with a diagnosis of painful HIV-DSP confirmed by neurological examination. All were receiving standard-of-care treatment for their neuropathy, which was defined as one conforming to the recommendations of Dworkin and colleagues [22]. Participants were excluded if they had a confounding medical condition (for example, diabetes mellitus) which would make the diagnosis of HIV-DSP unclear, or make it difficult to measure changes in pain as a result of the hypnosis intervention. Participants were required to remain on a stable pain treatment regimen during the course of the protocol. All participants were volunteers compensated for time and expenses. The study was approved by the Mount Sinai Medical Center Institutional Review Board (IRB). Informed consent was obtained from all participants prior to their entering the study.

Outcome Measures

In selecting the outcome measures, we set out to measure the following core domains: pain, quality of life (including physical function and carrying out of activities of daily living), emotional well-being, participant ratings, and adverse events. It will be noticed that these domains are congruent with the recommendations of the consensus group, Initiative on Methods, Measurement, and Pain Assessment in Clinical Trials [23,24].

Short Form McGill Pain Questionnaire (SFMQ) [25]. The SFMQ is one of the most thoroughly investigated and widely used pain evaluation instruments [26]. It has been used in a number of clinical trials for interventions for neuropathic pain (for example, [27,28,29]). The SFMQ has three independent parts: the total pain scale, the visual analog scale (VAS), and the present pain intensity (PPI) scale. The total pain scale consists of 15 verbal descriptors which participants rate each item on a 0–3 scale. The scale yields a summary score (total pain score), reflecting both the sensory and affective components of an individual's pain experience and was predefined as the primary outcome measure assessing pain relief. The total pain scale also yields two independent subscores, one reflecting the sensory, and the other, the affective components of an individual's pain experience. These subscores allowed us to address a further question: whether any observed reduction in the participants' pain score reflected change in the sensory experience, change in the affective experience, or both. The VAS consists of a 10-cm horizontal line anchored at the ends by the descriptors "No Pain" and "Worst Possible Pain." Participant places a vertical mark at the appropriate place on the horizontal line. The PPI consists of a ranked set of five verbal descriptors ranging from "No Pain" to "Excruciating Pain." The VAS and PPI were predefined as secondary outcome measures. The use of these two additional scales allowed us to address the question of whether any observed differences depended on the utilization of a particular type of pain measure.

Center for Epidemiological Studies Depression (CES-D) Scale [30]. The CES-D was specifically designed to measure depression-related symptoms in the general population and consists of 20 verbal descriptors rated on a 0–3 scale.

State Trait Anxiety Inventory [31]. This instrument consists of two separate forms: one measures current level of anxiety (i.e., anxiety as a state), the other, anxiety as an enduring pattern of personality (i.e., anxiety as a trait). Each form consists of 20 verbal descriptors rated on a 1–4 scale.

Medical Outcomes Study Quality of Life Measure for HIV-Infected Patients (MOS-QOL) [32]. This instrument is an adaptation of the SF-36 Health Survey [33], specifically designed to measure quality of life in HIV patients. It yields 11 scores, each one representing an independent quality of life factor. Each score is standardized and can range from 0 to 100. A composite score can be calculated based on the mean of the11 standardized subscores.

In addition to these measures, we kept records of adverse events, participant practice of self-hypnosis during the training period, and the degree to which participants rated at exit the helpfulness of the hypnosis intervention.

Hypnosis Intervention

The intervention was modeled on that used by Montgomery and colleagues [15]. Each session was approximately 70 minutes. All sessions were "one on one." In outline the sessions were as follows.

Session 1: The session began by introducing the participant to the concept and mechanics of hypnosis, and addressing any concerns they might have. Participant was then administered a sample hypnosis induction. After the induction, the hypnotist introduced the concept of self-hypnosis and guided the participant through a self-hypnosis procedure. Participant was given an audio compact disc (CD) (with CD player) to be used with self-hypnosis practice. The CD contained a recorded hypnosis induction specifically developed for this study by two of the co-authors (MCG and DD).

