

Comparison of Beneficial Effects of Kinesiotherapy for Seasonal and Non-Seasonal Depression

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Although kinesiotherapy is usually used for improvement of a person's endurance, mobility and strength, it can be also beneficial for different mood disorders including depression. We compared the clinical effects of several types of one-week mono and combined treatments in women with non-seasonal depression, seasonal depression and without depression. A week of kinesiotherapy was equally beneficial for non-seasonal and seasonal depression. A week of bright light therapy produced a similarly strong antidepressant response only in seasonal depressives. One-week therapies with exercise and/or bright light prevented relapse and produced further improvement after night sleep deprivation. However, if at least one of such treatment modalities ensured excellent response, there was no additional benefit from their combination. Since the specific feature of depression is that only in this illness a placebo effect can be very strong, these results highlighted once again the possibility that "visible" one-week interventions can work mostly as powerful placebos.

Keywords: *Kinesiotherapy, Bright Light, Sleep Deprivation, Antidepressant and Placebo Response, Depression.*

Introduction

Depression appears to be a much more common disease than other mental disorders. It is ranked fourth in the world in terms of the global burden of disease (Murray and Lopez 1996, Üstün et al. 2004). Therefore, it is of great practical importance to examine the possible clinical benefits offered by its treatment with antidepressants (Andrews 2001). However, the clinical trials have aroused concern among researchers and the lay public about efficacy of the conventional (pharmacological) antidepressant treatments. For instance, the general negative view that the public have about the benefits of medications (Jorm et al. 1997) was supported by clinical trials indicating that many pharmacological agents act non-specifically and are not distinctly superior to placebo treatments (Joffe et al. 1996, Moncrieff et al. 1998, Antonuccio et al. 1999, Khan et al. 2000, Kirsch et al. 2008, Moncrieff 2002, Walsh et al. 2002). The major problem with any antidepressant medications prescribed for depression is that there is no other illness in which the placebo effect is so large, either in absolute terms or as a proportion of the change in the treatment group. For instance, placebo groups

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comprise 60% of the progress recorded in the drug-treated groups, whereas it is only 23% in agoraphobia, 21% in obsessive-compulsive disorder and no progress at all in schizophrenia (Andrews 2001).

Physical activity has been shown to be beneficial in alleviating depression (Lawlor and Hopker 2001, Martinsen 2008). However, researchers are seriously concerned about the placebo action of kinesiotherapeutic interventions. Indeed, since depressed patients cannot be "blind" to such a therapy, they do not need to guess on which of the interventions is an active treatment. Consequently, a placebo response is expected to be enlarged due to "visibility" of the treatment with physical exercise. To resolve this problem researchers often focus on the differences between clinical effects of two "visible" treatments, one of which can be regarded as an active treatment and another as a placebo treatment.

In 2000, we published the preliminary results on comparison of the clinical effects of one-week mono-treatments with either bright light or physical exercise for non-seasonal and winter depression (Pinchasov et al. 2000). In the past 15 years, this study has been cited in more than a dozen systematic reviews and meta-analyses on exercise for depression (Cass 2001, Jorm et al. 2002, Mallikarjun and Oyebode 2005, Stathopoulou et al. 2006; Winkler et al. 2006, Westrin and Lam 2007, Peiser 2009, Ravindran et al. 2009, Rethorst et al. 2009, Krogh et al. 2011, Josefsson et al. 2014, Gühne et al. 2015, Mead et al. 2009). More recently, has posed the question of whether the reported results on photo- and kinesiotherapy can be included in the "alternative interventions" comparison or rather, if they can be judged as comparison of an active treatment (i.e., exercise) with a placebo treatment (i.e., bright light). Such necessity in distinguishing between active and placebo treatments was suggested by Ekkekakis (2015) due to a rising concern about efficacy of bright light therapy as a treatment for depression (National Collaborating Centre for Mental Health and the National Institute for Health and Clinical Excellence 2010: 450, Pichot and Jensen 1989, Light Therapy for Depression and Other Treatment of Seasonal Affective Disorder 2007; Hansen et al. 2008, Mårtensson et al. 2015). Two additional questions have been additionally asked in another publication: whether outcome assessors were blind to the treatment and whether an exercise treatment can last for only one week (Blumenthal and Ong 2009).

