

Antidepressant effect of alpha-lipoic acid: Brain-derived Neurotrophic Factor such as a new target for resistant depression

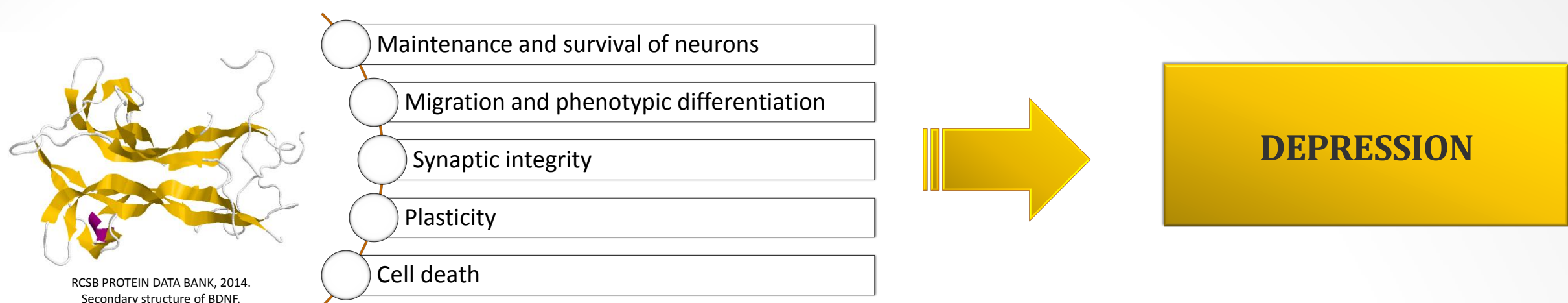
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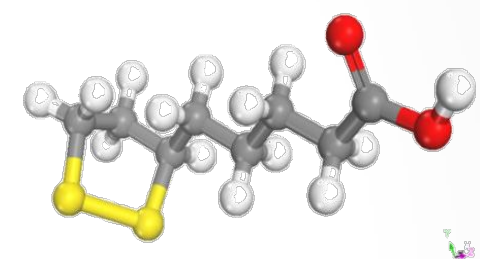
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PURPOSE