Session 2: This session had two main aims. First, to assure that the participant had mastered the techniques of self-hypnosis. Second, to identify the specific target goals the self-hypnosis would address, such as greater mobility. Participant performed a self-hypnosis induction. Any difficulties participant experienced were addressed. Participant's task for the coming week was to use self-hypnosis to achieve the identified target goals.

Session 3: The chief aim was to assure that participant could effectively use self-hypnosis independently of the hypnotist. The participant's target goals were reviewed and finalized. Participant performed a self-hypnosis induction addressing a target goal. Any difficulties the participant experienced were addressed.

Procedure

HIV patients with neuropathy learned of the study from leaflets, posters, and announcements in publications aimed at the HIV patient community, or through their health care providers. Those interested in participating contacted the study coordinator who arranged for an appointment to obtain informed consent and confirm their eligibility for the study.

The protocol consisted of nine visits over a 17-week period. The first three visits occurred at 3-week intervals prior to the hypnosis intervention. During each of these first three visits, the participant was administered the outcome measures described earlier. These visits were followed by the three weekly hypnosis sessions. Starting the week following the last hypnosis session, there were three visits, again at 3-week intervals during which the participants were again administered the outcome measures. Thus, each participant received a total of six identical evaluations, three preceding the treatment and three following the treatment.

Statistical Analyses

Inferential statistical analyses had two basic aims: 1) to assess whether the hypnosis intervention had an effect on the outcome variables; and 2) if there was an effect, to determine its time course during the 7-week period following the intervention; in other words how long the effect lasted. To these ends, we used analysis of variance (ANOVA) to analyze the outcome measures as a 2×3 two-factor within-subjects design [34]. The first factor was hypnosis treatment with two levels: *before treatment* and *after treatment*; the second factor was evaluation sequences of prehypnosis and posthypnosis outcome measures with three levels: *first evaluation*, *second evaluation*, and *third evaluation*. In this arrangement, the effect of the hypnosis would manifest itself as a main effect of hypnosis treatment, while any change in the time course of the effect would be detectable as a treatment $\times$ evaluation sequence interaction.

To determine whether the use of pain medications made any difference in the effects of hypnosis, we used a variation on this strategy. Specifically, we used ANOVA to analyze the McGill total pain scores as a $2 \times 3 \times 2$ split-plot design [35]. This design is similar to the two-factor within-subjects design used for the pain and quality of life measures, except that there is an added between-subjects factor of medications vs no medications. The presence of a hypnosis treatment $\times$ medication interaction would indicate that the use of pain medications affected the benefits of hypnosis. The possible effect of entry levels of depression were assessed using the same design. That is, the CES-D scores were also analyzed using ANOVA as a $2 \times 3 \times 2$ split-plot with the two-level between-subjects factor of high vs low level of depression at entry. The state anxiety scores were analyzed using analysis of covariance (ANCOVA) in the same fashion as the primary and secondary pain scores, with each participant's trait anxiety score added as a covariate to control for chronic levels of anxiety.

The primary analysis was a *per protocol analysis*: that is, the analysis included only participants who had completed all three postintervention evaluation visits. A secondary *intent to treat* analysis [36] was also performed, with missing data filled by last observation carried forward. Intent to treat was predefined as participating in at least one hypnosis session.

Table 1 Ethnic composition

Ethnicity	Number	Proportion (%)
African American	21	51
Hispanic	10	24
Non-Hispanic White	7	17
Non-Hispanic Multiracial	2	5
Unknown	1	2
Total	41	100

Results

A total of 63 prospective participants signed informed consent. Of these, 14 did not meet entry criteria. Prior to the hypnosis intervention, four were lost to follow-up, and four were hospitalized due to medical comorbidities unrelated to HIV-DSP. The remaining 41 patients completed the three-session hypnosis intervention. However, during the three postintervention evaluations, four participants missed one of the three post hypnosis evaluations, while one participant missed all three of the postintervention evaluations. Thus, 36 participants were available for the primary per protocol analysis, and 41 were available for the secondary intention to treat analysis.