Since the time of publication of this paper (Pinchasov et al. 2000) we have additionally collected and partially reported (Putilov 2013, Putilov et al. 2000, Danilenko and Putilov 2005, Putilov and Danilenko 2005a, 2005b) data on several more complex open and blind one-week clinical examinations of these and some other natural antidepressants. Therefore, the major purpose of the present paper was to address the issue of consideration of kinesio- and phototherapy as either "active treatments" "alternative interventions" or "no treatment" control by analyzing a larger set of data on more and less complex one-week antidepressant trials.

Method

Clinical effects of one-week antidepressant trials were tested during the winter season at the Medical Academic Hospital near Novosibirsk (55 degrees North) in 138 female study participants. They either did not suffer from depression (n=33) or they were diagnosed as having either seasonal (winter) depression (n=41) or non-seasonal depression (n=64). This sample included 54 participants in clinical trials investigating the therapeutic and physiological effects of one-week mono-treatments that were earlier reported in Pinchasov et al. (2000). The mono-treatments were either a 2-hr 2500 lux cool-white incandescent light from 14:00 to 16:00 or a 1-hr physical exercise from 13:00 to 14:00. Each of the mono-treatment groups included 9 study participants (9x3x2). The three conditions of the mono-treatments were: a) a night of total sleep deprivation followed by 2-hr bright light from 14:00 to 16:00 (n=20; 8 seasonal and 12 non-seasonal depressives), b) a night of total sleep deprivation followed by a 1-hr physical exercise under bright light from 12:00 to 13:00 (n=16; 5 seasonal and 11 non-seasonal depressives) and c) a night of total sleep deprivation followed by a 1-hr physical exercise under ordinary room light from 13:00 to 14:00 (n=12 non-seasonal depressives). Moreover, three additional groups included 36 participants left without antidepressant therapy for a week during which they passed through examination of their general physical health (10 seasonal, 11 non-seasonal depressives and 15 controls).

Both controls and patients were required to be free from psychotropic drugs, did not suffer from serious general and were not involved in regular physical activities prior to the study. Controls were additionally required to be free of psychiatric illness, sleep complaints and seasonal variations in mood and well-being. A history of seasonal difficulties was elicited by self-administration of the Seasonal Pattern Assessment Questionnaire (Rosenthal et al. 1984a). Additionally, the criteria of Rosenthal et al. (1984b) and a 2 to 3-yr history of complete summer remission were required for patients with winter depression (Danilenko and Putilov 1996). Non-seasonal depressives did not meet the criteria for denied seasonal pattern of their depression, but met the criteria for a major or minor depressive disorder or dysthymia (Spitzer et al. 1978).

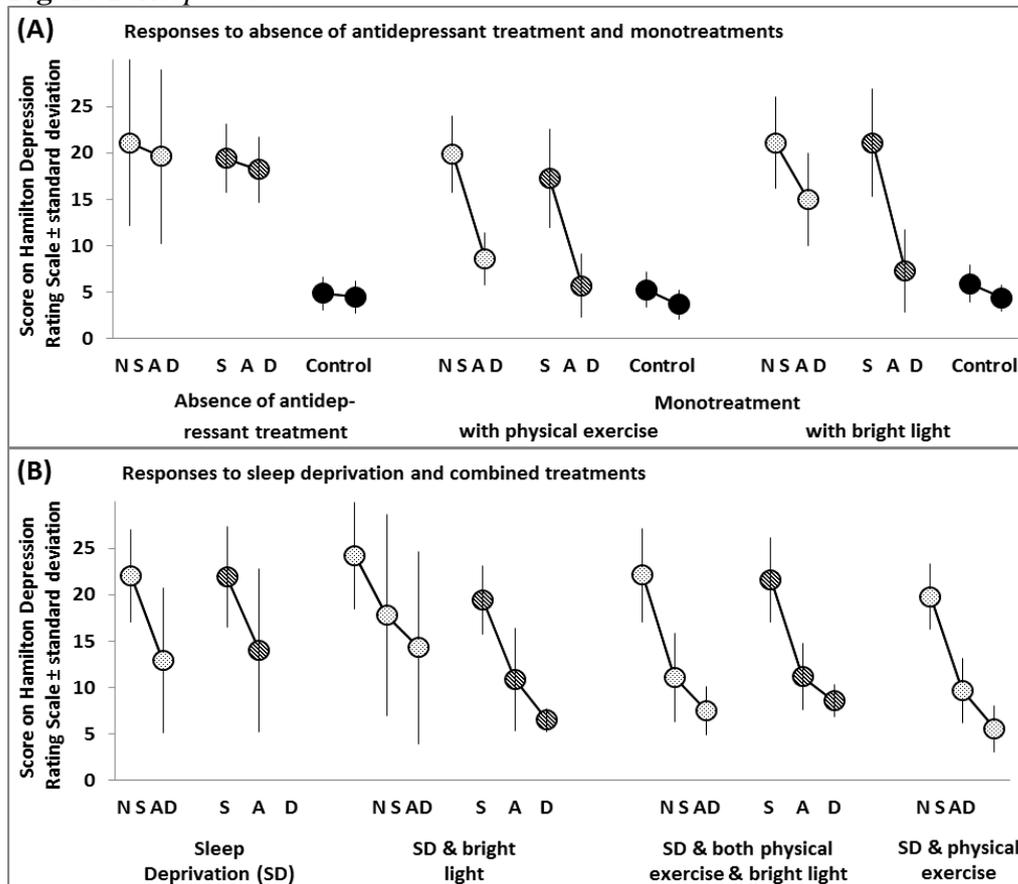
The 21-item Hamilton Depression Rating Scale (Hamilton 1967) was used for clinical response assessment. It was administered either twice (with a week interval) or three times: before and after total sleep deprivation and after consecutive 7-day treatment with light or/and exercise (Figure 1A or 1B, respectively). Differences between pre- and post-treatment conditions were examined with two-tailed paired student's *t*-test. Two-tailed unpaired student's *t*-test was applied to compare the reduction of depression scores in two different diagnostic groups or after two different one-week treatments.