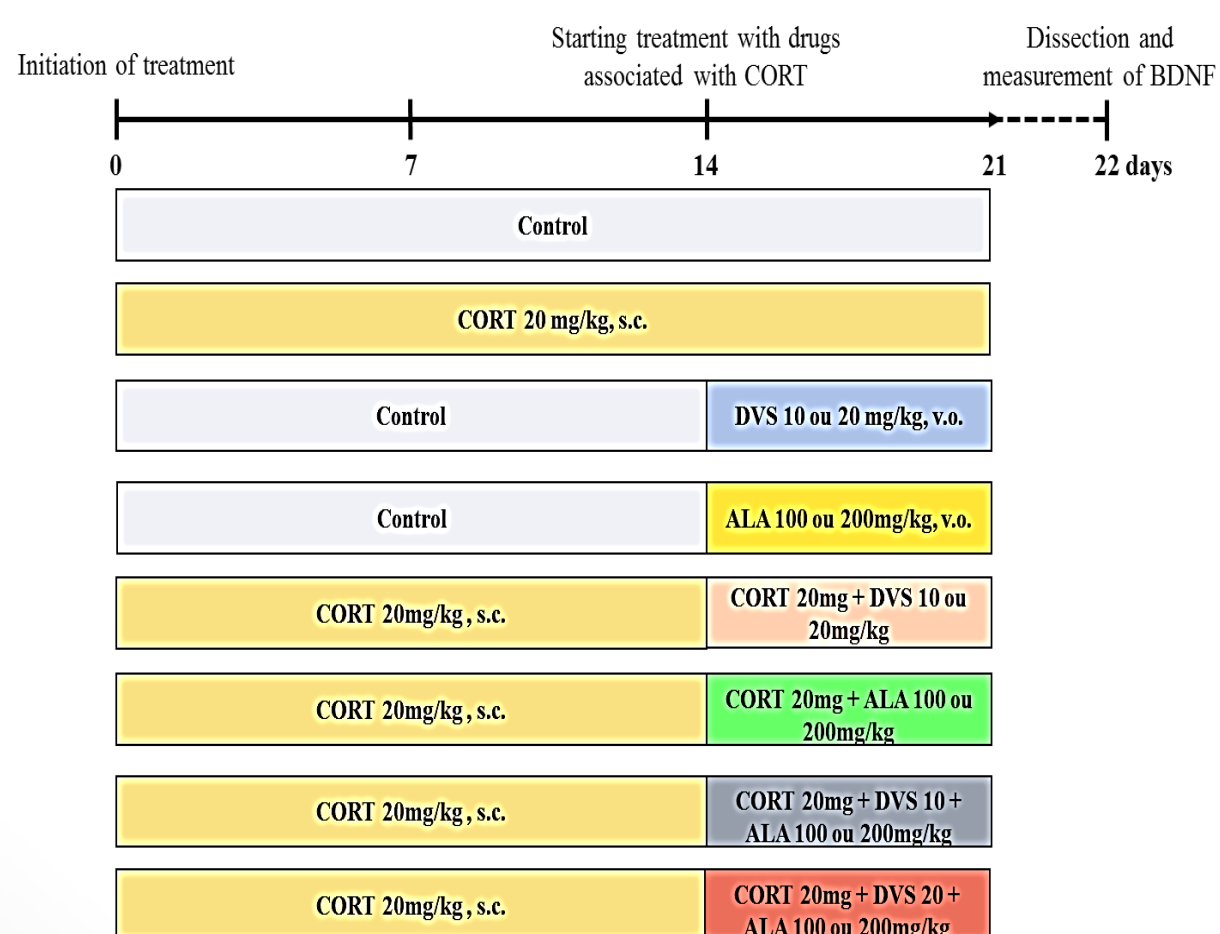


RATIONALE

Alpha lipoic-acid (ALA) has been used in the treatment of various diseases and has proved to be a very effective antioxidant substance. This study was designed to investigate the antidepressant effects of ALA on brain derived neurotrophic factor (BDNF) levels in the prefrontal cortex of mice treated only with ALA or in association with desvenlafaxine (DVS) in the chronic corticosterone (CORT) - resistant depression induced model.