Participant Characteristics

Mean age of participants participating in the study was 48. There were 30 males and 11 females. Median CD4 count was 409 and median viral load was 116. The median number of years since HIV diagnosis was 14; the median number of years since the diagnosis of HIV-DSP was 6. All but two of the 41 participants in the hypnosis sessions were on combination antiretroviral therapy.

The ethnic composition of the participants is shown in Table 1. It reflects the ethnic composition of the East Harlem community served by the Mount Sinai Hospital. The number of participants using each type of pain treatment is presented in Table 2. Some pain treatments were used from baseline through completion by 27 (66%) of the participants. As can be seen in Table 2, opiates/opioids and anticonvulsants, either alone or in combination with other treatments, account for the bulk of treatments used by our participants. As noted earlier, one requirement for retention in the protocol was that participants remained on a stable pain treatment regimen for all 17 weeks; no participant had to be dropped from the protocol for failure to maintain their regimens.

Pain Outcome Measures

Mean McGill total pain scores were calculated for each evaluation visit. These data are presented in Table 3. The data were analyzed using ANOVA as a 2 × 3 within-subjects two-factor design as described earlier. The analysis showed a main effect of hypnosis treatment ($F[1,35] = 16.06$, $P < 0.001$). The hypnosis treatment × evaluation sequence interaction was not statistically significant. These analyses show that there was a reduction in pain following hypnosis and that the reduction continued unchanged for at least 7 weeks. Further analyses showed that 26 out of 36 participants (72%) showed improvement on the primary outcome measure. Of those who improved, the mean improvement was 44%.

The VAS and PPI scores are shown in Tables 4 and 5. When analyzed in the same manner as the total pain score, they show the identical pattern: a main effect of hypnosis treatment: $F(1,35) = 11.1$, $P = 0.002$, for the VAS and $F(1,35) = 17.1$, $P < 0.001$ for the PPI with hypnosis treatment × sequence interaction which was not significant. These analyses show that the changes in pain ratings do not depend on using a particular pain rating method.

Additional analyses of the primary scores addressed three further questions: 1) Was there a difference in the effect of hypnosis on participants who receive medication for their pain vs those who did not? 2) Did the hypnosis intervention affect the sensory aspects of participants' pain experience, the affective aspects, or both? 3) Was there any relation between the amount of self-hypnosis practice between sessions and its efficacy in pain reduction?

To address the first question, we divided the participants into two groups: those receiving analgesic medication (i.e., opioids, anticonvulsants, or antidepressants) vs those who did not. These data are shown in Table 6. The ANOVA showed a main effect of hypnosis treatment $F(1,34) = 17.7$, $P > 0.001$, while the hypnosis treatment × medication interaction was not significant. These analyses show that there were similar benefits to hypnosis for participants on and off pain medications.

To address the second question, we separately analyzed the sensory and affective subscores of the McGill Total Pain Scale. These data are presented in Table 7. The sensory subscores showed a main effect of hypnosis treatment $F(1,35)$ 20.5, $P > 0.001$. On the other hand, the affective scores were only marginally significant

Table 2 Usage of pain medications by participants

Type of Medication	Used Alone	Used in Combination	Total Usage
Opiates/opioids	9	7	16
Anticonvulsants	4	4	8
NSAIDs	2	3	5
Antidepressants	2	0	2
CAM	0	1	1
Topical analgesic	0	1	1
Medical marijuana	0	1	1

CAM = complementary and alternative medicine; NSAIDs = nonsteroidal anti-inflammatory drugs.