Results

Neither clinically nor statistically significant mood improvement was detected in untreated groups (Figure 1A). In contrast, any type of one-week treatment produced significant reduction of depression score in both depressed and non-depressed subjects (Figure 1A).

Winter depression responded better than non-seasonal depression to monotreatment with bright light (65% vs. 30%, $t=4.8$, $p<0.001$). Moreover, the tendency for better response to physical exercise was noted (68% vs. 57%, $t=2.0$, $p=0.063$). However, the responses were similar (Figure 1B) for combination of sleep deprivation with physical exercise under bright light (60% vs. 65%, $t=-1.0$, $p=0.351$). Total night sleep deprivation improved mood in seasonally and non-seasonally depressed participants ($t=5.5$ and 9.9 , $p<0.001$). There was no difference in reductions of depression score between these two diagnostic groups (37% and 44%, respectively; $t=-1.0$, $p=0.330$).

Figure 1. Responses



In winter depression, bright light was found to be an effective treatment (Figure 1A). In non-seasonal depression, physical exercise alone or in combination with sleep deprivation was a significantly better treatment

compared to bright light mono-treatment ($p < 0.001$ for both). Besides, the combination of sleep deprivation with exercise was better treatment than its combination with bright light (71% vs. 44%, $t = 2.7$, $p = 0.013$). In treatments following sleep deprivation, further marked reductions of depression score were observed after either bright light exposure or exercise (Figure 1B).

Discussion

The results illustrated in Figure 1 were in full agreement with the results of several other trials of natural antidepressants for patients with seasonal (winter) depression and healthy controls (Putilov 2013, Putilov et al. 2000, Danilenko and Putilov 2005, Putilov and Danilenko 2005a, 2005b). Previously we found that bright light was an effective treatment irrespective of the time of the day (from 65% to 70%). All combined treatments for winter depression, including placebo, prevented relapse after sleep deprivation. However, further marked reductions of depression score were not detected after blind administration of either melatonin or placebo in the afternoon (i.e., the final reductions were 66% and 60% for two "visible" treatments, and only 34% and 54% for melatonin and placebo, respectively). The improvement observed in winter depressives after one week spent in a south region was even larger but, nevertheless, it was not significantly better than the effect of one-week treatment with bright light (81% vs. 70%).

In general, our results suggest that the significant final reductions of depression scores in both depressed and non-depressed women were observed after any type of one-week treatment, such as physical exercise on a bicycle ergometer, bright light exposure, melatonin or placebo intake in the afternoon and short vacation in a south region. The reductions were significant irrespective of whether these treatments were administered alone or in combination with one night of sleep deprivation. However, we also found that the combination of bright light with physical exercise did not bring additional benefits for winter depressives. It seems that there exists a saturation effect of such a short treatment. If, at least, one of two treatment modalities (physical exercise or bright light) ensured an excellent response (i.e., in winter depression), there is no additional benefit when they are combined.