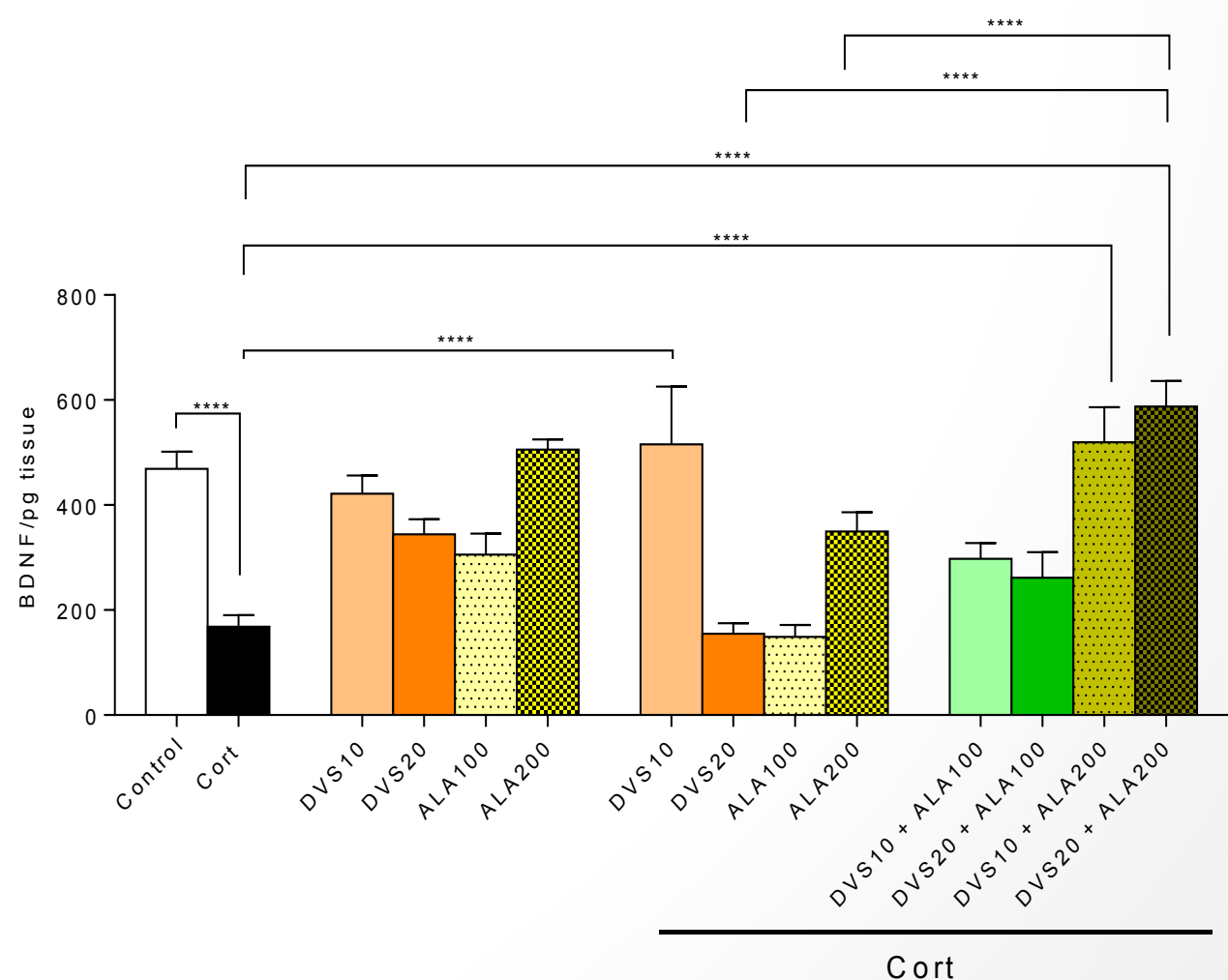


METHODS



RESULTS

Figure 1. Brain-derived Neurotrophic Factor levels in prefrontal cortex

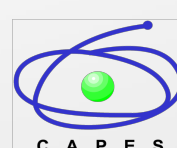


Statistical analysis was determined by one-way ANOVA followed by Tukey's test. For all analysis, $p < 0.05$ was considered significant. Abbreviations: CORT- corticosterone; DVS – desvenlafaxine; ALA- alpha-lipoic acid; MDA- malondialdehyde.

CONCLUSION

- ✓ Augmentation therapy with the addition of antioxidant drugs may be an important pharmacological approach for the treatment of depression
- ✓ Alpha-Lipoic Acid is an ideal antioxidant candidate as a promising agent to improve the therapeutics of depressive disorders
- ✓ Studies are needed to determine the neuroprotective mechanisms of ALA

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Antidepressant effect of alpha-lipoic acid: brain-derived neurotrophic factor as a new target for resistant depression

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Purpose: Brain-derived neurotrophic factor (BDNF), one of the major neurotrophic factors, plays an important role in the maintenance and survival of neurons, synaptic integrity and plasticity. Evidence suggests that BDNF is involved in depression, such that the level of BDNF is decreased in depressed patients and that antidepressants reverse this decrease [1]. Considering the significant involvement of neurotrophins in the pathophysiology of depression, this study was designed to investigate the antidepressant effects of the antioxidant alpha-lipoic acid (ALA) on BDNF levels in prefrontal cortex of mice treated only with alpha-lipoic acid (ALA) or in association with desvenlafaxine (DVS) in the chronic corticosterone (CORT)-induced resistant depression model [2].

Methods: The depression model was induced by repeated administrations of CORT (20mg/kg, subcutaneous) in mice over a period of 14 days. Between days 15 and 21, a randomized group of mice received DVS (10 or 20mg/kg, by gavage), ALA (100 or 200mg/kg, by gavage), or a combination of DVS (10 or 20mg/kg, by gavage) and ALA (100 or 200mg/kg, by gavage) along with the CORT injections for the remaining 7 days. Other groups of mice received DVS (10 or 20mg/kg, by gavage) or ALA (100 or 200mg/kg, by gavage) alone [3]. Twenty-four hours after the last administration, the animals were killed by decapitation and then removed prefrontal cortex (PFC) for the measurement of Brain-derived Neurotrophic Factor [1,2]. After homogenizing the brain areas in phosphate buffered saline (pH 7.4), BDNF levels in each sample were quantified by immunoenzymatic test according to manufacturer's instructions (ELISA, R & D Systems, USA). The results were expressed as picogram BDNF/g of tissue.

Results: CORT significantly decreased the levels of BDNF in prefrontal cortex compared with the control group [188 ± 21.3 (10)]. In mice treated with association CORT + ALA 200mg/kg, the levels of BDNF were significantly increased in prefrontal cortex [349.1 ± 36.6 (10)]. In the animals treated with CORT + DVS 10 or 20mg/kg or CORT + ALA 100mg/kg, there was no significant change in BDNF levels [123.6 ± 24.7 (7); 136.9 ± 20.1 (10); 168.0 ± 22.3 (9), respectively]. The addition of ALA 100 or 200mg/kg in the groups CORT + DVS 10 or 20mg/kg increased the BDNF levels, especially in combination with a dose of 200mg/kg of alpha-lipoic acid [445.8 ± 66.3 (9); 623.6 ± 48.9 (7), respectively].

Conclusion: These results suggest that augmentation therapy with the addition of antioxidant drugs may be an important pharmacological approach for the treatment of depression. They also contribute to the growing body of evidence implicating that ALA is an ideal antioxidant candidate as a promising agent to improve the therapeutics of depressive disorders. However, many studies also are needed to determine the neuroprotective mechanisms of ALA and to elucidate the mechanisms that may be effective in reducing the symptoms of depression.

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Keywords

Alpha-lipoic acid

Depression

Brain-derived Neurotrophic Factor