Table 3 McGill total pain score as a function of treatment and evaluation: means and (standard errors) (N = 36)

	Evaluation 1	Evaluation 2	Evaluation 3	Mean Score
Pretreatment	17.5 (1.44)	18.0 (1.46)	17.8 (1.43)	17.8 (1.45)
Posttreatment	13.4 (1.45)	13.3 (1.53)	12.8 (1.89)	13.2 (1.47)

$F(1,35)$, $P = 0.059$. As with the previously reported pain scores, the treatment × sequence interaction was not statistically significant. Comparing their effect sizes (as measured by *partial eta squared*): $\eta_p^2 = 0.369$ for the sensory score, and $\eta_p^2 = 0.098$ for the affective score. Using Cohen's classification [37], the former corresponds to a "large effect," while the latter corresponds to a "medium effect." These results point to the conclusion that the reduction in total pain scores was most associated with changes in the sensory experience of the participants, while the association with changes in the affective experience of the participants was comparatively smaller.

To address the third question, we reviewed the participants' self-reports of how many times they practiced self-hypnosis between training sessions. Median amount of practice outside of sessions was 6.5 times per week. Exploratory analyses using parametric and nonparametric statistics failed to reveal any systematic relationship between the amount of practice between the training sessions and reduction in total pain scores.

Other Outcome Measures

For analysis of the depression outcome measure (CES-D), we divided the participants into two groups, those who at

Table 4 McGill VAS pain scores as a function of treatment and evaluation (in centimeters): means and (standard errors) (N = 35)

	Evaluation 1	Evaluation 2	Evaluation 3	Mean Score
Pretreatment	5.90 (0.300)	6.04 (0.309)	5.89 (0.345)	5.94 (0.318)
Posttreatment	4.67 (0.390)	5.11 (0.408)	4.93 (0.406)	4.90 (0.401)

VAS = visual analog scale.

Table 5 McGill PPI score as a function of treatment and evaluation: means and (standard errors) (N = 36)

	Evaluation 1	Evaluation 2	Evaluation 3	Mean Score
Pretreatment	3.44 (0.130)	3.44 (0.152)	3.36 (0.150)	3.40 (0.144)
Posttreatment	2.92 (0.151)	2.89 (0.182)	2.86 (0.165)	2.90 (0.166)

PPI = present pain intensity.

Table 6 McGill total pain scores as a function of treatment and evaluation: medication (N = 23) vs no medication (N = 13): means and (standard errors)

	Evaluation 1	Evaluation 2	Evaluation 3	Mean Score
Pretreatment				
Medication	18.5 (1.71)	16.9 (1.78)	18.9 (1.79)	18.1 (1.76)
No medication	15.8 (2.64)	20.0 (2.55)	16.2 (2.40)	17.3 (2.53)
Posttreatment				
Medication	14.8 (1.83)	14.2 (1.86)	14.4 (1.81)	14.5 (1.84)
No medication	10.8 (2.34)	11.7 (2.73)	10.0 (1.99)	10.8 (2.37)

Table 7 McGill sensory and affective subscales as a function of treatment and evaluation: means and (standard errors) (N = 36)

	Evaluation 1	Evaluation 2	Evaluation 3	Mean Score
Sensory				
Pretreatment	13.7 (1.12)	14.1 (1.08)	14.1 (1.03)	14.0 (1.08)
Posttreatment	10.1 (1.08)	10.1 (1.15)	10.0 (1.04)	10.1 (1.09)
Affective				
Pretreatment	3.78 (0.470)	3.92 (0.529)	3.78 (0.515)	3.82 (0.505)
Posttreatment	3.27 (0.494)	3.17 (0.465)	2.78 (0.454)	3.07 (0.471)

entry exhibited high levels of depression-related symptoms (defined as CES-D > 17) and those with subclinical or low levels of depression-related symptoms (defined as CES-D $\leq$ 17). These data are presented in Table 8. The data were analyzed as a $2 \times 3 \times 2$ split-plot design, with hypnosis treatment and sequence the within-subjects factors, and entry level of depression the between-subjects factor. The results showed a main effect of treatment ($F[1,34] = 5.40$, $P = 0.0260$) and a treatment × entry depression level interaction ($F[1,34] = 7.03$, $P = 0.0120$). No other main effects or interactions were significant. These analyses support the conclusions, which would be gathered intuitively by examining Table 8: namely that the high-depression group experienced a decline in depression-related symptoms, but that the low-depression group remained unchanged.