All these findings can be understood in the framework of the idea of a strong modulating effect of placebo on the observed results of antidepressant treatment. When patients were asked to guess on which of two interventions was the active treatment (melatonin vs. placebo intake), these results were found to be the worse and similar for active and placebo treatments. They also were not found to be excellent when it was likely that a "visible" treatment can be regarded by a patient as being ineffective or less effective as compared to a more promising option (bright light vs. physical exercise for non-seasonal depression). Finally, a combination of two promising treatments did not

produce an additional improvement due to the absence of two separate specific actions of each of two "visible" treatments.

Thus, our results highlight the possibility that such "visible" one-week treatments as kinesiotherapy and phototherapy can work as powerful placebos. It seems that the psychology of depressed individuals is the most important mediator of clinical response to these treatments. In particular, the nature of depression suggests its high sensitivity to encouragement that comes from being involved in a novel antidepressant trial¹. Therefore, our results allow a recommendation to consider the effects of bright light and physical exercise under the category of Putilov (2013), for more detailed discussion on the nature of beneficial response to treatment for depression and evolutionary roots of placebo response "alternative interventions" in meta-analyses of beneficial action of photo- and kinesiotherapy for mood disorders. It is unlikely that these interventions can be classified as "no treatment" control. For instance, the results illustrated in Figure 1A suggested the absence of spontaneous recovery in the untreated condition. On the other hand, "visibility" of bright light and physical exercise interventions can be a cause of an extremely large contribution of placebo effect to outcomes of such interventions, and hence, they also cannot be definitely named "active treatments".

Depression scored in patients with non-seasonal depression, seasonal depression, and healthy controls (NSAD, SAD, and Control). Figure 1A depression ratings were obtained twice with a one-week interval either in the absence of treatment (left) or before and after one-week mono-treatments with physical exercise (middle) or bright light (right). Figure 1B Ratings were obtained during combined treatments before and after total sleep deprivation, SD and after the following one-week treatment with bright light and/or physical exercise.

It seems that, so far, only one of the natural treatments for depression, sleep deprivation, has been proved to produce a specific rather than a placebo effect. Although, psychotherapeutic mechanisms can contribute to its antidepressant action, they do not provide a complete explanation for the observed improvement of mood (Wu and Bunney 1990, Wirz-Justice and Van den Hoofdakker 1999). Moreover, the early studies ruled out the possibility to explain the antidepressant effect of sleep deprivation by the influence of such psychological factors as patients' positive expectations and attitudes, because favorite clinical responses were also documented when patients were told that this intervention served an aim of either diagnostic (Pflug and Tölle 1971) or biological rhythm assessment (Gerner et al. 1979). The remaining problem with antidepressant action of sleep deprivation is that this action is short-lived (till the morning following the first sleep episode) and other interventions are usually required for its stabilization. Nevertheless, we see no serious obstacles in recommending interventions with bright light and physical exercise as safe,

¹ See Putilov (2013) for more detailed discussion on the nature of beneficial response to treatment for depression and evolutionary roots of placebo response.

cheap, rapid and effective antidepressants. This is especially the case, for those seasonal and non-seasonal depressives who do not respond to drug medications, prefer unconventional and non-pharmacological treatments and suffer from depression in mild or moderate rather than severe, chronic or recurrent forms.

Conclusions

The results of natural antidepressant therapies for seasonal and non-seasonal depression revealed a highly significant clinical response of depressed female study participants to one-week mono - and combined treatments. We found that i) a one-week kinesiotherapy was equally beneficial for seasonal and winter depression, ii) a treatment with bright light produced a similarly strong antidepressant response only in winter depressives, iii) a week of bright light therapy and/or kinesiotherapy was able to prevent relapse after night sleep deprivation and iv) mood was even further improved in seasonal and winter depressives after such "visible" treatments. However, if at least one of treatment modalities ensured excellent response, there was no additional benefit from their combination. Therefore, it can be generally concluded that our results highlighted the possibility that most of these one-week treatments can work as powerful placebos.

Acknowledgments

The studies of AP were supported by the Russian Foundation for Basic Research (grants 07-06-00263-a, 10-06-00114-a, 13-06-00042-a, and 16-06-00235-a), and the Russian Foundation for Humanities (grants 06-06-00375-a, 12-06-18001-e, and 15-06-10403-a). We are thankful to Dr. Elena Y. Poljakova for her help in assessment of depression in some study participants.

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