Mean state anxiety scores are shown in Table 9. These data were analyzed using ANCOVA as a 2×3 two-factor within-subjects design with trait anxiety entered as a covariate. Neither the main effects nor any of the interactions were statistically significant. These analyses support the conclusion that there were no measurable changes in anxiety level associated with the treatment.

Mean MOS-QOL scores as a function of treatment level are shown in Table 10. The general QOL scores were analyzed in the same manner as the pain scores, i.e., as a 2×3 within-subjects two-factor design. The results showed improvement in the general score ($F[1,35] = 5.92$, $P = 0.020$). To identify the specific areas in which improvement occurred, each subscore was analyzed in the same fashion as the general QOL scores. The results showed positive changes in four areas: physical function ($F[1,35] = 9.82$, $P = 0.003$), role function ($F[1,35] = 4.76$, $P = 0.036$), pain-related well-being ($F[1,35] = 12.8$, $P = 0.001$), and perceived change in health status ($F[1,35] = 18.0$, $P < 0.001$). No interactions were statistically significant.

During the course of the study, there were six serious adverse events reported to the IRB, none of which were

Table 8 CES-D scores as a function of treatment and evaluation: high depression (N = 10) vs low depression (N = 26): means and (standard errors)

	Evaluation 1	Evaluation 2	Evaluation 3	Mean Score
Pretreatment				
High	26.7 (1.83)	20.6 (1.97)	23.7 (3.81)	23.7 (1.59)
Low	9.46 (0.977)	10.9 (1.64)	11.9 (1.85)	10.8 (2.54)
Posttreatment				
High	17.9 (3.77)	18.1 (3.70)	18.0 (3.83)	18.0 (3.16)
Low	11.3 (1.31)	10.0 (1.60)	12.0 (1.99)	11.1 (1.65)

Table 9 State anxiety scores as a function of treatment and evaluation: means and (standard errors) (N = 36)

	Evaluation 1	Evaluation 2	Evaluation 3	Mean Score
Pretreatment	33.8 (1.92)	32.4 (1.90)	35.4 (2.19)	33.8 (2.03)
Posttreatment	33.4 (1.73)	34.6 (2.22)	33.1 (2.24)	33.7 (2.01)

Table 10 Quality of life measures as a function of treatment and evaluation: means and (standard errors) (N = 36)

	Evaluation 1	Evaluation 2	Evaluation 3	Mean Score
Composite score*				
Pretreatment	61.7 (2.04)	62.6 (2.32)	58.6 (2.67)	61.0 (2.06)
Posttreatment	64.1 (2.98)	66.0 (2.87)	66.7 (2.95)	65.6 (2.76)
Subscores:				
Overall health perception				
Pretreatment	48.3 (3.24)	43.5 (3.56)	40.8 (3.92)	44.2 (3.60)
Posttreatment	45.8 (4.38)	47.1 (3.99)	44.6 (3.97)	45.8 (4.11)
Physical function*				
Pretreatment	65.0 (3.56)	66.6 (3.53)	63.6 (4.68)	65.1 (3.92)
Posttreatment	70.9 (3.53)	69.9 (3.89)	72.8 (3.81)	71.2 (3.74)
Role function*				
Pretreatment	44.4 (6.84)	51.4 (7.58)	44.4 (7.12)	46.8 (7.18)
Posttreatment	48.6 (7.58)	61.1 (6.43)	65.3 (7.13)	58.3 (7.22)
Social function				
Pretreatment	71.7 (3.77)	71.7 (3.68)	68.9 (4.40)	70.8 (3.95)
Posttreatment	65.6 (6.00)	73.9 (3.64)	71.7 (5.00)	70.4 (4.88)
Cognitive function				
Pretreatment	76.4 (3.56)	77.9 (3.35)	76.4 (3.52)	76.9 (3.48)
Posttreatment	75.4 (4.26)	80.7 (3.33)	80.1 (3.26)	78.8 (3.62)
Well-being: pain related*				
Pretreatment	48.6 (2.35)	49.3 (2.30)	46.4 (3.02)	48.1 (2.78)
Posttreatment	56.6 (3.47)	56.3 (3.19)	59.0 (3.25)	57.3 (3.31)
Well-being: mental health				
Pretreatment	75.4 (2.98)	75.7 (2.33)	72.9 (3.43)	74.7 (3.25)
Posttreatment	75.3 (3.18)	74.0 (3.60)	76.8 (3.45)	75.4 (3.41)
Well-being: energy/fatigue				
Pretreatment	56.9 (3.03)	58.6 (3.25)	55.7 (3.04)	57.1 (3.11)
Posttreatment	59.7 (3.38)	60.7 (3.39)	58.6 (3.80)	59.7 (3.11)
Well-being: health distress				
Pretreatment	73.2 (3.88)	73.1 (3.33)	71.5 (3.83)	72.6 (3.68)
Posttreatment	72.4 (4.67)	75.7 (3.75)	78.1 (3.97)	75.4 (4.13)
Well-being: quality of life				
Pretreatment	60.4 (2.88)	63.9 (2.89)	54.5 (3.57)	59.7 (3.15)
Posttreatment	64.6 (3.05)	60.4 (3.36)	62.5 (2.73)	62.6 (3.05)
Change in health*				
Pretreatment	57.6 (3.36)	56.9 (4.06)	49.3 (3.92)	54.6 (3.85)
Posttreatment	70.8 (4.40)	66.7 (4.11)	64.6 (4.50)	67.4 (4.33)

* Main effect of treatment significant with $\alpha = 0.05$.

deemed related to either the individual's participation in the study or to HIV-DSP. At exit from the protocol, participants rated how helpful they perceived the hypnosis intervention: 15 (43%) rated it as "Extremely Helpful," 6 (17%) rated it as "Very Helpful," while 14 (40%) rated it as "Somewhat Helpful." No participant rated it as "Not Helpful."

As noted earlier, the primary analyses of the data were per protocol, that is, utilizing the data from the 36 participants who completed the protocol. We repeated all of the earlier analyses using an intention to treat analysis, that is, for all 41 participants who had participated in at least one hypnosis session, with missing data supplied by carrying last observation forward. In all instances, the pattern of these analyses was identical to those reported earlier.

Discussion and Conclusions

The results of this study furnish preliminary evidence that hypnosis is effective for the management of painful HIV-DSP. There was a reduction not only in participants' pain levels, but also an improvement in their quality of life, and in participants with elevated levels of depression-related symptoms, a reduction in these symptoms. Further, these benefits were durable for at least 7 weeks following the intervention and occurred irrespective of whether or not participants were taking pain medications. There were no

serious adverse events related either to the intervention or HIV-DSP. At exit, participants uniformly found the intervention helpful.

These findings are of particular interest for two reasons. First, as we noted earlier there is little evidence for the effectiveness of pharmacological interventions for painful HIV-DSP. Second, as we also noted, the bulk of the literature addressing the effectiveness of hypnosis in pain management has concentrated in the area of acute rather than chronic pain.

We regard the results as justifying a more elaborate study of the possible benefits of hypnosis for management of painful HIV-DSP. Such a study could fruitfully address two limitations of the present study. First, while the within-subjects comparison is appropriate for a preliminary study such as reported here, a persuasive case for the usefulness of hypnosis in this population will ultimately require a between-subjects comparison where one group of participants receives either standard of care only or some comparison condition. Second, while the present results indicate that the benefits of hypnosis last for at least 7 weeks, longer term follow-ups are needed to determine the full extent of durability of the intervention, as well as whether follow-up sessions might be beneficial at periodic intervals. Such data will be necessary for pharmacoeconomic analyses to assess the cost-effectiveness of hypnosis interventions for HIV-DSP. It would also be appropriate to more extensively characterize the population with respect to HIV issues such as nadir CD4 count and past history of neurotoxic medications, and include as secondary outcome measures those which are clinician-reported outcomes [38,39].

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References

1 Ellis RJ, Rosario D, Clifford DB, et al. Continued high prevalence and adverse clinical impact of high immunodeficiency virus-associated sensory neuropathy in the era of combination antiretroviral therapy. Arch Neurol 2010;67:552–8.

2 Robinson-Papp J, Simpson D. Neuromuscular complications of Human Immunodeficiency Virus infection. Phys Med Rehabil Clin N Am 2008;19:81–96.

3 Robinson-Papp J, Gonzalez-Duarte A, Simpson DM, Rivera-Mindt M, Morgello S; Manhattan HIV Brain Bank. The roles of ethnicity and antiretrovirals in HIV-associated polyneuropathy: A pilot study. J Acquir Immune Defic Syndr 2009;51:569–73.

4 Phillips TJC, Cherry CL, Moss PJ, Rice ASC. Painful HIV-associated neuropathy. Pain Clin Updat 2010;18: 1–8.

5 Simpson DM, Tagliati M. Nucleoside analogue-associated peripheral neuropathy in human immunodeficiency virus infection. J AIDS 1995;9:153–61.

6 Verma S, Micsa E, Estanislao L, Simpson D. HIV Neuropathy. Curr Neurol Neurosci Rep 2004;4:62–7.

7 Wulff E, Wang A, Simpson D. HIV-associated peripheral neuropathy: Epidemiology, pathophysiology and treatment. Drugs 2000;59:1251–60.

8 Breitbart W, McDonald M, Rosenfeld B, et al. Pain in ambulatory AIDS patients—I: Pain characteristics and medical correlates. Pain 1996;58:315–21.

9 Rosenfeld B, Breitbart W, McDonald M, et al. Pain in ambulatory AIDS patients—II: Impact of pain on psychological functioning and quality of life. Pain 1996;68:323–8.

10 Finnerup NB, Sindrup SH, Jensen TS. The evidence for pharmacological treatment of neuropathic pain. Pain 2010;150:573–81.

11 Phillips TJC, Cherry CL, Cox S, Marshall SJ, Rice ASC. Pharmacological treatment of painful HIV-associated sensory neuropathy: A systematic review and meta-analysis of randomised controlled trials. Plos ONE 2010;5(12):e14433.

12 Montgomery G, DuHamel K, Redd W. A meta-analysis of hypnotically induced analgesia: How effective is hypnosis? Int J Clin Exp Hypn 2000;48:138–53.

13 Patterson R, Jensen M. Hypnosis and clinical pain. Psychol Bull 2003;129:495–521.

14 Lewis D. Hypnoanalgesia for chronic pain: The response to multiple inductions at one session and to separate single inductions. J R Soc Med 1992;85: 620–4.

15 Montgomery G, Weltz C, Seltz M, Bovbjerg D. Brief pre-surgery hypnosis reduces distress and pain in excisional breast biopsy patients. Int J Clin Exp Hypn 2002;50:17–32.

16 Montgomery GH, Bovbjerg DH, Schnur JB, et al. A randomized clinical trial of a brief hypnosis intervention to control side effects in breast surgery patients. J Natl Cancer Inst 2007;99:1304–12.

17 Lang EV, Rosen MP. Cost analysis of adjunct hypnosis with sedation during outpatient interventional radiologic procedures. Radiology 2002;222:375–82.

18 Edelson J, Fitzpatrick JL. A comparison of cognitive-behavioral and hypnotic treatments of chronic pain. J Clin Psychol 1989;45:316–23.

19 Elkins G, Jensen MP, Patterson DR. Hypnotherapy for the management of chronic pain. Int J Clin Exp Hypn 2007;55:275–87.

20 Jensen M, Patterson DR. Hypnotic treatment of chronic pain. J Behav Med 2006;29:95–124.

21 Haanen HC, Hoenderdos HT, van Romunde LK, et al. Controlled trial of hypnotherapy in the treatment of refractory fibromyalgia. J Rheumatol 1991;18:72–5.

22 Dworkin R, Backonja M, Rowbothan M, et al. Advances in neuropathic pain: Diagnosis, mechanisms, and treatment recommendations. Arch Neurol 2003;60:1524–34.

23 Turk DC, Dworkin RH, Allen RR, et al. Core outcome domains for chronic pain clinical trials: IMMPACT recommendations. Pain 2003;106:337–45.

24 Turk DC, Dworkin RH, Revicki D, et al. Identifying important outcome domains for chronic pain clinical trials: An IMMPACT survey of people with pain. Pain 2008;137:276–85.

25 Melzack R. The short-form McGill Pain Questionnaire. Pain 1987;30:191–7.

26 Katz J, Melzack R. The McGill Pain Questionnaire: Development, psychometric properties, and usefulness of the Long Form, Short Form, and Short Form-2. In: Turk D, Melzack R, eds. Handbook of Pain Assessment, 3rd edition. New York: The Guilford Press; 2011:45–66.

27 Backonja M, Beydoun A, Edwards KR, et al. Gabapentin for the symptomatic treatment of painful neuropathy in patients with diabetes mellitus: A randomized controlled trial. J Am Med Assoc 1998; 280:1831–36.

28 Gilron I, Bailey JM, Tu D, et al. Morphine, gabapentin, or their combination for neuropathic pain. N Engl J Med 2005;352:1324–34.

29 Dworkin RH, Corbin AE, Young JP, et al. Pregabalin for the treatment of postherpetic neuralgia: A randomized, placebo-controlled trial. Neurology 2003;60: 1274–83.

30 Radloff LS. The CES-D scale: A self-report depression scale for research in the general population. Appl Psychol Meas 1977;1:385–401.

31 Spielberger C. State-Trait Anxiety Inventory. Redwood City, CA: Mind Garden; 1981.

32 Wu AW, Revicki DA, Jacobson D, Malitz FE. Evidence for reliability, validity and usefulness of the Medical Outcomes Study HIV Health Survey (MOS-HIV). Qual Life Res 1997;6:481–93.

33 Ware J, Sherburne C. The MOS 36-item short-form health survey (SF-36): I. Conceptual framework and item selection. Med Care 1992;30:473–83.

34 Keppel G. Design and Analysis: A Researcher's Handbook, 3rd edition. Englewood Cliffs, NJ: Prentice-Hall; 1991.

35 Kirk R. Experimental Design: Procedures for the Behavioral Sciences, 2nd edition. Pacific Grove, CA: Brooks/Cole Publishing Company; 1982.

36 Hill AB. Principles of Medical Statistics, 7th edition. London: The Lancet Limited; 1961.

37 Cohen J. Statistical Power Analysis for the Behavioral Sciences, 2nd edition. Hillsdale, NJ: Erlbaum; 1988.

38 Willke RJ, Burke LB, Erickson P. Measuring treatment impact: A review of patient-reported outcomes and other efficacy endpoints in approved product labels. Control Clin Trials 2004;25:535–52.

39 Turk DC, Dworkin RH, Burke LB, et al. Developing patient-reported outcome measures for pain clinical trials: IMMPACT recommendations. Pain 2006;125: 208–15.